New palladium-catalyzed approaches to heterocycles and carbocycles

by

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has met the dissertation requirement of Iowa State University

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For the Major Program

To my wife, Chunrong Pan

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LIST OF ABBREVATIONS

Ac	acetyl
aq	aqueous
Bn	benzyl
br m	broad multiplet
br s	broad singlet
Bu	butyl
t-Bu	*tert*-butyl
cat.	Catalytic
concd	concentrated
d	doublet
dba	dibenzylideneacetone
dd	doublet of doublets
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplets
eq	equation
Et	ethyl
h	hour(s)
HRMS	high resolution mass spectroscopy
Hz	Hertz
IR	infrared

m	multiple
Me	methyl
mL	milliliter(s)
mol	mole(s)
mp	melting point
Ms	methanesulfonyl
MS	mass spectrometry
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
q	quartet
s	singlet
t	triplet
TBAC	tetra-*n*-butylammonium chloride
tert	tertiary
THF	tetrahydrofuran
TLC	thin-layer chromatography
Ts	*p*-toluenesulfonyl

ABSTRACT

The *tert*-butylimines of *o*-(1-alkynyl)benzaldehydes and analogous pyridinecarbaldehydes have been cyclized under very mild reaction conditions in the presence of I_2, ICl, PhSeCl, PhSCl and *p*-$O_2NC_6H_4SCl$ to give the corresponding halogen-, selenium- and sulfur-containing disubstituted isoquinolines and naphthyridines, respectively. Monosubstituted isoquinolines and naphthyridines have been synthesized by the metal-catalyzed ring closure of these same iminoalkynes. This methodology accommodates a variety of iminoalkynes and affords the anticipated heterocycles in moderate to excellent yields.

The Pd(II)-catalyzed cyclization of 2-(1-alkynyl)arylaldimines in the presence of various alkenes provides an efficient way to synthesize a variety of 4-(1-alkenyl)-3-arylisoquinolines in moderate to excellent yields. The introduction of an *ortho*-methoxy group on the arylaldimine promotes the Pd-catalyzed cyclization and stabilizes the resulting Pd(II) intermediate, improving the yields of the isoquinoline products.

Highly substituted naphthalenes have been synthesized by the palladium-catalyzed annulation of a variety of internal alkynes, in which two new carbon-carbon bonds are formed in a single step under relatively mild reaction conditions. This method has also been used to synthesize carbazoles, although a higher reaction temperature is necessary. The process involves arylpalladation of the alkyne, followed by intramolecular Heck olefination and double bond isomerization. This method accommodates a variety of functional groups and affords the anticipated highly substituted naphthalenes and carbazoles in good to excellent yields.

Novel palladium migration/arylation methodology for the synthesis of complex fused polycycles has been developed, in which one or more sequential Pd-catalyzed intramolecular migration processes involving C-H activation are employed. The chemistry works best with electron-rich aromatics, which is in agreement with the idea that these palladium-catalyzed C-H activation reactions parallel electrophilic aromatic substitution.

A relatively efficient synthesis of cyclopropanes has been developed using palladium-catalyzed C-H activation chemistry, in which two new carbon-carbon bonds are formed in a single step. This method involves the palladium-catalyzed activation of relatively unreactive C-H bonds, and provides a very efficient way to synthesize cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics.

GENERAL INTRODUCTION

Transition metal-catalyzed processes have proven to be extremely effective in organic synthesis. More specifically, palladium-catalyzed methodology has been extensively utilized in recent years.[1] The ability to create multiple carbon-carbon bonds from simple starting materials, the regio- and stereospecificity of the reactions, the exceptional tolerance for functional groups, the insensitivity to air or moisture, and the procedural ease with which the reactions can be carried out have all contributed to the success of palladium in organic synthesis.

The Larock group has shown in a series of recent papers that palladium-catalyzed cyclization or annulation methodology[2] can be effectively employed for the synthesis of indoles, isoindolo[2,1-*a*]indoles, benzofurans, benzopyrans, isocoumarins, α-pyrones, isoquinolines, carbolines and polycyclic aromatic hydrocarbons with a wide variety of substituent patterns. In this dissertation, extension of this approach to the synthesis of isoquinolines, naphthyridines, naphthalenes, carbazoles, and their derivatives have been investigated.

The ability of palladium to activate C-H bonds has been used extensively in organic synthesis.[3] In recent years, palladium-catalyzed C-H activation has received considerable attention due to the wide variety of reactions this metal will catalyze. Newly discovered palladium migration chemistry and the palladium-catalyzed activation of alkyl C-H bonds interests us as both an opportunity to study the behavior of palladium and an unusual pathway to construct complicated polycyclic compounds.

Dissertation Organization

This dissertation is divided into five chapters. Each of the chapters presented herein is written by following the guidelines for a full paper in the *Journal of Organic Chemistry* and is composed of the abstract, introduction, results and discussion, conclusion, experimental section, and references.

Chapter 1 discusses the synthesis of halogen-, selenium- and sulfur-containing disubstituted isoquinolines and naphthyridines by the electrophilic cyclization of the *tert*-butylimines of *o*-(1-alkynyl)benzaldehydes and analogous pyridinecarbaldehydes under very mild reaction conditions using I_2, ICl, PhSeCl, PhSCl and *p*-$O_2NC_6H_4SCl$ as electrophiles.

Chapter 2 investigates the Pd(II)-catalyzed cyclization of 2-(1-alkynyl)arylaldimines in the presence of various alkenes as an efficient way to synthesize a variety of 4-(1-alkenyl)-3-arylisoquinolines in moderate to excellent yields. Various imine substrates and alkenes have been studied. A mechanism for this transformation is proposed.

Chapter 3 presents a palladium-catalyzed annulation of a variety of internal alkynes to synthesize highly substituted naphthalenes. The process involves arylpalladation of the alkyne, followed by intramolecular Heck olefination and double bond isomerization. Highly substituted carbazoles have also been synthesized in good to excellent yields by this methodology.

Chapter 4 reports a novel palladium-catalyzed aryl-to-aryl migration. This reaction is both mechanistically and synthetically interesting, because it involves multiple C-H activation process and provides an unusual pathway for the synthesis of heterocyclic and carbocyclic compounds.

Chapter 5 describes a novel palladium-catalyzed activation of alkyl C-H bonds, which provides a novel way to synthesize cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics.

Finally, all of the ^{1}H and ^{13}C NMR spectra for the starting materials and reaction products have been compiled in appendices A-E following the general conclusions for this dissertation.

References

1. (a) Tsuji, J. *Palladium Reagents and Catalysis*; *J.* Wiley: Chichester, 1995 and references therein. (b) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985 and references therein.
2. For reviews, see: (a) Larock, R. C. *J. Organomet. Chem.* **1999**, *576*, 111. (b) Larock, R. C. Palladium-Catalyzed Annulation. In *Perspectives in Organopalladium Chemistry for the XXI Century*; Tsuji, J., Ed.; Elsevier Press: Lausanne, Switzerland, 1999; pp 111-124. (c) Larock, R. C. *Pure Appl. Chem.* **1999**, *71*, 1435.
3. (a) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (b) Li, C.-J. *Acc. Chem. Res.* **2002**, *35*, 533. (c) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1983**, *250*, 509. (d) Oyamada, J.; Jia, C.; Fujiwara, Y. *Chem. Lett.* **2002**, 2. (e) Oyamada, J.; Jia, C.; Fujiwara, Y. *Chem. Lett.* **2002**, 380. (f) Jia, C.; Piao, D.; Kitamura, T.; Fujiwara, Y. *J. Org. Chem.* **2000**, *65*, 7516.

CHAPTER 1. SYNTHESIS OF SUBSTITUTED ISOQUINOLINES BY ELECTROPHILIC CYCLIZATION OF IMINOALKYNES

A paper published in the *Journal of Organic Chemistry*

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Abstract

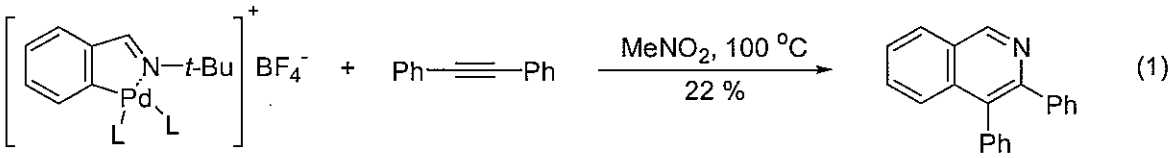
The *tert*-butylimines of *o*-(1-alkynyl)benzaldehydes and analogous pyridinecarbaldehydes have been cyclized under very mild reaction conditions in the presence of I_2, ICl, PhSeCl, PhSCl and *p*-$O_2NC_6H_4SCl$ to give the corresponding halogen-, selenium- and sulfur-containing disubstituted isoquinolines and naphthyridines, respectively. This methodology accommodates a variety of iminoalkynes and affords the anticipated heterocycles in moderate to excellent yields. Monosubstituted isoquinolines and naphthyridines have been synthesized by the metal-catalyzed ring closure of these same iminoalkynes. The silver-catalyzed ring closure is highly effective in cyclizing aryl, alkenyl, and alkyl-substituted iminoalkynes at 50 °C.

Introduction

The isoquinoline backbone appears in numerous natural products. Thus, the synthesis of isoquinolines has received much recent attention.[1] Although classical methods have been frequently employed in the total synthesis of isoquinoline alkaloids, these approaches often have drawbacks. For example, the Bischler-Napieralski,[2] Pictet-Spengler,[3] and Pomeranz-

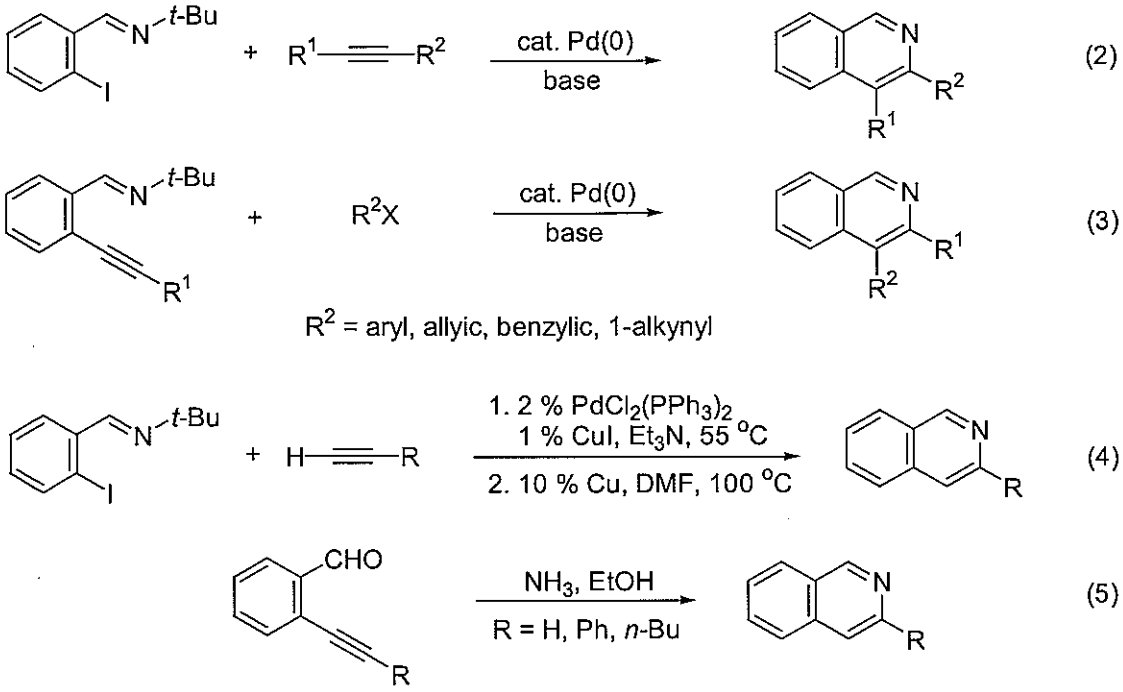
Fritsh[4] protocol require relatively strong acids to cyclize *E*-phenethylamines. Also, the Bischler-Napieralski[2] and the Pictet-Spengler[3] reactions afford dihydro- and tetrahydroisoquinolines, respectively. An additional step involving dehydrogenation is thus required to complete the synthesis of the isoquinoline.

Recently, substituted isoquinolines have been synthesized by employing palladium chemistry. Widdowson has published a synthesis of isoquinolines by the reaction of a cyclopalladated *N-tert*-butylarylaldimine and acrylonitrile.[5] His synthesis suffers from the use of stoichiometric amounts of palladium salts and high reaction temperatures (180-200 °C) for the final step. Heck has also reported the formation of 3,4-diphenylisoquinoline by the reaction of diphenylacetylene and a cyclopalladated *N-tert*-butylbenzaldimine tetrafluoroborate complex (eq 1).[6] This synthesis also utilizes a stoichiometric amount of palladium salts, which is not very practical in organic synthesis.



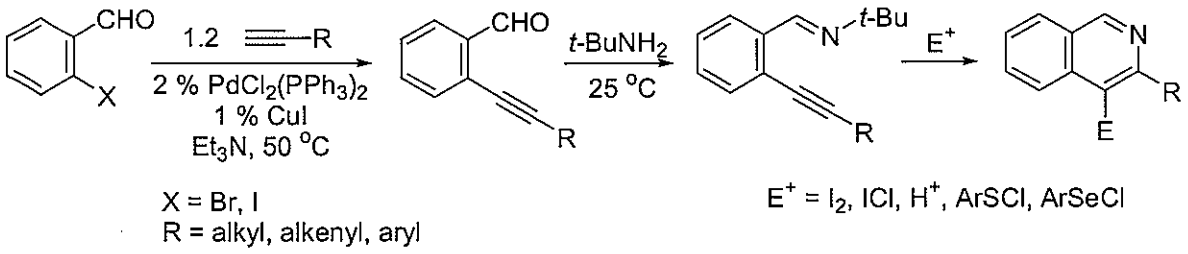
(1)

We have recently reported the formation of numerous 3,4-disubstituted isoquinolines by the palladium-catalyzed annulation of internal alkynes (eq 2)[7] and carbopalladation of the *tert*-butylimines of *o*-(1-alkynyl)benzaldehydes (eq 3).[8] 3-Substituted isoquinoline derivatives can be prepared by the palladium and copper-catalyzed cross coupling of terminal alkynes and subsequent ring closure by catalytic CuI (eq 4)[9] or by the reaction of *o*-(1-alkynyl)benzaldehydes with NH_3 (eq 5).[10]



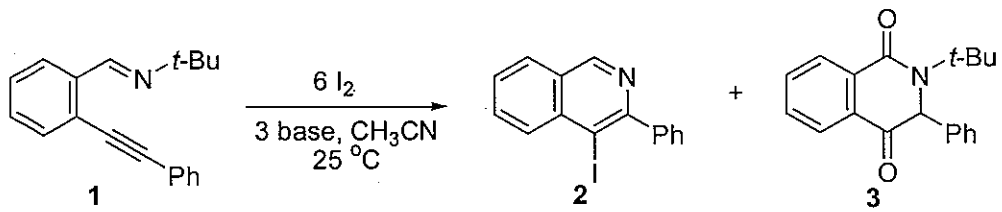
During the course of our isoquinoline annulation studies, we were encouraged to examine the electrophilic cyclization of our iminoalkynes by electrophiles other than organopalladium compounds in order to obtain 3,4-disubstituted isoquinolines (Scheme 1). The requisite iminoalkynes can be easily prepared by the Sonogashira reaction of a 2-halobenzaldehyde and a terminal alkyne, followed by reaction with *tert*-butylamine. We now wish to report that the electrophilic cyclization of the *tert*-butyl imines of *o*-(1-alkynyl)benzaldehydes and analogues provides a very efficient synthesis of a wide variety of substituted isoquinolines.

Scheme 1



Results and Discussion

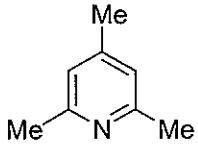
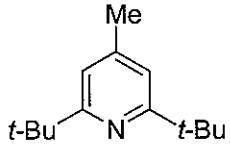
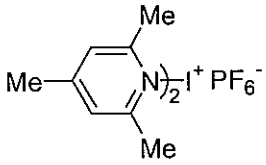
First, we studied the reaction of iminoalkyne **1** with I_2 in CH_3CN at room temperature in the presence of a variety of bases (eq 6). The results are summarized in Table 1, entries 1-11.



(6)

Table 1. Ring Closure of Iminoalkyne 1 by I_2 (eq 6).[a]

entry	base	time (h)	% yield of **2**[b]	% yield of **3**[b]
1	-	3	17	trace
2	$NaHCO_3$	3	36	24
3	Na_2CO_3	24	30	26
4	K_2CO_3	3	31	28
5	$NaOCO_2CH_3$	0.5	68	0
6	*t*-BuOK	3	17	0
7	*n*-$C_3H_7CO_2Na$	72	20	0
8	Et_3N	72	trace	0
9	pyridine[c]	72	20	0

10		72	32	trace
11		72	22	0
12[d]		72	30	0
13[e]		72	trace	0

[a] All reactions were run under the following conditions, unless otherwise described: 0.25 mmol of 1 and 0.75 mmol of the base in 7 ml of CH_3CN were stirred at room temperature under Ar for the specific period of time. [b] Isolated yields. [c] Pyridine (7 ml) were used as both the solvent and the base. [d] No I_2 was employed and 7 ml of CH_2Cl_2 were used as the solvent. [e] No I_2 was employed.

When no base was employed, this cyclization reaction only gave 17 % of the desired isoquinoline product 2 (entry 1). The addition of carbonate bases, such as $NaHCO_3$, Na_2CO_3 and K_2CO_3 increased the yields of 2 to 36 %, 30 % and 31 %, respectively (entries 2-4), while side product 3 was observed in 24 % to 28 % yields. The side product 3 probably arises from reaction of the intermediate isoquinolinium salt with water, hydroxide or the carbonate base (see the later mechanistic discussion). Surprisingly, the use of $NaOCO_2CH_3$[11] as the base (entry 5) produced a 68 % yield of 2 and none of the side product 3 was produced. This reaction was complete in 0.5 h. The very different results from the reaction of $NaOCO_2CH_3$ and the other carbonate bases can be explained by the fact that $NaOCO_2CH_3$ reacts with a proton to produce CO_2 and MeOH, while the reactions of a proton with the bases $NaHCO_3$, Na_2CO_3 or K_2CO_3 generate CO_2 and H_2O. The H_2O generated probably leads to the formation of side product 3 and thus results in low yields of 2. When a stronger

base, KO-*t*-Bu was employed, only a 17 % yield of 2 was observed (entry 6). The low yield may be a direct result of the fact that the imine appears to be unstable in the presence of this strong base. The reactions employing the less basic salt n-$C_3H_7CO_2Na$ and the organic base Et_3N were quite slow (entries 7 and 8). These reactions are not complete even in 3 days and give only a 20 % yield and a trace of 2, respectively. Pyridine and hindered pyridine derivatives, such as 2,4,6-trimethylpyridine and 2,6-di-*tert*-butyl-4-methylpyridine, have also been employed (entries 9-11). Although no side product 3 was produced, all of these reactions were slow and suffered low yields ranging from 20 % to 32 %. The use of *bis*-(2,4,6-trimethylpyridine)iodine(I) hexafluorophosphate, which is both a source of iodine cation and a potential base, failed to improve the yield of 2. A 30 % yield of 2 was observed when the reaction was carried out in CH_2Cl_2 (entry 12), while only trace amounts of 2 were produced in CH_3CN (entry 13). We have found that using less than 3 equivs of the base and 6 equivs of I_2 results in a lower yield. So we have chosen the following conditions as optimal for all subsequent experiments: 0.25 mmol of the iminoalkyne, 6 equivs of I_2, 3 equivs of $NaOCO_2CH_3$ in 7 ml of CH_3CN are stirred at room temperature for an appropriate amount of time. Most of the reactions are complete in 0.5 h and afford good to excellent yields of the corresponding iodoisoquinolines and iodonaphthyridines. The results using I_2 are summarized in Table 2, entries 1, 3, 4, 6, 8, 10, 12 and 13.

The stronger electrophilic reagent ICl has also been employed in these cyclizations and the corresponding cyclization products have been observed in yields comparable to those obtained using I_2, except for iminoalkynes 10 (compare entries 8 and 9) and 16 (compare entries 13 and 14). The reasons for this are not obvious. The reaction times are also usually

pretty similar to those of I_2. The results are summarized in Table 2, entries 2, 5, 7, 9, 11, and 14.

Of all of the electrophilic reagent examined, I_2 and ICl close the six-membered ring the fastest. Most of these reactions are complete in 0.5 h. The reactions of 1 with I_2 and ICl gave almost identical yields, 67 % and 68 % respectively (entries 1 and 2). When the iminoalkyne 4 bearing a cyclohexenyl group was allowed to react with I_2 (entry 3), the yield was similar to that of 1. This indicates that this electrophilic reaction can tolerate double bonds.

To further test the scope of this electrophilic ring closure, alkyl-substituted acetylenes, such as iminoalkynes *o*-(*t*-BuN=CH)C_6H_4C{ CR [R = cyclohexyl (38) or CH_2CH_2OTHP (40)] have been allowed to react with I_2 and ICl. Cacchi has reported that alkyl-substituted *o*-(1-alkynyl)phenols react with I_2 to give substituted iodobenzofurans.[11] However, in our chemistry, I_2 and ICl do not react with either of the alkyl-substituted iminoalkynes to afford the desired products and neither do PhSeCl or PhSCl as will be discussed later. The coordination of iodine to the carbon-carbon triple bonds in these iminoalkynes should result in a partial postive charge on the carbon next to the aromatic ring, since an aryl group stabilizes a carbocation better than an alkyl group. Obviously, the formation of isoquinolines from such an intermediate is impossible.

Table 2. Synthesis of Isoquinolines and Naphthyridines by the Reaction of Iminoalkynes and Electrophiles.[a]

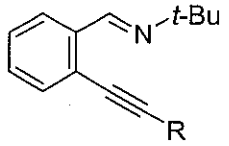
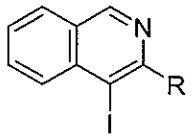
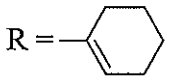
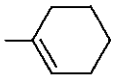
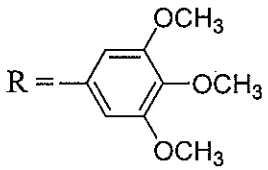
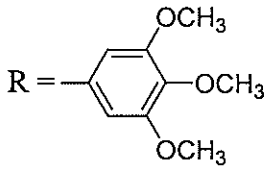
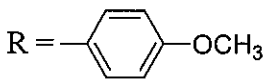
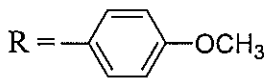
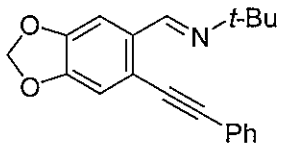
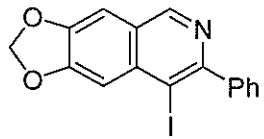
entry	iminoalkyne		electrophile	time (h)	product		% isolated yield
							
1	R = Ph	**(1)**	I_2[b]	0.5	R = Ph	**(2)**	68
2			ICl[c]	0.5		**(2)**	67
3	R = 	**(4)**	I_2[b]	0.5	R = 	**(5)**	67
4	R = 	**(6)**	I_2[b]	0.5	R = 	**(7)**	30
5			ICl[c]	0.5		**(7)**	24
6	R = 	**(8)**	I_2[b]	0.1	R = 	**(9)**	37
7			ICl[c]	0.5		**(9)**	40
8		**(10)**	I_2[b]	0.5		**(11)**	0
9			ICl[c]	0.5		**(11)**	52

Table 2 continued

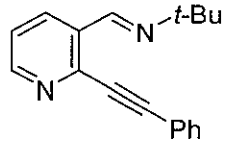
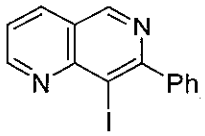
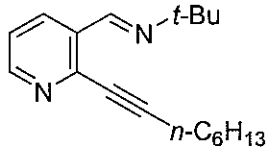
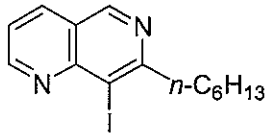
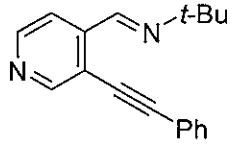
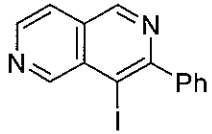
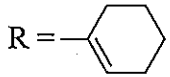
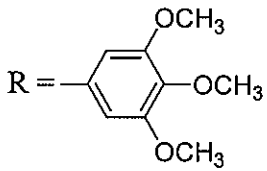
10		**(12)**	I_2[b]	0.5		**(13)**	90
11			ICl[c]	0.5		**(13)**	92
12		**(14)**	I_2[b]	0.5		**(15)**	76
13		**(16)**	I_2[b]	0.2		**(17)**	13
14			ICl[c]	24		**(17)**	72
							
15	**1**		PhSeCl	24	R = Ph	**(18)**	76
16	**4**		PhSeCl	24	R = 	**(19)**	96
17	**6**		PhSeCl	48	R = 	**(20)**	95

Table 2 continued

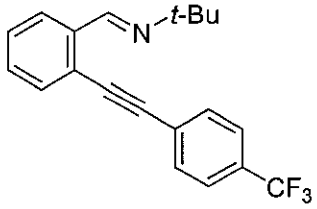
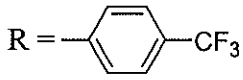
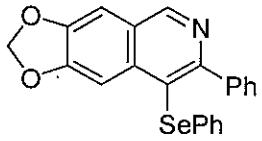
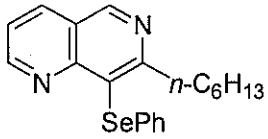
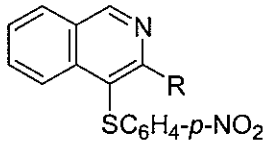
18		**(21)**	PhSeCl	72		**(22)**	18
19	**10**		PhSeCl	72		**(23)**	60
20	**16**		PhSeCl	72		**(24)**	80
21	**12**		PhSeCl	24		**(25)**	72
22	**14**		PhSeCl	72		**(26)**	61
							
23	**1**		p-$O_2NC_6H_4SCl$	48	R = Ph	**(27)**	46

Table 2 continued

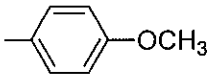
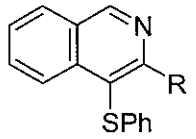
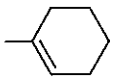
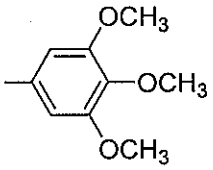
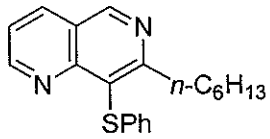
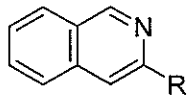
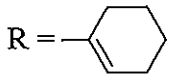
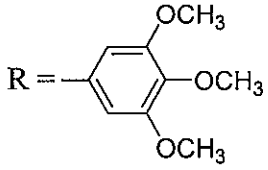
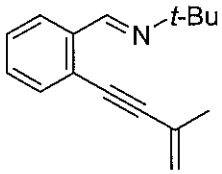
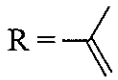
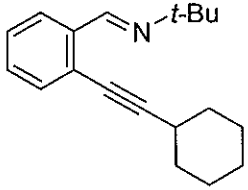
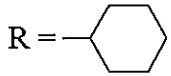
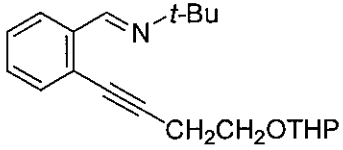
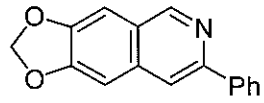
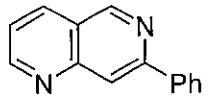
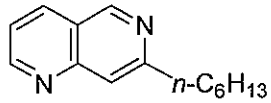
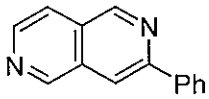
24	**4**	*p*-$O_2NC_6H_4SCl$	48	R = 	**(28)**	33
25	**8**	*p*-$O_2NC_6H_4SCl$	72	R = 	**(29)**	25
						
26	**4**	PhSCl	24	R = 	**(30)**	45
27	**6**	PhSCl	24	R = 	**(31)**	43
28	**14**	PhSCl	24		**(32)**	40
						
29	**1**	$AgNO_3$[d]	24	R = Ph	**(33)**	82
30		CuI[e]	3		**(33)**	100

Table 2 continued

31	**4**		$AgNO_3$[d]	24	R = 	**(34)**	78
32			CuI[e]	3		**(34)**	81
33	**6**		$AgNO_3$[d]	72	R = 	**(35)**	71
34		**(36)**	$AgNO_3$[d]	72	R = 	**(37)**	54
35		**(38)**	$AgNO_3$[d]	24	R = 	**(39)**	75
36			CuI[e]	6		**(39)**	93
37		**(40)**	$AgNO_3$[d]	24	R = CH_2CH_2OTHP	**(41)**	62
38			CuI[e]	5		**(41)**	83
39	**9**		$AgNO_3$[d]	24		**(42)**	56

15

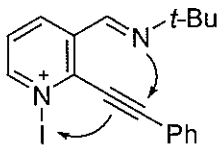
Table 2 continued

40	**11**	$AgNO_3$[d]	24		**(43)**	92
41	**13**	$AgNO_3$[d]	72		**(44)**	45
42	**15**	$AgNO_3$[d]	72		**(45)**	80

[a] All reactions were run under the following conditions, unless otherwise specified: 0.25 mmol of the iminoalkyne, 2 equivs of electrophile in 7 ml of CH_2Cl_2 at room temperature. [b] 0.25 Mmol of the iminoalkyne, 6 equivs of I_2, 3 equivs of $NaOCO_2CH_3$ in 7 ml of CH_3CN at room temperature. [c] 4 Equiv of ICl have been used. [d] 0.25 Mmol of the iminoalkyne, 5 mol % of $AgNO_3$ in 7 ml of $CHCl_3$ at 50 °C. [e] 0.25 Mmol of the iminoalkyne, 10 mol % of CuI in 5 ml of DMF at 100 °C.

While iminoalkyne **21**, *o*-(*t*-BuN=CH)$C_6H_4C\{CC_6H_4$-*p*-CF_3, bearing an electron-deficient arylethynyl group didn't react with I_2 or ICl at all, the introduction of an electron-rich arylethynyl group, as found in iminoalkynes **6** (entries 4 and 5) and **8** (entries 6 and 7) rather surprisingly resulted in low yields of the desired heterocyclic iodides. Similarly, none of the desired product has been obtained when iminoalkyne **10** with a methylenedioxo substituent is allowed to react with I_2 (entry 8), although all of the starting material is gone in 0.5 h. However, a 52 % yield of **11** was observed when ICl was employed as the electrophile (entry 9). This is possibly because ICl is a stronger electrophile than I_2.

From entries 10 and 11 in Table 2, one can see that the introduction of a pyridine ring into the starting material results in relatively high yields when either I_2 or ICl are employed as electrophiles. This might be explained by an intermediate such as **46**. The pyridine



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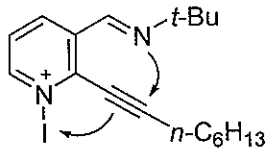
nitrogen might first coordinate to the electrophile to form a pyridinium cation. Because of this coordination, electrophilic attack of the triple bond might then occur in an intramolecular fashion. The intramolecular assistance significantly increases the yields for the reactions of I_2 and ICl from 68 % and 67 % for iminoalkyne **1** (entries 1 and 2) to 90 % and 92 % for iminoalkyne **12** (entries 10 and 11), respectively.

Alternatively, the presence of the pyridine moiety in iminoalkyne **12** may simply be directing the cationic charge of the intermediate iodonium ion to the more remote carbon of the alkyne, which should favor formation of the 6-membered ring isoquinoline. Whatever

the reason, the result is very encouraging, since it broadens the potential applications of this cyclization and improves its efficiency.

As described above, iminoalkynes derived from *o*-iodobenzaldehyde and acetylenes bearing simple alkyl groups do not react with I_2. However, iminoalkyne **14** can be cyclized by I_2 giving naphthyridine **15** in a 76 % yield (entry 12). Again, we believe that the key is the coordination of the electrophile to the pyridine nitrogen and formation of an intermediate like **4**.



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In an attempt to try to confirm this intramolecular assistance, iminoalkyne **16** has been allowed to react with I_2, and only a 13 % yield of **17** was obtained (entry 13). Compared to the reaction of **12** and I_2 (entry 10), the yield dropped from 90 % to 13 %. This may arise because **16** geometrically disfavors intramolecular assistance or it may simply be that we have now further removed the more electron-withdrawing nitrogen from the vicinity of the carbon-carbon triple bond. However, iminoalkyne **16** reacts with ICl to give naphthyridine **17** in 72 % yield, although this reaction requires 1 day to reach completion (entry 14). It is logical that ICl, a stronger electrophile than I_2, should work better in this reaction.

The next electrophilic reagent studied was PhSeCl. A variety of reaction conditions have been examined and the results are summarized in Table 3. Very similar yields, 74 % and 78 % respectively, of isoquinoline **18** have been obtained from iminoalkyne **1** using one or two equivs of PhSeCl (Table 3, entries 1 and 2). The concentration of the reactants seems

to play a minor role in this reaction. From entry 3, one can see that a more concentrated reaction actually gave a slightly lower yield. The reagent PhSeSePh failed to yield any of the corresponding isoquinoline (entry 4). Thus, we chose 0.25 mmol of the iminoalkyne, 2 equivs of PhSeCl in 7 ml of CH_2Cl_2 at room temperature as our standard reaction conditions for the reaction of PhSeCl and our iminoalkynes. In general, the reaction of iminoalkynes and PhSeCl requires 1-3 days and good to excellent yields of selenium-containing isoquinolines and naphthyridines are obtained (Table 2, entries 15-22). The major exception was iminoalkyne **21**, which gave only an 18 % yield after 3 days reaction time (entry 18).

Table 3. Optimization of the Cyclization Reaction Employing Se and S Electrophiles.[a]

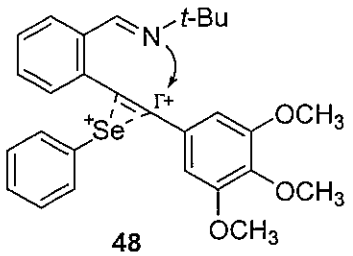
entry	electrophile	equiv of electrophile	temp (°C)	time (d)	% yield
1	PhSeCl	1	25 °C	1	74
2		2		1	78
3				1	70[b]
4	PhSeSePh			1	0
5	*p*-$NO_2C_6H_4SCl$			3	47
6				3	45[c]
7			60 °C	3	47

[a] All reactions were run using 0.25 mmol of **1** in 7 ml of CH_2Cl_2, unless otherwise specified. [b] Two ml of CH_2Cl_2 were used. [c] Two equivs of $ZnCl_2$ were added.

Cyclizations employing PhSeCl have generally proven quite successful. A 76 % yield of the isoquinoline product **18** has been obtained, when iminoalkyne **1** is allowed to react with PhSeCl (entry 15). When employing an iminoalkyne bearing a vinylic group on the

triple bond, a 96 % yield of selenium-containing isoquinoline **19** has been observed (entry 16). In contrast to the reactions of I_2 and ICl, the introduction of an electron-rich arylethynyl group into the iminoalkyne increases the yield from 76 % (entry 15) to 95 % (entry 17). However, the reaction of PhSeCl and iminoalkyne **21** bearing an electron-deficient arylethynyl group results in only an 18 % yield of isoquinoline (entry 18). Thus, electron-rich arylethynyl groups benefit the ring closure by PhSeCl, while an electron-deficient arylethynyl group disfavors cyclization. Obviously, the presence of an electron-rich arylethynyl group may be favoring the formation of the positive charge on the carbon necessary for formation of the six-membered ring. This supposition is confirmed by the reaction of **10** and PhSeCl, where the electron rich methylenedioxy group presumably favors cation formation on the "wrong" carbon of the alkyne, which results in a lower yield of selenium-substituted naphthalene (entry 19). Only a 60 % yield of **23** was obtained when **10** was allowed to react with PhSeCl. Although both iminoalkynes **6** (entry 17) and **10** (entry 19) have relatively electron-rich triple bonds, they afford quite different results. The lower yield of **23** can be explained as shown in Scheme 2. The positive charge on the alkyne carbon bearing the trimethoxyphenyl ring in intermediate **48** is better stabilized and therefore closure to a six-membered ring and formation of the isoquinoline product **20** are favored (entry 17). In intermediate **49**, more of the partial positive charge is located on the alkyne carbon bearing the methylenedioxyphenyl ring, which disfavors the formation of a six-membered ring and results in a decrease in the yield from 95 % (entry 17) to 60 % (entry 19).

Scheme 2



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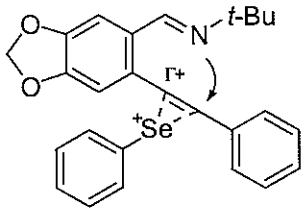
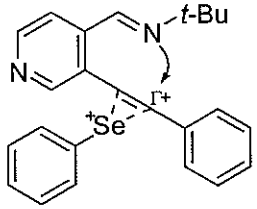


49



50

Although the electron density on both the triple bond and the imine nitrogen is decreased by the presence of a pyridine ring in compound **16**, we still obtain an 80 % yield from the reaction of iminoalkyne **16** and PhSeCl (entry 20). This may be explained by the fact that the partial positive charge in intermediate **50** (Scheme 2) is delocalized better by the phenyl group. Subsequent endo-6-trig attack apparently proceeds smoothly to form a stable isoquinoline product.

Iminoalkynes **12** and **14** also react with PhSeCl to give decent yields (entries 21 and 22). The success of these reactions may be the result of intramolecular assistance as described above. Alternatively, the presence of an electron-deficient pyridine ring may simply be favoring formation of an intermediate with a positive charge located on the carbon necessary to close the six-membered ring and disfavoring formation of the "wrong cation" on the carbon-carbon triple bond.

Unfortunately, when PhSeCl has been allowed to react with alkyl-substituted iminoalkynes, such as iminoalkynes *o*-(*t*-BuN=CH)C_6H_4C{ CR [R = cyclohexyl (**38**) or CH_2CH_2OTHP (**40**)], none of the desired product was observed. The results are similar to those from the reactions of I_2 and iminoalkynes **38** and **40**.

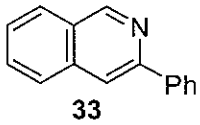
The electrophile p-$O_2NC_6H_4SCl$ has been examined under the optimal reaction conditions developed for PhSeCl. The isoquinoline product **27** expected from iminoalkyne **1** was obtained in a rather low yield of 47 % (Table 3, entry 5). The addition of the Lewis acid $ZnCl_2$ (entry 6) or an increase in the reaction temperature (entry 7) in an attempt to induce cyclization had little effect on the product yield, so the optimal reaction conditions for PhSeCl have been used in the reactions of p-$O_2NC_6H_4SCl$ and PhSCl[12] (Table 2, entries 23-28). In general, the yields of sulfur-containing isoquinolines from p-$O_2NC_6H_4SCl$ and PhSCl fall in the range of 25-46 %. The reactions producing nitro-containing products generally proceed in a slightly lower yield and require much longer reaction times.

The electrophile p-$O_2NC_6H_4SCl$ reacts with iminoalkynes **1**, **4** and **8** to produce the corresponding 4-(p-nitrophenylsulfenyl)isoquinoline derivatives in modest yields (entries 23-25). These yields are lower than those of reactions with I_2, ICl or PhSeCl. This is probably because this reagent is a weaker electrophile. Much better yields of the sulfur-containing isoquinolines were obtained when PhSCl was employed as the electrophile. As shown in entries 26-28, iminoalkynes **4**, **6** and **14** were allowed to react with PhSCl and the corresponding sulfide products **30-32** were obtained in yields ranging from 40 % to 45 %. All of these reactions were complete in 24 h. However, the reactions of PhSCl and the alkyl-substituted iminoalkynes **38** and **40** afforded none of the desired product. Thus, rather surprisingly, the pyridine-containing iminoalkyne **32** actually gives better results than the corresponding alkyl-substituted phenyl analogues. This may be due to intramolecular assistance by the pyridine as described earlier.

In order to synthesize monosubstituted isoquinolines, 10 mol % of CuI has been employed to close these same iminoalkynes to heterocycles with a hydrogen in the 4

position.[7] The results from these cyclizations are summarized in Table 2, entries 30, 32, 36 and 38. We now wish to report that catalytic amounts of $AgNO_3$ will effect the same transformation and the reaction occurs under milder reaction conditions, although the yields are often a bit lower. Thus, 0.25 mmol of iminoalkyne **1** have been allowed to react with 2 equivs of $AgNO_3$ in 7 ml of $CHCl_3$ at 50 °C (Table 4, entry 1). After 1 day, the monosubstituted isoquinoline **33** was obtained in a 90 % isolated yield. Further study indicated that 5 mol % of $AgNO_3$ is enough to close the six-membered ring in good yield (entries 2-4). The reaction failed when only 1 % of $AgNO_3$ was employed as the catalyst. Both $AgNO_3$ and AgOAc gave approximately the same yields for this ring closure (compare entries 3 and 5). Thus, the following standard conditions have been employed in all subsequent experiments: 0.25 mmol of the iminoalkyne and 5 mol % of $AgNO_3$ were stirred at 50 °C in 7 ml of $CHCl_3$ for the appropriate reaction time. The reaction takes 1-3 days at 50 °C and gives decent yields of the corresponding cyclization products (Table 2, entries 29, 31, 33-35, 37, and 39-42).

Table 4. Silver-catalyzed Ring Closure of Iminoalkyne 1.[a]

entry	silver salt (equivs)	solvent	product	% isolated yield
1	$AgNO_3$ (2.00)	$CHCl_3$	 **33**	90
2	(0.10)			80
3	(0.05)			82
4	(0.01)			0[b]
5	AgOAc (0.05)			80
6	$AgNO_3$ (2.00)	$CDCl_3$		69

[a] All reactions were run under the following conditions, unless otherwise specified: 0.25 mmol of iminoalkyne 1 and the indicated amount of silver salt in 7 ml of the solvent were stirred at 50 °C for 24 h. [b] After 24 h, there was only a minimal amount of the desired product present by TLC.

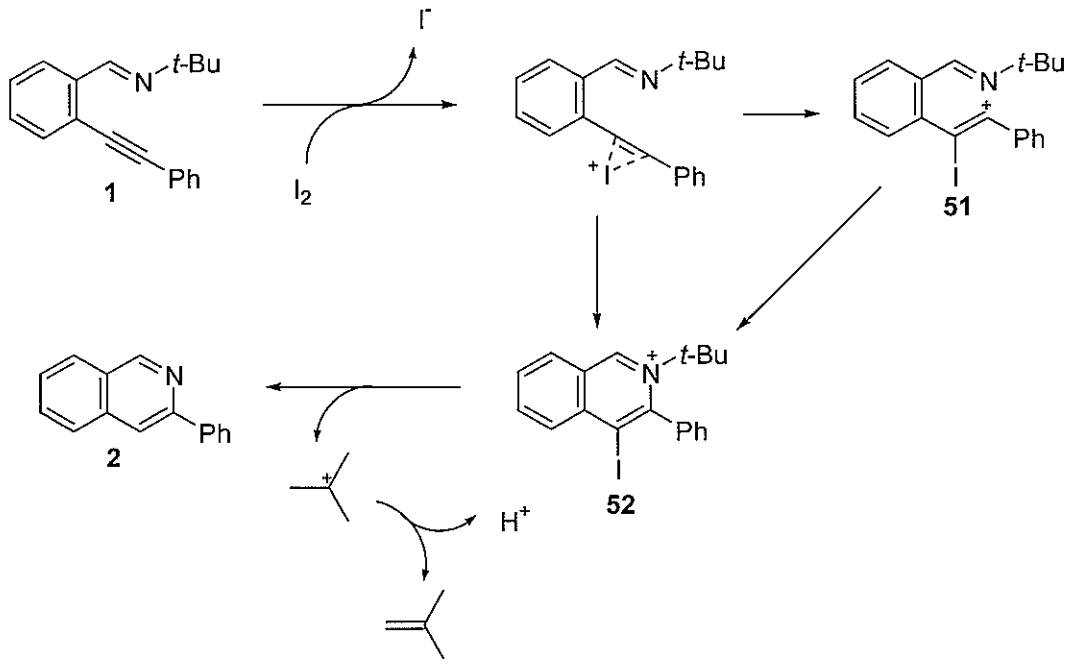
The source of the hydrogen atom ending up in the 4 position of the isoquinoline is not obvious. If the hydrogen atom comes from the solvent, the use of $DCCl_3$ would have resulted in a deuterated product (Table 4, entry 6). This was not the case as indicated by ^1H NMR spectroscopic analysis. Thus, we believe that the hydrogen is coming from the *tert*-butyl group of the imine or from small amounts of water present in the reaction.

As described above, alkyl-substituted *N*-(*o*-(1-alkynyl)benzylidene)-*tert*-butylamines failed to afford any of the desired isoquinolines when allowed to react with I_2, ICl, PhSeCl or *p*-$O_2NC_6H_4SCl$. However, iminoalkyne **38** and **40** do react with $AgNO_3$ or CuI to afford decent yields of the corresponding isoquinolines (Table 2, entries 35-38).

In general, the reactions of I_2 and ICl form the six-membered ring isoquinolines the fastest. In most cases, these reactions are complete in 0.5 h. However, the yields are less than those obtained from the reactions of PhSeCl, $AgNO_3$ or CuI. The reagents PhSCl and *p*-$O_2NC_6H_4SCl$ are the least efficient electrophilic reagents for this process, and their reactions require longer reaction times and result in lower yields.

For the reactions of I_2 or ICl and iminoalkyne **1**, we propose the mechanism shown in Scheme 3. First, the carbon-carbon triple bond of iminoalkyne **1** coordinates to the iodine cation generated from I_2 to generate an iodonium intermediate. This is followed by attack of the imine nitrogen on the activated triple bond to form intermediate **52**. Alternatively, the coordination of the iodine cation to the carbon-carbon triple bond may form a cationic intermediate like **51**, which cyclizes to intermediate **52**. The isoquinolinium salt **52** then presumably ionizes to produce the iodoisoquinoline **2** and a *tert*-butyl cation, which generates isobutylene.

Scheme 3



Conclusions

In conclusion, a procedure for the efficient synthesis of a wide variety of substituted isoquinolines has been developed which employs very mild reaction conditions. This methodology accommodates a variety of iminoalkynes and affords the anticipated substituted isoquinolines in moderate to excellent yields.

Experimental Section

General. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F) and visualization was effected with short wavelength UV light (254 nm) and basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 +

5 ml of NaOH (5 %) + 300 ml of H_2O]. All melting points are uncorrected. Low resolution mass spectra were recorded on a Finnigan TSQ700 triple quadrupole mass spectrometer (Finnigan MAT, San Jose, CA). High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. Elemental analyses were performed at Iowa State University on a Perkin Elmer 2400 CHNS/O Series II Analyzer. All reagents were used directly as obtained commercially unless otherwise noted. 2-Bromopyridine-3-carboxaldehyde,[13] 3-bromopyridine-4-carboxaldehyde[13] and PhSCl[14] were prepared according to literature procedures. The following starting materials were prepared as indicated.

2-(2-Propenylethynyl)benzyl alcohol. To a solution of 2-iodobenzyl alcohol (1.40 g, 6.0 mmol) and 2-methyl-1-buten-3-yne (0.47 g, 7.2 mmol) in Et_3N (24 ml) were added $PdCl_2(PPh_3)_2$ (84 mg, 2 mol %) and CuI (12 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 50 °C for 24 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography using 5:1 hexane/EtOAc to afford 0.97 g (94 %) of the desired compound as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.99 (dd, J = 0.9, 1.5 Hz, 3H), 2.72 (t, J = 6.0 Hz, 1H), 4.79 (d, J = 6.0 Hz, 2H), 5.31-5.33 (m, 1H), 5.40-5.42 (m, 1H), 7.22-7.33 (m, 2H), 7.40-7.44 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 23.7, 63.9, 86.0, 95.6, 121.3, 122.5, 126.8, 127.2, 127.5, 128.8, 132.2, 142.7.

Aldehydes Prepared

2-(2-Propenylethynyl)benzaldehyde. To a solution of 2-(2-propenylethynyl)benzyl alcohol (0.86 g, 5 mmol) in 75 ml of CH_2Cl_2 was added MnO_2 (6.52 g, 75 mmol). The

resulting mixture was stirred at 25 °C for 12 h. The extra MnO_2 was removed by filtration. The solvent was removed under reduced pressure and the oily residue was purified by flash column chromatography using 11:1 hexane/EtOAc to afford 0.73 g (86 %) of the desired compound as yellow oil: ^{1}H NMR ($CDCl_3$) Γ 2.02 (dd, J = 0.9, 1.2 Hz, 3H), 5.38-5.40 (m, 1H), 5.48-5.49 (m, 1H), 7.41-7.44 (m, 1H), 7.54-7.56 (m, 2H), 7.90-7.93 (m, 1H), 10.54 (d, J = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.4, 84.0, 97.7, 123.6, 126.4, 127.1, 127.3, 128.7, 133.4, 133.9, 136.0, 191.9.

General procedure for the preparation of other aldehydes. To a solution of the aryl halide (10.0 mmol) and the terminal alkyne (12.0 mmol, 1.2 equivs) in Et_3N (40 ml) were added $PdCl_2(PPh_3)_2$ (140 mg, 2 mol %) and CuI (20 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 50 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding arylalkyne.

2-(2-Phenylethynyl)benzaldehyde. 2-Bromobenzaldehyde (1.86 g, 10.0 mmol) and phenylacetylene (1.23 g, 12.0 mmol) were employed. Column chromatography using 20:1 hexane/EtOAc afforded 1.94 g (94 %) of the desired compound as a yellow oil with spectral properties identical to those previously reported. [15]

2-(2-Cyclohex-1-enylethynyl)benzaldehyde. 2-Bromobenzaldehyde (1.86 g, 10.0 mmol) and 1-ethynylcyclohexene (1.27 g, 12.0 mmol) were employed. Column chromatography using 25:1 hexane/EtOAc afforded 2.00 g (95 %) of the desired compound

as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.57-1.72 (m, 4H), 2.11-2.18 (m, 2H), 2.20-2.25 (m, 2H), 6.27 (m, 1H), 7.33-7.39 (m, 1H), 7.49-7.51 (m, 2H), 7.87 (dt, J = 1.2, 7.8 Hz, 1H), 10.52 (d, J = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 21.5, 22.3, 25.9, 29.0, 82.5, 98.6, 120.4, 127.1, 127.7, 128.1, 133.1, 133.8, 135.7, 136.9, 192.0.

2-(3,4,5-Trimethoxyphenylethynyl)benzaldehyde. 3,4,5-Trimethoxyiodobenzene (2.94 g, 10.0 mmol) and 2-ethynylbenzaldehyde (1.56 g, 12.0 mmol) were employed. Column chromatography using 9:1 hexane/EtOAc afforded 2.67 g (90 %) of the desired compound as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.89 (s, 3H), 3.90 (s, 6H), 6.80 (s, 2H), 7.46 (t, J = 7.2 Hz, 1H), 7.56-7.66 (m, 2H), 7.95 (d, J = 7.8 Hz, 1H), 10.66 (d, J = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 56.5, 61.2, 84.2, 96.6, 109.1, 117.5, 127.0, 127.5, 128.8, 133.4, 134.0, 136.0, 139.7, 153.4, 191.9.

2-(4-Methoxyphenylethynyl)benzaldehyde. 2-Bromobenzaldehyde (1.86 g, 10.0 mmol) and 4-methoxyphenylacetylene (1.58 g, 12.0 mmol) were employed. Column chromatography using 11:1 hexane/EtOAc afforded 2.20 g (93 %) of the desired compound as a yellow solid: mp 50-51 °C; ^{1}H NMR ($CDCl_3$) Γ 3.85 (s, 3H), 6.92 (d, J = 8.7 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.51 (d, J = 8.7 Hz, 2H), 7.58-7.66 (m, 2H), 7.95 (d, J = 8.1 Hz, 1H), 10.66 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.5, 83.9, 96.7, 114.3, 114.5, 127.3, 127.5, 128.4, 133.2, 133.4, 133.9, 135.8, 160.4, 192.1.

4,5-Methylenedioxy-2-(phenylethynyl)benzaldehyde. 2-Bromo-4,5-(methylenedioxy)benzaldehyde (2.30 g, 10.0 mmol) and phenylacetylene (1.22 g, 12.0 mmol) were employed. Column chromatography using 20:1 hexane/EtOAc afforded 2.40 g (96 %) of the desired compound as a yellow solid: mp 98-101 °C; ^{1}H NMR ($CDCl_3$) Γ 6.10

(s, 1H), 7.04 (s, 1H), 7.26 (s, 1H), 7.38-7.40 (m, 3H), 7.54-7.56 (m, 2H), 10.50 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 85.0, 95.4, 102.6, 106.3, 112.2, 122.5, 123.9, 128.8, 129.2, 131.8, 132.4, 148.9, 152.6, 190.3.

2-(Phenylethynyl)pyridine-3-carboxaldehyde. 2-Bromopyridine-3-carboxaldehyde[13] (1.88 g, 10.0 mmol) and phenylacetylene (1.22 g, 12.0 mmol) were employed. Column chromatography using 7:1 hexane/EtOAc afforded 1.85 g (96 %) of the desired compound as a yellow oil with spectral properties identical to those previously reported.[13a]

2-(1-Octyn-1-yl)pyridine-3- carboxaldehyde. 2-Bromopyridine-3-carboxaldehyde[13] (1.88 g, 10.0 mmol) and 1-octyne (0.98 g, 12.0 mmol) were employed. Column chromatography using 7:1 hexane/EtOAc afforded 2.04 g (95 %) of the desired compound as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 0.89-0.92 (m, 3H), 1.33-1.40 (m, 4H), 1.40-1.57 (m, 2H), 1.66-1.71 (m, 2H), 7.36-7.37 (m, 1H), 8.14-8.17 (m, 1H), 8.75-8.77 (m, 1H), 10.54-10.56 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.2, 19.7, 22.7, 28.3, 28.9, 31.5, 76.8, 98.8, 122.9, 131.9, 134.7, 146.8, 154.5, 191.5.

3-(Phenylethynyl)pyridine-4-carboxaldehyde. 3-Bromopyridine-4-carboxaldehyde[13] (1.88 g, 10.0 mmol) and phenylacetylene (1.22 g, 12.0 mmol) were employed. Column chromatography using 7:1 hexane/EtOAc afforded 1.89 g (95 %) of the desired compound as a yellow oil with spectral properties identical to those previously reported.[13a]

2-(4-Trifluoromethylphenylethynyl)benzaldehyde. 4-Iodobenzotrifluoride (2.72 g, 10.0 mmol) and 2-ethynylbenzaldehyde (1.56 g, 12.0 mmol) were employed. Column chromatography using 9:1 hexane/EtOAc afforded 2.33 g (85 %) of the desired compound as a yellow oil: ^{1}H NMR ($CDCl_3$) 7.49 (t, J = 7.5 Hz, 1H), 7.57-7.67 (m, 6H), 7.96 (d, J = 7.2

Hz, 1H), 10.62 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 87.4, 94.7, 125.7 (q, J = 15 Hz), 126.1, 126.3, 126.3, 127.8, 129.4, 132.1, 133.6, 134.0, 136.2, 191.4.

2-(Cyclohexylethynyl)benzaldehyde. 2-Bromobenzaldehyde (1.86 g, 10.0 mmol) and cyclohexylacetylene (1.30 g, 12.0 mmol) were employed. Column chromatography using 25:1 hexane/EtOAc afforded 2.00 g (94 %) of the desired compound as a yellow oil with spectral properties identical to those previously reported.[16]

2-(4-(Tetrahydropyran-2-yloxy)but-1-ynyl)benzaldehyde. 2-Bromobenzaldehyde (1.86 g, 10.0 mmol) and 2-(3-butynyloxy)tetrahydro-2*H*-pyran (1.85 g, 12.0 mmol) were employed. Column chromatography using 10:1 hexane/EtOAc afforded 2.30 g (90 %) of the desired compound as a yellow oil with spectral properties identical to those previously reported.[16]

Imines Prepared

***N*-(2-Phenylethynylbenzylidene)-*tert*-butylamine (1).** To 2-(2-phenylethynyl)benzaldehyde (1.04 g, 5.0 mmol) in a 4 dram vial was added *t*-$BuNH_2$ (6 equiv). The mixture was then stirred under an Ar atmosphere at room temperature for 24 h. The resulting mixture was extracted with ether. The combined organic layers were dried (Na_2SO_4) and filtered. Removal of the solvent afforded 1.27 g (98 %) of imine **1** as a yellow solid: mp 53-54 °C; ^{1}H NMR ($CDCl_3$) Γ 1.36 (s, 9H), 7.35-7.41 (m, 5H), 7.54-7.58 (m, 3H), 8.07-8.10 (m, IH), 8.95 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.0, 58.0, 86.9, 95.1, 123.3, 124.1, 126.6, 128.7, 128.8, 129.9, 131.7, 132.4 , 138.0, 154.4; IR ($CHCl_3$, cm^{-1}) 3060, 2214, 1637; HRMS Calcd for $C_{19}H_{19}N$: 261.1518. Found: 261.1518.

***N*-[2-(Cyclohex-1-enylethynyl)benzylidene]-*tert*-butylamine (4).** This imine was prepared from 2-(2-cyclohex-1-enylethynyl)benzaldehyde (1.06 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.22 g (92 %) of the imine **4** as a reddish oil: ^{1}H NMR ($CDCl_3$) Γ 1.32 (s, 9H), 1.59-1.74 (m, 4H), 2.13-2.20 (m, 2H), 2.22-2.27 (m, 2H), 6.23 (dddd, J = 1.8, 1.8, 6.0, 6.0 Hz, 1H), 7.29-7.33 (m, 2H), 7.39-7.45 (m, 1H), 7.98-8.05 (m, 1H), 8.82 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 21.6, 22.5, 25.9, 29.4, 29.9, 57.9, 84.3, 97.0, 120.8, 124.5, 125.9, 128.2, 129.7, 132.1, 135.6, 137.6, 154.6; IR (neat, cm^{-1}) 3062, 2200, 1637; HRMS Calcd for $C_{19}H_{23}N$: 265.1830. Found: 265.1831.

***N*-[2-(3,4,5-Trimethoxyphenylethynyl)benzylidene]-*tert*-butylamine (6).** This imine was prepared from 2-(3,4,5-trimethoxyphenylethynyl)benzaldehyde (1.48 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.47 g (84 %) of the imine **6** a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.36 (s, 9H), 3.89 (s, 9H), 6.77 (s, 2H), 7.35-7.38 (m, 2H), 7.53 (dd, J = 3.0, 6.0 Hz, 1H), 8.05 (dd, J = 3.6, 6.0 Hz, 1H), 8.92 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.9, 56.3, 58.0, 61.2, 86.1, 95.1, 108.9, 118.3, 124.0, 126.2, 128.8, 129.9, 132.2, 138.0, 139.3, 153.4, 154.3; IR (neat, cm^{-1}) 2958, 2206, 1698; HRMS Calcd for $C_{22}H_{25}NO_3$: 351.1834. Found: 351.1839.

***N*-[2-(4-Methoxyphenylethynyl)benzylidene]-*tert*-butylamine (8).** This imine was prepared from 2-(4-methoxyphenylethynyl)benzaldehyde (1.18 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.41 g (97 %) of the imine **8** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.34 (s, 9H), 3.84 (s, 3H), 6.90 (td, J = 2.1, 9.0 Hz, 2H), 7.32-7.36 (m, 2H), 7.47 (td, J = 2.1, 9.0 Hz, 2H), 7.50-7.54 (m, 1H), 8.04-8.07 (m, 1H), 8.92 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.0, 55.6, 58.1, 85.7, 95.2, 114.4, 115.4, 124.5, 126.1, 128.5, 129.9,

132.3, 133.2, 137.7, 154.7, 160.0; IR (neat, cm^{-1}) 2963, 2836, 1699; HRMS Calcd for $C_{20}H_{21}NO$: 291.1623. Found: 291.1626.

***N*-[(6-Phenylethynyl)benzo[1,3]dioxol-5-ylmethylene]-*tert*-butylamine (10).** This imine was prepared from 4,5-methylenedioxy-2-(phenylethynyl)benzaldehyde (1.25 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.53 g (100 %) of the imine **10** as a yellow solid: mp 88-90 °C; ^{1}H NMR ($CDCl_3$) Γ 1.32 (s, 9H), 6.02 (s, 2H), 6.97 (s, 1H), 7.36-7.39 (m, 3H), 7.50-7.53 (m, 2H), 7.57 (s, 1H), 8.85 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.1, 57.8, 86.9, 93.9, 101.9, 105.9, 111.3, 118.6, 123.4, 128.6, 131.6, 134.1, 148.8, 149.2, 153.7; IR ($CHCl_3$, cm^{-1}) 3018, 2969, 2904, 1612; HRMS Calcd for $C_{20}H_{19}NO_2$: 305.1416. Found: 305.1420.

***N*-[(2-Phenylethynyl)pyridin-3-ylmethylene]-*tert*-butylamine (12).** This imine was prepared from 2-(phenylethynyl)pyridine-3-carboxaldehyde (1.04 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.31 g (100 %) of the imine **12** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.35 (s, 9H), 7.29 (ddd, J = 0.3, 3.6, 6.0 Hz, 1H), 7.38-7.41 (m, 3H), 7.59-7.62 (m, 2H), 8.36 (dd, J = 1.5, 6.0 Hz, 1H), 8.63 (dd, J = 1.5, 3.6 Hz, 1H), 8.88 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.8, 58.4, 86.3, 94.5, 122.2, 123.3, 128.7, 129.4, 132.1, 133.9. 134.2, 143.5, 151.3, 152.5; IR (neat, cm^{-1}) 3057, 2967, 2928, 2218, 1699; HRMS Calcd for $C_{18}H_{18}N_2$: 262.1470. Found: 262.1475.

***N*-[2-(1-Octyn-1-yl)pyridin-3-ylmethylene]-*tert*-butylamine (14).** This imine was prepared from 2-(1-octyn-1-yl)pyridine-3- carboxaldehyde (1.08 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.35 g (100 %) of the imine **14** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 0.87-0.92 (m, 3H), 1.29-1.34 (m, 13H), 1.46-1.52 (m, 2H),

1.60-1.71 (m, 2H), 2.52 (t, J = 6.9 Hz, 2H), 7.23 (dd, J = 4.8, 7.8 Hz, 1H), 8.30 (dd, J = 1.8, 7.8 Hz, 1H), 8.55 (dd, J = 1.8, 4.8 Hz, 1H), 8.74 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.2, 19.7, 22.7, 28.6, 28.9, 29.8, 31.5, 58.2, 78.1, 96.6, 122.8, 133.7, 133.8, 144.1, 151.1, 152.9; IR (neat, cm^{-1}) 3056, 2961, 2928, 2858, 2227, 1636, 1578; HRMS Calcd for $C_{18}H_{26}N_2$: 270.2096. Found: 270.2099.

***N*-[3-(Phenylethynyl)pyridin-4-ylmethylene]-*tert*-butylamine (16).** This imine was prepared from 3-(phenylethynyl)pyridine-4-carboxaldehyde (1.04 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.27 g (97 %) of the imine **16** as a yellow solid: mp 91-92 °C; ^{1}H NMR ($CDCl_3$) Γ 1.35 (s, 9H), 7.38-7.40 (m, 3H), 7.54-7.56 (m, 2H), 7.91 (d, J = 3.9 Hz, 1H), 8.56 (d, J = 3.9 Hz, 1H), 8.81 (s, 2H); ^{13}C NMR ($CDCl_3$) Γ 29.7, 58.9, 83.8, 97.7, 119.5, 120.3, 122.6, 128.8, 129.3, 131.8, 144.2, 149.0, 152.5, 153.5; IR ($CHCl_3$, cm^{-1}) 3016, 2970, 2870, 2217, 1492; HRMS Calcd for $C_{18}H_{18}N_2$: 262.1470. Found: 262.1476.

***N*-[2-(4-Trifluoromethylphenylethynyl)benzylidene]-*tert*-butylamine (21).** This imine was prepared from 2-(4-trifluoromethylphenylethynyl)benzaldehyde (1.37 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.56 g (95 %) of the imine **21** as a yellow solid: mp 104-105 °C; ^{1}H NMR ($CDCl_3$) Γ 1.34 (s, 9H), 7.38-7.42 (m, 2H), 7.55-7.58 (m, 1H), 7.63 (s, 4H), 8.07-8.10 (m, 1H), 8.89 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.9, 58.2, 89.3, 93.4, 123.2, 125.5, 125.6 (q, J = 15.2 Hz), 126.4, 127.1, 129.4, 130.0, 130.2, 131.8, 132.6, 138.2, 153.9; IR ($CHCl_3$, cm^{-1}) 3019, 2970, 1755, 1323; HRMS Calcd for $C_{20}F_3H_{18}N$: 329.1391. Found: 329.1397.

***N*-[2-(2-Propenylethynyl)benzylidene]-*tert*-butylamine (36).** This imine was prepared from 2-(2-propenylethynyl)benzaldehyde (0.85 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.07 g (95 %) of the imine **36** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.30 (s, 9H), 2.03 (d, J = 0.6 Hz, 3H), 5.34 (d, J = 0.6 Hz, 1H), 5.43 (s, 1H), 7.27-7.35 (m, 2H), 7.45-7.47 (m, 1H), 8.03-8.05 (m, 1H), 8.82 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.7, 29.9, 58.0, 85.9, 96.3, 122.4, 124.1, 126.1. 126.8, 128.8, 129.9, 132.3, 137.9, 154.5; IR (neat, cm^{-1}) 2967, 2926, 2867, 1637; HRMS Calcd for $C_{16}H_{19}N$: 225.1517. Found: 225.1522.

***N*-[2-(Cyclohexylethynyl)benzylidene]-*tert*-butylamine (38).** This imine was prepared from 2-(cyclohexylethynyl)benzaldehyde (1.07 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.31 g (98 %) of the imine **38** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.31 (s, 9H), 1.35-1.45 (m, 3H), 1.50-1.63 (m, 3H), 1.73-1.81 (m, 2H), 1.85-1.92 (m, 2H), 2.68 (dddd, J = 3.6, 3.6, 12.3, 12.3 Hz, 1H), 7.26-7.31 (m, 2H), 7.37-7.43 (m, 1H), 7.98-8.03 (m, 1H), 8.83 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 24.8, 26.0, 29.8, 29.9, 32.7, 57.8, 78.0, 100.2, 124.9, 125.8, 127.9, 129.7, 132.2, 137.8, 154.8; IR (neat, cm^{-1}) 3062, 2224, 1683; HRMS Calcd for $C_{19}H_{25}N$: 267.1987. Found: 267.1987.

***N*-[2-(4-(Tetrahydropyran-2-yloxy)but-1-ynyl)benzylidene]-*tert*-butylamine (40).** This imine was prepared from 2-(4-(tetrahydropyran-2-yloxy)but-1-ynyl)benzaldehyde (1.29 g, 5.0 mmol) by the method used to prepare **1**. Removal of the solvent afforded 1.45 g (93 %) of the imine **40** as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.30 (s, 9H), 1.48-1.65 (m, 4H), 1.68-1.89 (m, 2H), 2.78 (t, J = 7.2 Hz, 2H), 3.48-3.56 (m, 1H), 3.67 (ddd, J = 7.2, 7.2, 9.6 Hz, 1H), 3.86-3.97 (m, 2H), 4.68 (t, J = 3.0 Hz, 1H), 7.26-7.31 (m, 2H), 7.37-7.42 (m, 1H),

7.97-8.03 (m, 1H), 8.78 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 19.5, 21.2, 25.5, 29.8, 30.7, 57.7, 62.3, 65.9, 78.8, 92.7, 98.9, 124.4, 125.9, 128.1, 129.7, 132.4, 137.8, 154.5; IR (neat, cm^{-1}) 3063, 2229, 1637; HRMS Calcd for $C_{20}H_{27}NO_2$: 313.2040. Found: 313.2042.

General procedure for the electrophilic cyclization of iminoalkynes by I_2, ICl, PhSeCl, PhSCl and *p*-$O_2NC_6H_4SCl$. The electrophile (6 or 2 equivs), the solvent (5 ml), and the base, where required (3 equivs), were placed in a 2 dram vial. The iminoalkyne (0.25 mmol) in 2 ml of the solvent was added dropwise to the vial. The vial was flushed with Ar and the reaction was stirred at room temperature for the indicated period of time. The reactions were monitored by TLC to establish completion. The reaction mixture was then diluted with 25 ml of ether, washed with either 25 ml of saturated $Na_2S_2O_3$ (for the reactions of I_2 and ICl) or saturated NaCl, dried (Na_2SO_4) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

4-Iodo-3-phenylisoquinoline (2). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 56 mg (68 %) (Table 2, entry 1) or 55 mg (67 %) (Table 2, entry 2) of the product from I_2 or ICl, respectively, as a yellow solid: mp 84-85 °C; ^{1}H NMR ($CDCl_3$) Γ 7.26-7.52 (m, 3H), 7.61-7.70 (m, 3H), 7.70-7.85 (m, 2H), 7.95 (d, J = 8.1 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 98.3, 128.1, 128.2, 128.3, 128.5, 130.3, 132.4, 132.6, 138.8, 143.9, 152.2, 157.4 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3055, 1630, 1549; HRMS Calcd for $C_{15}H_{10}IN$: 330.9858. Found: 330.9862.

3-(Cyclohex-1-enyl)-4-iodoisoquinoline (5). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 56 mg (67 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$)

Γ1.73-1.79 (m, 2H), 1.84-1.92 (m, 2H), 2.25-2.29 (m, 2H), 2.40-2.43 (m, 2H), 5.85 (s, 1H), 7.57-7.60 (m, 1H), 7.73-7.78 (m, 1H), 7.87 (d, J = 8.1 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 9.06 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ22.1, 22.9, 25.3, 28.5, 97.7, 127.6, 128.0, 128.2, 129.5, 132.0, 132.2, 138.7, 141.8, 152.1, 159.7; IR (neat, cm^{-1}) 3019, 2936, 1618; HRMS Calcd for $C_{15}H_{14}IN$: 335.0165. Found: 335.0168.

4-Iodo-3-(3,4,5-trimethoxyphenyl)isoquinoline (7). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 32 mg (30 %) (Table 2, entry 4) or 25 mg (24 %) (Table 2, entry 5) of the product from I_2 or ICl, respectively, as a yellow solid: mp 132-134 °C; ^{1}H NMR ($CDCl_3$) Γ3.92 (s, 6H), 3.93 (s, 3H), 6.86 (s, 2H), 7.69 (dt, J = 1.2, 7.5 Hz, 1H), 7.84 (dt, J = 1.5, 8.4 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.24 (dd, J = 0.6, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ56.4, 61.2, 98.3, 107.5, 128.2, 128.3, 128.3, 132.6, 132.7, 138.3, 138.9, 139.1, 152.0, 152.9, 156.9; IR ($CHCl_3$, cm^{-1}) 3017, 2939, 2836, 1586; HRMS Calcd for $C_{18}H_{16}IO_3N$: 421.0175. Found: 421.0182.

4-Iodo-3-(3-methoxyphenyl)isoquinoline (9). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 34 mg (37 %) (Table 2, entry 6) or 36 mg (40 %) (Table 2, entry 7) of the product from I_2 or ICl, respectively, as a yellow solid: mp 113-115 °C; ^{1}H NMR ($CDCl_3$) Γ3.88 (s, 3H), 7.01 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 9.0 Hz, 2H), 7.65 (dt, J = 0.9, 7.5 Hz, 1H), 7.81 (dt, J = 1.8, 8.4 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ55.6, 98.2, 113.5, 128.0, 128.1, 128.1, 131.5, 132.4, 132.6, 136.4, 138.9, 152.2, 156.9, 159.8; IR ($CHCl_3$, cm^{-1}) 3017, 2958, 2835, 2283, 1608, 1514; HRMS Calcd for $C_{16}H_{12}INO$: 360.9964. Found: 360.9970.

6-Iodo-7-phenyl-1,3-dioxolo[4,5-*g*]isoquinoline (11). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 48 mg (52 %) of the product as a dark sticky oil: ^{1}H NMR ($CDCl_3$) Γ 6.17 (s, 2H), 7.17 (s, 1H), 7.42-7.49 (m, 3H), 7.56-7.60 (m, 2H), 7.62 (s, 1H), 8.89 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 97.1, 102.4, 103.2, 109.6, 125.4, 128.1, 128.3, 129.9, 137.6, 144.1, 149.1. 149.8, 152.9, 156.6; IR ($CHCl_3$, cm^{-1}) 3018, 2926, 2855, 1473; HRMS Calcd for $C_{16}H_{10}INO_2$: 374.9756. Found: 374.9760.

8-Iodo-7-phenyl-1,6-naphthyridine (13). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 75 mg (90 %) (Table 2, entry 10) or 76 mg (92 %) (Table 2, entry 11) of the product from I_2 or ICl, respectively, as a yellow solid: mp 163-164 °C; ^{1}H NMR ($CDCl_3$) Γ 7.45-7.52 (m, 3H), 7.59-7.62 (dd, J = 3.3, 6.3 Hz, 1H), 7.69 (dd, J = 1.2, 6.0 Hz, 2H), 8.29 (dd, J = 1.5, 6.0 Hz, 1H), 9.16 (s, 1H), 9.21 (dd, J = 1.2, 3.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 101.8, 123.1, 123.4, 128.2, 128.9, 130.0, 136.4, 143.0, 151.1, 152.3, 156.0, 161.1; IR ($CHCl_3$, cm^{-1}) 3048, 1618; HRMS Calcd for $C_{14}H_9IN_2$: 331.9810. Found: 331.9816.

7- *n*-Hexyl-8-iodo-1,6-naphthyridine (15). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 65 mg (76 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 0.90 (t, J = 7.5 Hz, 3H), 1.31-1.51 (m, 6H), 1.77-1.88 (m, 2H), 3.31-3.36 (m, 2H), 7.53 (dd, J = 4.2, 8.1 Hz, 1H), 8.22 (dd, J = 1.5, 8.1 Hz, 1H), 9.06 (s, 1H), 9.15 (dd, J = 1.5, 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.2, 22.7, 29.3, 29.5, 31.8, 42.7, 102.3, 122.6, 122.6, 136.2, 150.6, 152.1, 155.5, 163.1; IR (neat, cm^{-1}) 3018, 2955, 2925, 2854, 1603, 1579; HRMS Calcd for $C_{14}H_{17}IN_2$: 340.0436. Found: 340.0441.

4-Iodo-3-phenyl-2,6-naphthyridine (17). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 11 mg (13 %) (Table 2, entry 13) or 60 mg (72 %) (Table 2, entry

14) of the product from I_2 or ICl, respectively, as a yellow solid: mp 150-151 °C; ^{1}H NMR ($CDCl_3$) Γ 7.47-7.54 (m, 3H), 7.62-7.66 (m, 2H), 7.70 (dd, J = 0.9, 5.7 Hz, 1H), 8.82 (d, J = 5.7 Hz, 1H), 9.23 (d, J = 0.6 Hz, 1H), 9.63 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 95.5, 118.6, 128.3, 128.9, 130.0, 130.4, 132.4, 142.6, 145.7, 151.5, 157.6, 158.8; IR ($CHCl_3$, cm^{-1}) 3018, 2927, 2854, 1568, 1533; HRMS Calcd for $C_{14}H_9IN_2$: 331.9810. Found: 331.9816.

3-Phenyl-4-(phenylselenyl)isoquinoline (18). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 69 mg (76 %) of the product as a yellow solid: mp 112-114 °C; ^{1}H NMR ($CDCl_3$) Γ 7.04-7.08 (m, 5H), 7.39-7.42 (m, 3H), 7.55-7.56 (m, 3H), 7.71 (ddd, J = 1.2, 6.9, 8.1 Hz, 1H), 8.02 (d, J = 7.5 Hz, 1H), 8.45 (d, J = 8.1 Hz, 1H), 9.35 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 121.8, 126.4, 127.8, 127.9, 128.3, 128.4, 128.4, 128.9, 129.4, 129.9, 130.1, 132.1, 133.3, 138.9, 142.0, 153.3, 158.4; IR ($CHCl_3$, cm^{-1}) 3056, 2924, 1575; HRMS Calcd for $C_{21}H_{15}N^{80}Se$: 361.0370. Found: 361.0378.

3-(Cyclohex-1-enyl)-4-(phenylselenyl)isoquinoline (19). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 88 mg (96 %) of the product as a yellow solid: mp 103-105 °C; ^{1}H NMR ($CDCl_3$) Γ 1.69-1.82 (m, 4H), 2.15-2.21 (m, 2H), 2.44-2.48 (m, 2H), 5.67-5.70 (m, 1H), 7.09-7.14 (m, 5H), 7.52-7.65 (m, 2H), 7.94 (d, J = 8.1 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H), 9.23 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.0, 22.9, 25.5, 29.1, 120.8, 126.1, 127.0, 128.1, 128.2, 128.4, 129.2, 129.3, 129.9, 131.4, 133.8, 138.4, 140.0, 153.1, 161.2; IR ($CHCl_3$, cm^{-1}) 3019, 2936, 1571; HRMS Calcd for $C_{21}H_{19}N^{80}Se$: 365.0684. Found: 365.0690.

4-Phenylselenyl-3-(3,4,5-trimethoxyphenyl)isoquinoline (20). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 107 mg (95 %) of the product as a yellow oil:

^{1}H NMR ($CDCl_3$) Γ 3.70 (s, 6H), 3.88 (s, 3H), 6.76 (s, 2H), 7.04-7.11 (m, 5H), 7.65 (dt, J = 0.6, 5.5 Hz, 1H), 7.75 (dt, J = 0.9, 5.8 Hz, 1H), 8.03 (d, J = 5.8 Hz, 1H), 8.49 (d, J = 6.3 Hz, 1H), 9.34 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 56.0, 61.0, 107.0, 121.0, 126.1, 127.7, 128.2, 128.3, 128.7, 129.4, 129.5, 132.0, 133.8, 137.7, 138.0, 139.1, 152.6, 153.3, 158.4; IR (neat, cm^{-1}) 3057, 2936, 2833, 1607; HRMS Calcd for $C_{24}H_{21}NO_3{}^{80}Se$: 451.0687. Found: 451.0695.

4-Phenylselenyl-3-(3-trifluoromethylphenyl)isoquinoline (22). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 19 mg (18 %) of the product as a yellow solid: mp 116-117 °C; ^{1}H NMR ($CDCl_3$) Γ 6.97-7.02 (m, 2H), 7.04-7.11 (m, 3H), 7.64 (d, J = 1.8 Hz, 4H), 7.68 (dt, J = 1.2, 8.4 Hz, 2H), 7.74 (dt, J = 1.5, 9.0 Hz, 1H), 8.05 (d, J = 0.84 Hz, 1H), 8.50 (d, J = 8.4 Hz, 1H), 9.35 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 122.3, 124.8 (q, J = 15.6 Hz), 126.6, 128.2, 128.4, 128.5, 128.7, 129.5, 129.9, 130.0, 130.3, 130.4, 132.2, 132.8, 138.8, 145.7, 153.6, 157.1; IR (neat, cm^{-1}) 2952, 2918, 2850, 1476; HRMS Calcd for $C_{22}F_3H_{14}N^{80}Se$: 429.0244. Found: 429.0250.

6-Phenylselenyl-7-phenyl-1,3-dioxolo[4,5-g]isoquinoline (23). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 53 mg (60 %) of the product as a yellow solid: mp 140-143 °C; ^{1}H NMR ($CDCl_3$) Γ 6.08 (s, 2H), 6.92-7.02 (m, 2H), 7.07-7.11 (m, 3H), 7.22 (s, 1H), 7.36-7.38 (m, 3H), 7.49-7.54 (m, 2H), 7.78 (s, 1H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 102.1, 103.6, 105.5, 125.6, 126.3, 127.8, 128.1, 129.4, 129.6, 129.9, 133.2, 135.4, 138.1, 142.5, 148.7, 151.1, 152.6, 158.2; IR ($CHCl_3$, cm^{-1}) 2958, 2962, 2855, 1516; HRMS Calcd for $C_{18}H_{15}NO_2{}^{80}Se$: 405.0268. Found: 405.0273.

3-Phenyl-4-phenylselenyl-2,6-naphthyridine (24). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 72 mg (80 %) of the product as a yellow solid:

mp 104-106 °C; ^{1}H NMR ($CDCl_3$) Γ 7.07-7.10 (m, 5H), 7.44-7.47 (m, 3H), 7.59-7.62 (m, 2H), 7.78 (d, J = 5.6 Hz, 1H), 8.74 (d, J = 5.6 Hz, 1H), 9.39 (s, 1H), 9.89 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 119.1, 121.6, 127.1, 128.1, 128.8, 129.6, 130.2, 130.4, 130.8, 132.3, 132.5, 141.1. 145.0, 152.5, 154.2, 159.7; IR ($CHCl_3$, cm^{-1}) 3061, 3017, 2930, 2360, 1570; HRMS Calcd for $C_{20}H_{14}N_2{}^{82}Se$: 364.0324. Found: 364.0330.

7-Phenyl-8-phenylselenyl-1,6-naphthyridine (25). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 66 mg (72 %) of the product as a yellow solid: mp 122-124 °C; ^{1}H NMR ($CDCl_3$) Γ 6.95-7.10 (m, 5H), 7.31-7.37 (m, 3H), 7.53-7.57 (m, 3H), 8.32 (dd, J = 1.8, 8.4 Hz, 1H), 9.17 (dd, J = 1.8, 4.2 Hz, 1H), 9.30 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 122.9, 123.0. 125.9, 126.5, 127.9, 128.4, 128.9, 129.9, 131.8, 132.7, 136.4, 141.6, 151.8, 152.7, 155.3, 160.8; IR ($CHCl_3$, cm^{-1}) 3017, 2976, 2283 (broad), 1601; HRMS Calcd for $C_{20}H_{14}N_2{}^{82}Se$: 364.0324. Found: 364.0331.

7-*n*-Hexyl-8-phenylselenyl-1,6-naphthyridine (26). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 56 mg (61%) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 0.83-0.87 (m, 3H), 1.24-1.36 (m, 6H), 1.67-1.76 (m, 2H), 3.31-3.36 (m, 2H), 7.09-7.13 (m, 3H), 7.20-7.24 (m, 2H), 7.50 (dd, J = 4.2, 8.4 Hz, 1H), 8.28 (dd, J = 1.8, 8.4 Hz, 1H), 9.14 (dd, J = 1.8, 4.2 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.2, 22.7, 29.5, 30.4, 31.8, 39.5, 122.2, 122.6, 124.4, 126.3, 129.1, 130.4, 133.0, 136.3, 151.8, 153.4, 155.4, 165.1; IR (neat, cm^{-1}) 3056, 2954, 2855, 1602; HRMS Calcd for $C_{20}H_{22}N_2{}^{80}Se$: 370.0948. Found: 370.0952.

3-Phenyl-4-(4-nitrophenylsulfenyl)isoquinoline (27). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 42 mg (47 %) of the product as a yellow solid:

mp 193-195 °C; ^{1}H NMR ($CDCl_3$) Γ 6.97-6.99 (m, 2H), 7.40-7.42 (m, 3H), 7.57-7.60 (m, 2H), 7.68-7.80 (m, 2H), 7.97-8.00 (m, 2H), 8.13 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 9.46 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 119.5, 124.4, 125.6, 126.1, 128.2, 128.3, 128.5, 128.8, 128.9, 129.7, 132.7, 138.1, 140.2, 145.4, 147.8, 154.6, 159.0; IR ($CHCl_3$, cm^{-1}) 3019, 2926, 1518; HRMS Calcd for $C_{21}H_{14}N_2O_2S$: 358.007. Found: 358.0781.

3-(Cyclohex-1-enyl)-4-(4-nitrophenylsulfenyl)isoquinoline (28). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 30 mg (33 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.67-1.77 (m, 4H), 2.13 (d, J = 0.5 Hz, 2H), 2.41 (d, J = 0.5 Hz, 2H), 5.78 (s, 1H), 6.98-7.01 (m, 2H), 7.59-7.74 (m, 2H), 7.98-8.16 (m, 3H), 8.18-8.20 (m, 1H), 9.35 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 21.9, 22.8, 25.5, 28.9, 118.8, 124.3, 125.4, 126.1, 126.6, 127.8, 128.3, 128.8, 129.8, 132.5, 138.1, 138.4, 148.7, 154.4, 161.9; IR ($CHCl_3$, cm^{-1}) 3019, 2932, 1517; HRMS Calcd for $C_{21}H_{18}N_2O_2S$: 362.1089. Found: 362.1094.

3-(4-Methoxyphenyl)-4-(4-nitrophenylsulfenyl)isoquinoline (29). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 21 mg (25 %) of the product as a yellow solid: mp 161-163 °C; ^{1}H NMR ($CDCl_3$) Γ 3.86 (s, 3H), 6.96 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 9.0 Hz, 2 H), 7.61 (d, J = 9.0 Hz, 2H), 7.69 (dt, J = 1.2, 7.8 Hz, 1H), 7.74 (dt, J = 1.2, 9.3 Hz, 1H), 8.01 (d, J = 8.7 Hz, 2H), 8.12 (dd, J = 0.9, 7.8 Hz, 1H), 8.26 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.5, 113.5, 118.6, 124.3, 125.5, 125.9, 128.0, 128.2, 128.7, 131.3, 132.6, 132.7, 138.2, 145.3, 148.0, 154.5, 158.7, 160.1; IR ($CHCl_3$, cm^{-1}) 3019, 2971, 2838, 1608, 1578, 1515; HRMS Calcd for $C_{22}H_{16}N_2O_3S$: 338.0082. Found: 338.0085.

3-(Cyclohex-1-enyl)-4-(phenylsulfenyl)isoquinoline (30). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 36 mg (45 %) of the product as a yellow solid:

mp 130-131 °C; ^{1}H NMR ($CDCl_3$) Γ 1.68-1.79 (m, 4H), 2.15-2.17 (m, 2H), 2.41-2.43 (m, 2H), 5.77-5.79 (m, 1H), 6.96-6.98 (m, 2H), 7.03-7.07 (m, 1H), 7.11-7.15 (m, 2H), 7.56 (t, J = 5.4 Hz, 1H), 7.65 (t, J = 5.4 Hz, 1H), 7.97(d, J = 6.0 Hz, 1H), 8.31 (d, J = 6.6 Hz, 1H), 9.26 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.0, 23.0, 25.5, 28.9, 121.4, 125.3, 126.0, 127.1, 127.2, 128.2, 128.2, 129.0, 129.2, 131.6, 138.3, 138.7, 138.7, 153.2, 161.2; IR ($CHCl_3$, cm^{-1}) 3019, 2936, 1630; HRMS Calcd for $C_{21}H_{19}NS$: 317.1238. Found: 317.1241.

4-Phenylsulfenyl-3-(3,4,5-trimethoxyphenyl)isoquinoline (31). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 43 mg (43 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.67 (s, 6H), 3.87 (s, 3H), 6.82 (s, 2H), 6.95 (d, J = 7.2 Hz, 2H), 7.06 (t, J = 7.2 Hz, 1H), 7.16 (t, J = 7.2 Hz, 2H), 7.67 (t, J = 7.2 Hz, 1H), 7.77 (t, J = 7.2 Hz, 1H), 8.07 (d, J = 4.0 Hz, 1H), 8.46 (d, J = 7.6 Hz, 1H), 9.38 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.9, 61.0, 106.9, 121.1, 125.3, 126.3, 126.4, 127.8, 128.3, 128.4, 129.2, 132.2, 136.3, 138.1, 138.8, 139.0, 152.7, 153.5, 158.4; IR ($CHCl_3$, cm^{-1}) 3015, 2939, 2860, 1585; HRMS Calcd for $C_{24}H_{21}NO_3S$: 403.1242. Found: 403.1246.

7- *n*-Hexyl-8-phenylsulfenyl-1,6-naphthyridine (32). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 32 mg (40 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 0.85 (t, J = 6.9 Hz, 3H), 1.24-1.37 (m, 6H), 1.67-1.76 (m, 2H), 3.30 (t, J = 8.4 Hz, 2H), 7.00-7.13 (m, 5H), 7.51 (dd, J = 4.2, 8.1 Hz, 1H), 8.30 (dd, J = 1.8, 8.1 Hz, 1H), 9.15 (dd, J = 1.8, 4.2 Hz, 1H), 9.29 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.2, 22.7, 29.5, 30.2, 31.8, 37.6, 122.3, 122.8, 124.4, 125.4, 127.2, 128.9, 136.4, 137.9, 151.8, 153.5, 155.6, 165.7; IR (neat, cm^{-1}) 3056, 2925, 2854, 2221, 1602; HRMS Calcd for $C_{20}H_{22}N_2S$: 322.1504. Found: 322.1508.

General procedure for the silver-catalyzed cyclization of iminoalkynes. 5 Mol % of $AgNO_3$ and 5 ml of $CHCl_3$ were placed into a 2 dram vial. The iminoalkyne (0.25 mmol) in 2 ml of $CHCl_3$ was added dropwise to the vial. The vial was then flushed with Ar and heated at 50 °C for the indicated period of time. The reaction mixture was cooled, diluted with 25 ml of ether, washed with 25 ml of saturated NaCl, dried (Na_2SO_4) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

General procedure for the copper-catalyzed cyclization of iminoalkynes. DMF (5 ml), the iminoalkyne (0.25 mmol), and CuI (5 mg, 0.025 mmol) were placed in a 2 dram vial. The vial was then flushed with Ar and heated in an oil bath at 100 °C for the indicated period of time. The reaction were monitored by TLC to establish completion. The reaction mixture was cooled, diluted with 25 ml of ether, washed with 25 ml of saturated NaCl, dried (Na_2SO_4) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

3-Phenylisoquinoline (33). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 42 mg (82 %) (Table 2, entry 29) or 51 mg (100 %) (Table 2, entry 30) of the product from $AgNO_3$ or CuI, respectively, as a yellow solid with spectral properties identical to those previously reported[17]: mp 102-103 °C (lit.[17] mp 101-102 °C).

3-(Cyclohexen-1-yl)isoquinoline (34). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 40 mg (78 %) (Table 2, entry 31) or 43 mg (81 %) (Table 2, entry 32) of the product from $AgNO_3$ or CuI, respectively, as a white solid: mp 114-115 °C; ^1H NMR ($CDCl_3$) Γ 1.69-1.77 (m, 2H), 1.83-1.91 (m, 2H), 2.30-2.38 (m, 2H), 2.56-2.62 (m,

2H), 7.04 (tt, J = 2.4, 3.6 Hz, 1H), 7.50 (dt, J = 0.6, 14.4 Hz, 1H), 7.59 (s, 1H), 7.65 (dd, J = 1.2, 6.9 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 9.20 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.4, 23.2, 26.2, 26.3, 114.3, 126.5, 126.9, 127.7, 127.7, 128.6, 130.4, 135.8, 136.8, 151.7, 152.6; IR ($CHCl_3$, cm^{-1}) 3060, 2919, 1621, 1574; MS *m/z* (rel intensity) 209 (100, M^+), 208 (89), 194 (42), 180 (51). Anal. Calcd for $C_{15}H_{15}N$: C, 86.09; H, 7.23; N, 6.69. Found: C, 86.03; H, 7.30; N, 6.73.

3-(3,4,5-Trimethoxyphenyl)isoquinoline (35). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 52 mg (71 %) of the product as a yellow solid: mp 122-124 °C; ^{1}H NMR ($CDCl_3$) Γ 3.93 (s, 3H), 4.00 (s, 6H), 7.38 (s, 2H), 7.58 (dt, J = 0.9, 7.5 Hz, 1H), 7.70 (dt, J = 0.9, 7.6 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.01 (s, 1H), 9.31 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 56.4, 61.2, 104.3, 116.3, 126.9, 127.2, 127.7, 127.8, 130.7, 135.4, 136.7, 138.8, 151.0, 152.4, 153.7; IR ($CHCl_3$, cm^{-1}) 3018, 2968, 2939, 1578; HRMS Calcd for $C_{18}H_{17}NO_3$: 295.1208. Found: 295.1211.

3-(2-Propenyl)isoquinoline (37). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 23 mg (54 %) of the product as a yellow solid: mp 66-68 °C; ^{1}H NMR ($CDCl_3$) Γ 2.32 (d, J = 0.4 Hz, 3H), 5.36 (d, J = 1.6 Hz, 1H), 6.20 (dd, J = 0.4, 1.6 Hz, 1H), 7.56 (dt, J = 1.2, 6.8 Hz, 1H), 7.70 (dt, J = 0.8, 7.2 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 20.9, 115.8, 115.9, 127.1, 127.2, 127.7, 127.9, 130.5, 136.6, 142.4, 151.8, 151.9; IR ($CHCl_3$, cm^{-1}) 3057, 3014, 2976, 1625, 1580; HRMS Calcd for $C_{12}H_{11}N$: 169.0892. Found: 169.0894.

3-Cyclohexylisoquinoline (39). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 40 mg (75 %) (Table 2, entry 35) or 49 mg (93 %) (Table 2, entry

36) of the product from $AgNO_3$ or CuI, respectively, as a white solid: mp 40-41 °C; ^{1}H NMR ($CDCl_3$) Γ 1.25-1.67 (m, 6H), 1.89 (dt, J = 2.7, 12.6 Hz, 2H), 2.06 (dd, J = 1.5, 12.9 Hz, 2H), 2.86 (tt, J = 3.3, 11.7 Hz, 1H), 7.47 (s, 1H), 7.52 (ddd, J = 1.2, 6.9, 8.1 Hz, 1H), 7.64 (td, J = 1.2, 6.9 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 9.21 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 26.4, 26.9, 33.3, 46.3, 116.2, 126.4, 126.5, 127.4, 127.6, 130.2, 136.8, 152.0, 160.3; IR ($CHCl_3$, cm^{-1}) 3055, 2926, 1628, 1585; HRMS Calcd for $C_{15}H_{17}N$: 211.1356. Found: 211.1361.

3-[2-(Tetrahydropyran-2-yloxy)ethyl]isoquinoline (41). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 39 mg (62 %) (Table 2, entry 37) or 52 mg (83 %) (Table 2, entry 38) of the product from $AgNO_3$ or CuI, respectively, as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.40-1.46 (m, 4H), 1.61-1.82 (m, 2H), 3.23 (t, J = 7.2 Hz, 2H), 3.42-3.48 (m, 1H), 3.76 (ddd, J = 3.3, 8.1, 11.7 Hz, 1H), 3.87 (ddd, J = 6.9, 9.6, 16.5 Hz, 1H), 4.18 (ddd, J = 6.9, 9.6, 16.8 Hz, 1H), 4.64 (ddd, J = 2.7, 2.7, 2.7 Hz, 1H), 7.54 (ddd, J = 1.2, 6.9, 9.3 Hz, 1H), 7.57 (s, 1H), 7.65 (ddd, J = 1.2, 6.6, 9.3 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 9.21 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 19.7, 25.6, 30.8, 38.5, 62.4, 67.1, 99.0, 119.3, 126.3, 126.7, 127.4, 127.6, 130.5, 136.6, 152.2, 152.6; IR ($CHCl_3$, cm^{-1}) 3054, 2942, 1628, 1588; HRMS Calcd for $C_{16}H_{19}NO_2$: 257.1416. Found: 257.1415.

3-Phenyl-6,7-(methylenedioxy)isoquinoline (42) Purification by flash chromatography (3:1 hexane/EtOAc) afforded 35 mg (56 %) of the product as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 6.10 (s, 1H), 7.16 (d, J = 7.1 Hz), 7.37-7.51 (m, 3H), 7.89 (s, 1H), 8.06 (d, J = 1.8 Hz, 1H), 9.06 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 101.9, 103.0, 103.4, 116.6, 125.3,

127.0, 128.5, 129.0, 135.3, 139.9, 148.6, 150.4, 150.8, 151.4; IR ($CHCl_3$, cm^{-1}) 3019, 2925, 1600, 1458; HRMS Calcd for $C_{16}H_{11}NO_2$: 249.0789. Found: 249.0793.

7-Phenyl-1,6-naphthyridine (43). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 47 mg (92 %) of the product as a pale yellow solid: mp 135-137 °C; ^1H NMR ($CDCl_3$) Γ 7.42-7.55 (m, 4H), 8.15-8.21 (m, 2H), 8.29 (ddd, J = 0.6, 1.8, 8.4 Hz, 1H), 8.35 (s, 1H), 9.09 (dd, J = 1.8, 4.2 Hz, 1H), 9.34 (d, J = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 118.0, 122.4, 122.9, 127.4, 129.1, 129.4, 135.8, 139.1, 151.6, 152.9, 155.3, 155.4; IR ($CHCl_3$, cm^{-1}) 3018, 2980, 1613; HRMS Calcd for $C_{14}H_{10}N_2$: 206.0844. Found: 206.0848.

7-*n*-Hexyl-1,6-naphthyridine (44). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 24 mg (45 %) of the product as a yellow oil: ^1H NMR ($CDCl_3$) Γ 0.88 (t, J = 4.2 Hz, 3H), 1.31-1.39 (m, 6H), 1.80-1.87 (m, 2H), 7.47 (dd, J = 4.5, 8.1 Hz, 1H), 7.75 (s, 1H), 8.26 (d, J = 8.1 Hz, 1H), 9.06 (dd, J = 1.5, 4.5 Hz, 1H), 9.23 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 22.8, 29.2, 29.9, 31.9, 38.5, 119.8, 121.9, 122.1, 135.8, 151.3, 152.5, 155.0, 160.6; IR ($CHCl_3$, cm^{-1}) 2956, 2929, 2857, 1619; HRMS Calcd for $C_{14}H_{18}N_2$: 214.1470. Found: 214.1472.

3-Phenyl-2,6-naphthyridine (45). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 41 mg (80 %) of the product as a yellow solid: mp 138-140 °C; ^1H NMR ($CDCl_3$) Γ 7.45 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.78 (d, J = 5.6, 1H), 8.13 (d, J = 7.6 Hz, 2H), 8.16 (s, 1H), 8.69, (d, J = 5.6 Hz, 1H), 9.37 (s, 1H), 9.41 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 115.1, 119.4, 127.2, 129.2, 129.3, 129.4, 131.4, 138.9, 144.6, 151.8, 152.4, 153.3; IR ($CHCl_3$, cm^{-1}) 3018, 2984, 1572; HRMS Calcd for $C_{14}H_{10}N_2$: 206.0844. Found: 206.0848.

Characterization of compound 3. A yellow oil (R_f = 0.25, 3:1 hexane/EtOAc): ^{1}H NMR ($CDCl_3$) Γ 1.42 (s, 9H), 5.73 (s, 1H), 7.17 (dd, *J* = 0.6, 4.8 Hz, 1H), 7.31 (dt, *J* = 0.6, 6.0 Hz, 2H), 7.49-7.54 (m, 3H), 7.65 (dd, *J* = 0.9, 6.3 Hz, 2H), 7.90 (td, *J* = 0.6, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.4, 57.2, 93.0, 121.5, 124.2, 129.0, 130.1, 130.6, 132.0, 132.5, 133.2, 134.5, 145.1, 169.9, 198.2; IR ($CHCl_3$, cm^{-1}) 3429, 3018, 2978, 1693; HRMS Calcd for $C_{19}H_{18}N_2O_2$: 292.1337. Found: 292.1343.

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CHAPTER 2. SYNTHESIS OF 4-(1-ALKENYL)ISOQUINOLINES BY PALLADIUM(II)-CATALYZED CYCLIZATION/OLEFINATION

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Abstract

A variety of 4-(1-alkenyl)-3-arylisoquinolines have been prepared in moderate to excellent yields by the Pd(II)-catalyzed cyclization of 2-(1-alkynyl)arylaldimines in the presence of various alkenes. The introduction of an *ortho*-methoxy group on the arylaldimine promotes the Pd-catalyzed cyclization and stabilizes the resulting Pd(II) intermediate, improving the yields of the isoquinoline products. Ketone-containing isoquinolines 36 and 49-51 have also been prepared by this process when unsaturated alcohols are employed as the alkenes.

Introduction

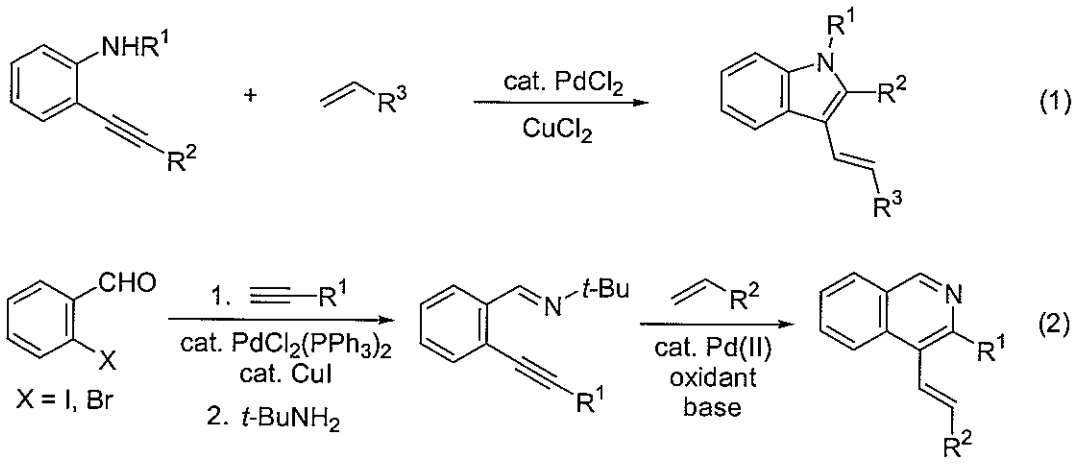
The synthesis of isoquinolines has received considerable attention due to the fact that the isoquinoline ring system is present in numerous naturally-occurring alkaloids.[1] Although classical methods have frequently been employed in the total synthesis of isoquinoline alkaloids, these approaches often have drawbacks. For example, the Bischler-Napieralski,[2] Pictet-Spengler,[3] and Pomeranz-Fritsch[4] protocols require relatively strong acids to cyclize *E*-phenethylamines. Also, the Bischler-Napieralski[2] and Pictet-Spengler[3] reactions afford

dihydro- and tetrahydroisoquinolines, respectively. An additional step involving dehydrogenation is thus required to complete the synthesis of the isoquinoline.

Substituted isoquinoline heterocycles have also been synthesized by employing palladium methodology. For instance, 3,4-disubstituted isoquinolines have been achieved by the annulation of internal alkynes by cyclopalladated *N,N*-dimethylbenzylamine complexes,[5] cyclopalladated *N-tert*-butylbenzaldimine tetrafluoroborates,[6] cyclopalladated *N-tert*-butylarylaldimines,[7] and *N-tert*-butyl-*o*-iodobenzaldimines plus a palladium catalyst.[8]

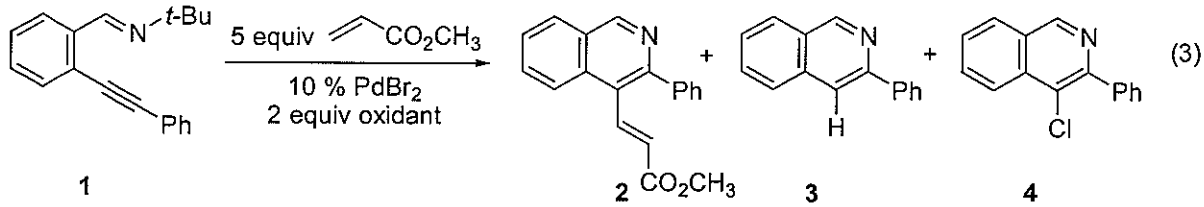
The transition metal-catalyzed cyclization of alkynes,[9] which possess nucleophilic centers in close proximity to the carbon-carbon triple bond, by *in situ* coupling/cyclization reactions,[10] and reactions promoted by vinylic, aryl, and alkynylpalladium complexes,[11] have also been shown to be extremely effective for the synthesis of a wide variety of carbo- and heterocycles.

The palladium(II)-catalyzed cyclization/olefination reaction of 2-(1-alkynyl)aniline derivatives to indoles has been reported by Sakamoto et al.[12] They report that the reaction of *N*-protected 2-(1-alkynyl)anilines with electron-deficient alkenes in the presence of $PdCl_2$ and $CuCl_2$ gives 2-substituted 3-(1-alkenyl)indoles (eq 1). Our interest in 4-(1-alkenyl)isoquinolines has prompted us to develop a convenient new synthesis of these isoquinolines by the Pd(II)-promoted cross coupling of a variety of alkenes and 2-(1-alkynyl)arylaldimines, which can be easily prepared from corresponding 2-halobenzaldehydes in two steps (eq 2).



Results and Discussion

Our initial studies on the synthesis of 4-(1-alkenyl)isoquinolines focused on the development of an optimum set of reaction conditions for their formation. A variety of Pd(II) catalysts, oxidants, bases, solvents and temperatures have been examined on the reaction of arylaldimine **1** and methyl acrylate (eq 3) and only some representative optimization reactions are summarized in Tables 1 and 2.



The optimization reactions shown in Table 1 employed 2 equiv of the oxidant (eq 3). In entry 1 (Table 1), benzaldimine **1** has been allowed to react with 5 equiv of methyl acrylate in the presence of 10 mol % of $PdBr_2$ under an O_2 balloon, and a 33 % yield of isoquinoline **2** was isolated in the absence of a base. However, the use of 2 equiv of $CuCl_2$ as the oxidant afforded none of the desired product, although all starting materials disappeared

within 20 h (entry 2). The use of $CuCl_2$ and the bases Et_3N, K_2CO_3 and NaOAc resulted in 10-20 % yields of the desired product **2** (entries 3-5). In entries 4 and 5, 4-chloro-3-phenylisoquinoline (**4**) was obtained in 15 % and 20 % yields, respectively.

Table 1. Optimization of the Reaction of Benzaldimine **1** and Methyl Acrylate by Examination of Different Oxidizing Reagents, Bases and Solvents (eq 3)[a]

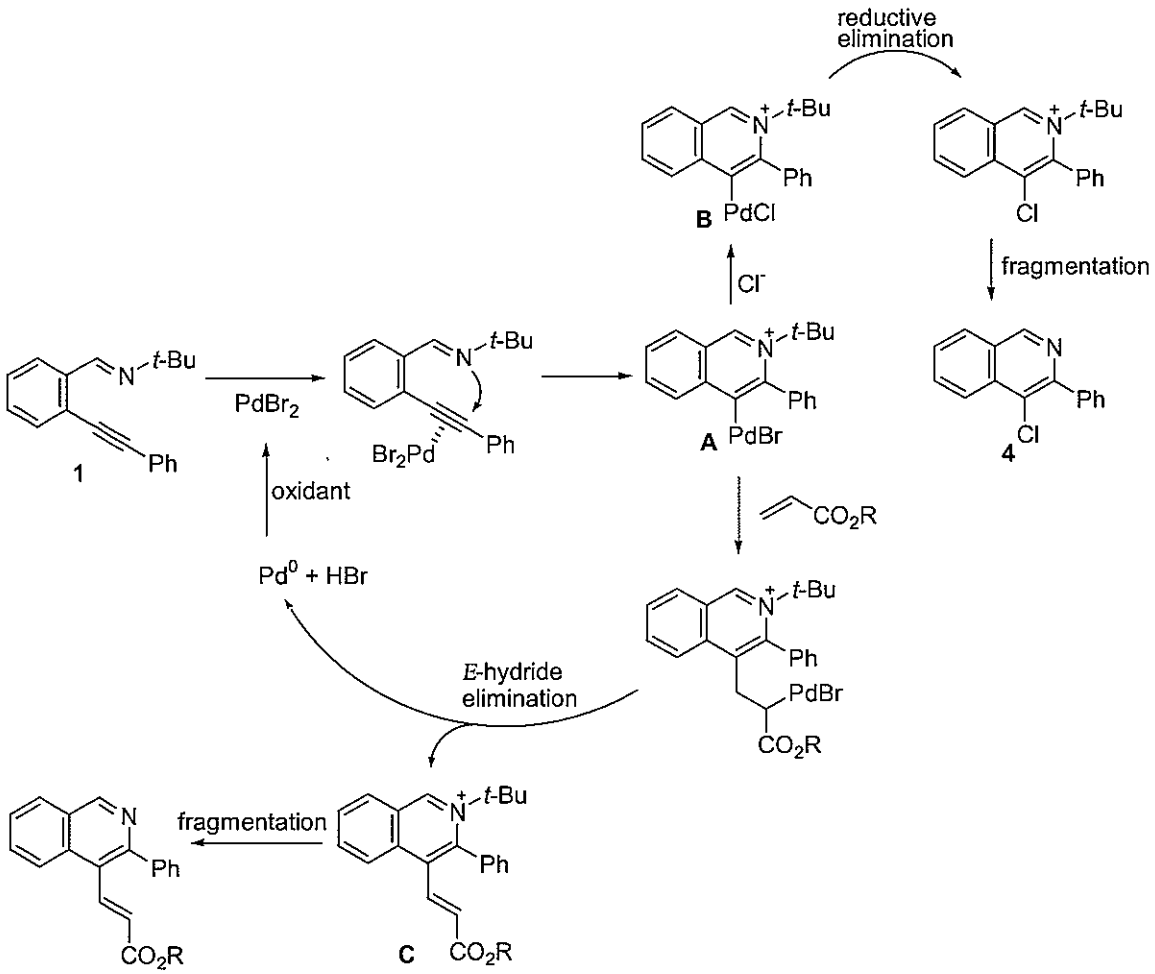
entry	oxidant	base	solvent	time (h)	**2** (%)[b]	**3** (%)[b]	**4** (%)[b]
1	O_2	--	DMF	24	33 (37[c])	20	0
2	$CuCl_2$	--	DMF	20	0	0	0
3	$CuCl_2$	Et_3N	DMF	36	10	15	trace
4	$CuCl_2$	K_2CO_3	DMF	36	17	trace	15
5	$CuCl_2$	NaOAc	DMF	36	20	trace	20
6	$Cu(OAc)_2$	NaOAc	DMF	24	35	0	0
7	$Cu(OAc)_2$	NaOAc	CH_3CN	12	18	25	0
8	$Cu(OAc)_2$	NaOAc	DMSO	12	61	5	0
9	$Cu(CO_3)_2$	NaOAc	DMSO	24	23	34	0
10	$Cu(NO_3)_2$	NaOAc	DMSO	24	37	19	0
11	benzoquinone	NaOAc	DMSO	24	40	30	0

[a] All reactions were run under the following reaction conditions: 0.25 mmol of benzaldimine **1**, 5 equiv of methyl acrylate, 10 mol % $PdBr_2$, 2 equiv of the oxidant, and 3 equiv of the base were stirred in 3 ml of the indicated solvent at 70 °C for the specified period of time. [b] Isolated yields. [c] Yield based on ^1H NMR spectroscopic analysis.

Possible mechanisms for the formation of isoquinolines **2** and **4** are shown in Scheme 1. The cyclization of benzaldimine **1** by $PdBr_2$ presumably forms intermediate **A**, which is an electron-deficient arylpalladium bromide. The *cis* addition of intermediate **A** to the carbon-carbon double bond of the olefin affords an alkylpalladium(II) intermediate, which

undergoes subsequent E-hydride elimination to afford intermediate **C** and Pd(0). Further fragmentation of the *tert*-butyl group from intermediate **C** generates the desired 4-(1-alkenyl)isoquinolines. The Pd(0) generated can be reoxidized back to $PdBr_2$ by the oxidant present in the reaction mixture.

Scheme 1



With the presence of excess chloride in the reaction mixture, the intermediate **A** is converted into intermediate **B** by halide exchange, because the Pd-Cl bond is much stronger than the Pd-Br bond.[13] Isoquinoline **4** is then generated by the reductive elimination of intermediate **B**, followed by fragmentation of the *tert*-butyl group. This reductive

elimination is apparently promoted by the presence of the copper salt, since arylpalladium halides do not normally undergo this process spontaneously. The use of $Cu(OAc)_2$ as the oxidant increased the yield of the desired isoquinoline **2** from 20 % (entry 5) to 35 % (entry 6). Obviously, the use of $Cu(OAc)_2$ eliminates the formation of intermediate **B** and eventual formation of the chloroisoquinoline **4**.

When CH_3CN was chosen as the solvent, an 18 % yield of isoquinoline **2** was isolated, alongside a 25 % yield of isoquinoline **3** (entry 7). However, the use of DMSO resulted in a 61 % yield of isoquinoline **2** and only a 5 % yield of **3** in 12 h (entry 8). Obviously, DMSO is a better solvent than DMF or CH_3CN for this isoquinoline olefination process, presumably due to improved oxidation of Pd(0) to Pd(II). Thus, DMSO has been chosen as the solvent for all subsequent optimization reactions. From entries 9-11, other oxidants $Cu(CO_3)_2$, $Cu(NO_3)_2$, and 1,4-benzoquinone have been employed and only 23-40 % yields of product **2** have been isolated. Based on the above results, the following reaction conditions have been chosen as the standard reaction conditions for procedure A: 0.25 mmol of benzaldimine, 5 equiv of the olefin, 10 mol % of $PdBr_2$, 2 equiv of $Cu(OAc)_2$, and 3 equiv of NaOAc are stirred in 3 mL of DMSO at 70 °C.

The drawback of procedure **A** is the use of 2 equiv of $Cu(OAc)_2$. We have therefore tried to develop an alternative procedure using only catalytic amounts of the copper reagent (eq 4). In this optimization study, it has been found that only catalytic amounts of $PdCl_2(PPh_3)_2$ in the presence of 10 mol % $CuCl_2$, 3 equiv of NaOAc and an O_2 atmosphere can cyclize benzaldimine **1**, affording a 38 % yield of isoquinoline **5** (entry 1, Table 2). Based on this reaction, various bases and additives have been examined and the results are summarized in entries 2-11.

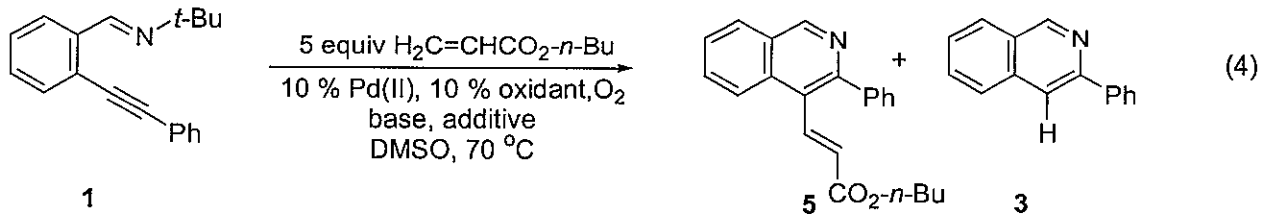


Table 2. Optimization of the Reaction of Benzaldimine **1** and *n*-Butyl Acrylate Using Catalytic Amounts of the Copper Reagent(eq 4)[a]

entry	catalyst	oxidant	base	additive	time (h)	% isolated yield of **5**	% isolated yield of **3**
1	$PdCl_2(PPh_3)_2$	$CuCl_2$	NaOAc	--	24	38	21
2			pyridine	--	24	48	9
3			Et_3N	--	28	46	12
4			Cs_2CO_3	--	24	trace[b]	20
5			K_2CO_3	--	28	29	18
6			$KHCO_3$	--	20	39	16
7			Na_2CO_3	--	20	47	12
8			$NaHCO_3$	--	14	51	11
9			$NaHCO_3$	TBAC	20	45	25
10			$NaHCO_3$	TBAB	20	46	15
11			$NaHCO_3$	TEAI	20	44	20

Table 2 continued

12	$PdCl_2$	$CuCl_2$	$NaHCO_3$	--	16	49	12
13	PdI_2			--	24	46	20
14	$Pd(O_2CCF_3)_2$			--	24	48	15
15	$Pd(OAc)_2$			--	20	45	11
16	$PdBr_2$			--	8	56	17
17	$PdBr_2$			PPh_3	20	48	17
18	$PdBr_2$			dppp	20	53	15
19	$PdBr_2$			dppe	18	51	11
20	$PdBr_2$	CuF_2		--	18	54	14
21		$Cu(OAc)_2$		--	19	45	27
22		$Cu(NO_3)_2$		--	24	45	21
23		$CuCO_3$		--	24	39	14
24		CuO		--	24	41	24
25		CuI		--	16	23	46

[a] All reactions were run under the following reaction conditions, unless otherwise specified: 0.25 mmol of benzaldimine **1**, 5 equiv of *n*-butyl acrylate, 10 mol % of the indicated Pd(II) salt, 10 mol % of the indicated oxidant and 3 equiv of the indicated base in 3 mL of DMSO were stirred at 70 °C for the specified period of time under a balloon of O_2. [b] Benzaldimine **1** was recovered in 40 % yield.

Table 3. Synthesis of Isoquinolines by Palladium(II)-Catalyzed Cyclization/Olefination[a]

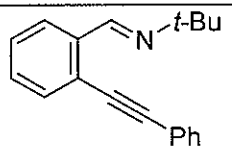
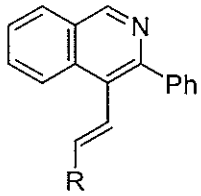
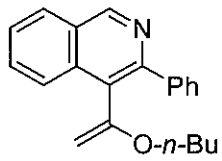
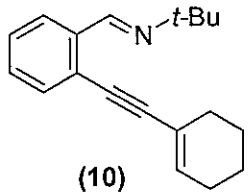
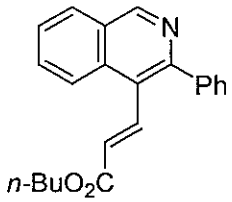
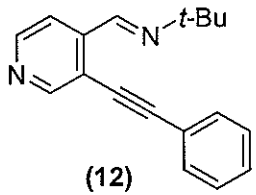
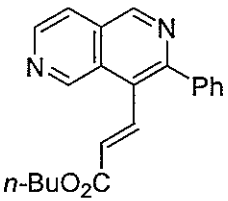
entry	arylaldimine	H_2C=CHR	procedure, time (h)	product	% isolated yield
1	 **(1)**	R = CO_2Me	A, 12	 R = CO_2Me **(2)**	61
2		R = CO_2-*n*-Bu	A, 10	R = CO_2-*n*-Bu **(5)**	61
3		R = CO_2-*n*-Bu	B, 8	R = CO_2-*n*-Bu **(5)**	56
4		R = CO_2-*t*-Bu	B, 24	R = CO_2-*t*-Bu **(6)**	50
5		R = Ph	B, 18	R = Ph **(7)**	53
6		R = CMe_2OH	B, 17	R = CMe_2OH **(8)**	34
7		R = O-*n*-Bu	B, 24	 **(9)**	31
8	 **(10)**	R = CO_2-*n*-Bu	B, 24	 **(11)**	41
9	 **(12)**	R = CO_2-*n*-Bu	B, 18	 **(13)**	51

Table 3 continued

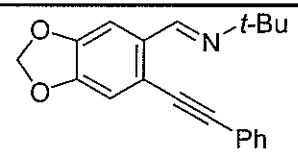
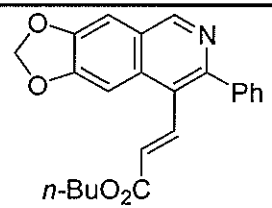
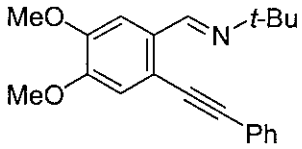
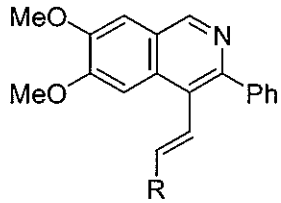
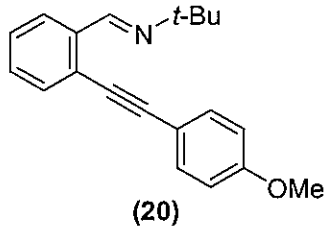
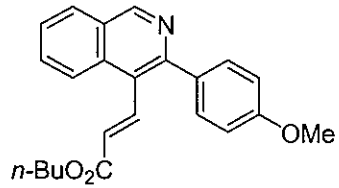
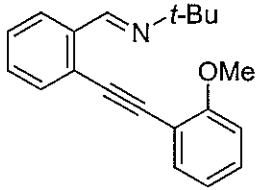
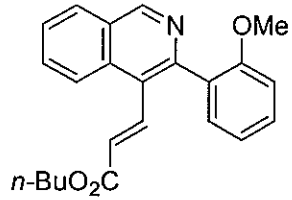
10	 **(14)**	R = CO_2-*n*-Bu	A, 18			43
11		R = CO_2-*n*-Bu	B, 24		**(15)**	48
12	 **(16)**	R = CO_2-*t*-Bu	B, 48		R = CO_2-*t*-Bu **(17)**	51
13		R = $CONMe_2$	B, 18		R = $CONMe_2$ **(18)**	51
14		R = SO_2CH_3	B, 17		R = SO_2CH_3 **(19)**	27
15	 **(20)**	R = CO_2-*n*-Bu	B, 24		**(21)**	35
16	 **(22)**	R = CO_2-*n*-Bu	A, 18		R = CO_2-*n*-Bu **(23)**	65
17		R = CO_2-*n*-Bu	B, 36		R = CO_2-*n*-Bu **(23)**	64
18		R = CO_2-*t*-Bu	B, 24		R = CO_2-*t*-Bu **(24)**	68
19		R = Ph	B, 72		R = Ph **(25)**	64
20		R = SO_2Ph	B, 72		R = SO_2Ph **(26)**	20
21		R = $CONMe_2$	B, 18		R = $CONMe_2$ **(27)**	65
22		R = CMe_2OH	B, 48		R = CMe_2OH **(28)**	25

Table 3 continued

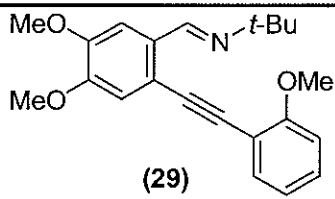
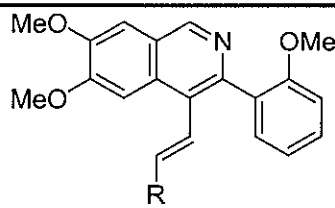
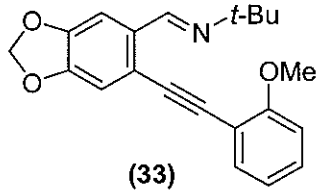
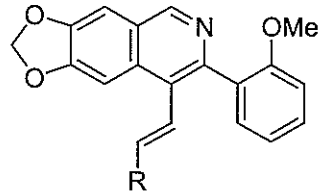
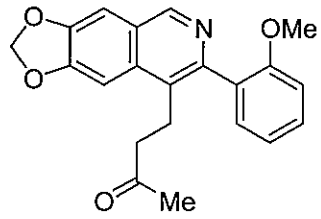
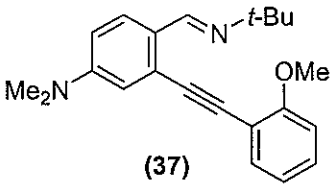
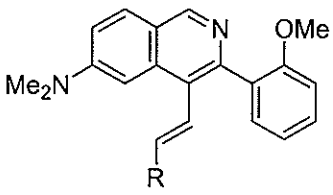
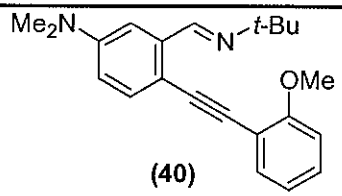
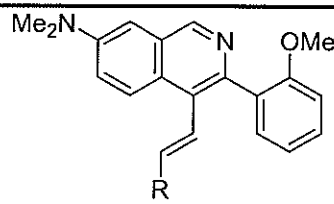
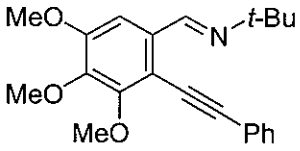
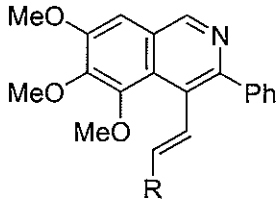
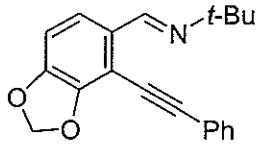
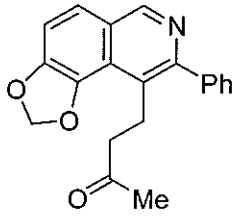
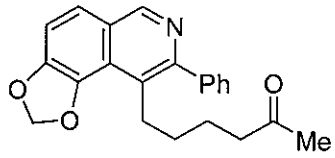
23	 **(29)**	R = CO_2-*t*-Bu	B, 14		R = CO_2-*t*-Bu **(30)**	92[b]
24		R = $CONMe_2$	B, 10		R = $CONMe_2$ **(31)**	97[b]
25		R = SO_2CH_3	B, 12		R = SO_2CH_3 **(32)**	52[b]
26	 **(33)**	R = CO_2-*t*-Bu	A, 12		R = CO_2-*t*-Bu **(34)**	61
27		R = CO_2-*t*-Bu	B, 10		R = CO_2-*t*-Bu **(34)**	82[b]
28		R = $CONMe_2$	B, 5		R = $CONMe_2$ **(35)**	89[b,c]
29		R = $CH(OH)CH_3$	B, 24		**(36)**	48
30	 **(37)**	R = CO_2-*t*-Bu	B, 16		R = CO_2-*t*-Bu **(38)**	69
31		R = CO_2-*t*-Bu	B, 2		R = CO_2-*t*-Bu **(38)**	67[b]
32		R = $CONMe_2$	B, 1.5		R = $CONMe_2$ **(39)**	70[b,d]

Table 3 continued

33	 **(40)**	$R = CO_2$-*t*-Bu	B, 12		$R = CO_2$-*t*-Bu **(41)**	71[b]
34		$R = CONMe_2$	B,16		$R = CONMe_2$ **(42)**	70[b]
35	 **(43)**	$R = CO_2$-*n*-Bu	A, 48		$R = CO_2$-*n*-Bu **(44)**	51[b]
36		$R = CO_2$-*t*-Bu	B, 36		$R = CO_2$-*t*-Bu **(45)**	62[b]
37		$R = CONMe_2$	B, 48		$R = CONMe_2$ **(46)**	50[b]
38		R = Ph	B,16		R = Ph **(47)**	78[b]
39	 **(48)**	$R = CH(OH)CH_3$	B, 72		$R = CH_3$ **(49)**	50
40		R = CH(OH)Ph	B, 4		R = Ph **(50)**	36[b]
41		$R = (CH_2)_2CH(OH)CH_3$	B, 8		**(51)**	27[b]

[a] See the text for the detailed reaction conditions for procedures A and B. [b] The reaction was run at 90 °C. [c] The product was isolated as a 73:27 mixture of *E*/*Z* isomers. [d] The product was isolated as a 91:9 mixture of *E*/*Z* isomers.

The use of 3 equiv of the organic bases pyridine or Et_3N afforded a 48 % (entry 2) or a 46 % (entry 3) yield of isoquinoline **5**, respectively. In entries 4-8, the carbonate salts Cs_2CO_3, K_2CO_3, $KHCO_3$, Na_2CO_3 and $NaHCO_3$ have been examined. The results show that the more soluble carbonate bases, such as Cs_2CO_3 (entry 4), disfavor the reaction and the less soluble carbonates, such as $NaHCO_3$ (entry 8), favor the formation of isoquinoline **5**. The addition of *n*-Bu_4NCl (TBAC), *n*-Bu_4NBr (TBAB) or Et_4NI (TEAI) resulted in a slight decrease in the yield of isoquinoline **5** (entries 9-11). Thus, the reaction conditions employed in entry 8, which are the best reaction conditions shown in entries 2-11, have been chosen for further optimization reactions employing a variety of Pd(II) catalysts and ligands. The results for this latter study are summarized in entries 12-19 in Table 2.

When catalytic amounts of $PdCl_2$, PdI_2, $Pd(O_2CCF_3)_2$, $Pd(OAc)_2$ or $PdBr_2$ have been employed, the desired product, isoquinoline **5**, was isolated in 45-56 % yields with $PdBr_2$ giving the best yield (entries 12-16). In entries 17-19, addition of the ligands, PPh_3, dppp or dppe resulted in a slight decrease in the yield of isoquinoline **5**. Again, the reaction conditions in entry 16, which have afforded the best result so far, have been chosen for further optimization.

Based on the reaction conditions in entry 16, a variety of oxidants have been examined and the results are summarized in entries 20-25. As mentioned above, a 56 % isolated yield of isoquinoline **5** was obtained in the presence of 10 mol % of $CuCl_2$ (entry 16). The use of 10 mol % CuF_2 gave a 54 % yield of isoquinoline **5** (entry 20). Other copper(II) reagents, such as $Cu(OAc)_2$, $Cu(NO_3)_2$, $CuCO_3$ and CuO have also been examined and isoquinoline **5** was isolated in 39-45 % yields (entries 21-24). The use of CuI, a copper(I) reagent as the

oxidant, resulted in a decrease in the yield of isoquinoline **5** from 56 % (entry 16) to 23 %, while the side product **3** was isolated in a 46 % yield (entry 25).[14]

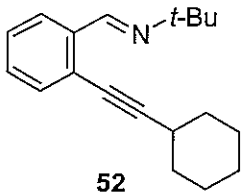
After the above optimization work, we have adopted the following standard reaction conditions using only a catalytic amount of Cu(II) reagent as procedure B: 0.25 mmol of arylaldimine, 5 equiv of the olefin, 10 mol % of $PdBr_2$, 10 mol % of $CuCl_2$, 3 equiv of $NaHCO_3$ in 3 mL of DMSO at 70 °C under an O_2 atmosphere.

By employing procedures A and B, a variety of 4-(1-alkenyl)- and 4-alkyl-3-arylisoquinolines have been prepared (Table 3). As mentioned above, using procedure A, isoquinoline **2** was isolated in a 61 % yield from the reaction of benzaldimine **1** and methyl acrylate (entry 1, Table 3). An identical yield of isoquinoline **5** was isolated from the reaction of benzaldimine **1** and *n*-butyl acrylate using procedure A (entry 2).

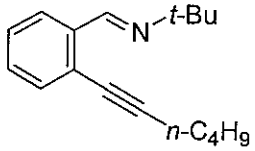
Several olefins, including electron-deficient and electron-rich alkenes, have been allowed to react with benzaldimine **1** using procedure B (entries 3-7). The use of *n*-butyl acrylate and *t*-butyl acrylate afforded a 56 % yield of isoquinoline **5** (entry 3) and a 50 % yield of isoquinoline **6** (entry 4), respectively. However, none of the desired isoquinoline product was observed when phenyl vinyl sulfone, an electron-deficient alkene, was allowed to react with benzaldimine **1**. The relatively electron-rich olefins, styrene and 2-methyl-3-buten-2-ol have been allowed to react with benzaldimine **1**. A 53 % yield of isoquinoline **7** (entry 5) and a 34 % yield of **8** (entry 6) were obtained, respectively. Instead of forming an internal alkene, the reaction of *n*-butyl vinyl ether afforded isoquinoline **9** bearing a terminal double bond, albeit in low overall yield (entry 7).[15]

Sakamoto et al. have reported that *N*-protected *alkyl*-substituted *o*-(1-alkynyl)anilines react with electron-deficient alkenes in the presence of $PdCl_2$ and $CuCl_2$ producing 2-

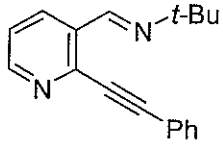
substituted 3-(1-alkenyl)indoles.[12] However, in our chemistry, the *N-tert*-butyl *alkyl*-substituted *o*-(1-alkynyl)benzaldimines **52** and **53** did not react with either electron-deficient or electron-rich terminal alkenes under either procedures A or B to afford isoquinoline products. Although *N-tert*-butyl *alkyl*-substituted *o*-(1-alkynyl)benzaldimines do not react with olefins, benzaldimine **10**, which is a *N-tert*-butyl *alkenyl*-substituted *o*-(1-alkynyl)benzaldimine, did react with *n*-butyl acrylate affording a 41 % isolated yield of isoquinoline **11** (entry 8).



52



53



54

The reaction of arylaldimine **54**, bearing a pyridine moiety, and olefins gave none of the desired product. However, when arylaldimine **12** with the alkynyl group attached to C-3 of the pyridine nucleus was allowed to react with *n*-butyl acrylate, naphthyridine **13** was isolated in a 51 % yield (entry 9).

It is known that electron-deficient aryl halides or vinylic halides disfavor the Heck reaction.[13] Thus, electron-donating groups have been introduced into the arylaldimine in order to increase the electron density in intermediate **A** (Scheme 1) and hopefully favor formation of the desired isoquinoline products. However, the experimental results indicate that the introduction of electron-donating groups into the arylaldimine does not really favor the isoquinoline olefination process, and instead results in a decrease in the yields of the desired isoquinoline products in most cases. For example, when benzaldimine **14** bearing a

methylenedioxo group on the benzylidene moiety was allowed to react with *n*-butyl acrylate using procedures A and B, the yield dropped from 61 % (entry 2) to 43 % (entry 10) or from 56 % (entry 3) to 48 % (entry 11), respectively. The reaction of **16**, another electron-rich arylaldimine, and *t*-butyl acrylate afforded isoquinoline **17** in a 51 % yield (entry 12), comparable to the 50 % yield from the reaction of benzaldimine **1** and *t*-butyl acrylate (entry 4). When *N*,*N*-dimethylacrylamide or methyl vinyl sulfone were allowed to react with arylaldimine **16**, a 51 % yield of isoquinoline **18** (entry 13) and a 27 % yield of isoquinoline **19** (entry 14) were obtained, respectively. The sulfone result is a bit surprising in view of our earlier failure to obtain any isoquinoline product from benzaldimine **1** and phenyl vinyl sulfone. The introduction of a *para*-methoxy group on the phenyl moiety resulted in the yield of the desired isoquinoline **21** dropping from 56 % (entry 3) to only 35 % (entry 15).

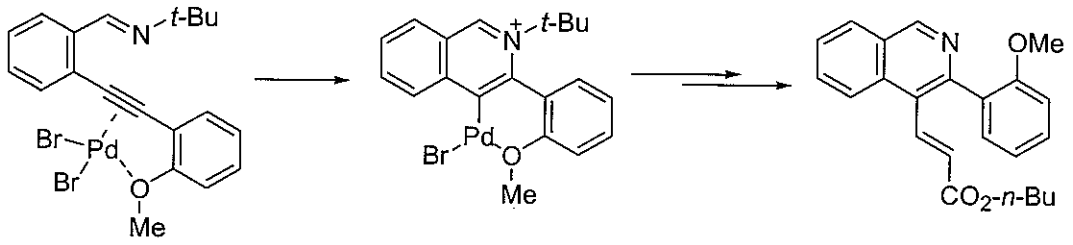
The presence of electron-donating groups increases the electron density of the carbon-carbon triple bond, which apparently disfavors cyclization by attack of the imine nitrogen on the activated triple bond and consequently results in low conversion of the arylaldimine to intermediate **A** and eventual formation of the isoquinoline (Scheme 1). Although the reactivity of intermediate **A** towards olefins is presumably improved by introducing electron-donating groups, the low conversion of arylaldimine to intermediate **A** results in a decrease in the overall yield of isoquinoline products.

The position of the electron-donating methoxy group in the arylaldimine is critical to the success of this process. Thus, the introduction of an *ortho*-methoxy group on the phenyl moiety facilitates isoquinoline formation. When benzaldimine **22** was allowed to react with *n*-butyl acrylate using procedures A and B, the yields increased to 65 % (entry 16) and 64 % (entry 17) from 61 % (entry 2) and 56 % (entry 3), respectively. Employing procedure B, a

variety of olefins have been allowed to react with arylaldimine **22** (entries 18-22). The reactions of **22** with *t*-butyl acrylate and styrene afforded a 68 % yield of isoquinoline **24** (entry 18) and a 64 % yield of isoquinoline **25** (entry 19), respectively. These yields are much better than the yields of 50 % and 53 % from the corresponding reactions of benzaldimine **1** (entries 4 and 5). As mentioned above, the reaction of benzaldimine **1** and phenyl vinyl sulfone gave none of the desired product. However, a 20 % yield of isoquinoline **26** was observed when benzaldimine **22** was allowed to react with phenyl vinyl sulfone (entry 20). When *N*,*N*-dimethylacrylamide was allowed to react with arylaldimine **22**, isoquinoline **27** was isolated in a 65 % yield (entry 21), much better than the yield of 51 % from the reaction of benzaldimine **16** and *N*,*N*-dimethylacrylamide (entry 13). The reaction of arylaldimine **22** and 2-methyl-3-buten-2-ol afforded isoquinoline **28** in a 25 % yield (entry 22). For some reason, this yield is lower than the 35 % yield obtained using benzaldimine **1** (entry 6).

The beneficial effects of an *ortho*-methoxy group can be explained by Scheme 2. Basically, the introduction of an *ortho*-methoxy group helps direct the $PdBr_2$ to the vicinity of the triple bond where attack by the imine nitrogen on the activated triple bond takes place generating an arylpalladium intermediate, which is stabilized by chelation with the *ortho*-methoxy group. Subsequent Heck olefination and fragmentation of the *t*-butyl group affords the desired isoquinoline olefin.

Scheme 2



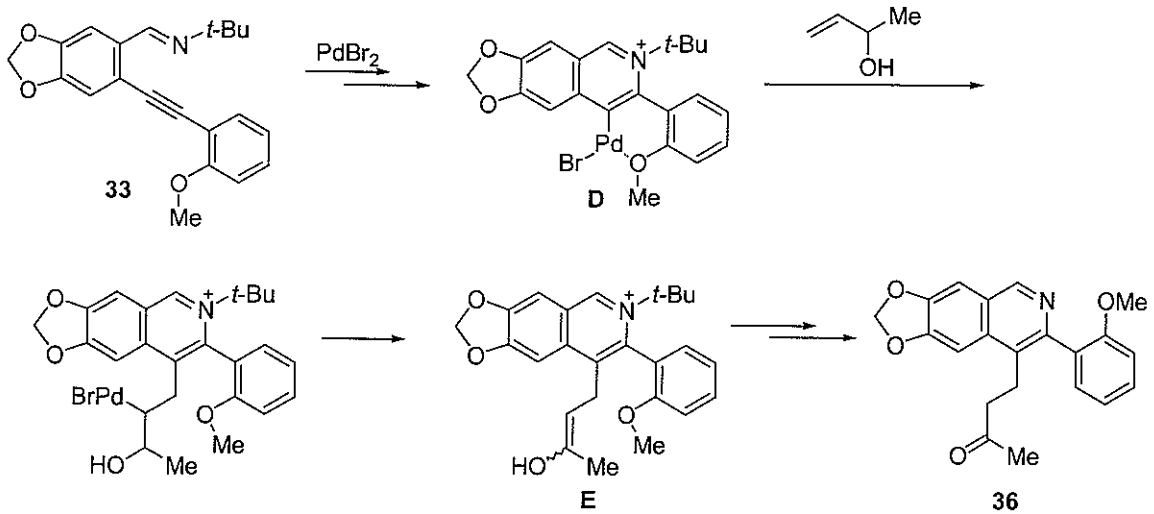
The reactions of benzaldimine **29** and *t*-butyl acrylate or *N,N*-dimethylacrylamide are very slow at 70 °C. These reactions were thus run at 90 °C and the corresponding isoquinolines **30** and **31** have been obtained in 92 % and 97 % yields, respectively (entries 23 and 24). Comparing the results from entries 12, 13, 18, 21, 23 and 24, one can see that both electronic effects and facilitation by the *ortho*-methoxy group play a role in forming isoquinolines **30** and **31** in such high yields. The *ortho*-methoxy group improves the conversion of the arylaldimine to intermediate **A** and the introduction of electron-donating groups on the arylaldimine moiety presumably increases the reactivity of intermediate **A** towards olefins,[14] affording mostly improved yields. When methyl vinyl sulfone was allowed to react with arylaldimine **29**, the yield of isoquinoline **32** increased to 52 % (entry 25) from the 27 % obtained without the *ortho*-methoxy group (entry 14).

Arylaldimine **33**, bearing a methylenedioxo group on the benzylidene moiety and an *ortho*-methoxy group on the phenyl moiety, has been allowed to react with several olefins (entries 26-29). The reactions of arylaldimine **33** with *t*-butyl acrylate afforded a 61 % (entry 26) or an 82 % (entry 27) yield of isoquinoline **34** using procedures A and B, respectively. For this specific arylaldimine, procedure A is not as efficient as procedure B. When *N,N*-dimethylacrylamide was allowed to react with arylaldimine **33**, an 89 % yield of isoquinoline

35 was isolated as a 73:27 *E/Z* mixture (entry 28). Comparing entries 23, 24, 27 and 28, one can see that the introduction of two methoxy groups onto the benzylidene moiety is much more efficient in promoting the Heck reaction than the introduction of a methylenedioxo group onto the benzaldimine moiety.

Unsaturated alcohols undergo reaction to afford ketone-containing products. Thus, 3-buten-2-ol has been allowed to react with arylaldimine **33** (entry 29). The corresponding ketone **36** was isolated in a 48 % yield. The formation of ketone **36** can be explained by the mechanism shown in Scheme 3. The cyclization of arylaldimine **33** by $PdBr_2$ affords an arylpalladium(II) intermediate **D**, which is stabilized by the *ortho*-methoxy group. The *cis* addition of intermediate **D** to 3-buten-2-ol results in an alkylpalladium bromide intermediate, which undergoes E hydride elimination to form enol **E**.[16] Subsequent tautomerization and fragmentation of intermediate **E** affords the desired ketone **36**.

Scheme 3

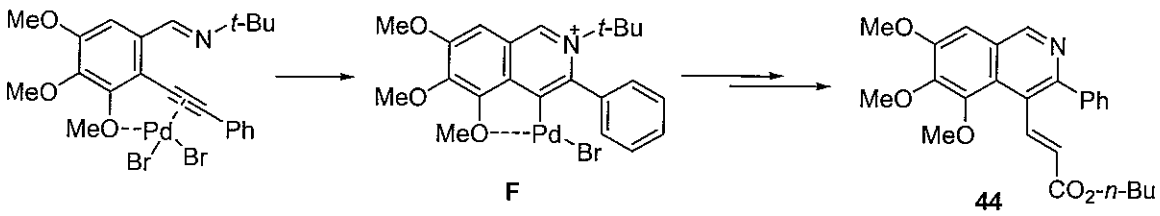


To further test the electronic effects of substituents on the isoquinoline olefination process, arylaldimines **37** and **40** have been prepared and allowed to react with *t*-butyl acrylate and *N*,*N*-dimethylacrylamide. The reaction of arylaldimine **37**, bearing a dimethylamino group *meta* to the alkynyl group, and *t*-butyl acrylate at 70 °C was complete in 16 h and afforded isoquinoline **38** in a 69 % yield (entry 30). When the reaction was run at 90 °C, it was complete in 2 h and gave isoquinoline **38** in a 67 % yield (entry 31). By employing *N*,*N*-dimethylacrylamide at 90 °C, the reaction was complete in 1.5 h and a 70 % yield of isoquinoline **39** was isolated as a 91:9 *E*/*Z* mixture (entry 32). While the introduction of a *meta*-dimethylamino group shortens the reaction time, the introduction of a dimethylamino group *para* to the alkynyl moiety slows the reaction down. Thus, arylaldimine **40** has been allowed to react with *t*-butyl acrylate and *N*,*N*-dimethylacrylamide at 90 °C affording a 71 % yield of isoquinoline **41** in 12 h (entry 33) and a 70 % yield of isoquinoline **42** in 16 h (entry 34). The reason for the slow reactions is apparently because the dimethylamino group *para* to the alkynyl group in arylaldimine **40** significantly increases the electron density on the carbon-carbon triple bond and has little influence on the electron density of the imine nitrogen, disfavoring attack of the imine nitrogen on the triple bond. However, the dimethylamino group in arylaldimine **37** significantly increases the electron density on the imine nitrogen, favoring attack of the imine nitrogen on the carbon-carbon triple bond. Thus, the reactions of arylaldimine **37** reach completion in shorter reaction times.

The reactions of arylaldimine **43** with *n*-butyl acrylate, *t*-butyl acrylate, *N*,*N*-dimethylacrylamide, and styrene gave the corresponding isoquinolines **44-47** in 51-78 % yields (entries 35-38). Similar to the reactions of arylaldimine **29**, the reactions of

arylaldimine **43** with olefins also involve electronic effects and facilitation by the *ortho*-methoxy group (Scheme 4). However, the reactions of arylaldimine **43**, having an *ortho*-methoxy group on the benzylidene moiety, are very slow. For example, when benzaldimine **43** was allowed to react with *n*-butyl acrylate or *N*,*N*-dimethylacrylamide, the reactions are not complete even in 48 h at 90 °C (entries 35 and 37). The reason is probably because the intermediate **F** (Scheme 4) is quite hindered, preventing approach of the olefins. Comparing the results from arylaldimine **29** (entries 23 and 24) with those of arylaldimine **43** (entries 36 and 37), we conclude that the introduction of an *ortho*-methoxy group onto the phenyl moiety promotes this isoquinoline olefination better than the introduction of an *ortho*-methoxy group onto the benzylidene moiety.

Scheme 4



To further test the effect of oxygen substituents in this isoquinoline olefination process, arylaldimine **48** has been prepared and allowed to react with olefins. The reaction of arylaldimine **48** and styrene afforded none of the desired product for reasons which are not obvious. When 3-buten-2-ol and 1-phenyl-2-propen-1-ol have been allowed to react with arylaldimine **48**, a 50 % yield of ketone **49** (entry 39) and a 36 % yield of ketone **50** were

obtained, respectively. Using procedure B, the reaction of arylaldimine **48** and 5-hexen-2-ol afforded compound **51** by palladium migration, albeit in a low yield (entry 41).[17]

Conclusions

An efficient and straightforward route to synthesize 4-(1-alkenyl)isoquinolines and 4-alkyl-3-arylisoquinolines containing a ketone group has been developed using a palladium(II)-catalyzed cyclization, followed by olefination (Heck reaction). A wide variety of olefins undergo this process in moderate to excellent yields with high regioselectivity being observed. The introduction of an *ortho*-methoxy group on the benzaldimine moiety promotes the Pd-catalyzed cyclization and stabilizes the resulting Pd(II) intermediate, improving the yields of the desired isoquinoline products. Moreover, the introduction of an *ortho*-methoxy group onto the phenyl moiety has been shown to promote this isoquinoline olefination more efficiently than the introduction of an *ortho*-methoxy group onto the benzylidene moiety. To form isoquinolines in high yields, both electronic effects and facilitation by an *ortho*-methoxy group are necessary.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. Low resolution mass spectra were recorded on a Finnigan TSQ700 triple quadrupole mass

spectrometer (Finnigan MAT, San Jose, CA). High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. All reagents were used directly as obtained commercially unless otherwise noted. All palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd. Compounds **1**,[1a] **10**,[1a] **12**,[1a] **14**,[1a] **20**,[1a] **52**,[1a] **53**,[12] **54**,[1a] 4-dimethylamino-2-iodobenzaldehyde,[8b] 5-dimethylamino-2-iodobenzaldehyde,[8b] 2-iodo-3,4,5-trimethoxybenzaldehyde,[8b] and *N*-(benzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine[14] were prepared according to previous literature procedures.

2-Methoxyphenyl trimethylsilyl acetylene. To a solution of the 2-iodoanisole (4.68 g, 20 mmol) and trimethylsilylacetylene (24 mmol, 1.2 equiv) in Et_3N (60 mL) were added $PdCl_2(PPh_3)_2$ (0.281 mg, 2 mol %) and CuI (38.2 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 55 °C. The reaction was complete in 2 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (15:1 hexane/EtOAc) to afford 4.05 g of the indicated product in 100 % yield as a yellow liquid: ^{1}H NMR ($CDCl_3$) Γ 0.27 (s, 9H), 3.87 (s, 3H), 6.85 (d, J = 8.8 Hz, 1H), 6.89 (dd, J = 0.8, 7.6 Hz, 1H), 7.25-7.30 (m, 1H), 7.44 (dd, J = 1.6, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 0.3, 56.0, 98.7, 101.4, 110.8, 112.4, 120.5, 130.2, 134.4, 160.5.

2-Methoxyphenylacetylene. A solution of KOH (5.06 g, 10 mmol) in 4 mL of water was added dropwise to 2-methoxyphenyl trimethylsilyl acetylene (2.04 g, 10 mmol) in 40 mL of CH_3OH under an Ar atmosphere at 25 °C. The mixture was stirred for another 0.5 h at 25 °C, and the CH_3OH was removed under vacuum. The residue was added to 20 mL of brine solution, and the mixture was extracted with EtOAc (3 x 20 mL), dried (Na_2SO_4),

filtered, and the solvent removed under vacuum. Purification by flash chromatography (7:1 hexane/EtOAc) afforded 1.15 g (10 mmol) of the indicated compound in a 100 % yield as a yellow liquid: ^{1}H NMR ($CDCl_3$) Γ 3.31 (s, 1H), 3.88 (s, 3H), 6.86 (d, J = 8.4 Hz, 1H), 6.90 (dd, J = 0.8, 7.6 Hz, 1H), 7.28-7.32 (m, 1H), 7.46 (dd, J = 1.6, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.9, 80.2, 81.3, 110.7, 111.3, 120.5, 130.4, 134.3, 160.7.

***N*-[4,5-Dimethoxy-2-(phenylethynyl)benzylidene]-*tert*-butylamine (16).** To a solution of 2-bromo-4,5-dimethoxybenzaldehyde (1.23 g, 5.0 mmol) and phenylacetylene (0.62 g, 6.0 mmol) in Et_3N (20 mL) were added $PdCl_2(PPh_3)_2$ (70 mg, 2 mol %) and CuI (10 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the reaction mixture was allowed to cool to 25 °C, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding arylalkyne. To the purified arylalkyne in a 4 dram vial was added *t*-$BuNH_2$ (12 equiv). The mixture was then stirred under an Ar atmosphere at 25 °C for 24 h. The resulting mixture was extracted with ether. The combined organic layers were dried (Na_2SO_4) and filtered. Removal of the solvent afforded 1.32 g of the indicated arylaldimine in a 82 % overall yield as a yellow solid: mp 137-140 °C; ^{1}H NMR ($CDCl_3$) Γ 1.35 (s, 9H), 3.95 (s, 3H), 4.00 (s, 3H), 7.01 (s, 1H), 7.36-7.38 (m, 3H), 7.52-7.55 (m, 2H), 7.63 (s, 1H), 8.86 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.1, 56.2, 56.3, 57.8, 86.9, 93.8, 107.9, 113.9, 117.1, 123.5, 128.5, 128.7, 131.5, 132.1, 149.9, 150.5, 153.9; IR ($CHCl_3$, cm^{-1}) 3019, 2969, 1681, 1593, 1507; HRMS Calcd for $C_{21}H_{23}O_2N$: 321.1729. Found: 321.1735.

***N*-[2-(*p*-Methoxyphenylethynyl)benzylidene]-*tert*-butylamine (22).** Using the procedure used to prepare arylaldimine **16,** 2-bromobenzaldehyde (0.93 g, 5.0 mmol) and *p*-methoxyphenylacetylene (0.79 g, 6.0 mmol) were employed to afford 1.06 g of the indicated arylaldimine in a 90 % overall yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.34 (s 9H), 3.84 (s, 3H), 6.90 (td, J = 2.1, 9.0 Hz, 2H), 7.32-7.36 (m, 2H), 7.47 (td, J = 2.1, 9.0 Hz, 2H), 7.50-7.54 (m, 1H), 8.04-8.07 (m, 1H), 8.92 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.0, 55.6, 58.1, 85.7, 95.2, 114.4, 115.4, 124.5, 126.1, 128.5, 129.9, 132.3, 133.2, 137.7, 154.7, 160.0; IR (neat, cm^{-1}) 2963, 2836, 1699; HRMS Calcd for $C_{20}H_{21}ON$: 291.1623. Found: 291.1626.

***N*-[4,5-Dimethoxy-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (29).** Using the procedure used to prepare arylaldimine **16**, 2-bromo-4,5-dimethoxybenzaldehyde (1.23 g, 5.0 mmol) and *o*-methoxyphenylacetylene (0.79 g, 6.0 mmol) were employed to afford 1.23 g of the indicated arylaldimine in a 70 % overall yield as a yellow solid: mp 124-126 °C; ^{1}H NMR ($CDCl_3$) Γ 1.35 (s, 9H), 3.92 (s, 3H), 3.94 (s, 3H), 3.99 (s, 3H), 6.92-6.98 (m, 2H), 7.03 (s, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.61 (s, 1H), 8.94 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.2, 55.9, 56.2, 57.6, 90.2, 91.3, 107.8, 110.8, 112.7, 113.9, 117.6, 120.7, 129.9, 132.0, 133.4, 149.8, 150.5, 154.6, 160.0 (one methoxy carbon is missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3019, 2967, 2838, 1634, 1598, 1507; HRMS Calcd for $C_{22}H_{25}O_3N$: 351.1834. Found: 351.1839.

***N*-[6-(*o*-Methoxy)phenylethynylbenzo[1,3]dioxol-5-ylmethylene]-*tert*-butylamine (33).** Using the procedure used to prepare arylaldimine **16**, 6-bromo-1,3-benzodioxole-5-carboxaldehyde (1.15 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.12 g of the indicated arylaldimine in a 67 % overall yield after recrystallization (EtOAc/hexane) as a yellow solid: mp 87-89 °C; ^{1}H NMR ($CDCl_3$) Γ 1.33

(s, 9H), 3.90 (s, 3H), 5.99 (s, 2H), 6.91 (d, J = 8.8 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 6.98 (s, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.57 (s, 1H), 8.92 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.1, 55.9, 57.7, 90.2, 90.9, 101.8, 105.7, 110.8, 111.3, 112.6, 119.0, 120.7, 129.9, 133.4, 133.8, 148.6, 149.1, 154.3, 160.1; IR ($CHCl_3$, cm^{-1}) 3017, 2968, 1612, 1476; HRMS Calcd for $C_{21}H_{21}O_3N$: 335.1521. Found: 335.1526.

***N*-[4-Dimethylamino-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (37).** Using the procedure used to prepare arylaldimine **16**, 4-dimethylamino-2-iodobenzaldehyde[8b] (1.38 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.57 g of the indicated arylaldimine in a 94 % overall yield as a yellow solid: mp 102-104 °C; ^{1}H NMR ($CDCl_3$) Γ 1.34 (s, 9H), 3.02 (s, 6H), 3.92 (s, 3H), 6.71 (dd, J = 2.4, 8.8 Hz, 1H), 6.82 (d, J = 2.8 Hz, 1H), 6.91-6.97 (m, 2H), 7.32 (dt, J = 1.6, 8.0 Hz, 1H), 7.51 (dd, J = 1.6, 7.6 Hz, 1H), 8.00 (br s, 1H), 8.90 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.2, 40.5, 55.9, 57.3, 90.2, 91.8, 110.8, 112.6, 113.1, 114.5, 120.7, 125.6, 126.1, 127.2, 130.0, 133.6, 151.4, 155.0, 160.2; IR ($CHCl_3$, cm^{-1}) 3018, 2968, 2400, 1596; HRMS Calcd for $C_{22}H_{16}ON_2$: 3340.2045. Found: 334.2050.

***N*-[5-Dimethylamino-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (40).** Using the procedure used to prepare arylaldimine **16**, 5-dimethylamino-2-iodobenzaldehyde[8b] (1.38 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.48 g of the indicated arylaldimine in a 89 % overall yield as a yellow solid: mp 118-120 °C; ^{1}H NMR ($CDCl_3$) Γ 1.35 (s, 9H), 3.03 (s, 6H), 3.92 (s, 3H), 6.72 (dd, J = 2.8, 8.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.94 (dd, J = 0.8, 7.6 Hz, 1H), 7.27 (dt, J = 1.6, 7.6 Hz, 1H), 7.38 (br s, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.47 (dd, J = 1.6, 7.6 Hz, 1H), 8.98 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.1, 40.6, 55.9, 57.7, 89.1, 92.3, 108.4, 110.8, 112.2, 113.5,

114.2, 120.7, 129.2, 133.2, 133.5, 138.7, 150.4, 155.8, 159.7; IR ($CHCl_3$, cm^{-1}) 3017, 2969, 1638, 1602; HRMS Calcd for $C_{22}H_{16}ON_2$: 334.2045. Found: 334.2050.

***N*-[2-(Phenylethynyl)-3,4,5-trimethoxybenzylidene]-*tert*-butylamine (43).** Using the procedure used to prepare arylaldimine **16**, 2-iodo-3,4,5-trimethoxybenzaldehyde[8b] (1.61 g, 5.0 mmol) and phenylacetylene (0.62 g, 6.0 mmol) were employed to afford 1.42 g of the indicated arylaldimine in a 81 % overall yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.33 (s, 9H), 3.92 (s, 3H), 3.97 (s, 3H), 4.03 (s, 3H), 7.35-7.37 (s, 3H), 7.43 (s, 1H), 7.52-7.55 (m, 2H), 8.85 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.1, 56.4, 58.0, 61.4, 61.7, 82.8, 98.1, 104.6, 112.4, 123.7, 128.5, 128.7, 131.5, 134.5, 144.1, 153.9, 154.3, 154.6; IR (neat, cm^{-1}) 3079, 3056, 2966, 2872, 2837, 1687, 1640, 1585, 1493; HRMS Calcd for $C_{22}H_{25}O_3N$: 351.1834. Found: 351.1839.

4-Iodo-1,3-benzodioxole-5-carboxaldehyde. To a solution of *N*-(benzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine[14] (1.03 g, 5.0 mmol) in 40 mL of THF at -78 °C was added 5.25 mmol of *n*-BuLi (2.5 M in hexane) dropwise over a 5 min period. The solution was stirred for 30 min at -78 °C and a solution of I_2 (2.68 g, 7.5 mmol) in 15 mL of THF was added dropwise. The resulting solution was warmed to 25 °C and stirred for 2 h. The reaction mixture was then quenched with water, extracted with ether, washed with satd aq $Na_2S_2O_3$, dried ($NaSO_4$), filtered, and the solvent was removed under reduced pressure. The residue was chromatographed using 3:1 hexane/EtOAc to afford 1.01 g of the indicated compound in a 70 % yield as a white solid: mp 130-132 °C; ^{1}H NMR ($CDCl_3$) Γ 6.16 (s, 2H), 6.86 (dd, J = 0.3, 8.1 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 9.90 (d, J = 0.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 76.0, 101.5, 108.3, 127.5, 128.8, 150.3, 150.9, 192.8.

***N*-(4-Phenylethynylbenzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine (48).** Using the procedure used to prepare arylaldimine **16**, 4-iodo-1,3-benzodioxole-5-carboxaldehyde (1.45 g, 5 mmol) and phenylacetylene (0.61 g, 6 mmol) were employed to afford 1.52 g of the indicated arylaldimine in a 100 % overall yield as a yellow solid: mp 128-129 °C; ^{1}H NMR ($CDCl_3$) Γ 1.34 (s, 9H), 6.10 (s, 2H), 6.84 (d, J = 8.0 Hz, 1H), 7.37-7.38 (m, 3H), 7.55-7.57 (m, 2H), 7.64 (d, J = 8.0 Hz, 1H), 8.77 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 30.0, 57.8, 80.8, 98.8, 102.1, 106.1, 109.0, 120.6, 122.9, 128.6, 128.9, 131.7, 131.8, 148.9, 153.4 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3018, 2969, 1644, 1616, 1458; HRMS Calcd for $C_{20}H_{19}O_2N$: 305.1416. Found: 305.1420.

General procedure A for the palladium-catalyzed formation of isoquinolines. Dried DMSO (3 mL), $PdBr_2$ (6.7 mg, 0.025 mmol), $Cu(OAc)_2$ (0.091 g, 0.50 mmol), NaOAc (0.062 g, 0.75 mmol) and the benzaldimine (0.25 mmol) were placed in a 4 dram vial. The contents were then stirred for 1 min, and the appropriate olefin (1.25 mmol) was added. The vial was sealed carefully and heated in an oil bath at 70 °C for the indicated period of time. The reaction was monitored by TLC to establish completion. The reaction mixture was cooled to 25 °C, diluted with 20 mL of EtOAc, washed with 20 mL of brine, dried (Na_2SO_4), and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column.

General procedure B for the palladium-catalyzed formation of isoquinolines. Dried DMSO (3 mL), $PdBr_2$ (6.7 mg, 0.025 mmol), $CuCl_2$ (3.4 mg, 0.025 mmol), $NaHCO_3$ (0.063 g, 0.75 mmol) and the benzaldimine (0.25 mmol) were placed in a 4 dram vial. The contents were then stirred for 1 min, and the appropriate olefin (1.25 mmol) was added. The vial was flushed with O_2 and heated in an oil bath at 70 °C or 90 °C under an O_2 balloon for

the indicated period of time. The reaction was monitored by TLC to establish completion. The reaction mixture was cooled to 25 °C, diluted with 20 mL of EtOAc, washed with 20 mL of brine, dried (Na_2SO_4), and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column.

Methyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (2). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 44 mg of the indicated compound in a 61 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.81 (s, 3H), 6.31 (d, J = 16.4 Hz, 1H), 7.41-7.49 (m, 3H), 7.61-7.63 (m, 2H), 7.67 (dd, J = 1.6, 8.4 Hz, 1H), 7.78 (dt, J = 1.6, 8.4 Hz, 1H), 8.02 (d, J = 16.0 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 8.24 (dd, J = 0.8, 8.8 Hz, 1H), 9.30 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 52.1, 123.9, 124.4, 126.3, 127.5, 127.6, 128.5, 128.5, 128.6, 130.6, 131.5, 134.5, 140.2, 141.6, 152.0, 152.9, 166.8; IR ($CHCl_3$, cm^{-1}) 3018, 2924, 2852, 1717, 1638; HRMS Calcd for $C_{19}H_{15}O_2N$: 289.1103. Found: 289.1108.

***n*-Butyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (5).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 51 mg (Table 3, entry 2) or 46 mg (entry 3) of the indicated compound as a yellow oil in a 61 % or a 56 % yield using Procedure A or B, respectively: ^{1}H NMR ($CDCl_3$) Γ 0.96 (t, J = 7.2 Hz, 3H), 1.37-1.46 (m, 2H), 1.64-1.72 (m, 2H), 4.43 (t, J = 6.8 Hz, 2H), 6.33 (d, J = 16.4 Hz, 1H), 7.42-7.49 (m, 3H), 7.63 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 7.2 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.99 (d, J = 16.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 8.8 Hz, 1H), 9.31 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.4, 30.9, 64.8, 123.9, 124.4, 126.6, 127.4, 127.6, 128.4, 128.5, 128.5, 130.6, 131.5, 134.4, 140.2, 141.3, 152.0, 152.8, 166.4; IR (neat, cm^{-1}) 3412, 3058, 2958, 2872, 1716, 1636, 1570; HRMS Calcd for $C_{22}H_{21}O_2N$: 331.1572. Found: 331.1577.

***t*-Butyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (6).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 41 mg of the indicated compound as a yellow oil in a 50 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.50 (s, 9H), 6.22 (d, J = 16.4 Hz, 1H), 7.38-7.49 (m, 3H), 7.62-7.67 (m, 3H), 7.75 (dt, J = 0.8, 6.8 Hz, 1H), 7.86 (d, J = 16.4 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 9.27 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.4, 81.0, 124.1, 124.6, 127.4, 127.6, 128.3, 128.4, 128.5, 130.6, 131.4, 134.4, 140.2, 140.3, 151.9, 152.7, 165.7 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3400, 3058, 2977, 2931, 1708, 1634, 1617, 1572, 1553; HRMS Calcd for $C_{22}H_{21}O_2N$: 331.1572. Found: 331.1577.

3-Phenyl-4-[(*E*)-2-phenylethen-1-yl]isoquinoline (7). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 41 mg of the indicated compound as a yellow oil in a 53 % yield: ^{1}H NMR ($CDCl_3$) Γ 6.89 (d, J = 16.8 Hz, 1H), 7.25-7.47 (m, 9H), 7.62 (dt, J = 1.2, 8.1 Hz, 1H), 7.71-7.74 (m, 3H), 8.02 (d, J = 7.8 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 9.27 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 124.7, 125.2, 126.6, 126.7, 127.1, 127.9, 127.9, 128.2, 128.2, 128.2, 128.9, 130.6, 130.8, 135.1, 136.8, 137.3, 141.1, 150.8, 151.4; IR ($CHCl_3$, cm^{-1}) 3058, 3024, 2972, 1697, 1666, 1617, 1495; HRMS Calcd for $C_{23}H_{17}N$: 307.1361. Found: 307.1366.

(*E*)-2-Methyl-4-(3-phenylisoquinolin-4-yl)-3-buten-2-ol (8). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 26 mg of the indicated compound as a white solid in a 34 % yield: mp 178-179 °C; ^{1}H NMR ($CDCl_3$) Γ 1.34 (s, 6H), 1.60 (br s, 1H), 5.92 (d, J = 16.5 Hz, 1H), 6.72 (d, J = 16.2 Hz, 1H), 7.34-7.37 (m, 1H), 7.40-7.45 (m, 2H), 7.59-7.64 (m, 3H), 7.73 (dd, J = 1.2, 6.9 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 8.17 (d, J =

5.4 Hz, 1H), 9.25 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.6, 71.5, 121.7, 124.8, 126.7, 127.1, 127.6, 127.7, 128.1, 128.1, 130.7, 130.7, 135.3, 141.2, 145.9, 150.9, 151.2; IR ($CHCl_3$, cm^{-1}) 3650, 3019, 2975, 2400, 1521; HRMS Calcd for $C_{20}H_{19}ON$: 289.1467. Found: 289.1471.

4-(1-*n*-Butoxyethen-1-yl)-3-phenylisoquinoline (9). The reaction mixture was chromatographed using 7:1 hexane/EtOAc to afford 24 mg of the indicated compound as a yellow oil in a 31 % yield: ^{1}H NMR ($CDCl_3$) Γ 0.92 (t, J = 7.6 Hz, 3H), 1.33-1.43 (m, 2H), 1.64-1.72 (m, 2H), 3.78 (t, J = 2.8 Hz, 2H), 4.12 (d, J = 2.4 Hz, 1H), 4.48 (d, J = 2.4 Hz, 1H), 7.35-7.45 (m, 3H), 7.61 (dt, J = 1.6, 8.4 Hz, 1H), 7.74 (dt, J = 1.6, 8.4 Hz, 1H), 7.78 (tt, J = 1.2, 6.8 Hz, 2H), 8.00 (d, J = 8.0 Hz, 1H), 8.08 (dd, J = 0.8, 8.8 Hz, 1H), 9.33 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.1, 19.6, 31.2, 67.7, 89.6, 125.5, 127.2, 127.2, 127.4, 127.7, 127.9, 128.1, 129.4, 130.9, 135.9, 141.2, 151.4, 152.5, 157.5; IR ($CHCl_3$, cm^{-1}) 3060, 3015, 2960, 2873, 1621, 1564, 1497; HRMS Calcd for $C_{21}H_{21}ON$: 303.1623. Found: 303.1627.

***n*-Butyl (*E*)-3-(3-cyclohexen-1-ylisoquinolin-4-yl)acrylate (11).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 34 mg of the indicated compound as a yellow oil in a 41 % yield: ^{1}H NMR ($CDCl_3$) Γ 0.99 (t, J = 7.2 Hz, 3H), 1.43-1.53 (m, 2H), 1.68-1.76 (m, 4H), 1.83-1.86 (m, 2H), 2.24-2.27 (m, 2H), 2.45-2.50 (m, 2H), 4.27 (t, J = 7.2 Hz, 2H), 5.85 (t, J = 1.6 Hz, 1H), 6.39 (d, J = 16.4 Hz, 1H) 7.59 (dt, J = 0.8, 7.2 Hz, 1H), 7.73 (dt, J = 1.2, 7.2 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 16.4 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 9.19 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.5, 22.2, 23.1, 25.9, 28.8, 30.9, 64.7, 122.9, 124.4, 124.9, 126.9, 127.4, 128.4, 131.2, 132.7, 134.4, 138.0, 141.6, 152.5, 155.1, 166.8; IR (neat, cm^{-1}) 2932, 2872, 1712, 1632; HRMS Calcd for $C_{22}H_{25}O_2N$: 335.1885. Found: 335.1892.

***n*-Butyl (*E*)-3-(3-phenyl-2,6-naphthyridin-4-yl)acrylate (13).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 42 mg of the indicated compound as a yellow solid in a 51 % yield: mp 86-88 °C; ^{1}H NMR ($CDCl_3$) Γ 0.96 (t, J = 7.2 Hz, 3H), 1.37-1.46 (m, 2H), 1.57-1.62 (m, 2H), 4.24 (t, J = 6.9 Hz, 2H), 6.43 (d, J = 16.5 Hz, 1H), 7.44-7.51 (m, 3H), 7.64 (dd, J = 1.5, 8.1 Hz, 2H), 7.85 (d, J = 5.7 Hz, 1H), 7.97 (d, J = 16.5 Hz, 1H), 8.78 (d, J = 5.7 Hz, 1H), 9.39 (s, 1H), 9.74 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.4, 30.8, 65.0, 119.4, 123.7, 128.1, 128.6, 128.7, 129.0, 129.2, 130.5, 139.2, 139.3, 144.8, 150.0, 152.0, 153.4, 165.9; IR ($CHCl_3$, cm^{-1}) 3019, 2965, 2874, 1712, 1638; HRMS Calcd for $C_{21}H_{20}O_2N_2$: 332.1525. Found: 332.1531.

***n*-Butyl (*E*)-3-(7-phenyl-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl)acrylate (15).** The reaction mixtures were chromatographed using 2:1 hexane/EtOAc to afford 40 mg or 45 mg of the indicated compound as a yellow solid in a 43 % (entry 10) or 48 % (entry 11) yield: mp 73-76 °C; ^{1}H NMR ($CDCl_3$) Γ 0.95 (t, J = 7.2 Hz, 3H), 1.36-1.44 (m, 2H), 1.62-1.70 (m, 2H), 4.20 (t, J = 6.8 Hz, 2H), 6.14 (s, 2H), 6.22 (d, J = 16.4 Hz, 1H), 7.24 (s, 1H), 7.38-7.47 (m, 3H), 7.51 (s, 1H), 7.56-7.58 (m, 2H), 7.92 (d, J = 16.4 Hz, 1H), 9.02 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.3, 30.8, 64.8, 101.1, 102.1, 103.8, 123.7, 125.1, 126.1, 128.3, 130.4, 132.8, 140.3, 141.8, 148.4, 150.4, 151.3, 152.2, 166.4 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3018, 2962, 1708, 1615; HRMS Calcd for $C_{23}H_{21}O_4N$: 375.1471. Found: 375.1475.

***t*-Butyl (*E*)-3-(6,7-dimethoxy-3-phenylisoquinolin-4-yl)acrylate (17).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 50 mg of the indicated compound as a yellow solid in a 51 % yield: mp 157-159 °C; ^{1}H NMR ($CDCl_3$) Γ 1.51 (s, 9H), 4.04 (s, 3H), 4.06 (s, 3H), 6.20 (d, J = 16.4 Hz, 1H), 7.26 (s, 1H), 7.37-7.47 (m, 4H),

7.60 (d, J = 6.8 Hz, 2H), 7.86 (d, J = 16.4 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.4, 56.3, 56.3, 80.9, 103.0, 106.0, 123.0, 123.8, 127.6, 128.2, 130.5, 131.0, 140.5, 140.9, 150.0, 150.4, 150.9, 153.8, 165.8 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3020, 2972, 2934, 2840, 1700, 1503; HRMS Calcd for $C_{24}H_{25}O_4N$: 391.1784. Found: 391.1792.

***N,N*-Dimethyl (*E*)-3-(6,7-dimethoxy-3-phenylisoquinolin-4-yl)acrylamide (18).** The reaction mixture was chromatographed using 1:3 hexane/EtOAc and 50:1 $CHCl_3/CH_3OH$ to afford 46 mg of the indicated compound as a yellow solid in a 51 % yield: mp 150-151 °C; ^{1}H NMR ($CDCl_3$) Γ 2.72 (s, 3H), 3.00 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.41 (d, J = 16.0 Hz, 1H), 7.26 (s, 1H), 7.32-7.38 (m, 2H), 7.43 (t, J = 8.0 Hz, 2H), 7.57-7.59 (m, 2H), 8.07 (d, J = 16.0 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.9, 37.0, 56.3, 56.4, 102.7, 105.8, 123.6, 124.0, 126.8, 127.7, 128.3, 130.3, 131.7, 137.9, 141.3, 149.5, 150.4, 150.8, 153.6, 166.2; IR ($CHCl_3$, cm^{-1}) 3444, 3006, 2934, 1649, 1618, 1505, 1467; HRMS Calcd for $C_{22}H_{22}O_3N_2$: 362.1630. Found: 362.1635.

6,7-Dimethoxy-3-phenyl-4-[(*E*)-2-methylsulfonylethen-1-yl]isoquinoline (19). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 25 mg of the indicated compound as a yellow solid in a 27 % yield: mp 196-198 °C; ^{1}H NMR ($CDCl_3$) Γ 2.80 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 6.47 (d, J = 15.6 Hz, 1H), 7.24 (s, 1H), 7.28 (s, 1H), 7.39-7.42 (m, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.53 (dd, J = 1.2, 7.6 Hz, 2H), 8.02 (d, J = 16.0 Hz, 1H), 9.12 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 42.6, 56.4, 56.5, 101.9, 106.1, 120.8, 123.6, 128.5, 128.6, 130.4, 131.1, 134.4, 140.4, 140.8, 150.7, 150.8, 151.3, 154.3; IR ($CHCl_3$, cm^{-1}) 3019, 2974, 2399, 1621, 1508; HRMS Calcd for $C_{20}H_{19}O_4SN$: 369.1035. Found: 369.1041.

***n*-Butyl (*E*)-3-[3-(*p*-methoxyphenyl)isoquinolin-4-yl]acrylate (21).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 32 mg of the indicated

compound as a yellow oil in a 35 % yield: ^{1}H NMR ($CDCl_3$) Γ 0.96 (t, J = 7.5 Hz, 3H), 1.36-1.49 (m, 2H), 1.64-1.74 (m, 2H), 3.87 (s, 3H), 4.24 (t, J = 6.6 Hz, 2H), 6.36 (d, J = 16.5 Hz, 1H), 7.00 (tt, J = 1.8, 7.8 Hz, 2H), 7.57-7.66 (m, 3H), 7.76 (dt, J = 1.8, 7.8 Hz, 1H), 8.97 (d, J = 16.5 Hz, 1H), 8.03 (d, J = 8.1 Hz, 1H), 8.25 (d, J = 8.7 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.0, 19.4, 30.9, 55.6, 64.8, 113.9, 123.4, 124.4, 126.3, 127.2, 127.4, 128.5, 131.5, 132.1, 132.7, 134.5, 141.7, 151.7, 152.8, 160.0, 166.6; IR (neat, cm^{-1}) 3057, 2958, 2872, 2836, 1708, 1633, 1607, 1552, 1463; HRMS Calcd for $C_{23}H_{23}O_3N$: 361.1678. Found: 361.1682.

***n*-Butyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (23).** The reaction mixtures were chromatographed using 2:1 hexane/EtOAc to afford 59 mg (entry 16) or 58 mg (entry 17) of the indicated compound as a yellow oil in a 65 % or a 64 % yield, respectively: ^{1}H NMR ($CDCl_3$) Γ 0.91 (t, J = 7.2 Hz, 3H), 1.31-1.36 (m, 2H), 1.57-1.64 (m, 2H), 3.72 (s, 3H), 4.13 (t, J = 6.8 Hz, 2H), 6.07 (d, J = 16.4 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.35-7.39 (m, 2H), 7.62 (t, J = 8.0 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.92 (d, J = 16.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H), 9.27 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.3, 30.8, 55.5, 64.6, 111.2, 121.0, 124.3, 125.3, 125.6, 127.4, 127.6, 128.3, 129.4, 130.1, 131.2, 131.6, 134.2, 141.2, 149.7, 152.6, 156.4, 166.6; IR (neat, cm^{-1}) 3059, 2958, 2872, 2835, 1716, 1638, 1601, 1494; HRMS Calcd for $C_{23}H_{23}O_3N$: 361.1678. Found: 361.1682.

***t*-Butyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (24).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 61 mg of the indicated compound as a yellow oil in a 68 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.47 (s, 9H), 3.74 (s, 3H), 6.04 (d, J = 16.4 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 7.07 (dt, J = 0.8, 7.4 Hz, 1H), 7.38-7.42

(m, 2H), 7.63 (dt, J = 0.8, 7.6 Hz, 1H), 7.75 (dt, J = 1.2, 8.4 Hz, 1H), 7.83 (d, J = 16.4 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.3, 55.5, 80.7, 111.2, 121.0, 124.4, 125.7, 127.0, 127.3, 127.6, 128.3, 129.5, 130.0, 131.1, 131.6, 134.2, 140.1, 149.7, 152.4, 156.4, 165.8; IR (neat, cm^{-1}) 3400, 3059, 2977, 2934, 2835, 1708, 1636, 1601, 1494; HRMS Calcd for $C_{23}H_{23}O_3N$: 361.1678. Found: 361.1682.

3-(*o*-Methoxyphenyl)-4-[(*E*)-2-phenylethen-1-yl]isoquinoline (25). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 54 mg of the indicated compound as a yellow oil in a 64 % yield: ^{1}H NMR ($CDCl_3$) Γ 3.71 (s, 3H), 6.71 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 7.05 (t, J = 8.4 Hz, 1H), 7.21-7.26 (m, 2H), 7.31-7.35 (m, 5H), 7.40 (dd, J = 1.6, 7.6 Hz, 1H), 7.62 (t, J = 8.4 Hz, 1H), 7.72 (dt, J = 1.2, 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.8 Hz, 1H), 9.25 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.7, 111.3, 120.9, 124.3, 124.9, 126.5, 127.0, 127.9, 128.1, 128.2, 128.8, 129.6, 130.4, 130.6, 131.7, 134.9, 135.8, 137.6, 149.1, 151.0, 156.6 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 3057, 3025, 2957, 2935, 2833, 2214, 1617, 1494; HRMS Calcd for $C_{24}H_{19}ON$: 337.1467. Found: 337.1473.

3-(*o*-Methoxyphenyl)-4-[(*E*)-2-phenylsulfonylethen-1-yl]isoquinoline (26). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 20 mg of the indicated compound as a yellow oil in a 20 % yield: ^{1}H NMR ($CDCl_3$) Γ 3.58 (s, 3H), 6.45 (d, J = 15.6 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.98 (t, J = 7.2 Hz, 1H), 7.27-7.31 (m, 2H), 7.50 (t, J = 8.0 Hz, 2H), 7.61-7.70 (m, 4H), 7.80 (dd, J = 0.8, 7.6 Hz, 1H), 8.02-8.08 (m, 3H), 9.30 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.5, 111.3, 121.1, 123.6, 123.7, 127.4, 127.7, 127.8, 128.5, 128.9, 129.5, 130.1, 131.3, 131.7, 133.4, 133.8, 134.0, 139.0, 140.4, 149.5, 153.3,

155.8; IR (neat, cm^{-1}) 3060, 2938, 2836, 1619, 1600, 1494; HRMS Calcd for $C_{24}H_{19}O_3NS$: 401.1086. Found: 401.1093.

***N,N*-Dimethyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (27).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc and pure EtOAc to afford 54 mg of the indicated compound as a yellow oil in a 65 % yield: ^{1}H NMR ($CDCl_3$) Γ 2.66 (s, 3H), 2.96 (s, 3H), 3.74 (s, 3H), 6.33 (d, J = 15.6 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 7.2 Hz, 1H), 7.36 (dt, J = 1.6, 8.0 Hz, 1H), 7.41 (dd, J = 1.6, 7.6 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.75 (dt, J = 1.2, 7.2 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 15.6 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.8, 37.0, 55.7, 111.3, 121.0, 124.3, 125.3, 126.7, 127.3, 127.4, 128.1, 129.6, 130.3, 130.9, 131.4, 134.7, 137.3, 148.8, 151.9, 156.3, 166.3; IR ($CHCl_3$, cm^{-1}) 3468, 3058, 3004, 2935, 2835, 2234, 1651, 1613; HRMS Calcd for $C_{21}H_{20}O_2N_2$: 332.1525. Found: 332.1531.

(*E*)-2-Methyl-4-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]-3-buten-2-ol (28). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 20 mg of the indicated compound as a yellow oil in a 25 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.20 (s, 6H), 3.74 (s, 3H), 5.75 (d, J = 16.0 Hz, 1H), 6.77 (d, J = 16.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 7.32-7.37 (m, 2H), 7.60 (d, J = 7.2 Hz, 1H), 7.70 (dt, J = 1.2, 7.6 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 9.24 (s, 1H) (the hydrogen from the OH group is missing); ^{13}C NMR ($CDCl_3$) Γ 29.6, 55.6, 71.2, 111.0, 120.7, 121.1, 124.6, 127.0, 127.6, 128.1, 128.3, 129.3, 130.5, 130.7, 131.6, 134.9, 144.8, 148.9, 150.9, 156.5; IR ($CHCl_3$, cm^{-1}) 3018, 2973, 1496; HRMS Calcd for $C_{21}H_{21}O_2N$: 319.1572. Found: 319.1576.

***t*-Butyl (*E*)-3-[6,7-dimethoxy-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (30).** The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 94 mg of the

indicated compound as a yellow oil in a 92 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.46 (s, 9H), 3.74 (s, 3H), 4.04 (s, 6H), 6.00 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.8 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 7.25 (s, 1H), 7.36-7.40 (m, 3H), 7.82 (d, J = 16.4 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 28.3, 55.4, 56.2, 56.3, 80.6, 102.8, 105.8, 111.0, 120.9, 123.8, 124.5, 126.2, 129.7, 130.8, 131.5, 140.6, 148.6, 149.8, 150.3, 153.6, 156.3, 165.9; IR (neat, cm^{-1}) 3400, 3060, 3004, 2975, 2835, 2255, 2211, 1701, 1624, 1578, 1505; HRMS Calcd for $C_{25}H_{27}O_5N$: 421.1889. Found: 421.1895.

***N*,*N*-Dimethyl (*E*)-3-[6,7-dimethoxy-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (31).** The reaction mixture was chromatographed using pure EtOAc and 50:1 $CHCl_3$/CH_3OH to afford 95 mg of the indicated compound as a yellow solid in a 97 % yield: mp 124-126 °C; ^{1}H NMR ($CDCl_3$) Γ 2.63 (s, 3H), 2.96 (s, 3H), 3.74 (s, 3H), 4.05 (s, 6H), 6.29 (d, J = 15.6 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 7.25 (s, 1H), 7.30-7.37 (m, 2H), 7.41 (dd, J = 1.6, 7.2 Hz, 1H), 8.02 (d, J = 15.6 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.7, 36.9, 55.7, 56.2, 56.4, 102.5, 105.7, 111.2, 121.0, 123.6, 124.7, 125.5, 129.3, 130.7, 131.4, 131.4, 137.6, 147.8, 149.4, 150.4, 153.4, 156.2, 166.3; IR ($CHCl_3$, cm^{-1}) 3547, 3011, 2937, 2836, 1649, 1618, 1499; HRMS Calcd for $C_{23}H_{24}O_4N_2$: 392.1736. Found: 392.1742.

6,7-Dimethoxy-3-phenyl-4-[(*E*)-2-methanesulfonylethen-1-yl]isoquinoline (32). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 51 mg of the indicated compound as a pale yellow solid in a 52 % yield: mp 212-214 °C; ^{1}H NMR ($CDCl_3$) Γ 2.66 (s, 3H), 3.77 (s, 3H), 4.06 (s, 3H), 4.06 (s, 3H), 6.34 (d, J = 15.6 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 7.14 (s, 1H), 7.27 (s, 1H), 7.37-7.43 (m,

2H), 8.02 (d, J = 15.6 Hz, 1H), 9.12 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 42.7, 55.8, 56.3, 56.5, 101.9, 105.9, 111.3, 121.3, 122.3, 123.6, 129.6, 130.0, 130.8, 131.6, 132.5, 140.5, 148.1, 150.6, 150.7, 154.0, 156.0; IR ($CHCl_3$, cm^{-1}) 3020, 2963, 2838, 1622, 1579; HRMS Calcd for $C_{21}H_{21}O_5SN$: 399.1140. Found: 399.1148.

***t*-Butyl (*E*)-3-{7-(*o*-methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}acrylate (34).** The reaction mixtures were chromatographed using 1:1 hexane/EtOAc to afford 62 mg or 83 mg of the indicated compound as a yellow oil in a 61 % (entry 26) or an 82 % (entry 27) yield: ^{1}H NMR ($CDCl_3$) Γ 1.47 (s, 9H), 3.74 (s, 3H), 5.97 (d, J = 16.4 Hz, 1H), 6.11 (s, 2H), 6.94 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 7.23 (s, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.37 (dt, J = 1.2, 8.0 Hz, 1H), 7.44 (s, 1H), 7.73 (d, J = 16.4 Hz, 1H), 9.00 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.3, 55.4, 80.6, 101.0, 101.9, 103.6, 111.1, 120.9, 125.1, 125.4, 126.6, 129.5, 129.9, 131.5, 132.6, 140.5, 148.3, 148.9, 150.1, 151.8, 156.4, 165.8; IR ($CHCl_3$, cm^{-1}) 2977, 2835, 1704, 1640; HRMS Calcd for $C_{24}H_{23}O_5N$: 405.1576. Found: 405.1584.

***N,N*-Dimethyl (*E*)-3-{7-(*o*-methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}acrylamide (35).** The reaction mixture was chromatographed using 1:3 hexane/EtOAc and pure EtOAc to afford 61 mg of the *E* isomer as a yellow oil and 23 mg of the *Z* isomer as a yellow oil in a 89 % overall yield. The following characterization data is for the pure major *E* isomer: ^{1}H NMR ($CDCl_3$) Γ 2.64 (s, 3H), 2.95 (s, 3H), 3.74 (s, 3H), 6.12 (s, 2H), 6.26 (d, J = 15.6 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 7.05 (dt, J = 0.8, 7.6 Hz, 1H), 7.23 (s, 1H), 7.34 (dt, J = 1.2, 8.0 Hz, 1H), 7.38 (dd, J = 1.6, 7.6 Hz, 1H), 7.41 (s, 1H), 7.90 (d, J = 15.6 Hz, 1H), 9.00 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.8, 37.0, 55.8, 100.9, 102.0, 103.5, 111.3, 121.0, 124.9, 125.1, 126.5, 129.5, 130.5, 131.4, 133.3, 137.7, 148.2, 148.5, 149.7, 151.8, 156.3, 166.3; IR

($CHCl_3$, cm^{-1}) 3006, 2937, 2836, 1650, 1614; HRMS Calcd for $C_{22}H_{20}O_4N_2$: 376.1423. Found: 376.1431.

4-{7-(*o*-Methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}butan-2-one (36). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 42 mg of the indicated compound as a yellow solid in a 48 % yield: mp 174-175 °C; ^{1}H NMR ($CDCl_3$) Γ 2.02 (s, 3H), 2.58-2.65 (m, 2H), 2.92-3.00 (m, 1H), 3.06-3.13 (m, 1H), 3.75 (s, 3H), 6.12 (s, 2H), 6.99 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.23-7.25 (m, 3H), 7.38 (dt, J = 1.2, 8.0 Hz, 1H), 8.94 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.3, 29.8, 43.7, 55.6, 99.8, 101.8, 104.0, 111.2, 120.9, 125.4, 128.5, 129.6, 130.3, 130.9, 133.3, 148.0, 148.5, 149.4, 151.6, 156.7, 207.9; IR ($CHCl_3$, cm^{-1}) 3018, 2963, 2837, 1713, 1603; HRMS Calcd for $C_{21}H_{19}O_4N$: 349.1314. Found: 349.1320.

***t*-Butyl (*E*)-3-[6-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (38).** The reaction mixtures were chromatographed using pure EtOAc to afford 70 mg or 68 mg of the indicated compound as a yellow oil in a 69 % (entry 30) or a 67 % (entry 31) yield: ^{1}H NMR ($CDCl_3$) Γ 1.45 (s, 9H), 3.14 (s, 6H), 3.74 (s, 3H), 6.02 (d, J = 16.4 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 7.02-7.06 (m, 2H), 7.19 (dd, J = 2.0, 8.8 Hz, 1H), 7.34-7.38 (m, 2H), 7.79 (d, J = 16.4 Hz, 1H), 7.83 (d, J = 9.2 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.3, 40.5, 42.8, 55.5, 80.3, 101.0, 111.0, 116.2, 120.9, 123.5, 125.3, 129.6, 129.6, 130.2, 131.5, 136.2, 141.1, 150.1, 151.3, 151.8, 156.4, 166.3; IR ($CHCl_3$, cm^{-1}) 2975, 2834, 1698, 1613; HRMS Calcd for $C_{25}H_{28}O_3N_2$: 404.2100. Found: 404.2107.

***N,N*-Dimethyl 3-[6-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (39).** The reaction mixture was chromatographed using pure EtOAc and 10:1 $CHCl_3/CH_3OH$ to afford 65 mg of a 91:9 *E/Z* mixture as determined by ^{1}H NMR

spectroscopy of a yellow oil in 89 % overall yield. ^{1}H NMR ($CDCl_3$) for the major *E* isomer: Γ 2.63 (s, 3H), 2.95 (s, 3H), 3.13 (s, 6H), 3.72 (s, 3H), 6.28 (d, J = 15.6 Hz, 1H), 6.91 (d, J = 8.8 Hz, 1H), 6.93 (s, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.19 (dd, J = 1.6, 9.2 Hz, 1H), 7.33 (dt, J = 1.2, 8.0 Hz, 1H), 7.38 (dd, J = 1.6, 7.6 Hz, 1H), 7.82 (d, J = 9.2 Hz, 1H), 7.98 (d, J = 15.6 Hz, 1H), 8.96 (s, 1H); additional ^{13}C NMR ($CDCl_3$) for the *E*/*Z* mixture Γ 35.7, 36.9, 40.5, 40.6, 41.1, 55.7, 100.7, 111.3, 116.3, 120.7, 120.8, 120.9, 124.0, 124.5, 129.3, 129.4, 131.3, 136.8, 138.1, 149.1, 150.8, 151.7, 156.3, 166.6 (except for two sp^3 carbons from the minor *Z* isomer, all other carbons are from the major *E* isomer); IR ($CHCl_3$, cm^{-1}) for the *E*/*Z* mixture 3006, 2937, 2836, 1650, 1614; HRMS Calcd for $C_{23}H_{25}O_2N_3$: 375.1947. Found: 375.1953.

***t*-Butyl (*E*)-3-[7-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (41).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 71 mg of the indicated compound as a yellow solid in a 71 % yield: mp 163-166 °C; ^{1}H NMR ($CDCl_3$) Γ 1.47 (s, 9H), 3.09 (s, 6H), 3.73 (s, 3H), 6.05 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 7.00 (s, 1H), 7.05 (t, J = 7.2 Hz, 1H), 7.36-7.38 (m, 3H), 7.78 (d, J = 16.4 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 9.10 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.3, 40.7, 55.4, 80.5, 105.4, 111.1, 120.7, 120.9, 125.2, 125.3, 126.3, 126.7, 129.6, 129.6, 129.8, 131.8, 140.8, 146.1, 149.1, 150.9, 156.6, 166.1; IR ($CHCl_3$, cm^{-1}) 3018, 2979, 2836, 1702, 1621; HRMS Calcd for $C_{25}H_{28}O_3N_2$: 404.2100. Found: 404.2107.

***N*,*N*-Dimethyl (*E*)-3-[7-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (42).** The reaction mixture was chromatographed using pure EtOAc and 20:1 $CHCl_3$/CH_3OH to afford 66 mg of the indicated compound yield as a yellow solid in a 70 % yield: mp 171-174 °C; ^{1}H NMR ($CDCl_3$) Γ 3.27 (s, 3H), 2.95 (s, 3H), 3.09 (s, 6H), 3.73 (s, 3H), 6.30 (d, J = 15.6 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 2.8 Hz, 1H), 7.04 (t, J =

7.6 Hz, 1H), 7.31-7.40 (m, 3H), 7.98 (s, 1H), 8.02 (t, J = 4.8 Hz, 1H), 9.09 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.8, 37.0, 40.7, 55.7, 105.2, 111.2, 120.5, 120.9, 124.7, 125.1, 126.2, 127.3, 129.2, 129.3, 130.7, 131.6, 137.8, 145.1, 149.2, 150.4, 156.4, 166.5; IR ($CHCl_3$, cm^{-1}) 3017, 2837, 2399, 1650, 1621, 1581; HRMS Calcd for $C_{23}H_{25}O_2N_3$: 375.1947. Found: 375.1953.

***n*-Butyl (*E*)-3-(3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl)acrylate (44).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 52 mg of the indicated compound as a yellow oil in a 51 % yield: ^{1}H NMR ($CDCl_3$) Γ 0.93 (t, J = 7.6 Hz, 3H), 1.32-1.39 (m, 2H), 1.57-1.63 (m, 2H), 3.81 (s, 3H), 4.02 (s, 3H), 4.04 (s, 3H), 4.12 (t, J = 6.4 Hz, 2H), 5.49 (d, J = 16.0 Hz, 1H), 7.12 (s, 1H), 7.31 (t, J = 6.8 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.52 (d, J = 7.6 Hz, 2H), 8.57 (d, J = 16.4 Hz, 1H), 9.09 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 19.3, 30.9, 56.3, 61.0, 61.4, 64.3, 102.6, 123.3, 123.7, 125.0, 127.1, 127.7, 128.2, 130.5, 140.8, 145.7, 146.6, 149.0, 150.3, 150.7, 154.0, 166.8; IR ($CHCl_3$, cm^{-1}) 3058, 2960, 2871, 1709, 1636, 1612, 1483; HRMS Calcd for $C_{25}H_{27}O_5N$: 421.1889. Found: 421.1897.

***t*-Butyl (*E*)-3-(3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl)acrylate (45).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 63 mg of the indicated compound as a yellow oil in a 62 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.45 (s, 9H), 3.81 (s, 3H), 4.02 (s, 3H), 4.03 (s, 3H), 5.41 (d, J = 16.0 Hz, 1H), 7.11 (s, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 7.6 Hz, 2H), 7.54 (d, J = 7.2 Hz, 2H), 8.46 (d, J = 16.4 Hz, 1H), 9.07 (d, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.3, 56.3, 60.9, 61.3, 80.2, 102.5, 123.8, 124.9, 125.0, 127.2, 127.6, 128.1, 130.6, 140.9, 144.6, 146.5, 149.0, 150.2, 150.6, 154.0, 166.0; IR (neat, cm^{-1}) 3392, 3058, 2976, 2937, 2840, 2253, 1698, 1636, 1611, 1484; HRMS Calcd for $C_{25}H_{27}O_5N$: 421.1889. Found: 421.1895.

***N,N*-Dimethyl (*E*)-3-[3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl]acrylamide (46).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc and 20:1 $CHCl_3/CH_3OH$ to afford 49 mg of the indicated compound as a white solid in a 50 % yield: mp 169-171 °C; ^{1}H NMR ($CDCl_3$) Γ 2.43 (s, 3H), 2.92 (s, 3H), 3.90 (s, 3H), 4.02 (s, 3H), 4.04 (s, 3H), 5.90 (d, J = 15.6 Hz, 1H), 7.11 (s, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.54 (d, J = 7.2 Hz, 2H), 8.43 (d, J = 15.6 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.6, 36.7, 56.3, 61.3, 61.3, 102.4, 124.7, 124.9, 125.1, 127.3, 127.3, 128.2, 130.7, 141.7, 141.8, 146.6, 149.4, 150.0, 150.8, 154.0, 166.8; IR ($CHCl_3$, cm^{-1}) 3017, 2941, 1648, 1611, 1580; HRMS Calcd for $C_{23}H_{24}O_4N_2$: 392.1736. Found: 392.1742.

5,6,7-Trimethoxy-3-phenyl-4-[(*E*)-2-phenylethen-1-yl]isoquinoline (47). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 77 mg of the indicated compound as a yellow solid in a 78 % yield: mp 133-135 °C; ^{1}H NMR ($CDCl_3$) Γ 3.74 (s, 3H), 4.02 (s, 3H), 4.03 (s, 3H), 6.12 (d, J = 16.4 Hz, 1H), 7.11 (s, 1H), 7.17-7.28 (m, 6H), 7.34 (t, J = 7.2 Hz, 2H), 7.60 (dd, J = 1.2, 8.0 Hz, 2H), 7.86 (d, J = 16.4 Hz, 1H), 9.06 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 56.2, 61.4, 61.4, 102.7, 125.4, 126.1, 126.2, 127.1, 127.3, 127.6, 128.0, 128.3, 128.7, 130.6, 133.9, 138.2, 141.9, 146.6, 149.4, 149.7, 151.0, 153.7; IR ($CHCl_3$, cm^{-1}) 3018, 2940, 1612, 1482; HRMS Calcd for $C_{26}H_{23}O_3N$: 397.1678. Found: 397.1685.

4-{8-Phenyl-1,3-dioxolo[4,5-*f*]isoquinolin-9-yl}butan-2-one (49). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 41 mg of the indicated compound as a yellow solid in a 50 % yield: mp 161-164 °C; ^{1}H NMR ($CDCl_3$) Γ 2.06 (s, 3H), 2.69 (dd, J = 6.0, 8.1 Hz, 2H), 3.31-3.36 (m, 2H), 6.17 (s, 2H), 7.30 (t, J = 7.2 Hz, 1H),

7.40-7.47 (m, 5H), 7.62 (d, J = 8.4 Hz, 1H), 9.04 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.5, 28.6, 44.5, 100.6, 110.6, 121.6, 122.9, 123.2, 124.2, 126.8, 127.3, 128.1, 139.6, 139.7, 146.8, 149.5, 151.5, 206.6; IR ($CHCl_3$, cm^{-1}) 3018, 1709, 1632, 1572, 1503; HRMS Calcd for $C_{20}H_{17}O_4N$: 319.1208. Found: 319.1212 .

1-Phenyl-3-{8-phenyl-1,3-dioxolo[4,5-*f*]isoquinolin-9-yl}propan-1-one (50). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 34 mg of the indicated compound as a yellow solid in a 36 % yield: mp 184-186 °C; ^{1}H NMR ($CDCl_3$) Γ 3.20-3.34 (m, 2H), 3.50-3.54 (m, 2H), 6.10 (s, 2H), 7.31 (d, J = 8.4 Hz, 1H), 7.37-7.54 (m, 8H), 7.63 (d, J = 8.4 Hz, 1H), 7.81 (dd, J = 1.2, 8.0 Hz, 2H), 9.06 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 25.3, 40.8, 101.9, 111.8, 122.9, 124.1, 124.7, 125.4, 128.0, 128.2, 128.6, 128.7, 129.3, 133.1, 136.8, 140.9, 140.9, 148.0, 150.7, 152.8, 199.1; IR ($CHCl_3$, cm^{-1}) 3018, 1685, 1632, 1598, 1580, 1503; HRMS Calcd for $C_{25}H_{19}O_3N$: 381.1365. Found: 381.1373.

6-{8-Phenyl-1,3-dioxolo[4,5-*f*]isoquinolin-9-yl}hexan-2-one (51). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 24 mg of the indicated compound as a yellow oil in a 27 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.54-1.58 (m, 4H), 2.06 (s, 3H), 2.29 (t, J = 7.2 Hz, 2H), 3.04 (t, J = 7.6 Hz, 2H), 6.20 (s, 2H), 7.29 (t, J = 8.4 Hz, 1H), 7.41-7.50 (m, 5H), 7.60 (d, J = 8.4 Hz, 1H), 9.02 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.6, 29.7, 29.8, 31.4, 43.1, 101.5, 111.5, 122.8, 123.7, 125.2, 125.7, 127.6, 128.1, 129.3, 140.8, 141.0, 147.7, 150.1, 152.0, 208.9; IR ($CHCl_3$, cm^{-1}) 3017, 2959, 1711, 1632, 1571, 1503, 1503; HRMS Calcd for $C_{22}H_{21}O_3N$: 347.4130. Found: 347.4136.

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CHAPTER 3. SYNTHESIS OF SUBSTITUTED NAPHTHALENES AND CARBAZOLES BY THE PALLADIUM-CATALYZED ANNULATION OF INTERNAL ALKYNES

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Abstract

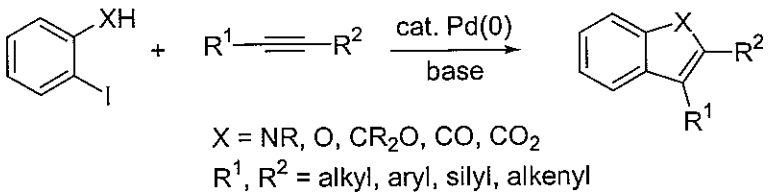
An efficient synthesis of highly substituted naphthalenes has been developed by the palladium-catalyzed annulation of a variety of internal alkynes, in which two new carbon-carbon bonds are formed in a single step under relatively mild reaction conditions. This method has also been used to synthesize carbazoles although a higher reaction temperature is necessary. The process involves arylpalladation of the alkyne, followed by intramolecular Heck olefination and double bond isomerization. This method accommodates a variety of functional groups and affords the anticipated highly substituted naphthalenes and carbazoles in good to excellent yields.

Introduction

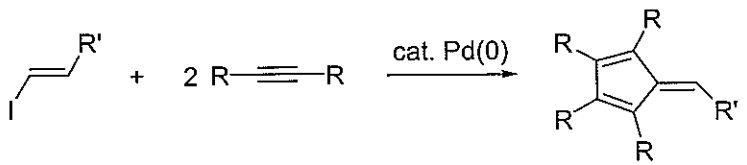
Highly substituted naphthalenes are common structural units in numerous biologically significant natural products and pharmaceuticals,[1] and improved methods for their construction are highly desirable.[2-6] Among the most important synthetic routes to such compounds are annulation via Fischer carbenes (the Dötz reaction)[3] and the palladium-

catalyzed cyclization of alkynes by arylsilyl triflates via *in situ* generation of highly reactive benzynes.[4] Another method of synthesis is based on the cyclopropane-shift reaction of diaryl(2-halogenocyclopropyl)methanols.[5] Very recently, substituted naphthalenes have been prepared using the gallium-catalyzed cyclization of carbonyl compounds or epoxides with alkynes.[6]

Annulation processes have proven quite valuable in organic synthesis because of the ease with which a variety of complicated hetero- and carbocycles can be rapidly constructed.[7] In our own laboratories, it has been demonstrated that palladium-catalyzed annulation[8] can be effectively employed for the synthesis of indoles,[9] isoindolo[2,1-*a*]indoles,[10] benzofurans,[11] benzopyrans,[12] isocoumarins,[11,12] α-pyrones,[12,13] indenones,[14] isoquinolines,[15] carbolines,[16] and polycyclic aromatic hydrocarbons[17] (eq 1). More recently, Takahashi et al. have reported that pentasubstituted fulvene derivatives can be prepared using the palladium-catalyzed annulation of disubstituted alkynes (eq 2).[18]



(1)

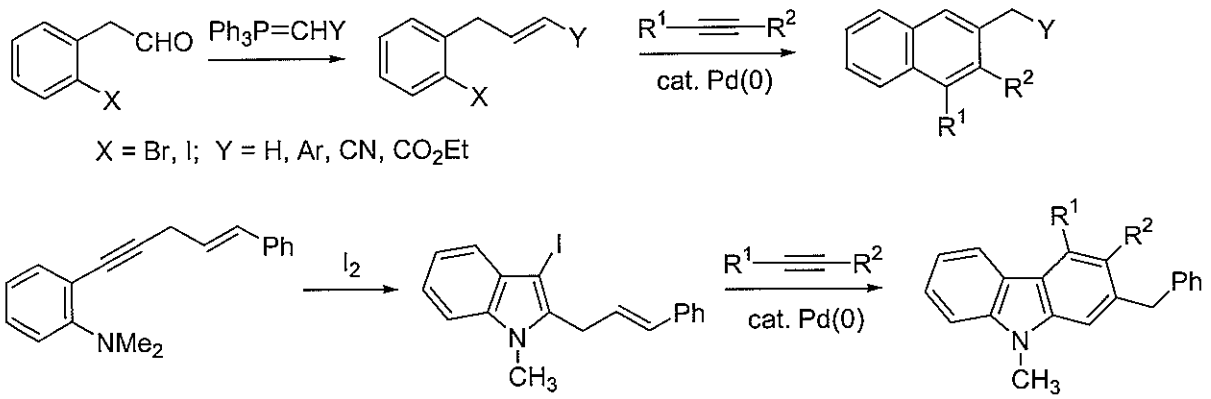


(2)

Due to our continuing interest in the palladium-catalyzed annulation of internal alkynes, we have investigated the reaction of internal alkynes and *o*-(2-alkenyl)aryl halides

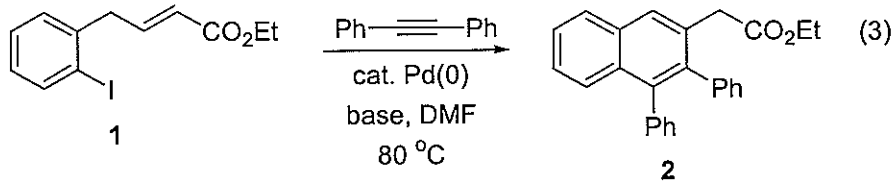
derived from aldehydes and ylides and have fully detailed this new naphthalene synthesis and its extension to the formation of substituted carbazoles (Scheme 1).

Scheme 1



Results and Discussion

Our initial studies focused on achieving optimal reaction conditions for the palladium-catalyzed annulation employing ethyl (*E*)-4-(2-iodophenyl)-2-butenoate (**1**). The reaction of aryl halide **1** and diphenylacetylene was chosen as the model system for optimization of this process (eq 3) and the results are summarized in Table 1.



1 **2** (3)

Table 1. Optimization of the Synthesis of Naphthalene **2** (eq 3)[a]

entry	alkyne (equiv)	catalyst	ligand	base	time (h)	% yield
1	2	10 % $Pd(OAc)_2$	--	3 NaOAc	12 h	58
2	2	10 % $Pd(OAc)_2$	--	3 Na_2CO_3	12 h	40
3	2	10 % $Pd(OAc)_2$	--	3 $NaHCO_3$	8 h	49
4	2	10 % $Pd(PPh_3)_4$	--	3 Na_2CO_3	24 h	trace
5	2	10 % $Pd(OAc)_2$	--	3 Bu_3N	10 h	71
6	2	10 % $Pd(OAc)_2$	--	3 Et_3N	12 h	76
7	2	10 % $Pd(OAc)_2$	--	3 pyridine	24 h	trace
8	2	5 % $Pd(OAc)_2$	--	3 Et_3N	10 h	80
9	1.2	5 % $Pd(OAc)_2$	--	3 Et_3N	12 h	58
10	5	5 % $Pd(OAc)_2$	--	3 Et_3N	12 h	81
11	2	5 % $Pd(OAc)_2$	--	3 Et_3N	12 h	80[b]
12	2	5 % $Pd(OAc)_2$	--	1.5 Et_3N	12 h	70
13	2	5 % $Pd(OAc)_2$	--	2 Et_3N	12 h	79
14	2	5 % $Pd(OAc)_2$	10 % PPh_3	2 Et_3N	12 h	86
15	2	5 % $Pd(OAc)_2$	10 % PPh_3	1.5 Et_3N	12 h	78

[a] All reactions were run under the following reaction conditions, unless otherwise specified: 0.25 mmol of aryl halide **1** and the indicated amount of diphenylacetylene were stirred in 3 mL of DMF at 80 °C in the presence of the specified amount of the indicated base, $Pd(OAc)_2$, and PPh_3. [b] One equiv of *n*-Bu_4NCl was added.

Using 10 mol % of $Pd(OAc)_2$ and 3 equiv of NaOAc afforded the desired naphthalene product **2** in a 58 % yield (entry 1, Table 1). Carbonate bases, such as Na_2CO_3 and $NaHCO_3$, gave naphthalene **2** in 40 % and 49 % yields respectively (entries 2 and 3). However, the use of $Pd(PPh_3)_4$ as a catalyst and Na_2CO_3 as a base gave only a trace of the desired product (entry 4). Our previous work has shown that carbonate bases usually work better for palladium-catalyzed annulation chemistry than organic bases.[9-17] However, it turned out that

organic bases work better than carbonate salts in this annulation chemistry. For example, when the organic bases *n*-Bu_3N and Et_3N were employed, the reaction of halide **1** gave 71 % and 76 % yields of naphthalene **2**, respectively, in the presence of 10 mol % of $Pd(OAc)_2$ (entries 5 and 6). This is probably because the ester group can be hydrolyzed in the presence of the carbonate bases and the resulting yield of naphthalene suffers. The use of pyridine afforded only a trace of the desired product (entry 7). Further optimization work showed that 5 mol % of $Pd(OAc)_2$ and 2 equiv of diphenylacetylene are necessary to achieve decent yields of naphthalene **2** (entries 8-10). In entry 11, the addition of 1 equiv of *n*-Bu_4NCl gave an 80 % yield, which is the same yield as the reaction without *n*-Bu_4NCl (entry 8). We have also explored the effects on the yield of other variables, such as the ligand and the amount of the base (entries 12-15). The optimal reaction conditions thus far developed employ 0.25 mmol of aryl halide **1**, 2 equiv of diphenylacetylene, 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3 and 2 equiv of Et_3N as a base in 3 mL of DMF stirred at 80 °C. This afforded an 86 % yield of naphthalene **2** (entry 14).

Using our optimal reaction conditions, the scope of the annulation process has been explored using a variety of substrates carefully selected in order to establish the generality of the process and its applicability to commonly encountered synthetic problems (Table 2). While the reaction of aryl halide **1** and diphenylacetylene afforded naphthalene **2** in an 86 % yield (entry 1), only a 61 % yield of naphthalene **3** was obtained from the reaction of aryl halide **1** and di(*p*- methoxyphenyl)acetylene (entry 2). The decrease in the yield of the reaction indicates that electron-rich diarylacetylenes disfavor the annulation chemistry. However, when an electron-deficient diarylacetylene, such as di(*p*-ethoxycarbonylphenyl)acetylene was allowed to react with aryl halide **1**, an 83 % yield of

Table 2. Synthesis of Substituted Naphthalenes and Carbazoles by the Palladium-Catalyzed Annulation of Internal Alkynes[a]

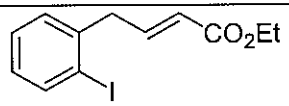
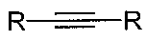
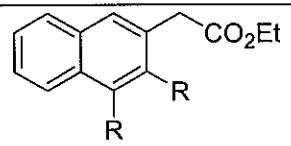
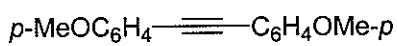
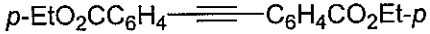
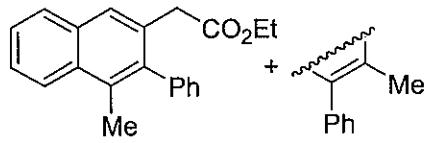
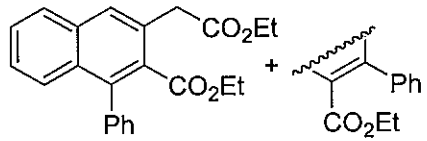
entry	haloalkene	alkyne	time (h)	product(s)	% isolated yield
	 **1**				
1			12	**2**	86
2			24	**3**	61
3			30	**4**	83
4			48	**5**	60
5			24	 **6** + **7**	75[b] (53 : 47)
6			12	 **8** + **9**	88[b] (76 : 24)

Table 2 continued

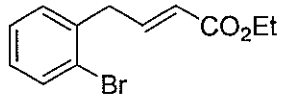
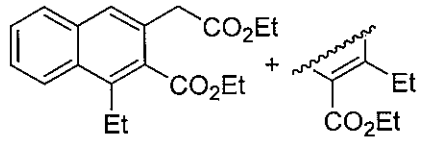
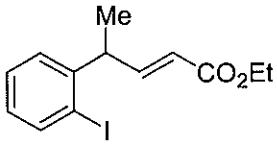
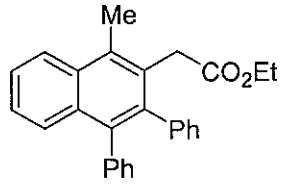
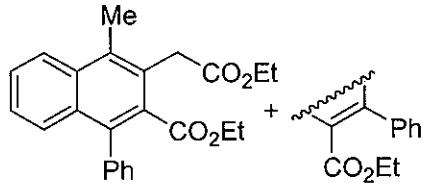
7	 **10**	Ph—≡—Ph	40	**2**	75
8		*n*-Pr—≡—*n*-Pr	72	**5**	46
9		Et—≡—CO_2Et	72	 **11 + 12**	52[b] (60 : 40)
10	 **13**	Ph—≡—Ph	26	 **14**	72
11		Ph—≡—CO_2Et	5	 **15 + 16**	86[b] (67 : 33)

Table 2 continued

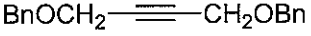
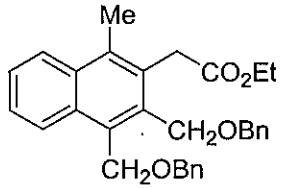
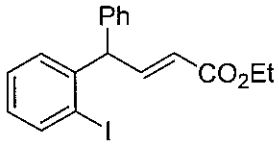
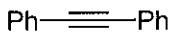
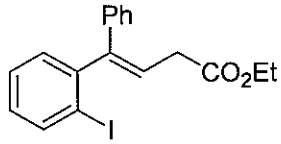
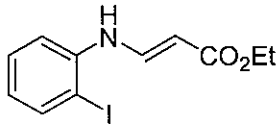
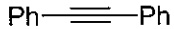
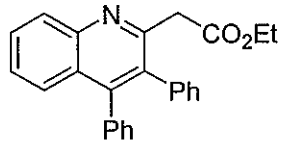
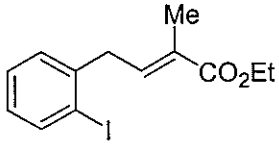
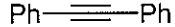
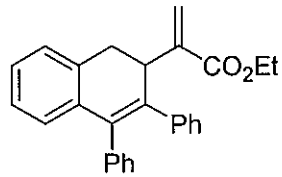
12			12	 **17**	56
13	 **18**		8	 **19**	48
14	 **20**		24	 **21**	0
15	 **22**		12	 **23**	73

Table 2 continued

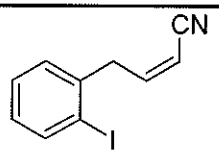
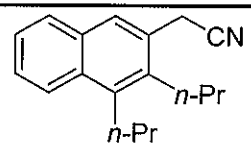
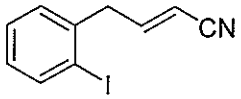
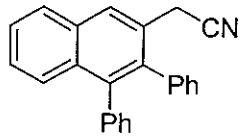
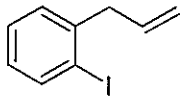
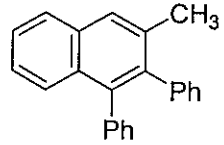
16	 **24**	*n*-Pr—≡—*n*-Pr	7	 **25**	74
17	 **27**	*n*-Pr—≡—*n*-Pr	7	**25**	72
18	**24**	Ph—≡—Ph	16	 **26**	45
19	**27**	Ph—≡—Ph	12	**26**	43
20	 **28**	Ph—≡—Ph	16	 **29**	32

Table 2 continued

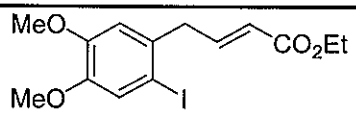
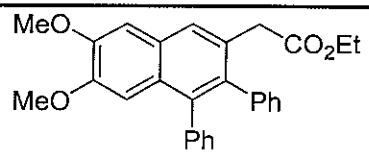
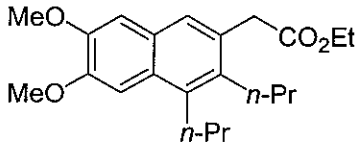
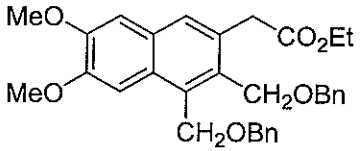
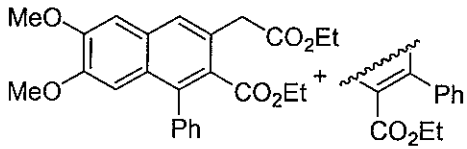
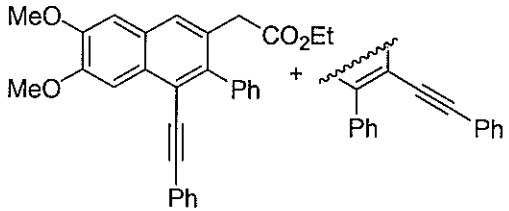
21	 **30**	Ph—≡—Ph	24	 **31**	71
22		*n*-Pr—≡—*n*-Pr	16	 **32**	73
23		$BnOCH_2$—≡—CH_2OBn	7	 **33**	60
24		Ph—≡—CO_2Et	12	 **34** + **35**	73 + 8
25		Ph—≡—≡—Ph	18	 **36** + **37**	66[b] (83 : 17)

Table 2 continued

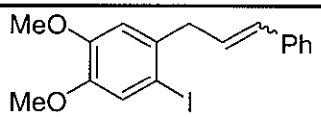
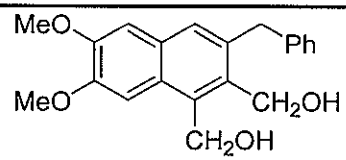
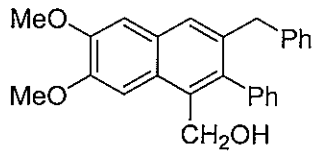
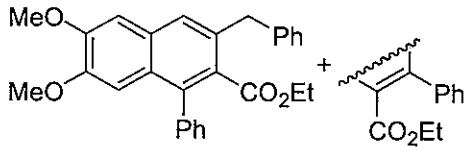
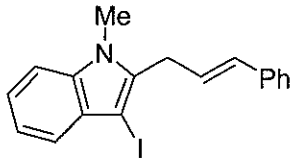
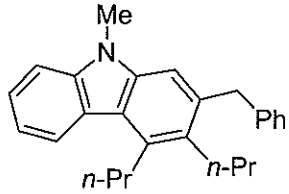
26	 **38**[c]	$HOCH_2—\equiv—CH_2OH$	16	 **39**	73
27		$HOCH_2—\equiv—Ph$	8	 **40**	31
28		$Ph—\equiv—CO_2Et$	8	 **41** + **42**	76 + 8
29	 **43**	*n*-Pr—≡—*n*-Pr	24	 **44**	33[d]

Table 2 continued

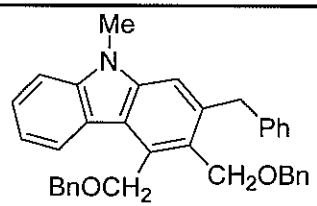
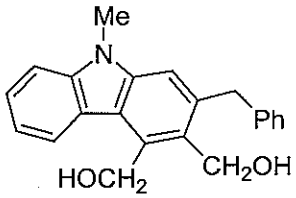
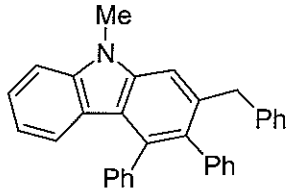
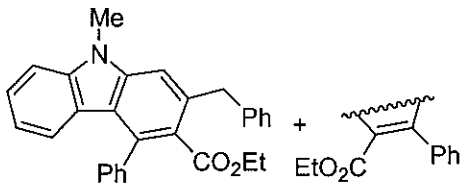
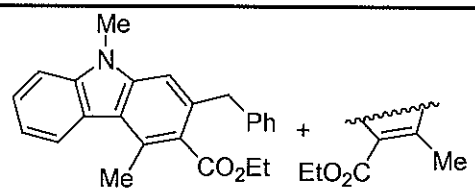
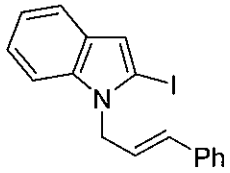
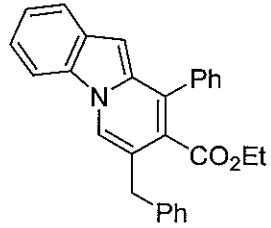
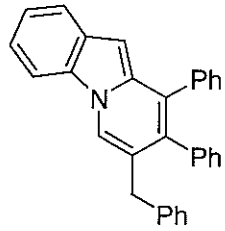
30	$BnOCH_2$—≡—CH_2OBn	4	 **45**	56[c]
31	$HOCH_2$—≡—CH_2OH	12	 **46**	41[e]
32	Ph—≡—Ph	24	 **47**	Trace[e,f]
33	Ph—≡—CO_2Et	16	 **48 + 49**	91[b,d] (60 : 40)

Table 2 continued

34		Me—≡—CO_2Et	72	 **50 + 51**	$78^{b,d}$ (82 : 18)
35	 **52**	Ph—≡—CO_2Et	7	 **53**	42
36		Ph—≡—Ph	12	 **54**	0

[a] All reactions were run under the following conditions, unless otherwise specified: 0.25 mmol of the aryl halide, 0.5 mmol of the alkyne, 0.5 mmol of Et_3N, 5 mol % of $Pd(OAc)_2$ and 10 mol % of PPh_3 were stirred in 3 mL of DMF at 80 °C under an Ar atmosphere. [b] The products are inseparable. [c] Compound **34** was prepared and utilized as a 55:45 mixture of *E/Z* isomers. [d] The reaction was run at 100 °C. [e] The reaction was run at 120 °C. [f] Sixty five percent of the starting materials were recovered.

naphthalene **4** was obtained (entry 3), comparable to the yield obtained from the reaction of aryl halide **1** and diphenylacetylene (entry 1). When 4-octyne, a dialkylacetylene, was allowed to react with aryl halide **1**, a 60 % yield of naphthalene **5** was obtained (entry 4).

To test the regioselectivity of this annulation process, 1-phenylpropyne was allowed to react with aryl halide **1** and a 53:47 mixture of two regioisomers **6** and **7** was obtained in a 75 % overall yield (entry 5). According to our previous work,[9-17] the bulkiness of the substituents on the acetylene plays a major role in determining the regioselectivity of alkyne insertion. The aryl moiety of the arylpalladium intermediate adds preferentially to the less hindered end of the carbon-carbon triple bond. In this naphthalene synthesis, the regioselectivity appears to be significantly lower than we have normally observed in the annulation of unsymmetrical alkynes. Similarly, the reaction of aryl halide **1** and ethyl phenylpropiolate afforded a 76:24 mixture of two regioisomers **8** and **9** (entry 6). In this case, the major product **8** results from aryl addition to the 3-position of the phenylpropiolate. Electronic effects appear to play a major role here. As in most Heck reactions, the aryl group of the initial Pd intermediate is more likely to add to the end of the carbon-carbon multiple bond furthest from the electron-withdrawing ester moiety, which results in naphthalene **8** as the major product.

The reactions of aryl halide **1** and 2-butyne-1,4-diol or 3-phenyl-2-propyn-1-ol failed to afford any recognizable product. It appears that the problem may be transesterification of the ester group by the acetylenic alcohols, which is further supported by the results described later. No recognizable naphthalene products could be obtained when bulky symmetrical or unsymmetrical alkynes, like di-*t*-butylacetylene, phenyl(trimethylsilyl)acetylene and 4,4-dimethyl-2-pentyne, were allowed to react with aryl halide **1**. Presumably, the problem here

is the difficulty in adding the hindered vinylic palladium intermediate across the relatively hindered internal alkene to place three bulky substituents in contiguous positions on the resulting carbocyclic ring.

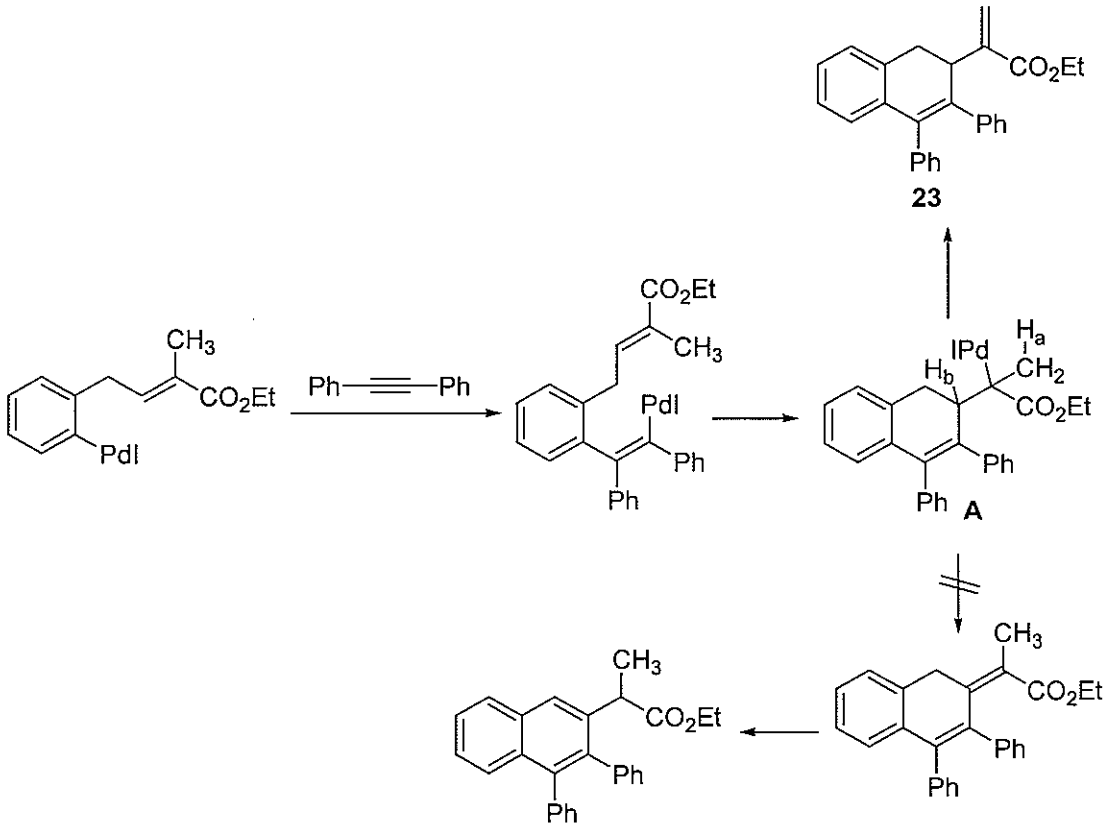
A synthetically interesting question is whether aryl bromides can also undergo this palladium-catalyzed annulation chemistry. To answer this question, compound **10** was prepared and employed in reactions with various alkynes. Generally, compared to the results from aryl iodide **1**, the annulation reactions of aryl bromide **10** with alkynes result in a longer reaction time and lower yields, although the reactions proceed smoothly (entries 7 and 8). The observed lower reactivity of the aryl bromide **10** is consistent with our other annulation chemistry.[9-17] Notice that the reaction of compound **10** and ethyl 2-pentynoate gave a 60:40 mixture of regioisomers **11** and **12** (entry 9).

In order to vary the linkage between the alkene and the iodoarene unit, substrates **13**, **18** and **20** have been prepared and employed in this annulation chemistry. The reaction of aryl iodide **13** and diphenylacetylene afforded a 72 % yield of the expected product (entry10), a little lower than the yield from the reaction of aryl halide **1** and diphenylacetylene (entry 1). When ethyl phenylpropiolate was allowed to react with compound **13**, a 67:33 mixture of regioisomers **15** and **16** was obtained in an 86 % overall yield (entry 11). Comparing the results from entries 6 and 11, it is clear that the introduction of a methyl group into the starting material decreases the regioselectivity of the annulation chemistry. When aryl halide **13** was allowed to react with 2-butyne-1,4-diol, none of desired product was obtain. However, the use of a benzyl protected 2-butyne-1,4-diol resulted in a 56 % yield (entry 12). While compound **13** underwent the annulation chemistry very well and gave good to excellent yields, the annulation reaction of aryl halides **18** and **20** gave none of the desired

products (entries 13 and 14). It is not too surprising that aryl halide **18** was isomerized to the more stable trisubstituted alkene **19** which was isolated in a 48 % yield after 8 h. Note that compound **19**, which is a possible starting material for this annulation chemistry, is relatively unstable under the reaction conditions employed. If the reaction of compound **18** is allowed to proceed for 28 h, compound **19** disappeared and no other significant product was observed. The readily prepared aryl halide **20** may also be undergoing double bond isomerization because no recognizable products could be isolated from its reaction with diphenylacetylene.

It is interesting that the reaction of aryl halide **22** and diphenylacetylene afforded compound **23** in a 73 % yield (entry 15). A mechanism for the formation of product **23** is shown in Scheme 2. From the intermediate **A** that is formed, there are two possible pathways for palladium *ß*-hydride elimination to occur. Intermediate **A** can eliminate H_b on the ring and eventually generate the naphthalene product after isomerization. The other pathway involves elimination of H_a from the methyl group which would afford compound **23** bearing a disubstituted terminal alkene. The result indicates that the elimination of H_a is much faster than that of H_b. This may be because the methyl group has three hydrogens increasing the chances of elimination. Alternatively, when the vinylic palladium iodide adds *cis* to the alkene, H_b is not *syn* to the alkylpalladium iodide generated. To undergo *ß*-hydride elimination, rotation of the C-C bond is necessary before H_b and PdI are aligned *cis* to each other for elimination. Thus, the elimination of H_a may be achieved before this rotation can actually occur.

Scheme 2



To examine whether the geometry of the carbon-carbon double bond affects the annulation process, nitriles **24** and **27**, which are *E*/*Z* isomers, were prepared and allowed to react with 4-octyne and diphenylacetylene (entries 16-19). When 4-octyne was employed, both reactions reached completion in 7 h and afforded very similar yields (entries 16 and 17). The reactions of nitriles **24** and **27** with diphenylacetylene also resulted in very similar yields (entries 18 and 19), although they gave lower yields than the reactions of 4-octyne. Notice that the reactions of diphenylacetylene also required a longer reaction time. This is probably because 4-octyne, which is an electron-rich alkyne, is more reactive than diphenylacetylene.

These results (entries 16-19) indicate that the geometry of the carbon-carbon double bond has little effect on this annulation process.

Since aryl halides bearing electron-deficient olefins work very well in this annulation chemistry, it was important to determine if the introduction of an electron-withdrawing group on the alkene is really necessary to achieve success. To answer this question, compound **28** was prepared and allowed to react with diphenylacetylene. Only a 32 % yield of naphthalene **29** was isolated (entry 20). It appears that the presence of an electron-withdrawing group, which presumably makes the olefin a better acceptor for the Heck reaction, facilitates this chemistry. In this comparision, however, we cannot rule out the possibility that the terminal alkene in aryl iodide **28** may be undergoing intermolecular Heck processes resulting in a lower yield.

The reactions of aryl halide **30,** bearing two methoxy groups on the aromatic ring, with symmetrical alkynes, such as diphenylacetylene, 4-octyne and 1,4-di(benzyloxy)-2-butyne afforded the corresponding naphthalenes **31-33** in 71 %, 73 % and 60 % yields, respectively (entries 21-23). When aryl halide **30** was allowed to react with ethyl phenylpropiolate, two regioisomers **34** (73 %) and **35** (8 % yield) were isolated (entry 24). Comparing this result with that from the reaction of aryl halide **1** and ethyl phenylpropiolate (entry 6), it appears that the introduction of electron-donating substituents, like methoxy groups, onto the arene moiety increases the regioselectivity in this annulation process. The use of a diyne afforded an 83:17 mixture of alkynes **36** and **37** in a 66 % overall yield (entry 25).

The phenyl-substituted aryl iodide **38** has been found to react well with 2-butyne-1,4-diol to produce naphthalene **39** in a 73 % yield (entry 26). This result confirms our suspicion that the earlier problem with alkynols had more to do with transesterification of the ester

group than any inherent problems with the alcohol functionality. Surprisely, only one regioisomer **40** was isolated, when 3-phenyl-2-propyn-1-ol was allowed to react with aryl halide **38** (entry 27), although the yield of 31 % was not very good. The reaction of aryl iodide **38** and ethyl phenylpropiolate afforded two regioisomers **41** (76 %) and **42** (8 %) with a yield and ratio of the two regioisomers similar to those from the reaction of **30** and ethyl phenylpropiolate (entry 24).

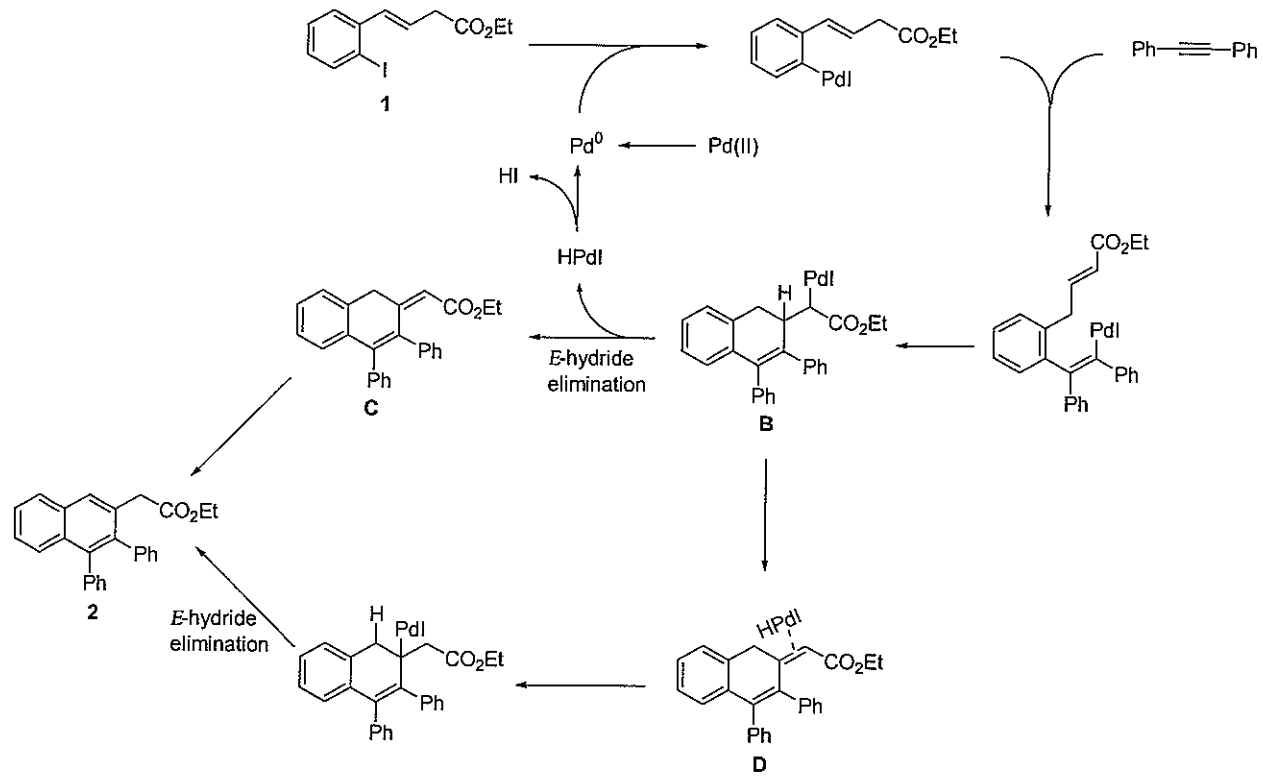
Carbazoles have attracted much attention due to their biological activity[19] and their potential as functional materials,[20] and the synthesis of carbazoles has been extensively studied.[21] Our palladium-catalyzed annulation chemistry provides an alternative, very efficient method to synthesize substituted carbazoles. Iodoindole **43** was first prepared using iodocyclization chemistry currently under investigation in our group.[22] This compound was allowed to react with a variety of alkynes, including symmetrical and unsymmetrical alkynes. While the reactions of 4-octyne, 2-butyne-1,4-diol and 1,4-di(benzyloxy)-2-butyne gave moderate yields ranging from 33 % to 56 %, the use of diphenylacetylene gave only a trace of the desired product (entries 29-32). The failure of the reaction of diphenylacetylene is probably a result of the fact that this alkyne appears to be less reactive than most other alkynes. Notice that for the carbazole synthesis, a higher reaction temperature is also required. There was no reaction at 80 °C when iodoindole **43** was employed. This may indicate that 5,6-fused ring systems are more difficult to form than 6,6-fused ring systems when employing this annulation chemistry. More reactive alkynes, such as ethyl phenylpropiolate and ethyl 2-butynoate have also been allowed to react with iodoindole **43** and better yields have been obtained (entries 33 and 34). The use of ethyl phenylpropiolate gave a 60:40 mixture of regioisomers **48** and **49** in a 91 % overall yield, which indicates that

the electronic effects appear to be more important than steric effects in this system (entry 33). Ethyl 2-butynoate, a less bulky alkyne, was allowed to react with iodoindole **43** and a 82:18 mixture of isomers **50** and **51** was isolated in a 78 % overall yield (entry 34). The results from entries 33 and 34 indicate that both electronic and steric effects play a role in the regioselectivity of the alkyne insertion and the electronic effect apparently outweighs the steric effect.

When compound **52** was allowed to react with two alkynes, the reaction of the more reactive ethyl phenylpropiolate gave a 42 % yield of compound **53** as a single isomer, while use of the less reactive diphenylacetylene results in none of the desired product (entries 35 and 36).

A mechanism for the reaction of aryl halide **1** and diphenylacetylene is proposed in Scheme 3. First of all, Pd(0) oxidatively inserts into the carbon-iodide bond of the aryl iodide to generate an arylpalladium species. Addition of the arylpalladium species to the carbon-carbon triple bond, followed by an intramolecular *cis*-addition to the carbon-carbon double bond, generates an alkylpalladium species **B**. Intermediate **B** can undergo *E*-hydride elimination forming intermediate **C**, which subsequently isomerizes to naphthalene **2**. Alternatively, the intermediate **B** may undergo reversible palladium hydride elimination to an alkene complex **D**, which undergoes readdition of the palladium hydride to the double bond with the opposite regiochemistry. Further palladium hydride elimination would produce the observed aromatic product.

Scheme 3



Conclusions

An efficient synthesis of highly substituted naphthalenes and carbazoles has been developed in which two new carbon-carbon bonds are formed in a single step under relatively mild reaction conditions. Both electronic and steric effects play a role in the regioselectivity of this process and the electronic effect predominates over the steric effect with certain ester-containing alkynes. The introduction of an electron-rich group onto the aryl halide increases the regioselectivity of this annulation process. When this method was employed to synthesize carbazoles, a higher reaction temperature was necessary due to the lower reactivity of the iodoindoles. This method accommodates a variety of functional

groups and generally affords the anticipated highly substituted naphthalenes and carbazoles in good to excellent yields.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise noted. All reagents were used directly as obtained commercially unless otherwise noted. Compounds **20**,[23] **28**,[24] (2-iodophenyl)acetaldehyde,[25] *N*,*N*-dimethylaniline,[26] and 2-iodoindole[27] were prepared according to previous literature procedures. The following starting materials were prepared as indicated.

Preparation of *o*-(2-Alkenyl)aryl halides.

Ethyl (*E*)-4-(2-iodophenyl)-2-butenoate (1). To a suspension solution of (carboethoxymethylene)triphenylphosphorane (5.22 g, 15.0 mmol) in 100 mL of CH_2Cl_2 was added dropwise a solution of 2-iodophenylacetaldehyde[25] (2.46 g, 10.0 mmol) in 20 mL of CH_2Cl_2 at 0 °C under an Ar atmosphere. The resulting mixture was stirred at 25 °C for 3 h and the solvent (CH_2Cl_2) was evaporated under reduced pressure. The solid residue was dissolved in 50 mL of hexane and the mixture was then stirred at 25 °C for 0.5 h. The Ph_3PO was filtered and the solvent (hexane) was removed under the reduced pressure. The oily residue was purified by flash chromatography (10:1 hexane/EtOAc) to afford 2.65 g of the

indicated compound as a colorless oil in an 84% yield: ^{1}H NMR ($CDCl_3$) Γ 1.27 (t, J = 7.2 Hz, 3H), 3.65 (dd, J = 1.5, 6.3 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 5.78 (td, J = 1.8, 15.6 Hz, 1H), 6.94 (dt, J = 1.8, 8.4 Hz, 1H), 7.06 (td, J = 6.3, 15.9 Hz, 1H), 7.19 (dd, J = 1.5, 7.5 Hz, 1H), 7.31 (dt, J = 1.2, 7.5 Hz, 1H), 7.84 (dd, J = 1.2, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.5, 43.5, 60.6, 100.9, 123.2, 128.8, 128.9, 130.2, 139.9, 140.9, 145.8, 166.6; IR (neat, cm^{-1}) 3058, 2978, 2923, 2850, 1717, 1652; HRMS Calcd for $C_{12}H_{13}IO$: 315.9960. Found: 315.9965.

Ethyl (*E*)-4-(2-bromophenyl)-2-butenoate (10). Using the procedure used to prepare aryl halide **1**, 2-bromophenylacetaldehyde[28] (2.01 g, 10.0 mmol) and (carboethoxymethylene)triphenylphosphorane (5.22 g 15.0 mmol) were employed to afford 1.82 g of the indicated compound as a colorless oil in a 68% yield: ^{1}H NMR ($CDCl_3$) Γ 1.27 (t, J = 6.8 Hz, 3H), 3.65 (dd, J = 1.2, 6.4 Hz, 2H), 4.17 (q, J = 7.2 Hz, 2H), 5.78 (td, J = 1.6, 15.6 Hz, 1H), 7.04-7.13 (m, 2H), 7.20 (dd, J = 1.6, 7.6 Hz, 1H), 7.26 (t, J = 7.2 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 38.7, 60.5, 123.1, 127.8, 127.9, 128.7, 130.9, 133.2, 137.5, 145.6, 166.6; IR (neat, cm^{-1}) 3058, 2980, 1719, 1654; HRMS Calcd for $C_{12}H_{13}BrO$: 268.0099. Found: 268.0103.

2-(2-Iodophenyl)propanal. To a suspension of (methoxymethyl)triphenylphosphonium chloride (2.87 g, 8.4 mmol) in dry THF (15 mL) was added KO-*t*-Bu (0.90 g, 8.0 mmol) portionwise under an Ar atmosphere at 25 °C. The resulting red suspension was stirred for 30 min at 25 °C and a solution of 2-iodoacetophenone (0.98 g, 4.0 mmol) in dry THF (5 mL) was added dropwise. After the reaction mixture was stirred at 25 °C for 1 h, the THF was removed under reduced pressure and hexane (30 mL) was added to the residue. The resulting suspension was stirred for 20

min and the Ph_3PO was removed by filtration. The filtrate was collected, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (20:1 hexane/EtOAc) on silica gel to afford 1.10 g of 2-(2-iodophenyl)-1-methoxypropene (*E*/*Z* = 90:10) in a 100 % yield as a yellow oil. To a solution of 2-(2-iodophenyl)-1-methoxypropene (*E*/*Z* = 90:10) (0.55 g, 2.0 mmol) in CH_2Cl_2 (10 mL) was added 1.2 mL of 47 % hydroiodic acid and the mixture was stirred under an Ar atmosphere at 25 °C for 40 min. The reaction was then diluted with 30 mL of CH_2Cl_2 and the excess acid was carefully neutralized by 30 mL of satd aq $NaHCO_3$, during which lots of bubbles were generated. The organic layer was collected, washed with 20 mL of brine, dried over Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (20:1 hexane/EtOAc) on silica gel to afford 0.36 g of 2-(2-iodophenyl)propanal in a 69 % yield as a colorless liquid: ^{1}H NMR ($CDCl_3$) Γ 1.40 (d, *J* = 6.8 Hz, 3H), 4.08 (q, *J* = 6.8 Hz, 1H), 6.99-7.03 (m, 1H), 7.06 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.35-7.39 (m, 1H), 7.93 (dd, *J* = 1.2, 8.0 Hz, 1H), 9.73 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.7, 56.9, 102.3, 128.6, 129.2, 129.5, 140.3, 141.4, 200.5.

Ethyl (*E*)-4-(2-iodophenyl)-2-pentenoate (13). To a suspension of (carboethoxymethylene)triphenylphosphorane (0.69 g, 1.95 mmol) in 5 mL of CH_2Cl_2 was added dropwise a solution of 2-(2-iodophenyl)propanal (0.34 g, 1.3 mmol) in 5 mL of CH_2Cl_2 at 0 °C under an Ar atmosphere. The resulting mixture was stirred at 25 °C for 3 h and the solvent (CH_2Cl_2) was evaporated under reduced pressure. The solid residue was dissolved in 20 mL of hexane and the mixture was then stirred at 25 °C for 0.5 h. The Ph_3PO was filtered and the solvent was removed under reduced pressure. The oily residue was purified by flash chromatography (20:1 hexane/EtOAc) to afford 0.41 g of the indicated

compound as a colorless oil in a 95 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.28 (t, J = 7.2 Hz, 3H), 1.39 (d, J = 7.2 Hz, 3H), 3.97-4.04 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 5.84 (dd, J = 2.0, 16.0 Hz, 1H), 6.90-6.95 (m, 1H), 9.08 (dd, J = 5.6, 16.0 Hz, 1H), 7.15 (dd, J = 1.6, 8.0 Hz, 1H), 7.30-7.34 (m, 1H), 7.85 (dd, J = 1.2, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.5, 19.7, 45.9, 60.6, 101.3, 121.0, 127.9, 128.8, 129.0, 140.0, 145.8, 151.3, 166.9; IR (neat, cm^{-1}) 3058, 2976, 2933, 2902, 1716, 1465; HRMS Calcd for $C_{13}H_{15}IO_2$: 330.0117. Found: 330.0123.

(2-Iodophenyl)phenylacetaldehyde. To a suspension of (methoxymethyl)triphenylphosphonium chloride (5.76 g, 16.8 mmol) in dry THF (25 mL) was added KO-*t*-Bu (1.80 g, 16.0 mmol) portionwise under an Ar atmosphere at 25 °C. The resulting reddish suspension was stirred for 30 min at 25 °C and a solution of 2-iodobenzophenone (2.46 g, 8.0 mmol) in THF (10 mL) was added dropwise. After the reaction mixture was stirred at 25 °C for 1 h, the solvent was removed under reduced pressure and hexane (50 mL) was added to the residue. The suspension was stirred for 20 min and the Ph_3PO was removed by filtration. The filtrate was collected, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (10:1 hexane/EtOAc) on silica gel to afford 2.68 g of 1-(2-iodophenyl)-2-methoxy-1-phenylethene (E/Z = 61:39) in 100 % yield as a pale yellow oil. To a solution of 1-(2-iodophenyl)-2-methoxy-1-phenylethene (E/Z = 61:39) (1.68 g, 5.0 mmol) in CH_2Cl_2 (15 mL) was added 3.0 mL of 47 % hydroiodic acid and the mixture was stirred under an Ar atmosphere at 25 °C for 3 h. Then the excess acid was carefully destroyed by 60 mL of satd aq $NaHCO_3$, during which lots of bubbles were generated. The organic layer was collected, washed with 50 mL of brine, dried over Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (15:1 hexane/EtOAc) on silica

gel to afford 0.91 g of (2-iodophenyl)phenylacetaldehyde in a 57 % yield as a pale yellow oil: ^{1}H NMR ($CDCl_3$) Γ 5.39 (s, 1H), 6.98-7.02 (m, 1H), 7.12 (dd, J = 1.6, 7.6 Hz, 1H), 7.22-7.24 (m, 2H), 7.30-7.40 (m, 4H), 7.92 (dd, J = 1.2, 8.0 Hz, 1H), 9.98 (d, J = 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 68.1, 102.7, 128.0, 128.7, 129.2, 129.5, 129.7, 130.3, 135.4, 139.8, 140.4, 198.1.

Ethyl (*E*)-4-(2-iodophenyl)-4-phenyl-2-butenoate (18). Using the procedure used to prepare aryl halide **13,** (2-iodophenyl)phenylacetaldehyde (0.84 g, 2.6 mmol) and (carboethoxymethylene)triphenylphosphorane (1.36 g, 3.9 mmol) were employed to afford 1.01 g of the indicated compound in a 100 % yield as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ1.28 (t, J = 7.2 Hz, 3H), 4.19 (q, J = 7.2 Hz, 2H), 5.27 (dd, J = 1.6, 6.0 Hz, 1H), 5.64 (dd, J = 1.6, 15.6 Hz, 1H), 6.93-6.97 (m, 1H), 7.11 (dd, J = 1.6, 7.6 Hz, 1H), 7.15-7.17 (m, 2H), 7.23-7.38 (m, 5H), 7.87 (dd, J = 1.2, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.5, 57.2, 60.7, 102.1, 123.8, 127.2, 128.7, 128.8, 129.0, 129.2, 130.1, 140.2, 140.4, 144.0, 149.2, 166.6; IR (neat, cm^{-1}) 3060, 2980, 1716, 1650, 1494; HRMS Calcd for $C_{18}H_{17}IO_2$: 392.0273. Found: 392.0279.

Ethyl (*E*)-4-(2-iodophenyl)-2-methyl-2-butenoate (22). Using the procedure used to prepare aryl halide **13,** (2-iodophenyl)acetaldehyde[25] (0.89 g, 3.6 mmol) and (carboethoxyethylene)triphenylphosphorane (1.67 g, 4.3 mmol) were employed to afford 1.19 g of the indicated compound in a 100 % yield as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 1.29 (t, J = 7.2 Hz, 3H), 1.97-1.98 (m, 3H), 3.62 (d, J = 7.5 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 6.78-6.84 (m, 1H), 6.90-6.95 (m, 1H), 7.18 (dd, J = 1.5, 7.5 Hz, 1H), 7.27-7.32 (m, 1H), 7.84 (dd, J = 1.2, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.1, 14.5, 40.4, 60.8, 100.8, 128.5, 128.8,

129.5, 129.7, 138.8, 139.8, 142.2, 168.2; IR (neat, cm^{-1}) 3054, 2979, 2930, 1708, 1648, 1251; HRMS Calcd for $C_{13}H_{15}IO_2$: 330.0117. Found: 330.0123.

(*Z*)-4-(2-Iodophenyl)-2-butenenitrile (24). Using the procedure used to prepare aryl halide **1,** 2-iodophenylacetaldehyde[25] (2.46 g, 10.0 mmol) and (triphenylphosphoranylidene)acetonitrile (4.52 g 15.0 mmol) were employed to afford 1.02 g of aryl halide **24** as a colorless oil in a 38 % yield and 1.10 g of aryl halide **27** as a colorless oil in a 41 % yield. Aryl halide **24**: ^{1}H NMR ($CDCl_3$) Γ 3.88 (d, J = 11.2 Hz, 2H), 5.47 (td, J = 1.2, 12.0 Hz, 1H), 6.60 (td, J = 7.6, 10.8 Hz, 1H), 6.97 (dt, J = 1.6, 7.6 Hz, 1H), 7.25 (dd, J = 1.2, 8.0 Hz, 1H), 7.33 (dt, J = 1.2, 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 43.1, 100.3, 100.9, 116.1, 129.1, 129.1, 130.1, 139.9, 140.2, 151.5; IR (neat, cm^{-1}) 3062, 2219, 1619; HRMS Calcd for $C_{10}H_8IN$: 268.9702. Found: 268.9705.

(*E*)-4-(2-Iodophenyl)-2-butenenitrile (27). ^{1}H NMR ($CDCl_3$) Γ 3.67 (dd, J = 2.4, 8.0 Hz, 2H), 5.25 (td, J = 2.8, 22.0 Hz, 1H), 6.84 (td, J = 8.4, 29.6 Hz, 1H), 6.98 (dt, J = 2.0, 16.0 Hz, 1H), 7.17 (dd, J = 2.0, 10.0 Hz, 1H), 7.34 (dt, J = 1.6, 10.0 Hz, 1H), 7.86 (dd, J = 1.6, 10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 44.3 100.7, 101.7, 117.4, 129.1, 129.3, 130.2, 139.4, 140.1, 152.5; IR ($CHCl_3$, cm^{-1}) 3017, 2224, 1631; HRMS Calcd for $C_{10}H_8IN$: 268.9702. Found: 268.9705.

(2-Iodo-4,5-dimethoxyphenyl)acetaldehyde. To a solution of (2-iodo-4,5-dimethoxyphenyl)acetic acid[29] (14.5 mmol) in dried THF (50 mL) was added dropwise 8.0 mL of 2.0 M $BH_3{\cdot}SMe_2$ (16.0 mmol) in THF at 0 °C. Considerable gas was generated during addition of the $BH_3{\cdot}SMe_2$. The resulting mixture was stirred for 12 h at 25 °C and the solvent was removed under reduced pressure to afford crude 2-(2-iodo-4,5-dimethoxyphenyl)ethanol.

DMSO (2.06 mL, 31.9 mmol) was added dropwise into a solution of $(COCl_2)_2$ (1.39 mL, 16.0 mmol) in CH_2Cl_2 (20 mL) at – 60 °C ($CHCl_3$ and dry ice), in which considerable gas was generated. The colorless mixture was stirred for 10 min at – 60 °C. Then, a solution of the crude 2-(2-iodo-4,5-dimethoxyphenyl)ethanol in 10 mL CH_2Cl_2 was added dropwise to the reaction vessel and the reaction mixture turned a cloudy white. The resulting reaction mixture was further stirred for 30 min at – 60 °C and Et_3N (72.5 mmol) was added. After being stirred for 10 min, the reaction mixture was then diluted with water (50 mL) at – 60 °C, warmed up to 25 °C, washed with 1N HCl (50 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The extracts were combined and dried over Na_2SO_4. The solvent was removed and the liquid chromatographed (3:1 hexane/EtOAc) to afford 1.11 g of the desired compound as a yellow solid in a 25 % overall yield: mp 53-56 °C; ^{1}H NMR ($CDCl_3$) Γ 3.82 (s, 2H), 3.85 (s, 3H), 3.87 (s, 3H), 6.71 (s, 1H), 7.28 (s, 1H), 9.74 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 54.5, 56.2, 56.4, 89.1, 113.6, 122.0, 128.4, 149.2, 149.9, 198.9.

Ethyl (*E*)-4-(2-iodo-4,5-dimethoxyphenyl)-2-butenoate (30). Using the procedure used to prepare aryl iodide **1,** (2-iodo-4,5-dimethoxyphenyl)acetaldehyde (1.53 g, 5.0 mmol) and (carboethoxymethylene)triphenylphosphorane (2.61 g, 7.5 mmol) were employed to afford 1.37 g of the indicated compound as a pale yellow oil in a 73% yield: ^{1}H NMR ($CDCl_3$) Γ 1.28 (t, J = 6.8 Hz, 3H), 3.59 (dd, J = 2.0, 6.0 Hz, 2H), 3.85 (s, 3H), 3.86 (s, 3H), 4.18 (q, J = 7.2 Hz, 2H), 5.76 (td, J = 1.6, 15.6 Hz, 1H), 6.69 (s, 1H), 7.01 (td, J = 9.2, 21.6 Hz, 1H), 7.23 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 43.1, 56.2, 56.4, 60.5, 88.5, 112.7, 121.9, 122.8, 133.1, 146.1, 148.6, 149.8, 166.7; IR (neat, cm^{-1}) 2977, 2904, 2839, 1715, 1651; HRMS Calcd for $C_{14}H_{17}IO_4$: 376.0171. Found: 376.0177.

1-(2-Iodo-4,5-dimethoxyphenyl)-3-phenylpropene (38). To a white suspension of benzyltriphenylphosphonium chloride (2.92 g, 7.5 mmol) in 100 mL of dried THF was added dropwise 2.5 M of *n*-BuLi (3.0 mL, 7.5 mmol) at 0 °C. The resulting reddish solution was then warmed up to 25 °C and stirred for 30 min before use. Using the procedure used to prepare aryl iodide **1**, (2-iodo-4,5-dimethoxyphenyl)acetaldehyde (1.53 g, 5.0 mmol) and (phenylmethylene)triphenylphosphorane (7.5 mmol) were employed to afford 1.71 g of a 55:45 mixture of *E*/*Z* stereoisomers as a colorless oil in a 90 % overall yield: ^{1}H NMR ($CDCl_3$) Γ 3.59 (dd, J = 1.2, 6.0 Hz, 2H), 3.69 (dd, J = 2.0, 7.2 Hz, 2H), 3.80 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 5.76 (td, J = 6.4, 11.2 Hz, 1H), 6.29 (td, J = 6.4, 16.0 Hz, 1H), 6.44 (d, J = 16.0 Hz, 1H), 6.64 (d, J = 11.6 Hz, 1H), 6.73 (s, 1H), 6.77 (s, 1H), 7.18-7.39 (m, 12H); additional ^{13}C NMR ($CDCl_3$) Γ 39.8, 44.0, 56.1, 56.2, 56.4, 88.3, 88.5, 112.2, 112.7, 121.8, 126.3, 126.3, 126.4, 127.1, 127.4, 128.0, 128.5, 128.7, 128.7, 128.9, 130.0, 130.8, 131.7, 135.3, 136.0, 137.3, 137.6, 148.1, 148.2, 149.6, 149.7 (one sp^3 carbon from one of the methoxy groups is missing due to overlap); IR (neat, cm^{-1}) 3079, 3055, 3002, 2933, 2905, 2837, 1596, 1567; HRMS Calcd for $C_{17}H_{17}IO_2$: 380.0273. Found: 380.0280.

(*E*)-1-Phenyl-1-penten-4-yne. To a stirred mixture of cinnamyl bromide (1.97 g, 10.0 mmol) and CuCl (0.099 g, 1.0 mmol) in dry THF (40 mL) was added dropwise a solution of ethynylmagnesium bromide in THF (0.5 M, 20 mL) at 25 °C. The resulting mixture was then stirred at 25 °C for 5 min and at 50 °C for 14 h. It was allowed to cool to room temperature and washed with 50 mL of brine. The organic layer was collected, dried over Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The oily residue was purified by flash chromatography (hexane) on silica gel to afford 0.67 g (47 % yield) of the indicated compound as a colorless liquid: ^{1}H NMR ($CDCl_3$) Γ 2.18 (t, J = 2.4 Hz, 1H), 3.13-3.15 (m,

2H), 6.16 (td, J = 5.6, 16.0 Hz, 1H), 6.67 (d, J = 16.0 Hz, 1H), 7.22-7.24 (m, 1H), 7.29-7.32 (m, 2H), 7.36-7.38 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 22.2, 70.9, 81.4, 123.8, 126.5, 127.6, 128.7, 131.8, 137.2.

***N,N*-Dimethyl-2-(*E*-5-phenyl-4-penten-1-ynyl)aniline.** To a solution of $PdCl_2(PPh_3)_2$ (42.1 mg, 0.06 mmol), *N,N*-dimethyl-2-iodoaniline[26] (0.74 g, 3.0 mmol) and (*E*)-1-phenyl-1-penten-4-yne (0.51 g, 3.6 mmol) in Et_3N (15 mL) was added CuI (5.71 mg, 0.03 mmol). The resulting mixture was stirred for 10 min under an Ar atmosphere and was heated to 50 °C. After 6 h, the reaction was allowed to cool to 25 °C. The ammonium salt was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (20:1 hexane/EtOAc) on silica gel to afford 0.64 g (92 % yield) of the indicated compound as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 2.93 (s, 6H), 3.44 (dd, J = 2.0, 5.6 Hz, 2H), 6.27 (td, J = 5.6, 16.0 Hz, 1H), 6.76 (d, J = 16.0 Hz, 1H), 6.86-6.90 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 7.20-7.25 (m, 2H), 7.29-7.33 (m, 2H), 7.37-7.39 (m, 2H), 7.43 (dd, J = 1.6, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.7, 43.9, 82.1, 92.2, 116.4, 117.3, 121.0, 124.6, 126.4, 127.5, 128.7, 128.9, 131.6, 134.6, 137.4, 155.0.

3-Iodo-1-methyl-2-[*E*-3-phenylpro-2-enyl]-1*H*-indole (43). To a solution of *N,N*-dimethyl-2-(*E*-5-phenyl-4-penten-1-ynyl)aniline (0.58 g, 2.2 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of I_2 (0.67 g, 1.2 equiv) in CH_2Cl_2 (15 mL) under an Ar atmosphere at 25 °C. The reaction mixture was stirred at 25 °C for 3 h and diluted with 30 mL of CH_2Cl_2. The excess I_2 was destroyed by adding 50 mL of satd aq $Na_2S_2O_3$. The organic layer was washed with 50 mL of brine, dried over Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (10:1 hexane/EtOAc) to afford 0.73 g of the indicated compound as a

yellow solid: mp 85-87 °C; ^{1}H NMR ($CDCl_3$) Γ 3.72 (s, 3H), 3.79 (dd, J = 1.2, 5.6 Hz, 2H), 6.24 (td, J = 5.6, 16.0 Hz, 1H), 6.33 (d, J = 16.0 Hz, 1H), 7.17-7.31 (m, 8H), 7.43 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 31.0, 59.0, 109.5, 120.5, 121.0, 122.4, 125.4, 126.3, 127.6, 128.7, 130.1, 131.8, 137.1, 137.8, 138.8 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3055, 3025, 2929, 1674, 1386; HRMS Calcd for $C_{18}H_{16}IN$: 373.0328. Found: 373.0332.

2-Iodo-1-(*E*-3-phenylprop-2-enyl)-1*H*-indole (52). To a suspension of NaH (0.18 g, 4.5 mmol) in dry DMF (15 mL) was added dropwise a solution of 2-iodoindole[27] (0.73 g, 3.0 mmol) in THF (10 mL) at 0 °C, during which lots of bubbles were generated. The resulting yellow suspension was stirred at 0 °C for 1 h and a solution of cinnamyl bromide (0.59 g, 3.0 mmol) in dry THF (2 mL) was added dropwise at 0 °C. After the reaction mixture was stirred at 0 °C for 20 min, it was warmed up to 25 °C, diluted with 50 mL of Et_2O, and washed with 50 mL of brine. The organic layer was collected, dried over Na_2SO_4, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (30:1 hexane/EtOAc) on silica gel to afford 0.61 g of the compound **52** as a white solid: mp 99-101 °C; ^{1}H NMR ($CDCl_3$) Γ 4.95 (d, J = 4.8 Hz, 2H), 6.24 (td, J = 4.8, 16.0 Hz, 1H), 6.36 (d, J = 16.0 Hz, 1H), 6.84 (s, 1H), 7.07-7.11 (m, 1H), 7.12-7.16 (m, 1H), 7.21-7.29 (m, 5H), 7.35 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 7.6 Hz 1H); ^{13}C NMR ($CDCl_3$) Γ 49.2, 83.3, 110.1, 112.6, 119.8, 120.2, 122.1, 124.3, 126.7, 128.0, 128.7, 130.1, 132.4, 136.4, 137.7; IR ($CHCl_3$, cm^{-1}) 3077, 3019, 2913, 1455, 1434; HRMS Calcd for $C_{17}H_{14}IN$: 359.0171. Found: 359.0179.

General procedure for preparation of the naphthalenes and carbazoles. To a mixture of the alkyne (0.50 mmol), $Pd(OAc)_2$ (2.8 mg, 0.025 mmol), PPh_3 (6.6 mg, 0.05

mmol), and Et_3N (55.0 mg, 0.5 mmol) in 2 mL of DMF was added dropwise a solution of the aryl halide (0.25 mmol) in 1 mL of DMF. The resulting mixture was then stirred under an Ar atmosphere at the indicated temperature (see Table 2 in the text). The reaction was monitored by TLC to establish completion. When the reaction was complete, the reaction mixture was allowed to cool to 25 °C, poured into brine (25 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were concentrated and the residue was purified by column chromatography on silica gel to afford the corresponding naphthalene(s) or carbazole(s).

Ethyl (1,2-diphenylnaphth-3-yl)acetate (2). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 79 mg or 69 mg of the indicated product as a white solid in an 86 % (entry 1) or a 75 % (entry 7) yield, respectively: mp 85-87 °C; ^{1}H NMR ($CDCl_3$) Γ 1.15 (t, J = 7.2 Hz, 3H), 3.61 (s, 2H), 4.02 (q, J = 7.2 Hz, 2H), 7.02 (d, J = 6.8 Hz, 2H), 7.09-7.22 (m, 8H), 7.35 (t, J = 7.6 Hz, 1H), 7.45-7.49 (m, 2H), 7.85 (s, 1H), 7.87 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 40.5, 60.9, 126.1, 126.2, 126.6, 126.7, 127.0, 127.6, 127.7, 127.8, 128.9, 130.6, 131.2, 132.2, 133.0, 139.4, 139.5, 139.6, 139.8, 172.1 (one sp^2 carbon is missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3056, 3021, 2982, 2933, 1950, 1731, 1601; HRMS Calcd for $C_{26}H_{22}O_2$: 366.1620. Found: 366.1620.

Ethyl [1,2-di(4-methoxyphenyl)naphth-3-yl]acetate (3). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford 65 mg of the indicated compound as a yellow oil in a 61 % yield: ^{1}H NMR ($CDCl_3$) Γ 1.15 (t, J = 7.2 Hz, 3H), 3.61 (s, 2H), 3.74 (s, 3H), 3.77 (s, 3H), 4.02 (q, J = 9.6 Hz, 2H), 6.69-6.77 (m, 2H), 6.93 (dd, J = 2.8, 8.8 Hz, 2H), 7.00 (dd, J = 1.6, 11.2 Hz, 2H), 7.34 (dt, J = 1.6, 9.2 Hz, 1H), 7.45-7.51 (m, 2H), 7.82 (s, 1H), 7.86 (d, J = 10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 40.6, 55.2, 55.3, 60.7, 113.2,

113.2, 126.0, 126.1, 127.1, 127.8, 128.6, 131.6, 131.8, 132.1, 132.3, 132.6, 132.9, 139.4, 139.6, 158.1, 172.2 (two sp^2 carbons are missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3015, 2958, 2933, 2836, 1893, 1731, 1609; HRMS Calcd for $C_{28}H_{26}O_4$: 426.1831. Found: 426.1837.

Ethyl [1,2-di(4-ethoxycarbonylphenyl)naphth-3-yl]acetate (4). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 106 mg of the indicated compound as a yellow oil in an 83 % yield: ^1H NMR ($CDCl_3$) Γ 1.14 (t, J = 7.2 Hz, 3H), 1.38 (t, J = 6.8 Hz, 3H), 1.38 (t, J = 7.2 Hz, 3H), 3.58 (s, 2H), 4.01 (q, J = 7.2 Hz, 2H), 4.32-4.38 (m, 4H), 7.13 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.35-7.40 (m, 2H), 7.48-7.52 (m, 1H), 7.85-7.91 (m, 6H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 14.5, 40.2, 61.0, 61.1, 126.6, 126.6, 126.7, 128.0, 129.1, 129.1, 129.6, 130.5, 130.6, 131.1, 131.6, 133.1, 138.3, 138.4, 144.0, 144.3, 166.5, 166.6, 171.7 (two sp^3 carbons from ethoxy groups and two sp^2 carbons are missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3021, 2983, 2937, 2906, 2872, 1716, 7608; HRMS Calcd for $C_{32}H_{30}O_6$: 510.2042. Found: 510.2049.

Ethyl (1,2-di-*n*-propylnaphth-3-yl)acetate (5). The reaction mixture was chromatographed using 20:1 hexane/EtOAc to afford 45 mg or 35 mg of the indicated product as a yellow in a 60 % (entry 4) or a 46 % (entry 8) yield, respectively: ^1H NMR ($CDCl_3$) Γ 1.08 (t, J = 7.5 Hz, 3H), 1.11 (t, J = 7.5 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.48-1.61 (m, 2H), 1.62-1.75 (m, 2H), 2.74-2.79 (m, 2H), 3.01-3.06 (m, 2H), 3.80 (s, 2H), 4.16 (q, J = 7.2 Hz, 2H), 7.35-7.46 (m, 2H), 7.57 (s, 1H), 7.73 (dd, J = 1.5, 8.4 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 15.0, 24.5, 24.7, 31.2, 32.4, 40.1, 61.0, 124.2, 125.0, 125.8, 128.3, 128.5, 131.5, 131.9, 132.5, 136.7, 137.0, 172.2 (one sp^3 carbon is missing due

to overlap); IR (neat, cm^{-1}) 3069, 2958, 2870, 1735, 1597; HRMS Calcd for $C_{20}H_{26}O_2$: 298.1933. Found: 298.1937.

Ethyl (1-methyl-2-phenylnaphth-3-yl)acetate (6) and ethyl (2-methyl-1-phenylnaphth-3-yl)acetate (7). The reaction mixture was chromatographed using 20:1 hexane/EtOAc to afford 57 mg of a 53:47 mixture of regioisomers **6/7** as determined by ^1H NMR spectral analysis of the yellow oil in a 75 % overall yield. ^1H NMR ($CDCl_3$) for the major regioisomer **6**: Γ 1.26 (t, J = 7.2 Hz, 3H), 2.16 (s, 3H), 3.86 (s, 2H), 4.19 (q, J = 7.2 Hz, 2H), 7.20-7.52 (m, 8H), 7.73 (s, 1H), 7.79 (d, J = 4.8 Hz, 1H). ^1H NMR ($CDCl_3$) for the minor regioisomer **7**: Γ 1.13 (t, J = 7.2 Hz, 3H), 2.37 (s, 3H), 3.51 (s, 2H), 3.99 (q, J = 7.2 Hz, 2H), 7.20-7.52 (m, 7H), 7.67 (s, 1H), 7.83 (dd, J = 1.2, 4.8 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) for the mixture Γ 14.3, 14.4, 16.8, 17.7, 40.6, 40.6, 60.8, 61.1, 124.6, 125.3, 125.8, 125.9, 126.2, 126.5, 127.2, 127.2, 127.3, 127.6, 128.4, 128.5, 128.6, 128.9, 129.9, 130.4, 131.2, 131.9, 132.0, 132.2, 132.5, 132.6, 132.9, 132.9, 139.3, 139.8, 140.4, 140.8, 171.9, 172.1; IR (neat, cm^{-1}) for the mixutre 3056, 3022, 2981, 2934, 2870, 1731, 1599, 1572; HRMS Calcd for $C_{21}H_{20}O_2$: 304.1463. Found: 304.1467.

Ethyl (2-ethoxycarbonyl-1-phenylnaphth-3-yl)acetate (8) and ethyl (1-ethoxycarbonyl-2-phenylnaphth-3-yl)acetate (9). The reaction mixture was chromatographed using 7:1 hexane/EtOAc to afford 80 mg of a 76:24 mixture of regioisomers **8/9** as determined by ^1H NMR spectroscopy of the yellow oil in an 88 % overall yield. ^1H NMR ($CDCl_3$) for the major regioisomer **8**: Γ 0.87 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 6.8 Hz, 3H), 3.94 (s, 2H), 3.95 (q, J = 7.2 Hz, 2H), 4.16 (q, J = 6.8 Hz, 2H), 7.28-7.59 (m, 8H), 7.79-7.87 (m, 2H). ^1H NMR ($CDCl_3$) for the minor regioisomer **9**: Γ 0.91 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 6.8 Hz, 3H), 3.61 (s, 2H), 3.98-4.10 (m, 4H), 7.28-7.59 (m, 8H), 7.79-

7.87 (m, 2H). ^{13}C NMR ($CDCl_3$) for the mixture Γ 13.6, 13.8, 14.2, 14.3, 39.7, 39.7, 60.9, 61.0, 61.1, 61.2, 125.0, 126.7, 127.0, 127.2, 127.3, 127.7, 127.8, 127.9, 128.0, 128.1, 128.1, 128.5, 129.0, 129.6, 129.8, 130.3, 130.8, 130.9, 131.4, 131.8, 132.3, 132.7, 133.7, 138.3, 138.4, 138.5, 139.2, 169.0, 169.2, 171.3, 171.5 (one sp^2 carbon is missing due to overlap); IR (neat, cm^{-1}) for the mixutre 3057, 2981, 2936, 2903, 2872, 1731, 1622, 1596; HRMS Calcd for $C_{23}H_{22}O_4$: 362.1518. Found: 362.1522.

Ethyl 3-(2-ethoxy-2-oxoethyl)-1-ethyl-2-naphthoate (11) and ethyl 3-(2-ethoxy-2-oxoethyl)-2-ethyl-1-naphthoate (12). The reaction mixture was chromatographed using 7:1 hexane/EtOAc to afford 41 mg (52 % yield) of a 60:40 mixture of regioisomers **11/12** as determined by ^{1}H NMR spectroscopic analysis of the yellow oil. ^{1}H NMR ($CDCl_3$) for the major regioisomer **11**: Γ 1.22-1.27 (m, 3H), 1.34-1.48 (m, 6H), 3.09 (q, J = 7.5 Hz, 2H), 3.81 (s, 2H), 4.16 (q, J = 7.2 Hz, 2H), 4.44 (q, J = 7.2 Hz, 2H), 7.41-7.56 (m, 2H), 7.64 (s, 1H), 7.76-7.82 (m, 1H), 8.05-8.09 (m, 1H). ^{1}H NMR ($CDCl_3$) for the minor regioisomer **12**: Γ 1.22-1.27 (m, 6H), 1.34-1.48 (m, 3H), 2.82 (q, J = 7.5 Hz, 2H), 3.83 (s, 2H), 4.17 (q, J = 7.2 Hz, 2H), 4.54 (q, J = 7.2 Hz, 2H), 7.41-7.56 (m, 2H), 7.68-7.71 (m, 1H), 7.76-7.82 (m, 2H). ^{13}C NMR ($CDCl_3$) for the mixture Γ 14.4, 14.4, 14.4, 14.6, 15.5, 15.9, 24.2, 24.7, 39.0, 40.0, 61.2, 61.3, 61.5, 61.6, 124.5, 124.6, 126.0, 126.7, 126.9, 127.0, 128.0, 128.2, 128.6, 128.8, 129.6, 130.7, 131.0, 131.5, 131.6, 131.8, 132.0, 134.1, 137.9, 138.7, 170.0, 170.2, 171.3, 171.6; IR (neat, cm^{-1}) for the mixture 3060, 2979, 2937, 1728, 1449; HRMS Calcd for $C_{19}H_{22}O_4$: 314.1518. Found: 314.1522.

Ethyl (1-methyl-3,4-diphenyl-2-naphthyl)acetate (14). The reaction mixture was chromatographed using 30:1 hexane/EtOAc to afford 68 mg (72 % yield) of the indicated compound as a white solid: mp 80-82 °C; ^{1}H NMR ($CDCl_3$) Γ 1.18 (t, J = 7.1 Hz, 3H), 2.72

(s, 1H), 3.69 (s, 2H), 4.08 (q, J = 7.1 Hz, 2H), 7.01-7.21 (m, 10H), 7.32-7.38 (m, 1H), 7.48-7.54 (m, 2H), 8.16 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 15.8, 38.0, 60.8, 124.3, 125.8, 126.0, 126.4, 126.6, 127.6, 127.7, 127.7, 129.3, 130.5, 131.3, 132.1, 132.3, 133.0, 137.5, 139.9, 140.1, 141.0, 171.9; IR ($CHCl_3$, cm^{-1}) 3018, 1729, 1216; HRMS Calcd for $C_{27}H_{24}O_2$: 380.1776. Found: 380.1781. Anal. Calcd: C, 85.22; H, 6.35. Found: C, 84.83; H, 6.49.

Ethyl 3-(2-ethoxy-2-oxoethyl)-4-methyl-1-phenyl-2-naphthoate (15) and ethyl 3-(2-ethoxy-2-oxoethyl)-4-methyl-2-phenyl-1-naphthoate (16). The reaction mixture was chromatographed using 7:1 hexane/EtOAc to afford 64 mg (86 % yield) of a 67:33 mixture of regioisomers **15/16** as determined by ^{1}H NMR spectroscopic analysis of the yellow oil. ^{1}H NMR ($CDCl_3$) for the major regioisomer **15**: Γ 0.89 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 3.95 (s, 2H), 3.96 (q, J = 7.2 Hz, 2H), 4.14 (q, J = 7.2 Hz, 2H), 7.26-7.59 (m, 8H), 8.12-8.14 (m, 1H). ^{1}H NMR ($CDCl_3$) for the minor regioisomer **16**: Γ 0.91 (t, J = 7.2 Hz, 3H), 1.18 (t, J = 7.2 Hz, 3H), 3.67 (s, 2H), 4.02 (q, J = 7.2 Hz, 2H), 4.08 (q, J = 7.2 Hz, 2H), 7.26-7.59 (m, 7H), 7.85-7.87 (m, 1H), 8.12-8.14 (m, 1H). ^{13}C NMR ($CDCl_3$) for the mixture Γ 13.7, 13.9, 14.4, 14.4, 15.5, 15.9, 37.1, 37.5, 60.9, 61.1, 61.1, 61.2, 124.5, 124.6, 125.7, 125.9, 126.2, 126.6, 126.9, 127.0, 127.7, 127.7, 127.8, 128.1, 128.1, 128.8, 129.1, 129.9, 130.7, 130.8, 131.5, 132.1, 133.1, 133.2, 133.9, 135.5, 136.4, 138.5, 138.6, 139.6, 169.5, 169.9, 171.0, 171.5; IR (neat, cm^{-1}) for the mixture 3059, 2980, 2937, 1717, 1228; HRMS Calcd for $C_{24}H_{24}O_4$: 376.1675. Found: 376.1680.

Ethyl {3,4-bis[(benzyloxy)methyl]-1-methyl-2-naphthyl}acetate (17). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 65 mg of the indicated compound as a yellow solid in a 56 % yield: mp 82-83 °C; ^{1}H NMR ($CDCl_3$) Γ 1.18 (t, J =

7.2 Hz, 3H), 2.64 (s, 3H), 4.01 (s, 2H), 4.05 (q, J = 7.2 Hz, 2H), 4.49 (s, 2H), 4.55 (s, 2H), 4.70 (s, 2H), 4.91 (s, 2H), 7.23-7.36 (m, 10H), 7.47-7.50 (m, 2H), 8.04-8.07 (m, 1H), 8.11-8.14 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 15.8, 36.2, 60.9, 65.4, 66.6, 72.8, 72.9, 124.7, 125.3, 126.1, 126.2, 128.0, 128.3, 128.4, 128.6, 128.6, 130.4, 131.6, 132.2, 133.2, 134.4, 134.9, 138.2, 138.4, 171.7 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3065, 3026, 2975, 2867, 1728, 1326; HRMS Calcd for $C_{31}H_{32}O_4$: 468.2301. Found: 468.2312.

Ethyl *E*-4-(2-iodophenyl)-4-phenyl-3-butenoate (19). The reaction mixture was chromatographed using 15:1 hexane/EtOAc to afford 47 mg (48 % yield) of the indicated compound as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.25 (t, J = 7.2 Hz, 3H), 2.92 (dd, J = 8.0, 16.4 Hz, 1H), 3.05 (dd, J = 6.4, 16.4 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 6.44-6.47 (m, 1H), 7.02-7.06 (m, 1H), 7.19 (dd, J = 1.6, 7.6 Hz, 1H), 7.24-7.30 (m, 5H), 7.39-7.43 (m, 1H), 7.92 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.5, 35.6, 60.9, 100.0, 121.7, 126.8, 127.7, 128.5, 128.6, 129.2, 130.8, 139.4, 139.7, 144.1, 146.0, 171.6; IR (neat, cm^{-1}) 3059, 2981, 1717; HRMS Calcd for $C_{18}H_{17}IO_2$: 392.0273. Found: 392.0279.

Ethyl 2-(3,4-diphenyl-1,2-dihydronaphthalen-2-yl)acrylate (23). The reaction mixture was chromatographed using 15:1 hexane/EtOAc to afford 69 mg (73 % yield) of the indicated compound as a yellow solid: mp 135-137 °C; ^{1}H NMR ($CDCl_3$) Γ 1.31 (t, J = 7.2 Hz, 3H), 2.99 (dd, J = 2.4, 16.0 Hz, 1H), 3.47 (dd, J = 7.2, 16.0 Hz, 1H), 4.01 (dd, J = 1.6, 7.2 Hz, 1H), 4.20-4.25 (m, 2H), 5.80-5.81 (m, 1H), 6.28 (d, J = 1.2 Hz, 1H), 6.80 (d, J = 7.6 Hz, 1H), 7.00-7.13 (m, 10H), 7.20-7.22 (m, 3H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 34.5, 41.3, 61.1, 126.5, 126.5, 126.6, 126.8, 127.0, 127.6, 127.7, 128.3, 128.4, 128.8, 131.2, 133.6, 136.9, 137.2, 138.6, 138.9, 139.7, 142.0, 167.1; IR (CH_2Cl_2, cm^{-1}) 3054, 3020, 2981, 2899, 1709, 1264; HRMS Calcd for $C_{27}H_{24}O_2$: 380.1776. Found: 380.1784.

(3,4-Di-*n*-propylnaphthyl)acetonitrile (25). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 46 mg or 45 mg of the indicated compound as a yellow solid in a 74 % (entry 16) or a 72 % (entry 17) yield, respectively: mp 76-78 °C; ^{1}H NMR ($CDCl_3$) Γ 1.10 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H), 1.52-1.62 (m, 2H), 1.63-1.72 (m, 2H), 2.71-2.75 (m, 2H), 3.01-3.06 (m, 2H), 3.88 (s, 2H), 7.44 (dt, J = 0.8, 7.6 Hz, 1H), 7.50 (dt, J = 1.2, 7.6 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.79 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 15.0, 15.0, 22.8, 24.4, 24.7, 31.1, 32.1, 118.4, 124.2, 125.6, 126.6, 126.8, 126.8, 128.6, 132.2, 132.4, 135.3, 137.6; IR ($CHCl_3$, cm^{-1}) 3065, 3019, 2960, 2872, 2251, 1598; HRMS Calcd for $C_{18}H_{21}N$: 251.1674. Found: 251.1679.

(3,4-Diphenyl-2-naphthyl)acetonitrile (26). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 36 mg or 34 mg of the indicated compound as a yellow solid in 45 % (entry 18) or 43 % (entry 19) yield: mp 193-195 °C; ^{1}H NMR ($CDCl_3$) Γ 3.61 (d, J = 0.9 Hz, 2H), 7.02-7.10 (m, 4H), 7.17-7.25 (m, 6H), 7.38-7.44 (m, 1H), 7.49-7.57 (m, 2H), 7.95 (d, J = 8.1 Hz, 1H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.5, 118.4, 126.6, 126.8, 126.9, 127.1, 127.2, 127.3, 127.8, 127.9, 128.4, 130.2, 131.0, 132.4, 132.9, 138.2, 138.7, 138.7, 140.1 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 3020, 2254, 1487, 1442; HRMS Calcd for $C_{24}H_{17}N$: 319.1361. Found: 319.1366.

3-Methyl-1,2-diphenylnaphthalene (29). The reaction mixture was chromatographed using hexane to afford 24 mg (32 % yield) of the indicated compound as a white solid: mp 147-148 °C; ^{1}H NMR ($CDCl_3$) Γ 2.26 (d, J = 0.6 Hz, 3H), 7.01-7.05 (m, 2H), 7.08-7.24 (m, 8H), 7.28-7.34 (m, 1H), 7.42-7.48 (m, 2H), 7.77 (s, 1H), 7.82-7.85 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.1, 125.5, 125.9, 126.3, 126.5, 127.0, 127.3, 127.6, 127.6, 127.7, 130.3, 131.2,

131.5, 133.1, 134.6, 138.8, 139.6, 140.1, 140.8; IR ($CHCl_3$, cm^{-1}) 3019, 1489, 1442, 1215; HRMS Calcd for $C_{23}H_{18}$: 294.1408. Found: 294.1413.

Ethyl (6,7-dimethoxy-1,2-diphenylnaphth-3-yl)acetate (31). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 75 mg of the indicated compound as a white solid in a 71 % yield: mp 142-145 °C; ^1H NMR ($CDCl_3$) Γ 1.15 (t, J = 7.2 Hz, 3H), 3.57 (s, 2H), 3.69 (s, 3H), 4.02 (s, 3H), 4.03 (q, J = 7.2 Hz, 2H), 6.76 (s, 1H), 7.01-7.03 (m, 2H), 7.08-7.21 (m, 9H), 7.71 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.3, 40.3, 55.8, 56.1, 60.8, 105.8, 106.2, 126.5, 126.6, 127.2, 127.6, 127.7, 127.7, 128.9, 129.3, 130.7, 131.0, 138.0, 138.1, 139.7, 140.1, 149.6, 149.7, 172.3; IR ($CHCl_3$, cm^{-1}) 3057, 3020, 2982, 2956, 2831, 1733, 1623, 1599, 1566; HRMS Calcd for $C_{28}H_{26}O_4$: 426.1831. Found: 426.1837.

Ethyl (6,7-dimethoxy-1,2-dipropyl-3-naphthyl)acetate (32). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 66 mg (73 % yield) of the indicated compound as a pale yellow solid: mp 94-96 °C; ^1H NMR ($CDCl_3$) Γ 1.07 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.47-1.60 (m, 2H), 1.63-1.77 (m, 2H), 2.71-2.76 (m, 2H), 2.95-3.01 (m, 2H), 3.76 (s, 2H), 3.96 (s, 3H), 4.00 (s, 3H), 4.17 (q, J = 7.2 Hz, 2H), 7.04 (s, 1H), 7.22 (s, 1H), 7.44 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 15.0, 15.1, 24.2, 24.6, 31.5, 32.3, 40.0, 55.9, 55.9, 61.0, 103.4, 106.9, 126.8, 127.4, 128.3, 129.8, 135.3, 135.3, 148.8, 149.4, 172.5; IR ($CHCl_3$, cm^{-1}) 3020, 2958, 2871, 1729, 1510, 1473; HRMS Calcd for $C_{22}H_{30}O_4$: 358.2144. Found: 358.2148.

Ethyl [1,2-di(benzyloxy)methyl-6,7-dimethoxy-3-naphthyl]acetate (33). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 72 mg (60 % yield) of the indicated compound as a white solid: mp 83-85 °C; ^1H NMR ($CDCl_3$) Γ 1.20 (t, J = 7.2 Hz, 3H), 3.84 (s, 2H), 3.86 (s, 3H), 3.97 (s, 3H), 4.07 (q, J = 7.2 Hz, 2H), 4.52 (s, 2H),

4.53 (s, 2H), 4.70 (s, 2H), 4.88 (s, 2H), 7.04 (s, 1H), 7.30-7.37 (m, 11H), 7.58 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.4, 39.5, 55.9, 56.0, 61.0, 65.6, 66.1, 72.7, 72.8, 103.8, 106.5, 128.0, 128.0, 128.2, 128.4, 128.4, 128.6, 128.6, 129.5, 129.7, 130.4, 132.4, 132.5, 138.4, 138.4, 149.8, 149.9, 172.1; IR ($CHCl_3$, cm^{-1}) 3019, 2939, 1727, 1509, 1259; HRMS Calcd for $C_{32}H_{34}O_6$: 514.2355. Found: 514.2362.

Ethyl (2-ethoxycarbonyl-6,7-dimethoxy-1-phenylnaphth-3-yl)acetate (34). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 77 mg of naphthalene **34** as a colorless oil in 73 % yield and 8 mg of naphthalene **35** as a pale yellow oil in an 8 % yield. Naphthalene **34**: ^{1}H NMR ($CDCl_3$) Γ 0.86 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 3.72 (s, 3H), 3.89 (s, 2H), 3.93 (q, J = 7.2 Hz, 2H), 4.00 (s, 3H), 4.16 (q, J = 7.2 Hz, 2H), 6.85 (s, 1H), 7.12 (s, 1H), 7.37 (d, J = 7.6 Hz, 2H), 7.40-7.46 (m, 3H), 7.64 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.7, 14.4, 39.7, 55.8, 56.1, 61.0, 61.0, 105.7, 106.2, 127.1, 127.7, 128.0, 128.2, 130.1, 130.2, 130.2, 137.8, 139.1, 150.0, 150.5, 169.6, 171.6 (one sp^2 carbon is missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3021, 2981, 2937, 1731, 1625; HRMS Calcd for $C_{25}H_{26}O_2$: 422.1729. Found: 422.1734. Naphthalene **35**: ^{1}H NMR ($CDCl_3$) Γ 0.89 (dt, J = 1.5, 7.2 Hz, 3H), 1.15 (dt, J = 1.5, 7.2 Hz, 3H), 3.56 (s, 2H), 3.96-4.05 (m, 5H), 4.08-4.19 (m, 5H), 7.13 (s, 1H), 7.19 (s, 1H), 7.27-7.47 (m, 5H), 7.73 (s, 1H).

Ethyl [6,7-dimethoxy-2-phenyl-1-(phenylethynyl)-3-naphthyl]acetate (36) and ethyl [6,7-dimethoxy-1-phenyl-2-(phenylethynyl)-3-naphthyl]acetate (37). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 74 mg (66 % yield) of a 83:17 mixture of regioisomers **36/37** as determined by ^{1}H NMR spectroscopic analysis of the yellow oil. ^{1}H NMR ($CDCl_3$) for the major regioisomer **36**: Γ 1.23 (t, J = 7.2 Hz, 3H), 3.74 (s, 2H), 4.00 (s, 3H), 4.04 (s, 3H), 4.18 (q, J = 7.2 Hz, 2H), 6.89 (s, 1H), 7.12 (s, 1H), 7.14-

7.55 (m, 10H), 7.63 (s, 1H). ^{1}H NMR ($CDCl_3$) for the minor regioisomer **37**: Γ 1.16 (t, J = 7.2 Hz, 3H), 3.59 (s, 2H), 4.00-4.05 (m, 5H), 4.08 (s, 3H), 7.14-7.55 (m, 11H), 7.67 (s, 1H), 7.77 (s, 1H). Additional ^{13}C NMR ($CDCl_3$) for the mixture Γ 14.3, 14.4, 39.9, 41.1, 55.8, 56.0, 56.1, 60.9, 61.1, 87.9, 88.3, 97.1, 98.2, 105.4, 105.5, 106.5, 106.5, 119.4, 119.5, 123.8, 127.0, 127.2, 127.5, 127.6, 128.1, 128.2, 128.3, 128.4, 128.6, 129.1, 129.3, 130.3, 130.8, 131.3, 131.3, 131.4, 139.6, 140.3, 142.3, 142.5, 149.8, 150.2, 150.2, 150.7, 171.9, 172.0 (five sp^2 carbons and one sp^3 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3057, 3020, 2980, 1731, 1506, 1255; HRMS Calcd for $C_{30}H_{26}O_4$: 450.1831. Found: 450.1839.

3-Benzyl-1,2-di(hydroxylmethyl)-6,7-dimethoxynaphthalene (39). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 63 mg of the indicated compound as a white solid in a 73 % yield: mp 170-172 °C; ^{1}H NMR ($CDCl_3$) Γ 2.28 (br s, 2H), 4.00 (s, 3H), 4.03 (s, 3H), 4.26 (s, 2H), 4.83 (s, 2H), 5.15 (s, 2H), 7.08 (s, 1H), 7.14 (d, J = 6.8 Hz, 2H), 7.20 (dt, J = 2.0, 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.28 (dt, J = 2.0, 8.4 Hz, 1H), 7.49 (s, 1H), 7.54 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 40.4, 56.1, 56.1, 58.9, 59.8, 103.0, 106.7, 126.6, 127.4, 128.7, 128.9, 129.0, 129.9, 134.9, 135.1, 136.0, 141.4, 150.0, 150.1; IR ($CHCl_3$, cm^{-1}) 3415 (br), 3019, 2972, 2953, 2903, 2829, 1625, 1602; HRMS Calcd for $C_{21}H_{22}O_4$: 338.1518. Found: 338.1525.

(3-Benzyl-6,7-dimethoxy-2-phenyl-1-naphthyl)methanol (40). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 30 mg (31 % yield) of the indicated compound as a yellow solid: mp 144-146 °C; ^{1}H NMR ($CDCl_3$) Γ 1.45 (br s, 1H), 3.80 (s, 2H), 4.00 (s, 3H), 4.04 (s, 3H), 4.75 (s, 2H), 6.88-6.91 (m, 2H), 7.05-7.20 (m, 6H), 7.34-7.38 (m, 3H), 7.48 (s, 1H), 7.54 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 40.5, 56.1, 56.2, 60.5, 103.7, 106.8,

125.9, 126.7, 127.3, 127.8, 128.3, 128.3, 129.2, 129.4, 129.9, 132.7, 135.7, 139.4, 139.9, 141.1, 149.7, 150.0; IR ($CHCl_3$, cm^{-1}) 3354 (br), 3016, 2940, 1509; HRMS Calcd for $C_{26}H_{24}O_3$: 384.1725. Found: 384.1731.

Ethyl 3-benzyl-6,7-dimethoxy-1-phenyl-2-naphthoate (41) and ethyl 3-benzyl-6,7-dimethoxy-2-phenyl-1-naphthoate (42). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 81 mg of compound **41** (76 % yield) as a pale yellow solid and 9 mg of compound **42** (8 % yield) as a yellow oil. Naphthalene **41**: mp 129-131 °C; ^{1}H NMR ($CDCl_3$) Γ 0.77 (t, J = 7.2 Hz, 3H), 3.71 (s, 3H), 3.80 (q, J = 7.2 Hz, 2H), 3.97 (s, 3H), 4.19 (s, 2H), 6.83 (s, 1H), 7.05 (s, 1H), 7.18-7.33 (m, 5H), 7.36-7.47 (m, 6H); NOE: H^a-H^b; ^{13}C NMR ($CDCl_3$) Γ 13.7, 39.6, 55.8, 56.1, 60.8, 105.5, 106.3, 126.3, 126.4, 126.9, 127.7, 128.2, 128.5, 129.6, 130.0, 130.3, 131.2, 133.5, 136.9, 138.7, 140.4, 149.7, 150.3, 169.9; IR ($CHCl_3$, cm^{-1}) 3057, 3024, 2962, 1713, 1507; HRMS Calcd for $C_{28}H_{26}O_4$: 426.1831. Found: 426.1831. Anal. Calcd: C, 78.85; H, 6.15. Found: C, 78.69; H, 6.18. Naphthalene **42**: ^{1}H NMR ($CDCl_3$): Γ 0.89 (t, J = 7.2 Hz, 3H), 3.90 (s, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 4.01 (q, J = 7.2 Hz, 2H), 6.91-6.93 (m, 2H), 7.07 (s, 1H), 7.14-7.21 (m, 6H), 7.30-7.34 (m, 3H), 7.55 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 13.9, 39.8, 56.1, 56.1, 61.2, 103.7, 106.4, 124.4, 126.0, 127.4, 128.0, 128.4, 129.0, 129.2, 130.0, 130.5, 135.4, 137.2, 139.4, 141.0, 150.0, 150.4, 169.7 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3021, 2937, 1714, 1506; HRMS Calcd for $C_{28}H_{26}O_4$: 426.1831. Found: 426.1831.

2-Benzyl-9-methyl-3,4-dipropyl-9*H*-carbazole (44). The reaction mixture was chromatographed using 20:1 hexane/EtOAc to afford 29 mg (33 % yield) of the indicated compound as a pale yellow solid: mp 113-115 °C; ^{1}H NMR ($CDCl_3$) Γ 1.02 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 1.46-1.55 (m, 2H), 1.77-1.84 (m, 2H), 2.70-2.74 (m, 2H), 3.19-

3.23 (m, 2H), 3.73 (s, 3H), 4.24 (s, 2H), 7.02 (s, 1H), 7.16-7.24 (m, 4H), 7.25-7.30 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.41-7.45 (m, 1H), 8.07 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 15.1, 15.1, 23.5, 25.3, 29.1, 31.3, 32.7, 40.7, 108.3, 108.5, 118.9, 120.0, 122.4, 123.0, 124.8, 126.1, 128.5, 128.9, 130.3, 136.8, 137.1, 140.0, 141.4, 141.8; IR ($CHCl_3$, cm^{-1}) 3018, 2957, 2930, 1597, 1216; HRMS Calcd for $C_{26}H_{29}N$: 355.2300. Found: 355.2310.

2-Benzyl-3,4-bis[(benzyloxy)methyl]-9-methyl-9*H*-carbazole (45). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 72 mg (56 % yield) of the indicated compound as a pale yellow solid: mp 112-114 °C; ^{1}H NMR ($CDCl_3$) Γ 3.73 (s, 3H), 4.27 (s, 2H), 4.43 (s, 2H), 4.57 (s, 2H), 4.62 (s, 2H), 5.11 (s, 2H), 7.06 (d, J = 7.2 Hz, 2H), 7.16-7.25 (m, 5H), 7.28-7.35 (m, 10H), 7.42-7.46 (m, 1H), 8.06 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.2, 40.1, 65.7, 66.4, 72.8, 72.8, 108.4, 110.9, 115.5, 119.3, 121.5, 122.6, 123.3, 125.4, 126.1, 127.0, 127.9, 127.9, 128.5, 128.5, 128.5, 128.9, 132.7, 138.4, 138.5, 138.6, 141.5, 141.5, 141.7 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3015, 1597, 1216; HRMS Calcd for $C_{36}H_{33}NO_2$: 511.2511. Found: 511.2520.

2-Benzyl-3,4-bis(hydroxymethyl)-9-methyl-9*H*-carbazole (46). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 34 mg (41 % yield) of the indicated compound as a yellow solid: mp 191-193 °C; ^{1}H NMR (CD_3OD) Γ 3.31 (s, 1H), 3.31 (s, 1H), 3.75 (s, 3H), 4.35 (s, 2H), 4.84 (s, 2H), 5.30 (s, 2H), 7.12-7.23 (m, 6H), 7.27 (s, 1H), 7.38-7.44 (m, 2H), 8.26 (d, J = 8.0 Hz, 1H); ^{13}C NMR (CD_3OD) Γ 29.2, 40.9, 58.5, 59.6, 109.6, 111.7, 120.2, 122.1, 123.7, 124.1, 126.5, 127.1, 129.5, 129.8, 130.1, 136.0, 139.7, 142.6, 142.9, 143.1; IR ($CHCl_3$, cm^{-1}) 3397 (br), 3060, 3019, 2924, 1598, 1215; HRMS Calcd for $C_{22}H_{21}NO_2$: 331.1572. Found: 331.1579.

Ethyl 2-benzyl-9-methyl-4-phenyl-9*H*-carbazole-3-carboxylate (48) and ethyl 2-benzyl-9-methyl-3-phenyl-9*H*-carbazole-4-carboxylate (49). The reaction mixture was chromatographed using 20:1 hexane/EtOAc to afford 106 mg (91 % yield) of a 60:40 mixture of regioisomers **48/49** as determined by ^{1}H NMR spectroscopic analysis of the yellow oil. Carbazole **48**: ^{1}H NMR ($CDCl_3$) Γ 0.80 (t, J = 7.2 Hz, 3H), 3.79 (s, 3H), 3.84 (q, J = 7.2 Hz, 2H), 4.30 (s, 2H), 6.91-6.95 (m, 2H), 7.15 (s, 1H), 7.18-7.23 (m, 1H), 7.27-7.40 (m, 6H), 7.46-7.50 (m, 5H); ^{13}C NMR ($CDCl_3$) Γ 13.7, 29.4, 40.3, 60.8, 108.5, 109.0, 119.3, 119.5, 122.3, 122.8, 125.8, 126.1, 126.3, 127.9, 128.4, 128.6, 129.5, 129.6, 135.9, 136.6, 139.4, 140.9, 141.5, 141.9, 170.2; IR ($CHCl_3$, cm^{-1}) 3062, 2981, 1709, 1593; HRMS Calcd for $C_{29}H_{25}O_2N$: 419.1885. Found: 419.1892. Carbazole **49**: ^{1}H NMR ($CDCl_3$) Γ 0.94 (t, J = 7.2 Hz, 3H), 3.81 (s, 3H), 4.01 (s, 2H), 4.11 (dq J = 2.0, 7.2 Hz, 2H), 6.94-6.96 (m, 2H), 7.12-7.25 (m, 6H), 7.29-7.34 (m, 4H), 7.39 (d, J = 8.4 Hz, 1H), 7.46-7.50 (m, 1H), 7.97 (d, J = 8.0 Hz, 1H). Additional ^{13}C NMR ($CDCl_3$) for the mixture: Γ 13.8, 13.9, 29.4, 29.4, 40.2, 40.3, 60.8, 61.3, 108.5, 108.7, 109.0, 111.1, 117.6, 119.2, 119.5, 121.1, 121.9, 122.3, 122.8, 125.8, 126.0, 126.1, 126.3, 127.2, 127.8, 127.9, 127.9, 128.4, 128.4, 128.5, 129.1, 129.5, 130.6, 131.4, 135.8, 136.6, 137.3, 139.3, 139.4, 140.7, 140.9, 141.4, 141.5, 141.8, 141.9, 169.8, 170.2 (three sp^2 carbons missing due to overlap).

Ethyl 2-benzyl-4,9-dimethyl-9*H*-carbazole-3-carboxylate (50) and ethyl 2-benzyl-3,9-dimethyl-9*H*-carbazole-4-carboxylate (51). The reaction mixture was chromatographed using10:1 hexane/EtOAc to afford 69 mg (78 % yield) of a 82:18 mixture of regioisomers **50/51** as determined by ^{1}H NMR spectroscopic analysis of the yellow oil. Carbazole **50**: ^{1}H NMR ($CDCl_3$) Γ 1.26 (t, J = 7.2 Hz, 3H), 2.85 (s, 3H), 3.77 (s, 3H), 4.23, (s, 2H), 4.28 (q, J = 7.2 Hz, 2H), 7.03 (s, 1H), 7.20-7.30 (m, 6H), 7.39 (d, J = 8.4 Hz, 1H),

7.46-7.49 (m, 1H), 8.18 (d, J = 7.6 Hz, 1H); NOE: H^a-H^b; ^{13}C NMR ($CDCl_3$) Γ 14.3, 18.3, 29.3, 40.5, 61.2, 107.9, 108.6, 119.5, 120.0, 122.8, 123.6, 125.5, 126.3, 126.4, 128.5, 129.3, 131.3, 136.1, 141.0, 141.4, 141.7, 171.0; IR ($CHCl_3$, cm^{-1}) 3057, 3027, 2983, 2901, 1710, 1596; HRMS Calcd for $C_{24}H_{23}O_2N$: 357.1729. Found: 357.1734. Carbazole **51**: ^{1}H NMR ($CDCl_3$) Γ 1.45 (t, J = 7.2 Hz, 3H), 2.33 (s, 3H), 3.76 (s, 3H), 4.19 (s, 2H), 4.59 (q, J = 7.2 Hz, 2H), 7.13-7.30 (m, 7H), 7.34-7.39 (m, 1H), 7.42-7.49 (m, 1H), 7.89 (dd, J = 1.2, 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.6, 16.4, 29.3, 40.8, 61.7, 108.7, 111.6, 117.8, 119.2, 121.1, 121.4, 124.3, 126.0, 126.3, 127.8, 128.7, 128.9, 137.5, 139.8, 140.4, 141.6.

Ethyl 7-benzyl-9-phenylpyrido[1,2-*a*]indole-8-carboxylate (53). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 34 mg (41 % yield) of the indicated compound as a yellow oil: ^{1}H NMR (CD_3OD) Γ 0.92 (t, J = 7.2 Hz, 3H), 4.01 (q, J = 7.2 Hz, 2H), 5.28 (d, J = 2.0 Hz, 2H), 6.90 (s, 1H), 7.04-7.08 (m, 1H), 7.20-7.28 (m, 3H), 7.33-7.52 (m, 11 H); ^{13}C NMR (CD_3OD) Γ 13.8, 43.5, 61.4, 104.2, 109.1, 120.6, 121.7, 123.6, 128.0, 128.2, 128.4, 128.5, 128.6, 128.8, 129.2, 129.3, 129.6, 132.5, 134.4, 136.3, 136.9, 138.5, 168.3 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 3056, 3026, 2979, 2933, 1717, 1134; HRMS Calcd for $C_{28}H_{23}NO_2$: 405.1729. Found: 405.1735.

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CHAPTER 4. SYNTHESIS OF FUSED POLYCYCLES BY 1,4-PALLADIUM MIGRATION CHEMISTRY

A paper submitted to the *Journal of Organic Chemistry*

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Abstract

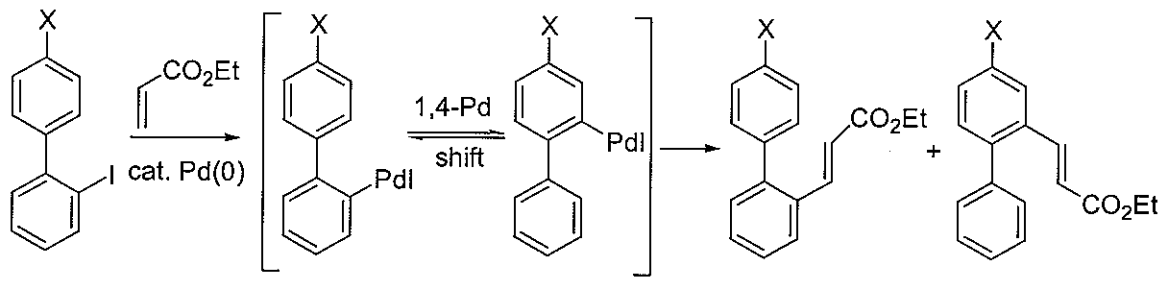
Novel palladium migration/arylation methodology for the synthesis of complex fused polycycles has been developed, in which one or more sequential Pd-catalyzed intramolecular migration processes involving C-H activation are employed. The chemistry works best with electron-rich aromatics, which is in agreement with the idea that these palladium-catalyzed C-H activation reactions parallel electrophilic aromatic substitution.

Introduction

The ability of palladium to activate C-H bonds has been used extensively in organic synthesis.[1] In recent years, palladium-catalyzed C-H activation has received considerable attention due to the wide variety of reactions this metal will catalyze. For instance, catalytic amounts of Pd salts have been used to effect the addition of C-H bonds of electron-rich arenes to alkenes and alkynes and effect carbonylation.[2] We have previously reported the synthesis of 9-benzylidene-9*H*-fluorenes by Pd-catalyzed intramolecular C-H activation involving the rearrangement of organopalladium intermediates derived from aryl halides and internal alkynes.[3] Similarly, intramolecular C-H activation in organopalladium intermediates

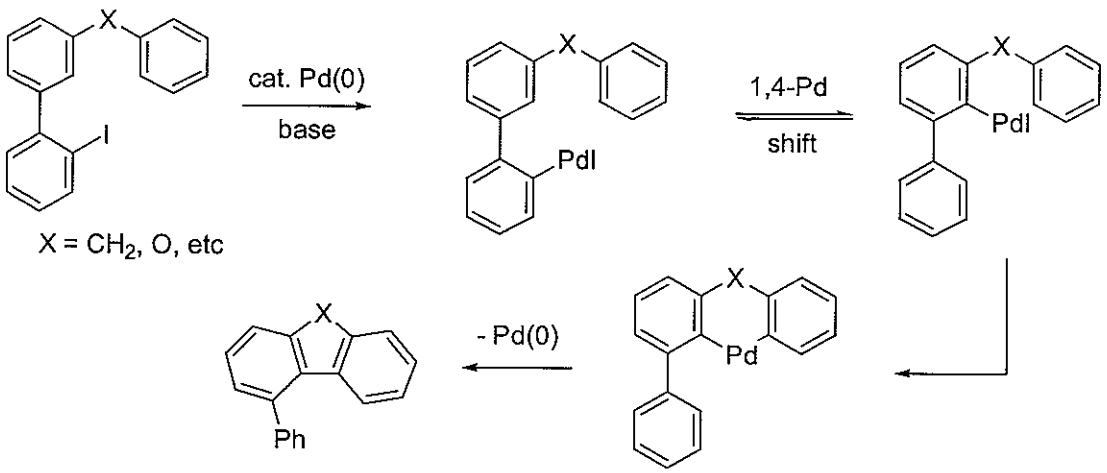
derived from *o*-halobiaryls leads to a 1,4-palladium migration (Scheme 1).[4] We have already shown that such intermediates can be trapped by Heck, Suzuki and alkyne annulation reactions.[4,5] We have recently reported that this aryl-to-aryl palladium migration process, followed by arylation, provides a novel, new route to a wide variety of carbo- and heterocycles.[6] Herein, we now wish to report further details regarding this aryl-aryl migration and also vinylic-aryl migration chemistry, followed by intramolecular arylation.

Scheme 1



Our strategy involves palladium C-H activation and 1,4-palladium migration within a biaryl, which generates key arylpalladium intermediates, which subsequently undergo C-C bond formation by intramolecular arylation producing fused polycycles (Scheme 2). This process represents a very powerful new tool for the preparation of complex molecules, which might be difficult to prepare by any other present methodology.

Scheme 2

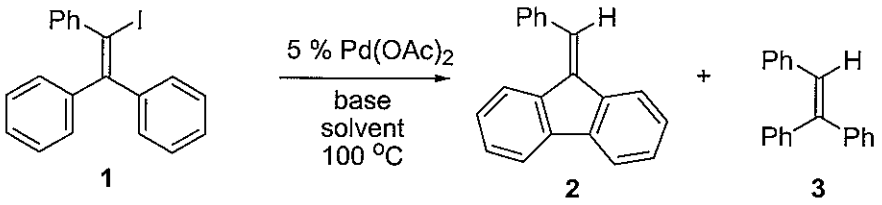


Results and Discussion

In order to obtain an optimum set of reaction conditions for migration, we have reinvestigated the palladium-catalyzed transformation of 1-iodo-1,2,2-triphenylethene (**1**) to 9-benzylidene-9*H*-fluorene (**2**) as our model system[3] (Table 1). While this system may not be the most obvious for a study of aryl to aryl Pd migrations, we had previously accumulated substantial data on this system. To begin with, we carried out this reaction using our previously reported conditions[3] and obtained a 73 % yield of the desired compound **2**, along with a 15 % yield of triphenylethene (**3**) (entry 1). The first variable to be examined was the ligand on palladium. We examined phosphines other than PPh_3. Entries 2 and 3 indicate that P(*o*-tol)$_3$ and $CH_2(PPh_2)_2$ (dppm) are superior to PPh_3 in affording higher yields of the fluorene **2**. However, the reactions with all of these phosphine ligands required 3 d to reach completion. In order to shorten this relatively lengthy reaction time, we eliminated *n*-Bu_4NCl (TBAC) and found that the reaction was complete after only 1 d (entry 4). Unfortunately, this led to a much lower yield of the desired compound **2** (47 %), and the

yield of reduced product **3** increased to 47 %. In order to investigate whether DMF was the hydride source for the reduction of **1** to **3**, we carried out this reaction using other solvents,

Table 1. Palladium-catalyzed cyclization of 1-iodo-1,2,2-triphenylethene (**1**) to 9-benzylidenefluorene (**2**).[a]



1 **2** **3**

entry	ligand (mol %)	base	chloride source	solvent	time (d)	% yield **2**	% yield **3**
1	PPh_3 (10)	NaOAc	TBAC[b]	DMF	3	73	15
2	P(*o*-tol)$_3$ (10)	NaOAc	TBAC	DMF	3	75	20
3	dppm[c] (5)	NaOAc	TBAC	DMF	3	79	15
4	dppm (5)	NaOAc	-	DMF	1	47	47
5	dppm (5)	NaOAc	-	DMA	1.5	52	48
6	dppm (5)	NaOAc	-	NMP	1	46	46
7	dppm (5)	NaOAc	-	DMSO	1	-	-
8	dppm (5)	pyridine	-	DMF	1	-	-
9	dppm (5)	*i*-Pr_2NEt	-	DMF	1	-	-
10	dppm (5)	Na_2CO_3	-	DMF	1	70	26
11	dppm (5)	$NaHCO_3$	-	DMF	1	65	23
12	dppm (5)	Na_2CO_3[d]	-	DMF	1	-	47
13	dppm (5)	Cs_2CO_3	-	DMF	1	74	22
14	dppm (5)	CsOAc	-	DMF	2	90	4
15	dppm (5)	CsO_2CCMe_3	-	DMF	1	96	4
16	dppm (5)	CsO_2CCMe_3	-	DMA	1	59	17[e]
17	dppe[f] (5)	CsO_2CCMe_3	-	DMF	1	90	10
18	dppm (5)	*n*-Bu_4NOAc	-	DMF	1	<10	-

[a]The reaction was run using 0.25 mmol of 1-iodo-1,2,2-triphenylethene (**1**), 5 mol % of $Pd(OAc)_2$ and 4 mL of solvent at 100 °C. [b]TBAC = *n*-Bu_4NCl. [c]Dppm = 1,1-*bis*(diphenylphosphino)methane. [d]One equiv of NaI was added. [e]Twenty four percent of **1** was recovered. [f]Dppe = 1,2-*bis*(diphenylphosphino)ethane.

such as DMA, NMP, and DMSO (entries 5-7). DMSO gave none of the desired fluorene **2** or any reduction product **3**. The amount of reduction was more or less the same in the other

solvents. Thus, we continued our investigation using DMF as the reaction solvent.

We also examined the effect of various bases on the yields of **2** and **3**, including organic bases, such as pyridine and diisopropylethylamine (entries 8 and 9). These bases were ineffective in promoting the reaction and TLC analysis of the reaction mixtures indicated only the presence of the starting vinylic halide **1**. The use of Na_2CO_3 as the base provided **2** in a 70 % yield, but we also obtained a 26 % yield of reduced product **3** (entry 10). The base $NaHCO_3$ provided a 65 % yield of **2** and a 23 % yield of **3** (entry 11). We believe that the solubility of these bases in the reaction mixture may be playing a critical role in determining the outcome. Thus, once again we used Na_2CO_3 as the base, but this time we added 1 equiv of NaI, which is completely soluble in DMF, as an additive to promote a sodium common ion effect intended to make Na_2CO_3 less soluble in the reaction mixture. Indeed, this experiment revealed that under such reaction conditions only the reduced product **3** was produced in a 47 % yield (entry 12). None of the desired product **2** was observed (compare entries 10 and 12). Although there may be a number of other effects going on under these reaction conditions, it seemed logical to assume that the yield of the reaction would improve by using more soluble inorganic bases. Thus, the use of Cs_2CO_3, which presumably has better solubility than other alkali carbonates in DMF,[7] provided a slightly higher 74 % yield of compound **2**, along with a 22 % yield of the reduced product **3**. Similarly, the use of very soluble CsOAc as the base provided a 90 % yield of the desired product **2**, along with 4 % of the reduced product **3** after 2 d (entry 14). We subsequently found that cesium pivalate (CsO_2CCMe_3), unlike any other previously studied base, was completely soluble in DMF at 100 °C. In this case, we obtained an impressive 96 % yield of the desired compound **2**, along with only a small amount of the reduced product **3** (4 %) after only 1 d (entry 15). Clearly, cesium pivalate is far superior as

a base in this reaction, and its high solubility in DMF seems to explain this phenomena. To illustrate, we carried out the reaction of **1** under conditions identical to those described in entry 15, but we used DMA instead of DMF as the solvent, in which cesium pivalate is not completely soluble. Under these conditions, we obtained a relatively low 59 % yield of the desired compound **2**, along with a 17 % yield of the reduced product **3** (entry 16). Twenty four percent of the starting vinylic iodide **1** was also obtained. Finally, to test whether dppm was indeed critical to this reaction, we carried out the transformation using another chelating phosphine ligand, namely 1,2-*bis*(diphenylphosphino)ethane (dppe), and we obtained a 90 % yield of **2**, along with a 10 % yield of the reduced product **3** (entry 17). As a result of this optimization work, our optimal set of reaction conditions for this transformation are those listed in entry 15 of Table 1. Notice that the newly developed conditions catalyze the transformation of **1** to **2** in high yield and much shorter reaction time than our earlier reported procedure (entry 1).[3] The variable most critical to the success of this process appears to be the highly soluble cesium pivalate base. Surprisingly, the use of *n*-Bu_4NOAc as the base, which is also completely soluble in DMF under reaction conditions identical to those described in entry 15, failed to promote this reaction, affording only trace amounts of the desired product **2** after 1 d (entry 18). Thus, not only the solubility, but also the exact nature of the base, appears critical in determining the reaction yield. It is interesting to note that the work of Buchwald, Hartwig and Fu has demonstrated that steric congestion imposed on palladium by bulky, electron-rich ligands facilitates both the oxidative addition and reductive elimination steps involving palladium, and gives rise to more effective catalyst systems.[8] However, nothing is apparently known about the effects of using a sterically hindered base,

such as pivalate, in palladium chemistry, and whether or not it may give similar results to those obtained using bulky ligands.

With an apparently "optimal" set of reaction conditions for palladium migration chemistry at our disposal, we proceeded to study the sequential Pd-catalyzed migration/arylation of various 3'-substituted 2-iodobiphenyls (Table 2). We began by allowing 3'-benzyl-2-iodobiphenyl (**4**) to react under our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react. However, by simply increasing the reaction temperature to 110 °C, we were able to obtain the desired compound **5** in a 40 % yield (entry 1). The disappointingly low yield obtained with this substrate might be explained by the poor reactivity of the benzyl moiety as an intramolecular trap. To test this idea, we carried out the reaction with the more electron-rich 2-iodo-3'-phenoxybiphenyl (**6**) and obtained the desired 4-phenyldibenzofuran (**7**) in an impressive 89 % yield (entry 2). Clearly, these results indicate that the electron-rich oxygen-substituted phenyl ring is superior as an arylating agent. Our finding that electron-rich arenes are superior to electron-neutral arene traps is consistent with literature reports indicating that the ease of C-H activation by palladium parallels electrophilic aromatic substitution.[9] Similarly, we were able to selectively obtain 3-chloro-5-phenyldibenzofuran (**9**) in an 82 % yield from 3-(*p*-chlorophenoxy)-2-iodobiphenyl (**8**) under our standard conditions, while leaving the chloro functionality intact (entry 3).

Table 2. Sequential 1,4-Palladium Migration, Followed by Intramolecular Arylation[a]

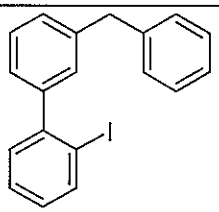
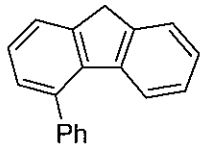
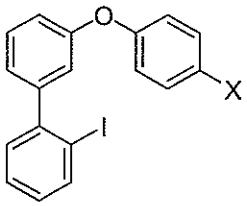
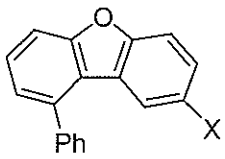
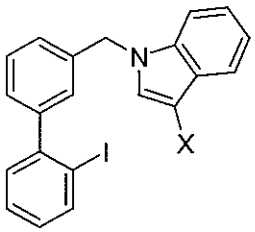
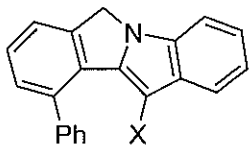
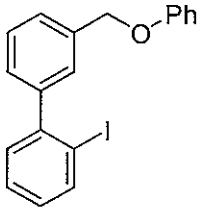
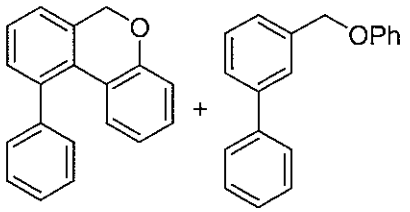
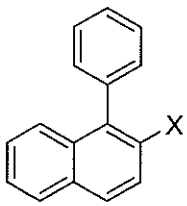
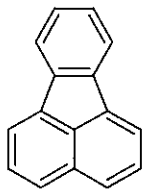
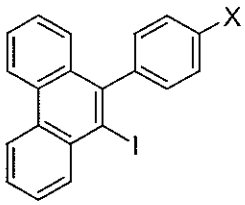
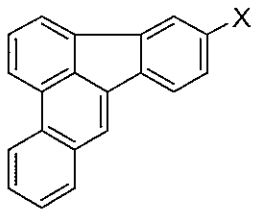
entry	substrate		product(s)		time (d)	yield[b] (%)
1		**4**		**5**	3[c]	40
2	 X = H	**6**		**7**	1[c]	89
3	X = Cl	**8**		**9**	1[c]	82
4	 X = H	**10**		**11**	1	70
5	X = Me	**12**		**13**	1	71
6		**14**	 **15** **16**		2[d]	75 (60 : 40)
7	 X = I	**17**		**18**	1[c]	81
8	X = Br	**19**			3[c]	70
9	 X = H	**20**		**21**	2[c]	78 (18)
10	X = OMe	**22**		**23**	2[c]	71 (22)
11	X = CO_2Et	**24**		**25**	2[c]	50 (20)

Table 2 continued

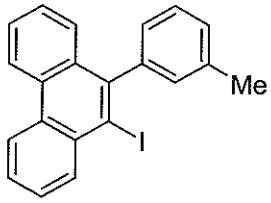
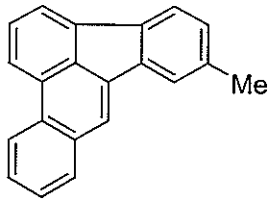
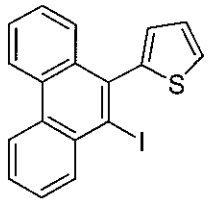
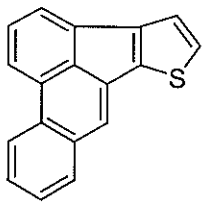
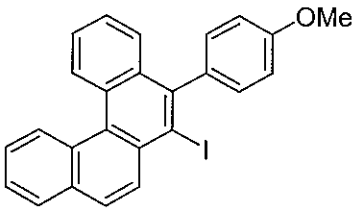
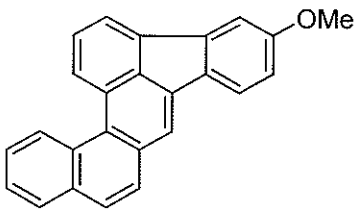
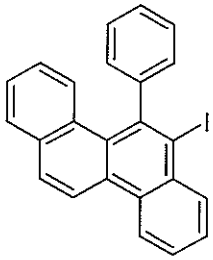
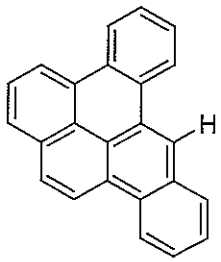
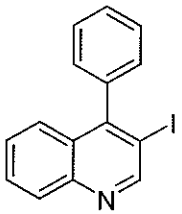
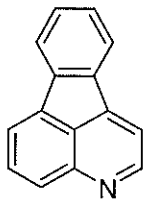
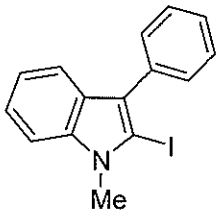
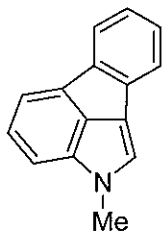
12		**26**		**27**	2[c]	56 (37)
13		**28**		**29**	2[c]	0
14		**30**		**31**	2[c]	65
15		**32**		**33**	2[c]	0 (80)
16		**34**		**35**	2.5[c]	54
17		**36**		**37**	2[c]	0

Table 2 continued

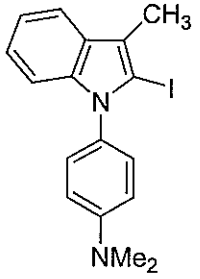
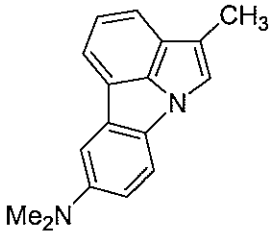
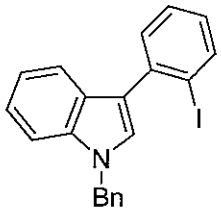
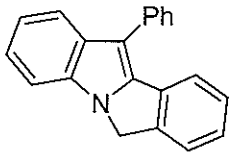
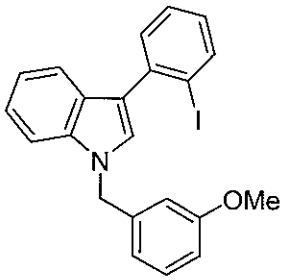
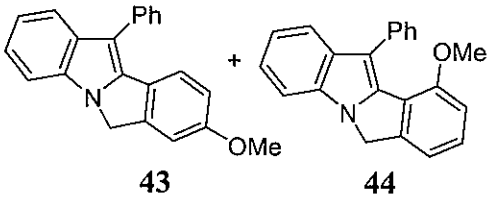
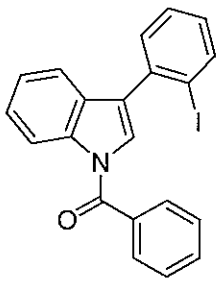
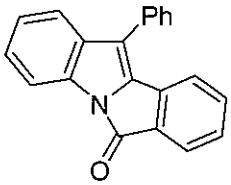
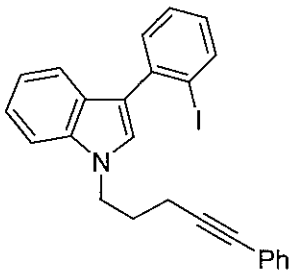
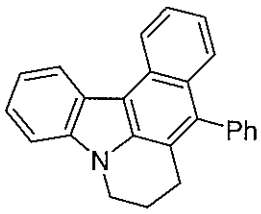
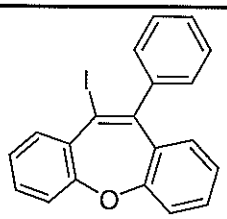
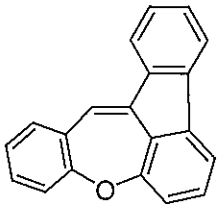
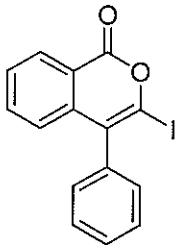
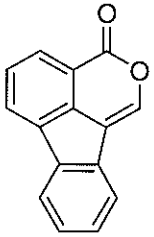
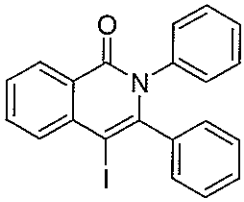
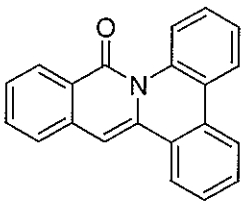
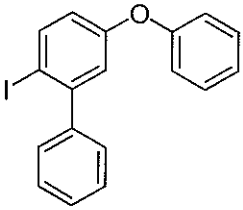
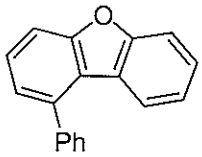
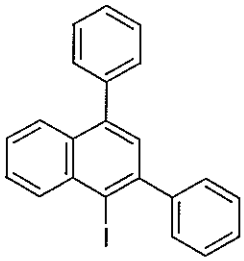
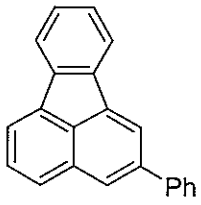
18		**38**		**39**	2[c]	0
19		**40**		**41**	1	92[e]
20		**42**	 **43** **44**		0.5	78 + 12
21		**45**		**46**	1	33
22		**47**		**48**	0.5	65

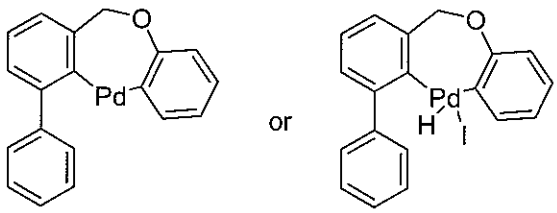
Table 2 continued

23		**49**		**50**	2[c]	80
24		**51**		**52**	2	0
25		**53**		**54**	5[c]	0 (12)
26		**55**		**4**	1	88 (<5)
27		**56**		**57**	14	0 (62)[c]

[a] The reaction was carried out under the following standard conditions employing 0.25 mmol of the aryl halide, 5 mol % $Pd(OAc)_2$, 5 mol % dppm, and 2 equivs of CsO_2CCMe_3 in DMF (4 mL) at 100 °C unless otherwise noted. [b] The yield in parentheses corresponds to the GC yield of product in which the C-I bond has been reduced to a C-H. [c] The reaction temperature was increased to 110 °C. [d] The reaction temperature was increased to 120 °C. [e] The yield was determined by ^1H NMR spectroscopy.

Motivated by the ease of preparation of the following starting materials and by the knowledge that electron-rich arenes are apparently superior as intramolecular traps for our arylpalladium intermediates, we synthesized the indole derivatives **10** and **12**. To our great satisfaction, compound **10** smoothly underwent the desired reaction, producing the relatively strained isoindoloindole **11** in a 70 % yield (entry 4). Surprisingly, compound **12** produced the strained and sterically congested 2-methylisoindoloindole **13** in a comparable 71 % yield (entry 5). We next examined the possibility of using an intramolecular arylation to form six-membered rings. Unfortunately, 3-(2-iodophenyl)benzyl phenyl ether (**14**) failed to react under our standard reaction conditions. Even at 110 °C, the reaction was sluggish, so the temperature was increased to 120 °C, in which case the reaction was complete after 2 d. Unfortunately, a 60:40 inseparable mixture of the desired compound **15** and the reduced product **16** was obtained in a 75 % overall yield (entry 6). Clearly, the formation of a six-membered ring is not as favorable as five-membered ring formation (compare entries 2 and 6). This might be due to the difficulty in forming a seven-membered ring palladacycle (Figure 1).

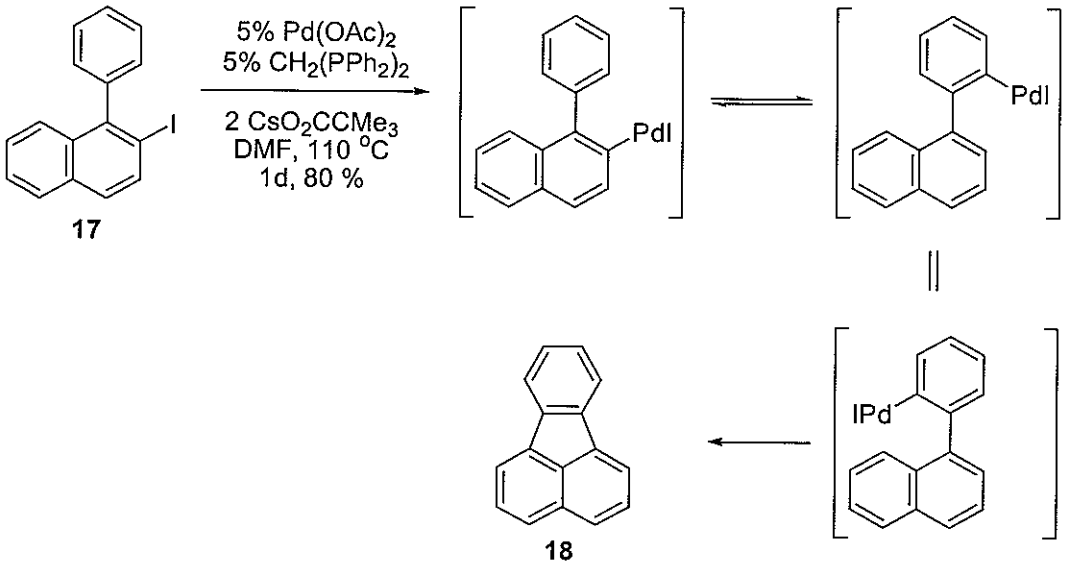
Figure 1. Unfavorable seven-membered ring palladacycle intermediates



We proceeded to investigate the sequential migration/arylation reaction of more complex polyaromatic compounds. In theory, 2-iodo-1-phenylnaphthalene (**17**) should afford fluoranthene (**18**) using our methodology. Mechanistically, the palladium must first undergo a 1,4-palladium migration from the 2-position of the naphthalene to the *o*-position of

the phenyl substituent, followed by arylation at the 8-position of the naphthalene (Scheme 3). Although the reaction did not proceed at 100 °C, at 110 °C compound **17** produced the

Scheme 3



17 **18**

desired compound **18** in an 81 % yield (entry 7). Similarly, 2-bromo-1-phenylnaphthalene (**19**) produced the desired fluoranthene (**18**) in a 70 % yield, indicating that this aryl bromide also undergoes the desired transformation, but in a somewhat lower yield and a longer reaction time.

Another interesting example of this migration/arylation chemistry involves the rearrangement of easily prepared 9-iodo-10-arylphenanthrenes[10] to benz[*e*]acephenanthrylenes (entries 9-12). In this case, the palladium migrates from the 9 position of the phenanthrene to the *ortho* position of the aryl substituent, followed by cyclization onto the 1 position of the phenanthrene. Indeed, the reaction of 9-iodo-10-phenylphenanthrene (**20**) under our standard reaction conditions at 110 °C produced the

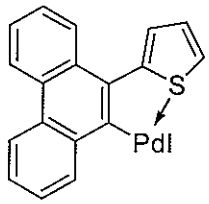
desired benz[*e*]acephenanthrylene (**21**) in a 78 % yield (entry 9). We proceeded to investigate electronic effects in this phenanthrene reaction by looking at different substituents on the phenyl moiety. As expected, the use of an electron-donating methoxy group in compound **22** gave a good yield (71 %) of the corresponding benz[*e*]acephenanthrylene **23**, although the yield was slightly lower than that of the parent system (entry 10). As expected, the introduction of an electron-withdrawing CO_2Et group in the *para* position of the phenyl substituent was detrimental to the reaction, producing compound **25** in only a 50 % yield. All of these phenanthrene reactions gave approximately a 20 % yield of the corresponding reduction product.

We have also studied the regioselectivity of the migration by using an *m*-tolyl moiety in the 10-position of the 9-iodophenanthrene (entry 12). Compound **26** has two available positions for palladium migration, the more sterically-congested neighboring 2 position or the remote 6 position of the phenyl ring. The palladium-catalyzed cyclization of compound **26** generated compound **27** exclusively in a 56 % yield, alongside a significant amount of reduction product (37 %). This result indicates that palladium migration occurs exclusively onto the less sterically-congested 6 position of the phenyl moiety and that the presence of a methyl group apparently completely inhibited migration to the more hindered 2 position or at least cyclization of that intermediate to the corresponding polycyclic product.

We next tried to prepare the more strained fused thiophene **29** from phenanthrene **28**. Unfortunately, this reaction led to a very complex mixture, which produced none of the desired compound **29** as far as we could tell. Besides the unfavorable ring strain associated with the final product **29**, intramolecular sulfur chelation of the intermediate 10-(thiophen-2-

yl)phenanthren-9-ylpalladium iodide might be inhibiting the palladium migration step (Figure 2).

Figure 2. Intramolecular palladium chelation by sulfur.



The relatively electron-rich benzo[*e*]phenanthrene **30** also underwent the migration/arylation reaction, producing the highly conjugated hexacyclic compound **31** in a 65 % yield (entry 14). Unfortunately, compound **32** failed to generate the desired hexacycle **33** under our reaction conditions at 110 °C (entry 15). Only reduction product was isolated in an 80 % yield. This example once again indicates that intramolecular cyclization to form a six membered ring is apparently rather unfavorable.

Having studied the palladium-catalyzed transformation of a variety of polycyclic aromatic halides, we switched our attention to heterocyclic aromatic compounds. To begin with, we carried out the reaction of 3-iodo-4-phenylquinoline (**34**) under our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react. Fortunately, by simply increasing the reaction temperature to 110 °C, we obtained the desired indeno[1,2,3-*de*]quinoline (**35**) in a 54 % yield. Again the modest yield obtained with this electron-deficient substrate is consistent with our previous observations that electron-deficient substrates do not perform as well as more electron-rich substrates (compare entries 7 and 16). We also allowed 2-iodo-1-methyl-3-phenylindole (**36**) to react under our standard reaction

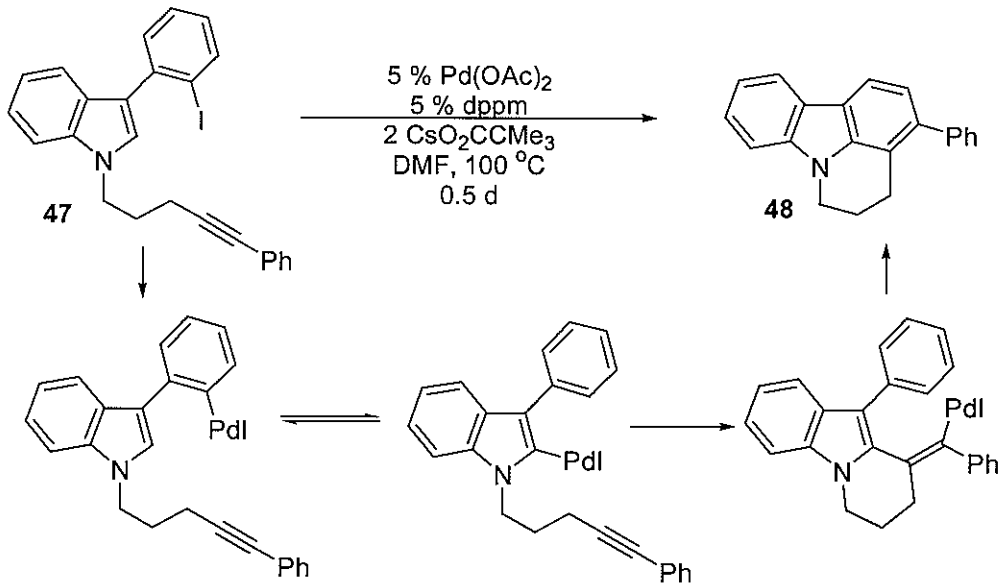
conditions at 110 °C, but failed to obtain the desired tricyclic compound **37** (entry 17). A similar negative result was obtained with iodoindole **38** (entry 18). The poor results obtained with substrates **36** and **38** can be explained in terms of the unfavorable ring strain of the corresponding products **37** and **39**. In addition, we have previously established, using Heck trapping experiments, that palladium prefers to reside on the indole moiety in such substrates.[4,5]

To confirm our suspicion that the palladium prefers to migrate to a more electron-rich position, because of the relatively easy activation of an electron-rich C-H bond,[4,5,9] compound **40** was allowed to react under our migration conditions and indole **41** was produced in a 92 % yield in 1 d at 100 °C (entry 19). From the results of entries 1 and 19, it appears that the high efficiency of palladium migration to a relatively electron-rich ring allows the sequential migration/arylation to proceed smoothly at a lower temperature and in a shorter reaction time, although the benzyl group is not a particularly good arylating agent. When a methoxy group was introduced onto the benzyl group, this migration/arylation reaction afforded a mixture of indoles **43** and **44** in 78 % and 12 % yields, respectively (entry 20). This result is consistent with our previous observation (see entry 12) that the palladium intermediate is more likely to form the final carbon-carbon bond at the less hindered position of the aryl terminus. When compound **45**, which has an electron-deficient aryl terminus, was allowed to react under the standard migration conditions, a 33 % yield of product **46** was isolated (entry 21). This is consistent with electron-deficient termini giving lower yields.

We have also examined the possibility of trapping palladium migration species by alkynes. Thus, we have carried out the palladium-catalyzed sequential migration/alkyne insertion/arylation of aryl halide **47** in the hope that the arylpalladium intermediate generated

by a 1,4-Pd shift via through-space C-H activation could be trapped by alkyne insertion-annulation chemistry described earlier by us (Scheme 4).[11] The reaction was carried out under our standard migration conditions and carbazole **48** was isolated in a 65 % yield (entry 22). It is important to note that this reaction was complete in 0.5 d at 100 °C, consistent with the particularly facile migration of Pd to the electron-rich indole ring system. Although we cannot rule out the possibility that this reaction is proceeding by direct endocyclic addition of the initial arylpalladium species to the alkyne triple bond and subsequent ring closure onto the indole to give product **48**, this seems unlikely since exocyclic addition is more common. This successful alkyne insertion chemistry suggests that there is the exciting possibility of trapping aryl- and other organopalladium intermediates generated by a 1,4-Pd shift by many other synthetically useful palladium methodologies, such as amination and annulation. We are presently examining such possibilities.

Scheme 4

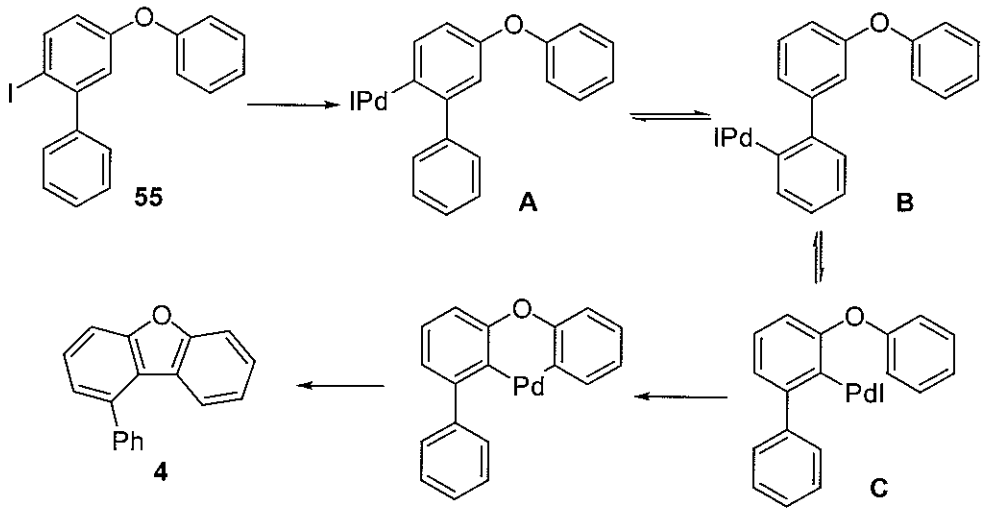


While our efforts have focused on synthesizing polycyclic compounds in which the key 1,4-palladium shift occurs from an aryl to another aryl position, we wanted to establish that our methodology could also make use of a vinylic to aryl palladium migration to generate the key intermediate for the intramolecular arylation step. We have already shown one example of such a transformation in converting compound **1** to **2** (Table 1). Another illustration of this process involves the use of 9-iodo-10-phenyldibenz[*b,f*]oxepine (**49**). The reaction of this relatively electron-rich substrate produced the desired pentacyclic compound **50** in an 80 % yield (entry 23). On the other hand, treating the electron-deficient 3-iodo-4-phenylisocoumarin (**51**) under our standard reaction conditions gave a complex mixture, and we failed to isolate any of the desired tricyclic compound **52** (entry 24). This disappointing result was not unexpected, since our previous experience with compound **51** has indicated that palladium easily catalyzes its decomposition. Our last attempt to generate polycycles from vinylic iodides involved the use of isoquinolone **53** (entry 25). This substrate suffers the disadvantage that the intramolecular arylation step requires the formation of a six-membered ring. As expected, the reaction of substrate **53** under our standard reaction conditions at 110 °C failed to produce the desired pentacyclic product **54**. After 5 d of reaction, we were only able to isolate the reduction product *N*-phenyl-3-phenylisoquinolone[12] in a 12 % yield.

A mechanistically interesting question is whether the arylpalladium intermediate can migrate more than once and still effect synthetically useful chemistry. To examine this possibility, 2-iodo-5-phenoxybiphenyl (**55**) was allowed to react under our migration conditions and an 88 % yield of double migration product **4** was isolated (entry 26 and

Scheme 5). Mechanistically, the palladium first inserts into the aryl iodide bond to form intermediate **A**, which migrates to the phenyl unit by through-space C-H activation. The metal moiety in the first migration intermediate **B** can return to the original aromatic ring in either the position from which it originally migrated (**A**) or migrate to the position *ortho* to the phenoxy group (**C**), where it can be trapped by arylation. Note that the yield for this double migration chemistry is very similar to that from the single migration chemistry (entry 2) and the success of this double palladium migration indicates that multiple migration processes are entirely feasible.

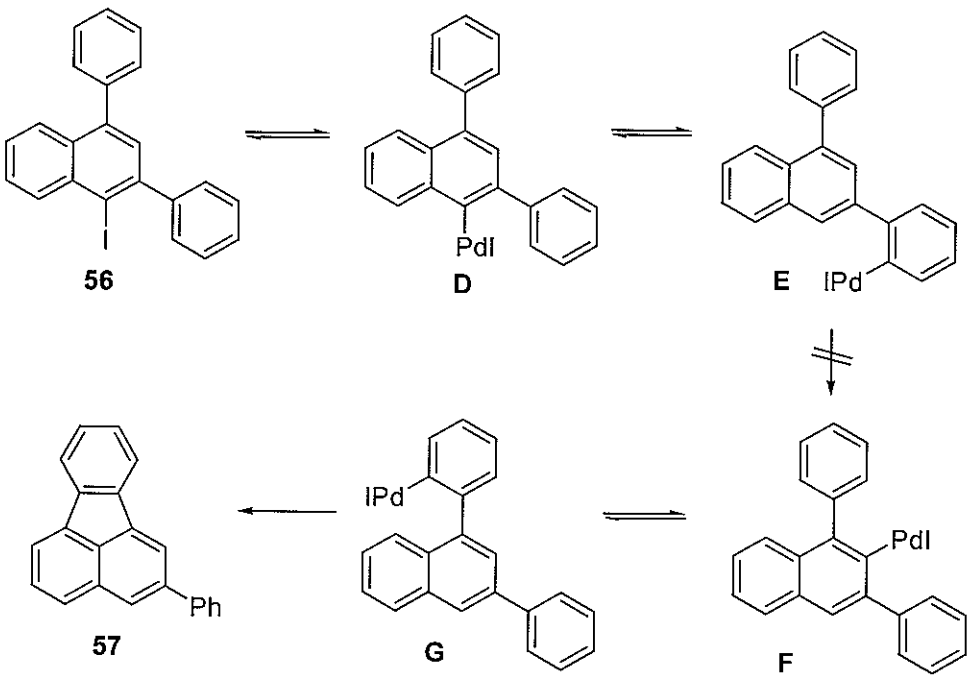
Scheme 5



One attempt to extend this chemistry to a triple migration process has been unsuccessful. The reaction of iodonaphthalene **56** under our standard migration conditions afforded none of the desired triple migration product **57**, producing instead a 62 % yield of the reduction product (entry 27). The reason for this failure to afford compound **57** is

indicated in Scheme 6. While we would anticipate that intermediates **D** and **E** should be easily formed, we believe that the problem lies in getting the relatively unhindered species **E** to migrate the palladium to the more hindered position present in **F**. Instead the palladium presumably migrates back to the less hindered position present in intermediate **D**. This is consistent with our previous observation in entries 12 and 20 that palladium is more likely to migrate to or form a new C-C bond at a less hindered position. Therefore, the palladium intermediates only equilibrate between **D** and **E**, and eventually produce the reduced 1,3-diphenylnaphthalene.

Scheme 6

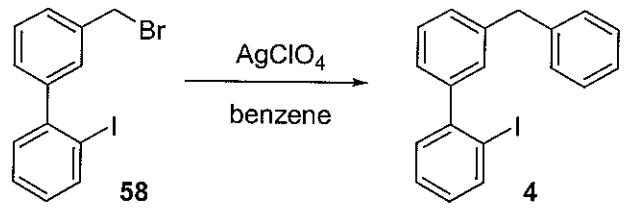


Conclusions

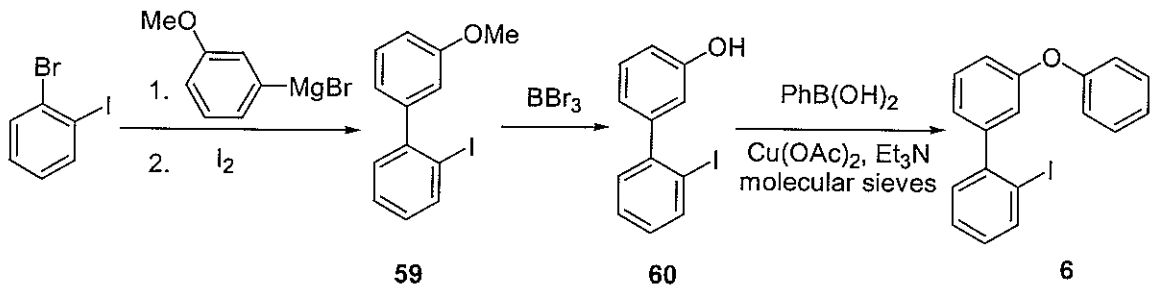
In conclusion, we have developed novel methodology for the synthesis of complex fused polycycles employing two or more sequential Pd-catalyzed intramolecular processes involving C-H activation. This methodology exploits relatively facile aryl to aryl and vinylic to aryl palladium migrations, followed by intramolecular arylation to prepare a wide variety of carbocycles and heterocycles. This chemistry works best with electron-rich aromatics, which is in agreement with the idea that these palladium-catalyzed C-H activation reactions parallel electrophilic aromatic substitution. The success of our double palladium migration for the conversion of biphenyl 55 to dibenzofuran 4 indicates that multiple migration processes can be employed to produce novel new routes to a variety of polycycles. Finally, our demonstration that this chemistry is applicable to alkyne insertion processes as well opens up still further unique routes to polycylic products.

Experimental Section

General procedures. All ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. Compounds **19**,[13] **20**,[13] **36**,[13] and **49**[13] were prepared according to literature procedures.



3'-Benzyl-2-iodobiphenyl (4). This biphenyl was prepared from 3'-bromomethyl-2-iodobiphenyl (**58**)[13] by following a procedure from the literature.[14] To a suspension of $AgClO_4$ (0.28 g, 1.4 mmol) in benzene (4.0 mL) was added compound **58** (0.261 g, 0.7 mmol) in benzene (4.0 mL) and the resulting mixture was stirred overnight at room temperature in the dark. The reaction mixture was diluted with diethyl ether (50 mL), filtered and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography using 50:1 hexane/EtOAc to afford 0.187 g (72 %) of the indicated compound **4** as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 4.03 (s, 3H), 6.97-7.01 (m, 1H), 7.15-7.34 (m, 11H), 7.92 (dd, J = 1.0, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 42.0, 98.8, 126.2, 127.1, 128.2, 128.2, 128.3, 128.6, 128.8, 129.1, 130.1, 130.2, 139.6, 140.8, 141.0, 144.3, 146.6; IR (CH_2Cl_2) 3056, 3025, 2917, 1601, 1583, 1494, 1461 cm^{-1}; HRMS *m/z* 370.0224 (calcd for $C_{19}H_{15}I$, 370.0218).

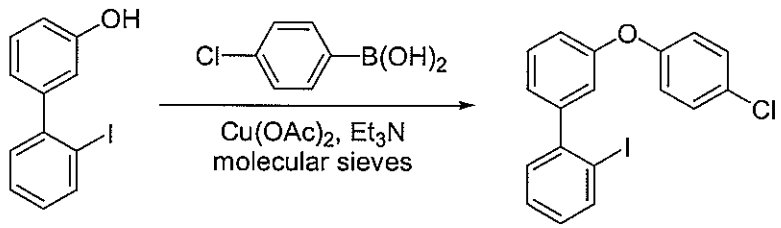


2-Iodo-3'-methoxybiphenyl (59). Compound **59** was prepared by a procedure reported by Hart *et al.*[15] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10

mL) was added slowly (90 min) to a solution of 3-methoxyphenylmagnesium bromide [prepared from 3-bromoanisole (1.87 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10 % aq $NaHSO_3$ (35 mL) and the organic layer was separated and washed with brine (20 mL). Finally, the organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 30:1 hexane/EtOAc to afford 0.620 g (40 %) of the desired compound **59** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 3.84 (s, 3H), 6.88-6.95 (m, 3H), 7.01-7.05 (m, 1H), 7.29-7.38 (m, 3H), 7.95 (dd, J = 1.2, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.4, 98.5, 113.4, 115.0, 121.8, 128.1, 128.9, 129.1, 130.1, 139.6, 145.5, 146.5, 159.1; HRMS *m/z* 309.9859 (calcd for $C_{13}H_{11}IO$, 309.9855).

2-Iodo-3'-phenoxybiphenyl (6). This biphenyl was prepared in two steps from 2-iodo-3-methoxybiphenyl (**59**). To a solution of compound **59** (0.97 g, 3.14 mmol) in CH_2Cl_2 (20 mL) at -78 °C was added 1.0 M BBr_3 in CH_2Cl_2 (4.1 mL, 4.1 mmol). The resulting solution was allowed to warm to room temperature and stirred for 2 h. The mixture was worked up with ice (15 g) and extracted with diethyl ether (75 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography using 3:1 hexane/EtOAc to afford 0.91 g (98 %) of 3-(2-iodophenyl)phenol (**60**) as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 5.04 (br s, 1H), 6.80-6.81 (m, 1H), 6.85-6.90 (m, 2H), 7.00-7.05 (m, 1H), 7.25-7.31 (m, 2H), 7.37 (dt, J = 0.8, 7.6 Hz, 1H), 7.94 (dd, J = 0.8, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 98.4, 114.7, 116.4, 122.0, 128.1, 128.9, 129.3, 130.0, 139.5, 145.8, 146.2, 155.0. 3-(2-Iodophenyl)phenol (**60**) was phenylated

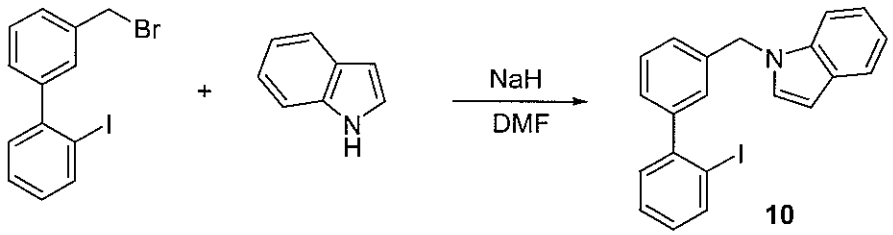
by a literature procedure.[16] A suspension of 3-(2-iodophenyl)phenol (0.222 g, 0.75 mmol), phenylboronic acid (0.183 g, 1.5 mmol), $Cu(OAc)_2$ (0.163 g, 0.90 mmol), Et_3N (0.38 g, 3.75 mmol), and 5 Angstrom molecular sieves (0.2 g) in CH_2Cl_2 (6.0 mL) was stirred under O_2 (1 atm) for 2 d at room temperature. The reaction mixture was diluted with diethyl ether (50 mL), filtered, and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography using 15:1 hexane/EtOAc to afford 0.129 g (46 %) of the indicated compound **6** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 7.00-7.12 (m, 7H), 7.25-7.40 (m, 5H), 7.92 (dd, J = 1.2, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 98.4, 118.2, 119.1, 119.8, 123.4, 124.2, 128.2, 129.0, 129.4, 129.8, 130.0, 139.6, 145.9, 146.0, 156.8, 157.1; IR (CH_2Cl_2) 3058, 1578, 1488, 1460, 1222, cm^{-1}; HRMS *m/z* 372.0020 (calcd for $C_{18}H_{13}IO$, 372.0011).



60 **8**

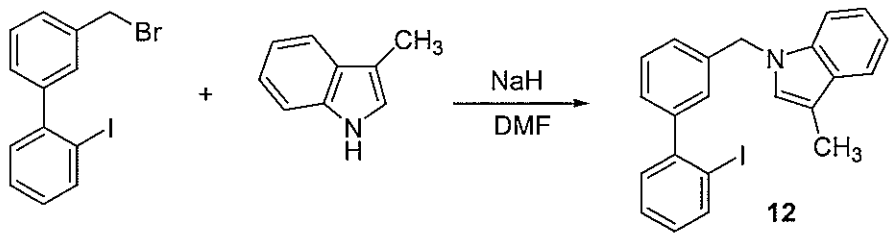
2-Iodo-3'-(*p*-chlorophenoxy)biphenyl (8). This biphenyl was prepared by a procedure similar to that used for compound **6**. A suspension of 3-(2-iodophenyl)phenol (**60**) (0.222 g, 0.75 mmol), *p*-chlorophenylboronic acid (0.235 g, 1.5 mmol), $Cu(OAc)_2$ (0.163 g, 0.90 mmol), Et_3N (0.38 g, 3.75 mmol), and 5 Angstrom molecular sieves (0.2 g) in CH_2Cl_2 (6.0 mL) was stirred under O_2 (1 atm) for 2 d at room temperature. The reaction mixture was diluted with diethyl ether (50 mL), filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 30:1 hexanes/ethyl acetate to afford 79.5 mg (26 %) of the indicated compound **8** as a clear oil:

^{1}H NMR ($CDCl_3$) Γ 6.96-7.09 (m, 6H), 7.27-7.41 (m, 5H), 7.93 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 98.4, 118.2, 119.9, 120.3, 124.6, 128.2, 128.4, 129.1, 129.6, 129.8, 130.0, 139.6, 145.8, 146.0, 155.8, 156.4; IR (CH_2Cl_2) 3057, 1576, 1484, 1460, 1228 cm^{-1}; HRMS *m/z* 405.9632 (calcd for $C_{18}H_{12}ICIO$, 405.9621).



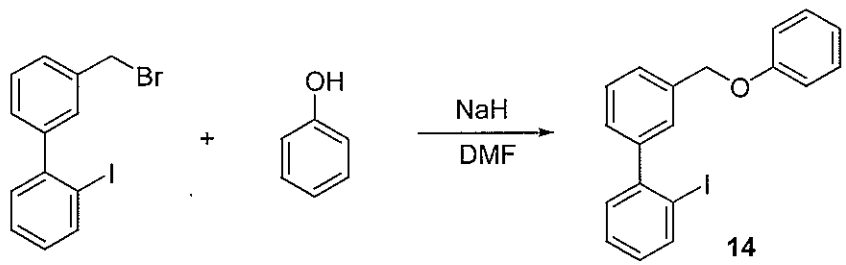
10

1-[3-(2-Iodophenyl)benzyl]indole (10). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 ^{0}C was added 1*H*-indole (0.117 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (**58**)[13] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.335 g (88 %) of the desired compound **10** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 5.34 (s, 2H), 6.54 (d, J = 2.8 Hz, 1H), 6.98 (td, J = 7.6, 1.6 Hz, 1H), 7.09-7.23 (m, 7H), 7.30-7.34 (m, 3H), 7.64 (d, J = 7.6 Hz, 1H), 7.90 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 50.1, 98.6, 101.9, 109.9, 119.6, 121.1, 121.8, 126.2, 128.0, 128.2, 128.4, 128.6, 128.6, 128.9, 129.0, 130.1, 136.4, 137.4, 139.6, 144.6, 146.1; IR (CH_2Cl_2) 3052, 2972, 2922, 2863, 1462, 1437, 1316 cm^{-1}; HRMS *m/z* 409.0334 (calcd for $C_{21}H_{16}IN$, 409.0328).



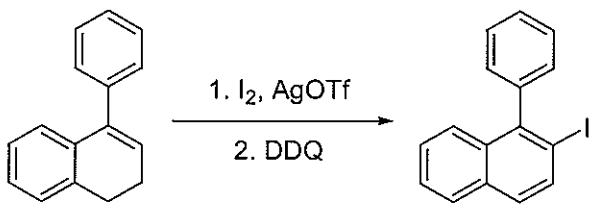
12

1-[3-(2-Iodophenyl)benzyl]-3-methylindole (12). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 ^{0}C was added 3-methyl-1*H*-indole (0.131 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (**58**)[1] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.362 g (92 %) of the desired compound **12** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 2.33 (d, J = 0.8 Hz, 3H), 5.29 (s, 2H), 6.92-6.92 (m, 1H), 6.97-6.99 (m, 1H), 7.10-7.24 (m, 6H), 7.27-7.34 (m, 3H), 7.56-7.58 (m, 1H), 7.90-7.92 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 10.1, 50.1, 98.8, 109.9, 111.2, 119.1, 119.3, 121.9, 126.2, 126.4, 128.2, 128.4, 128.7, 128.7, 129.2, 129.3, 130.3, 136.9, 137.9, 139.8, 144.7, 146.4; IR (CH_2Cl_2) 3052, 2914, 1611, 1465, 1330, 1012 cm^{-1}; HRMS *m/z* 423.0491 (calcd for $C_{22}H_{18}IN$, 423.0484).



14

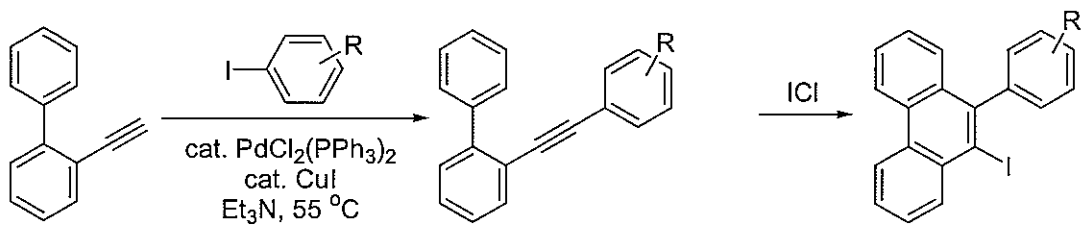
3-(2-Iodophenyl)benzyl phenyl ether (14). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 ^{0}C was added phenol (0.094 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, 3'-bromomethyl-2-iodobiphenyl (**58**)[13] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.359 g (100 %) of the desired compound **14** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 5.13 (s, 2H), 6.96-7.04 (m, 4H), 7.26-7.33 (m, 4H), 7.39-7.46 (m, 4H), 7.94-7.96 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 69.9, 98.6, 115.0, 121.1, 126.8, 128.3, 128.4, 128.5, 129.0, 129.0, 129.6, 130.2, 137.0, 139.6, 144.5, 146.4, 158.8; IR (CH_2Cl_2) 3056, 2919, 1598, 1494, 1238 cm^{-1}; HRMS *m/z* 386.0172 (calcd for $C_{19}H_{15}IO$, 386.0168).



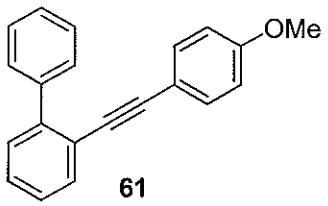
17

2-Iodo-1-phenylnaphthalene (17). To a solution of 3,4-dihydro-1-phenylnaphthalene (1.30 g, 6.3 mmol) and I_2 (2.24 g, 8.8 mmol) in anhydrous CH_3CN (15 mL) was added dropwise AgOTf (1.75 g, 6.8 mmol) in anhydrous CH_3CN (20 mL). The resulting mixture was stirred at room temperature in the dark for 1 h. The reaction was diluted with diethyl

ether (70 mL) and washed with satd aq $Na_2S_2O_3$ (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was dissolved in benzene (25 mL). To this solution was added DDQ (2.86 g, 12.6 mmol) and the reaction was heated at 65 °C for 2 d. The resulting mixture was filtered and washed with 10 % aq Na_2CO_3 (25 mL). The organic layer was filtered, dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified by silica gel column chromatography using 50:1 hexane/EtOAc to afford 1.47 g (70 %) of the indicated compound **17** as a clear oil: ^{1}H NMR ($CDCl_3$) Γ 7.22-7.26 (m, 2H), 7.32-7.34 (m, 1H), 7.38-7.56 (m, 6H), 7.80-7.83 (m, 1H), 7.95 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 98.7, 126.5, 127.0, 127.4, 128.1, 128.1, 128.7, 129.3, 130.2, 133.1, 133.6, 135.8, 143.5, 144.7; IR (CH_2Cl_2) 3053, 1577, 1502, 1442, 1382, 1306 cm^{-1}; HRMS *m/z* 329.9910 (calcd for $C_{16}H_{11}I$, 329.9906).

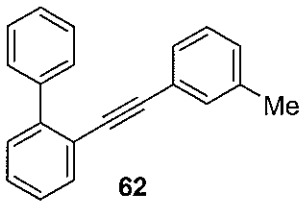


General procedure for preparation of the 2-(arylethynyl)biphenyls. To a solution of the corresponding aryl iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4.0 mL) were added $PdCl_2(PPh_3)_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was then heated under an N_2 atmosphere at 55 ϴC for 3 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding product.



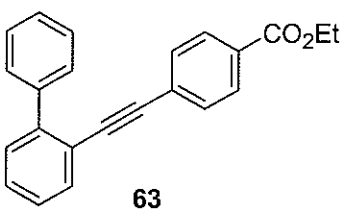
61

2-[(4-Methoxyphenyl)ethynyl]biphenyl (61). 2-Ethynylbiphenyl[17] and 4-iodoanisole were employed. Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.21 g (74 %) of the product as a clear liquid: ^{1}H NMR ($CDCl_3$) Γ 3.80 (s, 3H), 6.84 (dd, J = 2.4, 6.9 Hz, 2H), 7.30 (dd, J = 2.1, 6.9 Hz, 2H), 7.34-7.50 (m, 6H), 7.64-7.73 (m, 3H); ^{13}C NMR ($CDCl_3$) Γ 55.5, 88.4, 92.5, 114.2, 115.9, 122.2, 127.3, 127.6, 128.1, 128.4, 129.6, 129.7, 132.9, 133.1, 140.9, 143.9, 159.8.



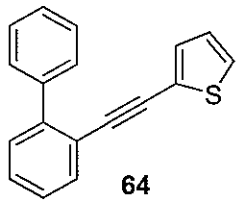
62

2-[(3-Methylphenyl)ethynyl]biphenyl (62). 2-Ethynylbiphenyl[17] and 3-iodotoluene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.26 g (95 %) of the product as a clear liquid: ^{1}H NMR ($CDCl_3$) Γ 2.34 (s, 3H), 7.12-7.22 (m, 4H), 7.33-7.53 (m, 6H), 7.67-7.74 (m, 3H); ^{13}C NMR ($CDCl_3$) Γ 21.5, 89.3, 92.7, 122.0, 123.5, 127.3, 127.7, 128.2, 128.4, 128.7, 128.7, 129.3, 129.7, 129.7, 132.2, 133.1, 138.2, 140.9, 144.1.



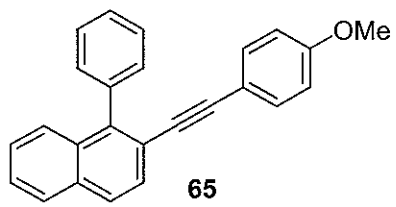
63

Ethyl 4-(biphen-2-ylethynyl)benzoate (63). 2-Ethynylbiphenyl[17] and ethyl 4-iodobenzoate were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.27 g (84 %) of the product as a white solid: mp 58-60 °C; ^{1}H NMR ($CDCl_3$) Γ 1.38 (t, J = 6.9 Hz, 3H), 4.36 (q, J = 7.2 Hz, 2H), 7.32-7.48 (m, 8H), 7.64-7.66 (m, 3H), 7.96 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) Γ 14.6, 61.3, 91.7, 92.6, 121.3, 127.4, 127.9, 128.2, 128.3, 129.3, 129.63, 129.64, 129.8, 129.9, 131.4, 133.2, 140.6, 144.5, 166.3.



64

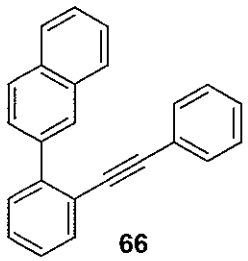
2-(Biphen-2-ylethynyl)thiophene (64). 2-Ethynylbiphenyl[17] and 2-iodothiophene were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.22 g (85 %) of the product as a light yellow liquid: ^{1}H NMR ($CDCl_3$) Γ 6.98-7.00 (m, 1H), 7.15-7.17 (m, 1H), 7.25-7.27 (m, 1H), 7.37-7.55 (m, 6H), 7.66-7.75 (m, 3H); ^{13}C NMR ($CDCl_3$) Γ 85.9, 93.5, 121.6, 123.8, 127.3, 127.4, 127.5, 127.8, 128.3, 129.0, 129.6, 129.8, 131.8, 132.8, 140.7, 144.0.



65

2-[(4-Methoxyphenyl)ethynyl]-1-phenylnaphthalene (65). 2-Iodo-1-phenylnaphthalene and 4-ethynylanisole[18] were employed. Purification by flash chromatography (20:1 hexane/EtOAc) afforded 0.27 g (82 %) of the product as a clear oil:

^{1}H NMR ($CDCl_3$) Γ 3.81 (s, 3H), 6.82 (dd, J = 6.9, 2.1 Hz, 2H), 7.17 (dd, J = 6.9, 2.1 Hz, 2H), 7.43-7.60 (m, 7H), 7.68-7.72 (m, 2H), 7.83-7.94 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 55.4, 88.9, 93.5, 114, 115.7, 120.7, 126.4, 126.6, 126.8, 127.6, 127.6, 128.1, 128.2, 128.4, 130.9, 132.4, 133.0, 133.1, 139.3, 142.8, 159.7.

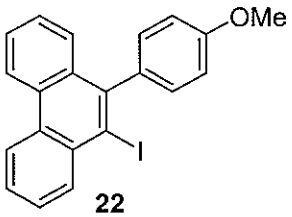


66

2-[2-(Phenylethynyl)phenyl]naphthalene (66). 2-(2-Iodophenyl)naphthalene[15] and phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.29 g (96 %) of the product as a light yellow liquid: ^{1}H NMR ($CDCl_3$) Γ 7.24-7.58 (m, 10H), 7.70-7.72 (m, 1H), 7.86-7.97 (m, 4H), 8.17 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 89.7, 92.7, 122.0, 123.6, 126.2, 126.3, 127.4, 127.5, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9, 130.0, 131.6, 132.9, 133.3, 133.5, 138.3, 144.0 (one sp^2 carbon missing due to overlap).

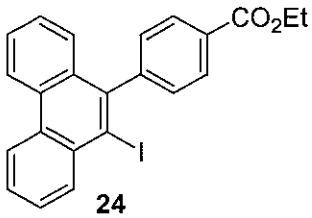
General procedure for synthesis of the phenanthrenes[10]

The following procedure was used to prepare phenanthrenes **22**, **24**, **26**, **28**, **30** and chrysene **32**. To a solution of 2-(arylethynyl)biphenyl (0.30 mmol) in CH_2Cl_2 (3 mL) under N_2 was added ICl (1.2 equiv) in CH_2Cl_2 (0.5 mL) at -78 ϴC. The reaction mixture was stirred at -78 ϴC for 1 h unless otherwise indicated. The reaction mixture was then diluted with diethyl ether (50 mL), washed with 25 mL of satd aq $Na_2S_2O_3$, dried ($MgSO_4$), and filtered. The solvent was evaporated under reduced pressure and the product was purified by chromatography on a silica gel column.



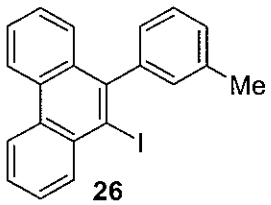
22

9-Iodo-10-(4-methoxyphenyl)phenanthrene (22). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.122 g (99 %) of the product as a white solid: mp 170-171 °C; ^{1}H NMR ($CDCl_3$) Γ 3.94 (s, 3H), 7.09 (dd, J = 2.1, 6.6 Hz, 2H), 7.21 (dd, J = 2.1, 6.6 Hz, 2H), 7.40-7.49 (m, 2H), 7.64-7.72 (m, 3H), 8.45-8.49 (m, 1H), 8.67-8.78 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 55.6, 107.7, 114.0, 122.8, 122.9, 127.2, 127.3, 127.7, 128.3, 129.0, 130.5, 130.8, 131.3, 132.7, 132.9, 135.0, 138.2, 145.3, 159.4; IR (neat) 3066, 3024, 2834, 1610 cm^{-1}; HRMS *m/z* 410.0172 (calcd for $C_{21}H_{15}IO$, 410.0168).



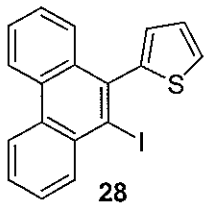
24

Ethyl 4-(10-iodophenanthren-9-yl)benzoate (24). The reaction mixture was stirred at room temperature for 1 h. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.136 g (100 %) of the product as a white solid: mp 152-153 °C; ^{1}H NMR ($CDCl_3$) Γ 1.46 (t, J = 7.2 Hz, 3H), 4.47 (q, J = 7.2 Hz, 2H), 7.30-7.45 (m, 4H), 7.66-7.75 (m, 3H), 8.26 (dd, J = 1.8, 6.6 Hz, 2H), 8.45-8.49 (m, 1H), 8.68-8.78 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 14.6, 61.4, 106.0, 122.9, 123.0, 127.4, 127.5, 128.0, 128.4, 128.5, 130.1, 130.3, 130.4, 130.5, 130.8, 132.1, 132.5, 134.9, 144.6, 150.0, 166.7; IR (CH_2Cl_2) 3069, 2979, 1714 cm^{-1}; HRMS *m/z* 452.0278 (calcd for $C_{23}H_{17}IO_2$, 452.0273).



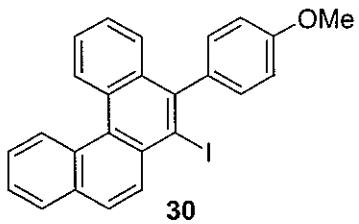
26

9-Iodo-10-(3-methylphenyl)phenanthrene (26). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.117 g (99 %) of the product as a white solid: mp 134-135 °C; ^{1}H NMR ($CDCl_3$) Γ 2.44 (s, 3H), 7.07-7.09 (m, 2H), 7.30-7.32 (m, 1H), 7.41-7.45 (m, 3H), 7.63-7.70 (m, 3H), 8.45-8.48 (m, 1H), 8.67-8.73 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 21.7, 106.5, 122.6, 122.7, 127.1, 127.1, 127.5, 128.1, 128.4, 128.5, 128.8, 130.3, 130.6, 130.6, 132.5, 132.5, 134.7, 138.1, 145.4, 145.5 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3067, 2971, 2921, 1602, 1563 cm^{-1}; HRMS *m/z* 394.0226 (calcd for $C_{21}H_{15}I$, 394.0219).



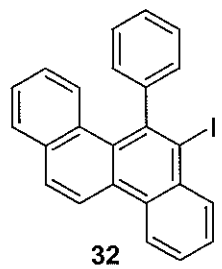
28

9-Iodo-10-(thiophen-2-yl)phenanthrene (28). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.111 g (96 %) of the product as a white solid: mp 140-142 °C; ^{1}H NMR ($CDCl_3$) Γ 7.06-7.08 (m, 1H), 7.23-7.26 (m, 1H), 7.45-7.76 (m, 6H), 8.44-8.49 (m, 1H), 8.66-8.75 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 110.5, 122.7, 122.9, 126.5, 127.2, 127.5, 128.2, 128.4, 128.7, 128.8, 130.3, 131.1, 132.6, 133.2, 135.3, 138.4, 146.5; IR (neat) 2925, 1464, 1216 cm^{-1}; HRMS *m/z* 385.9631 (calcd for $C_{18}H_{11}IS$, 385.9626).



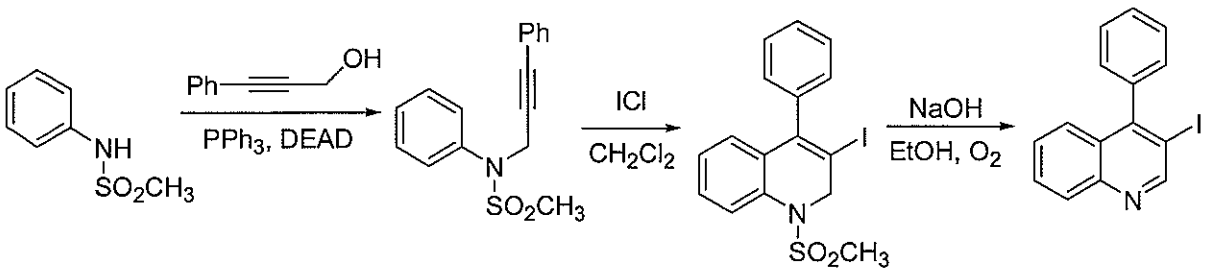
30

6-Iodo-5-(4-methoxyphenyl)benzo[*c*]phenanthrene (30). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.138 g (97 %) of the product as a white solid: mp 186-187 °C; ^{1}H NMR ($CDCl_3$) Γ 3.94 (s, 3H), 7.08-7.12 (m, 2H), 7.23-7.26 (m, 2H), 7.42-7.47 (m, 1H), 7.57-7.69 (m, 4H), 7.94 (d, J = 9.0 Hz, 1H), 8.04-8.06 (m, 1H), 8.42 (d, J = 9.0 Hz, 1H), 9.01-9.04 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 55.6, 107.3, 114.1, 126.4, 126.6, 126.7, 126.8, 128.4, 128.4, 128.6, 128.6, 128.8, 129.0, 129.7, 130.2, 131.3, 131.5, 132.4, 133.8, 133.8, 138.0, 145.0, 159.4; IR (neat) 2950, 1606, 1506 cm^{-1}; HRMS *m/z* 460.0330 (calcd for $C_{25}H_{17}IO$, 460.0324).



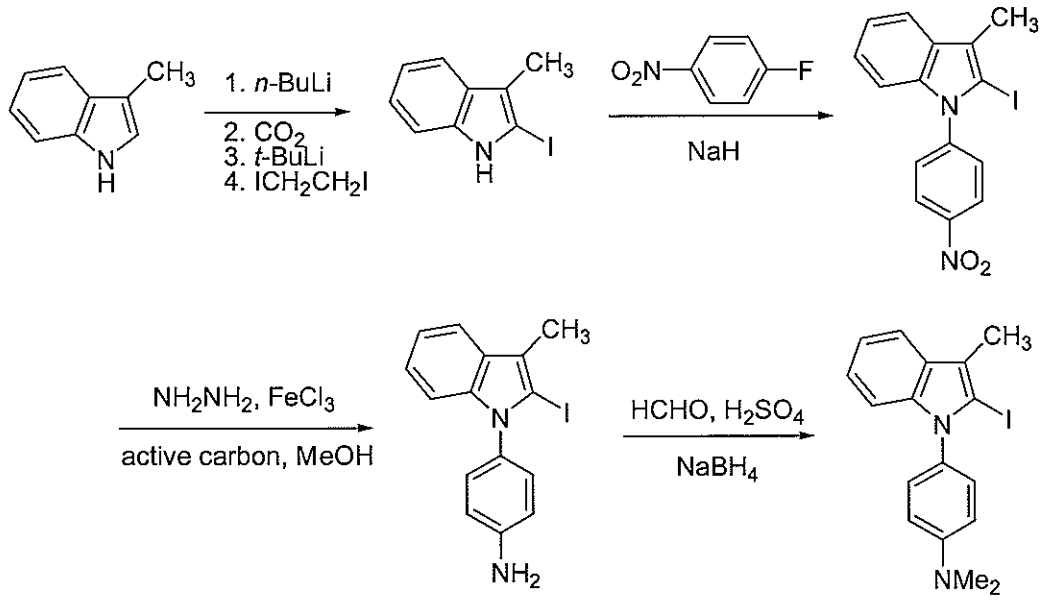
32

6-Iodo-5-phenylchrysene (32). Purification by flash chromatography (40:1 hexane/EtOAc) afforded 98 mg (76%) of the product as a yellow solid: mp 168-169 °C; ^{1}H NMR ($CDCl_3$) Γ 7.07 (t, J = 6.9 Hz, 1H), 7.33-7.57 (m, 7H), 7.71-7.76 (m, 2H), 8.89 (d, J = 6.5 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 8.56-8.60 (m, 1H), 8.78 (d, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) Γ 111.5, 121.3, 123.7, 125.4, 126.1, 127.7, 128.2, 128.4, 128.6, 128.9, 129.0, 129.2, 129.3, 130.4, 130.7, 130.8, 131.1, 133.5, 133.8, 135.3, 144.3, 150.0; IR (neat) 2922 cm^{-1}; HRMS *m/z* 430.0025 (calcd for $C_{24}H_{15}I$, 430.0219).



3-Iodo-4-phenylquinoline (34). To a solution of *N*-phenylmethanesulfonamide[19] (0.513 g, 3.0 mmol), PPh_3 (1.18 g, 4.5 mmol) and 3-phenylpropargyl alcohol (0.594 g, 4.5 mmol) in anhydrous THF (30 mL) at 0 °C was added DEAD (0.784 g, 4.5 mmol). The resulting solution was stirred at 0 °C for 1 h and an additional 3 h at room temperature. The mixture was washed with brine (30 mL) and the organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to obtain 0.534 g (63 %) of *N*-phenyl-*N*-(3-phenyl-2-propyn-1-yl)methanesulfonamide as a white solid: mp 76-77 °C; ^{1}H NMR ($CDCl_3$) Γ 3.08 (s, 3H), 4.67 (s, 2H), 7.34-7.46 (m, 8H), 7.62-7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 39.2, 42.3, 84.4, 86.3, 122.3, 127.7, 128.4, 128.7, 129.1, 129.7, 131.9, 140.5. To a solution of *N*-phenyl-*N*-(3-phenyl-2-propyn-1-yl)methanesulfonamide (71.2 mg, 0.25 mmol) in CH_2Cl_2 (3.0 mL) at -78 °C was added ICl (48.7 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL) and the resulting solution was stirred at this temperature for 1 h. The reaction mixture was washed with satd aq $Na_2S_2O_3$ (20 mL) and the organic layer dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 82.2 mg (80 %) of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline as a white solid: mp 173-175 °C; ^{1}H NMR ($CDCl_3$) Γ 2.89 (s, 3H), 4.82 (s, 2H), 6.80 (dd, J = 7.8, 1.2 Hz, 1H), 7.11-7.16 (m, 3H), 7.30-

7.33 (m, 1H), 7.44-7.48 (m, 3H), 7.62 (dd, J = 8.1, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 38.6, 56.7, 92.0, 126.9, 127.2, 127.2, 128.6, 128.8, 129.0, 129.2, 130.7, 134.5, 140.3, 143.9. A solution of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline (0.103 g, 0.25 mmol) and NaOH (0.10 g, 2.5 mmol) in EtOH (10 mL) was stirred at 50 °C under O_2 (1 atm) for 12 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to afford 76.1 mg (92 %) of the desired compound **34** as a white solid: mp 131-132 °C; ^{1}H NMR ($CDCl_3$) Γ 7.25-7.28 (m, 2H), 7.42-7.48 (m, 2H), 7.52-7.55 (m, 3H), 7.69-7.74 (m, 1H), 8.12 (d, J = 8.8 Hz, 1H), 9.24 (s, 1H); ^{13}C NMR ($CDCl_3$) Γ 96.4, 126.8, 127.4, 128.7, 129.0, 129.1, 129.5, 129.8, 140.4, 147.2, 152.4, 156.6 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3061, 2918, 1566, 1501, 1485 cm^{-1}; HRMS *m/z* 330.9864 (calcd for $C_{15}H_{10}IN$, 330.9858).



38

2-Iodo-3-methylindole. To a solution of 3-methylindole (2.64 g, 20.0 mmol) in 55 mL of dry THF was added dropwise 8.4 mL of *n*-BuLi (2.5 M in hexane) at –78 °C under an Ar atmosphere. The resulting suspension was stirred at –78 °C for 20 min. Carbon dioxide was bubbled through the reaction mixture for 30 min to form a clear yellow solution. The reaction mixture was allowed to warm to 25 °C and the solvent was removed under reduced pressure. To the residue was added 50 mL of dry THF and the suspension was cooled to -78 °C. 12.5 Ml of *t*-BuLi (1.7 M pentane) was added to the suspension and the resulting orange reaction mixture was stirred at -78 °C for 1 h. A solution of ICH_2CH_2I (5.64 g, 20.0 mmol) in 15 mL of dry THF was added dropwise and the resulting yellow solution was stirred at -78 °C for 1 h. Then the reaction mixture was allowed to warm to 25 °C and washed with 50 mL of satd aqueous NH_4Cl. The organic layer was collected, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column (5:1 hexane/EtOAc) to afford 4.98 g of 2-iodo-3-methylindole as a yellow oil in 97 % yield with spectral properties identical to those previously reported.[20]

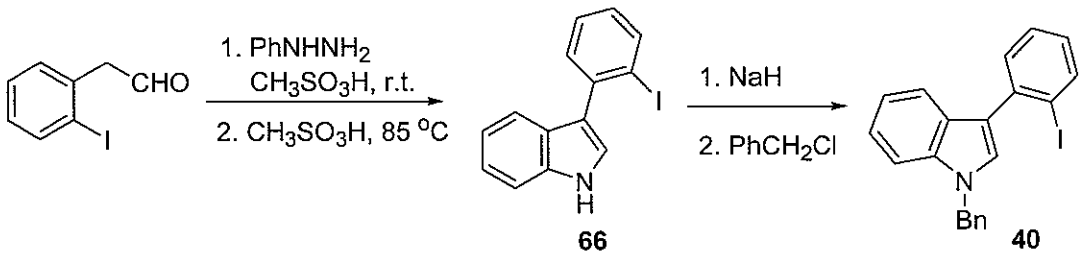
2-Iodo-3-methyl-1-(4-nitrophenyl)indole. To a suspension of NaH (5.5 mmol) in 20 mL of DMF was added 1.28 g of 2-iodo-3-methylindole (5.0 mmol) at 0 °C under an Ar atmosphere and lots of bubbles were generated. The resulting yellow suspension was stirred at 0 °C for 40 min and a solution of 1-fluoro-4-nitrobenzene (0.846 g, 6.0 mmol) in 10 mL of DMF was added dropwise. After 12 h, the reaction was diluted with 30 mL of Et_2O and washed with 30 mL of brine. The organic layer was collected, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (15:1 hexane/EtOAc) to afford 1.07 g of the indicated compound in a 57 % yield as a yellow solid: mp 123-126 °C; ^{1}H NMR ($CDCl_3$) 2.39 (s, 3H), 7.13-7.20 (m, 3H), 7.54-7.60 (m, 3H),

8.37-8.42 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 12.8, 85.2, 110.3, 118.9, 121.1, 121.5, 123.4, 124.9, 129.2, 129.5, 139.3, 144.7, 147.0.

1-(4-Aminophenyl)-2-iodo-3-methylindole. To a 6 dram vial was added 0.80 g of 2-iodo-3-methyl-1-(4-nitrophenyl)indole (2.1 mmol), 17 mL of CH_3OH, 8.5 mg of $FeCl_3$•$6H_2O$ (0.32 mmol), 4.3 mg of active carbon (3.6 mmol), and 0.21 mL of NH_2NH_2•H_2O (4.2 mmol). The resulting mixture was stirred at 25 °C for 5 min and was heated to 70 °C (a sealed tube reaction). After 7 h, the reaction was allowed to cool to 25 °C and filtered. The colorless filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (2:1 hexane/EtOAc) to afford 0.60 g of the indicated compound in an 82 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) 2.38 (s, 3H), 3.94 (br s, 2H), 6.78-6.80 (m, 2H), 7.06-7.10 (m, 5H), 7.54-7.56 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 12.7, 88.8, 110.9, 115.4, 118.0, 118.2, 119.7, 122.2, 128.5, 130.2, 140.1, 146.7 (one sp^2 carbon missing due to overlap).

1-(4-Dimethylaminophenyl)-2-iodo-3-methylindole (38). To a mixture of formaldehyde (37% of aqueous solution, 0.40 mL, 4.98 mmol) and H_2SO_4 (3 M, 0.69 mL, 2.1 mmol) was added a slurry of $NaBH_4$ (0.22 g, 5.8 mmol) and 1-(4-aminophenyl)-2-iodo-3-methylindole (0.29 g, 0.83 mmol) in 7 mL of THF at 0 °C. Lots of bubbles were generated in this process and the resulting yellow suspension was stirred at 0 °C for 10 min. The reaction mixture was diluted with 30 mL of Et_2O, and washed with satd aq $NaHCO_3$ (30 mL) and brine (20 mL). The organic layer was collected, dried over $NaSO_4$, and filtered. Removal of solvent under reduced pressure afforded 0.26 g of the indicated compound in an 83 % yield as a yellow solid: mp 149-150 °C; ^{1}H NMR ($CDCl_3$) 2.38 (s, 3H), 3.04 (s, 6H), 6.79 (d, J = 8.8 Hz, 2H), 7.05-7.10 (m, 3H), 7.16 (d, J = 8.8 Hz, 2H), 7.54-7.56 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 12.7, 40.7, 89.3, 111.0, 112.3, 117.8, 118.2, 119.6, 122.1, 128.1, 128.4, 129.9,

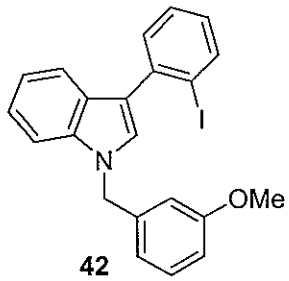
140.2, 150.3; IR (CH_2Cl_2) 3053, 2986, 1524 cm^{-1}; HRMS *m/z* 376.0441 (calcd for $C_{17}H_{17}IN_2$, 376.0437).



3-(2-Iodophenyl)indole (66). To a solution of (2-iodophenyl)acetaldehyde[21] (0.738 g, 3.0 mmol) in 15 mL of absolute ethanol was added 0.356 g of $PhNHNH_2$ (3.3 mmol) and 57.6 mg of CH_3SO_3H (0.6 mmol). The resulting yellow solution was then stirred at room temperature for 1 h. Another 0.519 g of CH_3SO_3H (5.4 mmol) was then added to the reaction mixture and the reaction was stirred at 85 °C. After 2 d, the reaction was complete and was allowed to cool to room temperature. The ethanol was removed under reduced pressure and the residue was diluted with Et_2O (30 mL), washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (5:1 hexane/EtOAc) to afford 0.41 g of compound **66** (43 % yield) as a yellow oil: ^1H NMR ($CDCl_3$) Γ 7.01-7.05 (m, 1H), 7.14-7.18 (m, 1H), 7.23-7.27 (m, 1H), 7.38-7.49 (m, 4H), 7.54 (d, *J* = 8.0 Hz, 1H), 8.01 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.27 (br s, 1H); ^{13}C NMR ($CDCl_3$) Γ 101.0, 111.5, 120.3, 120.4, 122.6, 123.8, 126.8, 128.2, 128.5, 131.6, 135.8, 140.0, 140.1 (one sp^2 carbon missing due to overlap).

1-Benzyl-3-(2-iodophenyl)indole (40). To a suspension of 30 mg of NaH (0.75 mmol, 60 % in mineral oil) in DMF (2 mL) was added dropwise a solution of compound **66** (0.16 g, 0.5 mmol) in DMF (4 mL) at 0 °C. A lot of bubbles were generated. The resulting brown

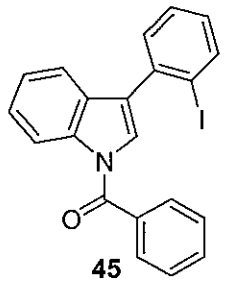
solution was stirred at 0 °C for 45 min and a solution of $PhCH_2Cl$ (0.127 g, 1.0 mmol) in DMF (1 mL) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 12 h. The reaction mixture was diluted with Et_2O (30 mL), washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (20:1 hexane/EtOAc) to afford 0.155 g of the indicated compound **40** (76 % yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 5.38 (s, 2H), 6.98-7.02 (m, 1H), 7.12-7.16 (m, 1H), 7.18-7.33 (m, 8H), 7.37-7.41 (m, 1H), 7.49 (dd, J = 1.6, 7.6 Hz, 1H), 7.54-7.56 (m, 1H), 7.99 (dd, J = 1.2, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 50.4, 101.1, 110.1, 119.2, 120.1, 120.4, 122.3, 127.1, 127.5, 127.9, 128.1, 128.2, 128.4, 129.0, 131.6, 136.3, 137.5, 140.0, 140.1; IR (neat) 3055, 3029, 2921, 1613, 1585 cm^{-1}; HRMS *m/z* 409.0335 (calcd for $C_{21}H_{16}IN$, 409.0328).



42

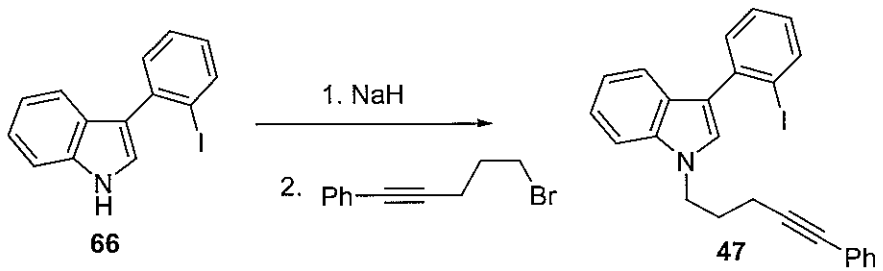
1-(3-Methoxybenzyl)-3-(2-iodophenyl)indole (42). Using the procedure to prepare compound **40**, but employing 0.16 g of 3-methoxybenzyl chloride (1.0 mmol) afforded 0.193 g of the indicated compound **42** in an 88 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.72 (s, 3H), 5.34 (s, 2H), 6.71 (s, 1H), 6.77-6.81 (m, 2H), 6.98-7.02 (m, 1H), 7.12-7.15 (m, 1H), 7.18-7.24 (m, 2H), 7.31-7.33 (m, 2H), 7.37-7.40 (m, 1H), 7.48-7.50 (m, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 50.3, 55.4, 101.1, 110.1, 112.7, 113.2, 119.2, 119.3, 120.1, 120.4, 122.3, 127.5, 128.1, 128.2, 128.4, 130.0, 131.6, 136.2, 139.1,

140.0, 140.0, 160.2; IR (neat) 3051, 2934, 1586, 1490 cm^{-1}; HRMS *m/z* 439.0439 (calcd for $C_{22}H_{18}ION$, 439.0433).



45

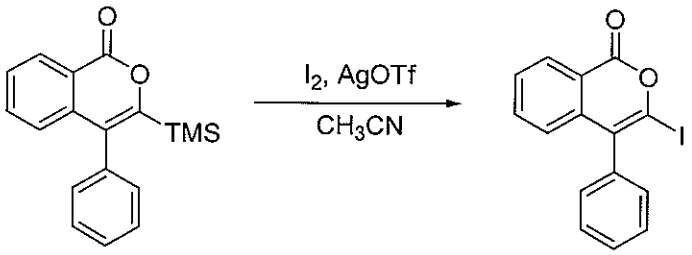
1-Benzoyl-3-(2-iodophenyl)indole (45). Using the procedure to prepare compound **40**, but employing of 0.14 g of benzoyl chloride (1.0 mmol) afforded 0.190 g of the indicated compound **45** in a 90 % yield as a pale yellow solid: mp 102-103 °C; ^1H NMR ($CDCl_3$) Γ 7.04-7.08 (m, 1H), 7.32-7.36 (m, 1H), 7.40-7.46 (m, 5H), 7.51-7.55 (m, 2H), 7.58-7.63 (m, 1H), 7.81-7.84 (m, 2H), 7.98 (d, J = 7.6 Hz, 1H), 8.49-8.51 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 100.2, 116.7, 120.5, 124.3, 125.3, 125.5, 126.5, 128.3, 128.8, 129.6, 129.6, 130.1, 131.3, 132.3, 134.6, 136.1, 138.1, 140.1, 168.9; IR (neat) 3051, 1686, 1450, 1364 cm^{-1}; HRMS *m/z* 423.0129 (calcd for $C_{21}H_{14}ION$, 423.0120).



66 **47**

3-(2-Iodophenyl)-1-(5-phenyl-4-pentynyl)indole (47). To a suspension of NaH (45.7 mg, 1.14 mmol, 60 % in mineral oil) in DMF (3 mL) was added dropwise a solution of compound **66** (0.243 g, 0.76 mmol) in DMF (5 mL) at 0 °C. A lot of bubbles were generated.

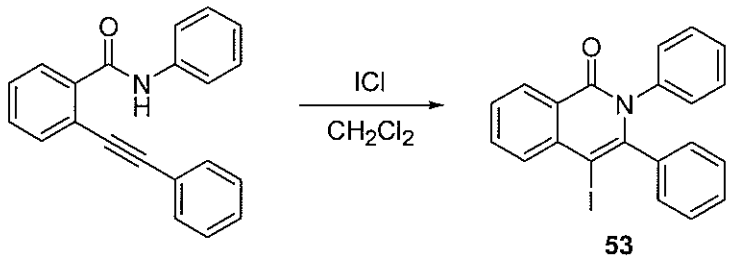
The resulting brown solution was stirred at 0 °C for 45 min and a solution of 5-bromo-1-phenyl-1-pentyne (0.34 g, 1.52 mmol) in DMF (2 mL) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 12 h, diluted with Et_2O (30 mL), washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (20:1 hexane/EtOAc) to afford 0.30 g of the indicated compound **47** (85 % yield) as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 2.13-2.22 (m, 2H), 2.45 (t, J = 8.8 Hz, 2H), 4.41 (t, J = 8.8 Hz, 2H), 6.98-7.03 (m, 1H), 7.12-7.23 (m, 1H), 7.23-7.33 (m, 4H), 7.37-7.50 (m, 6H), 7.54-7.56 (m, 1H), 8.00 (dd, J = 1.6, 10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 17.0, 29.1, 45.1, 82.3, 88.6, 101.1, 109.8, 118.7, 120.0, 120.4, 122.1, 123.8, 127.5, 128.0, 128.1, 128.2, 128.3, 128.5, 131.5, 131.8, 135.9, 140.1 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3053, 2985, 1613, 1596, 1548 cm^{-1}; HRMS *m/z* 461.0647 (calcd for $C_{25}H_{20}IN$, 461.0641).



51

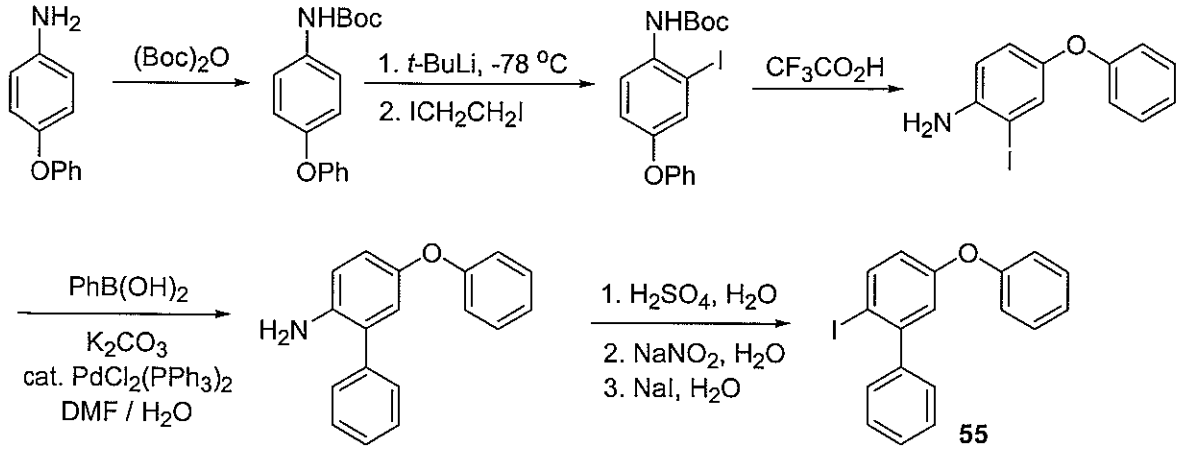
3-Iodo-4-phenylisocoumarin (51). A solution of 4-phenyl-3-(trimethylsilyl)isocoumarin[22] (0.435 g, 1.48 mmol), I_2 (1.13 g, 4.45 mmol), and AgOTf (0.76 g, 2.96 mmol) in CH_3CN (20 mL) was heated at 55 °C for 5 d. The reaction mixture was diluted with diethyl ether (100 mL), and washed with satd aq $Na_2S_2O_3$ (30 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to obtain 0.498 g (97 %) of the indicated compound **51** as a yellow solid. Recrystallization from

hexanes/ethyl acetate afforded the indicated compound **51** as a yellow solid: mp 170-171 °C, ^{1}H NMR ($CDCl_3$) Γ 6.97 (d, J = 8.0 Hz, 1H), 7.26-7.28 (m, 2H), 7.50-7.56 (m, 4H), 7.59-7.63 (m, 1H), 8.31 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 107.9, 119.6, 125.6, 127.4, 128.7, 128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2; IR (CH_2Cl_2) 1736 cm^{-1}; HRMS *m/z* 347.9652 (calcd for $C_{15}H_9IO_2$, 347.9647).



53

4-Iodo-2,3-diphenyl-2*H*-isoquinolin-1-one (53). To a solution of *N*-phenyl-2-(phenylethynyl)benzamide[23] (74.2 mg, 0.25 mmol) in CH_2Cl_2 (3.0 mL) at room temperature was added ICl (48.7 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL) and the resulting solution was stirred at this temperature for 1 h. The reaction mixture was washed with satd aq $Na_2S_2O_3$ (20 mL) and the organic layer dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 42.3 mg (40 %) of the indicated compound **53** as a yellow solid: mp 129-130 °C; ^{1}H NMR ($CDCl_3$) Γ 7.08-7.11 (m, 1H), 7.20-7.30 (m, 3H), 7.33-7.38 (m, 4H), 7.57-7.64 (m, 3H), 7.67-7.72 (m, 1H), 8.03-8.06 (m, 1H), 8.84-8.87 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 75.2, 124.1, 125.1, 125.1, 125.4, 128.1, 128.7, 128.7, 130.5, 130.9, 132.0, 132.7, 135.7, 140.6, 145.0, 147.8, 152.1; IR (CH_2Cl_2) 2916, 2849, 1642, 1586, 1488, 1445 cm^{-1}; HRMS *m/z* 423.0131 (calcd for $C_{15}H_9IO_2$, 423.0120).



***N*-(4-Phenoxyphenyl)-2,2-dimethylpropanamide.** To a solution of 4-phenoxyaniline (3.33 g, 18.0 mmol) in 70 mL of dried THF was added $(Boc)_2O$ (4.71 g, 21.6 mmol) and the resulting yellow solution was refluxed at 80 °C for 6 h. The solvent was removed under reduced pressure and the reddish residue was recrystallized using hexane and EtOAc to afford 4.84 g of the indicated compound (85 % yield) as white needles: mp 109-111 °C; ^{1}H NMR ($CDCl_3$) Γ 1.52 (s, 9H), 6.43 (br s, 1H), 6.95-6.98 (m, 4H), 7.06 (t, J = 3.6 Hz, 1H), 7.29-7.34 (m, 4H); ^{13}C NMR ($CDCl_3$) Γ 28.6, 80.7, 118.3, 120.2, 120.5, 123.0, 129.9, 134.2, 152.6, 153.2, 158.1.

***N*-(2-Iodo-4-phenoxyphenyl)-2,2-dimethylpropanamide.** To a solution of *N*-(4-phenoxyphenyl)-2,2-dimethylpropanamide (2.57 g, 9.02 mmol) in 20 mL of dry diethyl ether was added dropwise 10.6 mL of *t*-BuLi (1.7 M in pentane, 18.04 mmol) at -78 °C under Ar. The pale orange solution turned a pale yellow color when half of the *t*-BuLi solution had been added and eventually to yellow when all of the *t*-BuLi solution was added. The resulting yellow solution was then stirred at -78 °C for 30 min. A solution of ICH_2CH_2I (2.81 g, 9.92 mmol, recrystallized from diethyl ether) in 20 mL of dry ether was added dropwise to the reaction mixture and the resulting orange solution was stirred at -78 °C for

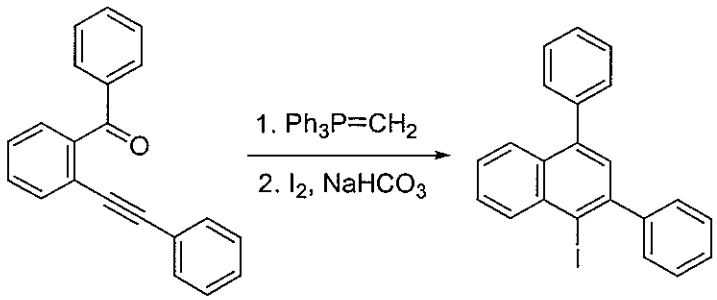
another 30 min. The reaction mixture was allowed to warm up to room temperature and quenched by 50 mL of water. The organic layer was separated and dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (15:1 hexane/EtOAc) to afford 2.3 g of the desired compound (62 % yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 1.53 (s, 9H), 6.68 (br s, 1H), 6.96-6.98 (m, 2H), 7.02 (dd, J = 2.4, 8.8 Hz, 1H), 7.08-7.12 (m, 1H), 7.30-7.35 (m, 2H), 7.42 (d, J = 2.8 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 28.5, 81.3, 89.5, 118.6, 120.2, 121.6, 123.6, 129.3, 130.0, 134.9, 153.0, 153.0, 157.4.

2-Iodo-4-phenoxyaniline. To a solution of *N*-(2-iodo-4-phenoxyphenyl)-2,2-dimethylpropanamide (0.82 g, 2.0 mmol) in 10 mL of CH_2Cl_2 was added dropwise 2.0 mL of TFA at 0 °C and the reaction was allowed to warm up to room temperature. The resulting colorless mixture was stirred at room temperature for 16 h, diluted with 20 mL of CH_2Cl_2, washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (5:1 hexane/EtOAc) to afford 0.56 g of the indicated compound (91 % yield) as a pale orange solid: mp 54-56 °C; ^{1}H NMR ($CDCl_3$) Γ 4.00 (s, 2H), 6.74 (d, J = 8.7 Hz, 1H), 6.88-6.91 (m, 2H), 6.93-6.95 (m, 1H), 7.01-7.07 (m, 1H), 7.26-7.32 (m, 2H), 7.36 (d, J = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 83.8, 115.2, 117.6, 121.6, 122.8, 129.9, 130.3, 143.5, 148.8, 158.6.

4-Phenoxy-2-phenylaniline. To a 50 mL round-bottom flask was added $PdCl_2(PPh_3)_2$ (0.103 g, 0.147 mmol), $PhB(OH)_2$ (0.358 g, 2.94 mmol), K_2CO_3 (0.406 g, 2.94 mmol), 2-iodo-4-phenoxyaniline (0.457 g, 1.47 mmol), 15 mL of DMF and 3 mL of H_2O. The whole mixture was then stirred at room temperature for 5 min, flushed with Ar and heated to 70 °C for 3 h. The reaction was allowed to cool to room temperature, diluted with diethyl ether (30

mL), washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (5:1 hexane/EtOAc) to afford 0.342 g of the indicated compound (88 % yield) as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.71 (br s, 2H), 6.75-6.77 (m, 1H), 6.87-6.90 (m, 2H), 6.97-7.03 (m, 3H), 7.25-7.35 (m, 3H), 7.41-7.60 (m, 4H); ^{13}C NMR ($CDCl_3$) Γ 116.9, 117.5, 120.4, 122.2, 122.3, 127.6, 129.0, 129.1, 129.2, 129.7, 139.1, 139.9, 148.9, 159.0.

2-Iodo-5-phenoxybiphenyl (55). To a solution of 4-phenoxy-2-phenylaniline (0.383 g, 1.47 mmol) in DME (4 mL) was added dropwise 3 mL of water containing 0.6 mL of conc H_2SO_4 (95 %). The resulting yellow mixture was cooled to 0 °C and a solution of $NaNO_2$ (0.152 g, 2.21 mmol) in water (1 mL) was added over 10 min. The yellow reaction mixture was stirred at 0 °C for 20 min and a solution of NaI (1.10 g, 7.35 mmol) in water (3 mL) was added dropwise at 0 °C. The reaction mixture turned black when the NaI solution was added. After 10 min, the reaction was diluted with Et_2O (30 mL), and washed by satd $Na_2S_2O_3$ (30 mL), water (30 mL), and brine (30 mL). The organic layer was collected, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (30:1 hexane/EtOAc) to afford 0.44 g of the indicated compound **55** (81 % yield) as a yellow solid: mp 68-70 °C; ^{1}H NMR ($CDCl_3$) Γ 6.73 (dd, J = 3.0, 8.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 7.04-7.06 (m, 2H), 7.11-7.15 (m, 1H), 7.31-7.43 (m, 7H), 7.85 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 90.4, 119.4, 119.5, 120.5, 124.1, 128.0, 128.2, 129.4, 130.1, 140.6, 143.9, 148.2, 156.6, 158.0; IR (CH_2Cl_2) 3056, 2981, 1583, 1561, 1490 cm^{-1}; HRMS *m/z* 372.0019 (calcd for $C_{18}H_{13}IO$, 372.0011).

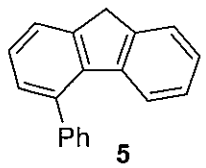


56

1-Iodo-2,4-diphenylnaphthalene (56). To a yellow suspension of $Ph_3P=CH_2$ (1.5 mmol) in THF (8 mL) [prepared by the reaction of 0.57 g of methyltriphenylphosphonium bromide (1.6 mmol) in 8 mL of THF and 0.6 mL of *n*-BuLi (2.5 M in hexane, 1.5 mmol) at 0 °C for 30 min] was added a solution of 2-(phenylethynyl)acetophenone (1.0 mmol) in THF (3 mL). After 1 h, TLC analysis showed that the reaction was not complete and another 1.0 mmol of $Ph_3P=CH_2$ in THF (5 mL) was added to the reaction mixture. The reaction reached completion in 10 min. The solvent was removed under reduced pressure and 30 mL of hexane was added to the residue. After being stirred at 25 °C for 20 min, the mixture was filtered to remove the phosphonium salt. Removal of the solvent under reduced pressure afforded a colorless residue. The colorless residue was added to a stirred mixture of $NaHCO_3$ (0.25 g, 3.0 mmol), I_2 (1.54 g, 6.0 mmol) and CH_3CN (15 mL). The reaction was complete after 20 min at 25 °C. The reaction mixture was diluted with Et_2O (30 mL) and washed by satd aqueous $Na_2S_2O_3$ (30 mL). The organic layer was collected, dried over $NaSO_4$, filtered, and the solvent was removed under reduced pressure. The residue was purified by chromatograph (50:1 hexane/EtOAc) to afford 0.39 g of the indicated compound **56** in a 97 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 7.38-7.50 (m, 12H), 7.58-7.63 (m, 1H), 7.88 (d, J = 8.1 Hz, 1H), 8.43 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 103.6, 126.8, 126.9, 127.8, 128.2, 128.2, 128.6, 128.9, 129.8, 130.2, 131.5, 134.1, 135.3, 139.9, 140.9,

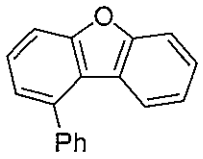
146.0, 146.2 (one sp^2 carbon missing due to overlap); IR (neat) 3058, 3028, 2927, 1599 cm^{-1}; HRMS *m/z* 406.0225 (calcd for $C_{22}H_{15}I$, 406.0218).

Representative procedure for the palladium-catalyzed migration reactions. The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-*bis*(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol) and CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol) in DMF (4 mL) were stirred under Ar at 100 °C for the specified period of time. The reaction mixture was allowed to cool to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by flash chromatography on silica gel.



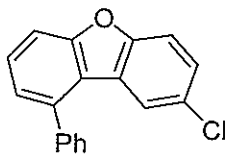
5

1-Phenyl-9*H*-fluorene (5). Compound **4** (92.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 3 d. The reaction mixture was chromatographed using 30:1 hexane/EtOAc to afford 24.2 mg (40 %) of the indicated compound **2** as a colorless oil: ^1H NMR ($CDCl_3$) Γ 3.95 (s, 2H), 6.94 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.19-7.22 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.45-7.55 (m, 7H); ^{13}C NMR ($CDCl_3$) Γ 37.0, 122.9, 124.0, 124.8, 126.3, 126.4, 127.5, 128.5, 128.8, 129.2, 137.9, 138.7, 141.3, 141.6, 143.7, 143.9 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3056, 3025, 1454, 1417, 1478 cm^{-1}; HRMS *m/z* 242.1101 (calcd for $C_{19}H_{14}$, 242.1096).



7

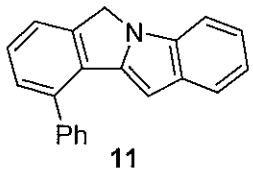
1-Phenyldibenzofuran (7). Compound **6** (93.0 mg, 0.25 mmol) or compound **55** (93.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixtures were chromatographed using 30:1 hexane/EtOAc to afford 54.4 mg (89 %) (entry 2, Table 2) or 54.0 mg (88 %) (entry 8, Table 2) of the indicated compound **7**, respectively, as a white solid: mp 62-63 °C (lit[24] mp 63-64 °C); ^{1}H NMR ($CDCl_3$) Γ 7.10-7.14 (m, 1H), 7.24-7.26 (m, 1H), 7.37-7.42 (m, 1H), 7.46-7.64 (m, 9H); ^{13}C NMR ($CDCl_3$) Γ 110.5, 111.6, 121.8, 122.3, 122.5, 123.9, 124.0, 127.1, 127.1, 127.9, 128.6, 129.0, 138.0, 140.0, 156.4, 156.5. The other spectral properties were identical to those previously reported.[24]



9

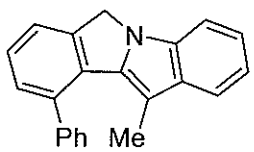
7-Chloro-1-phenyldibenzofuran (9). Compound **8** (0.101 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 57.1 mg (82 %) of the indicated compound **9** as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 7.25 (dd, J = 6.8, 1.2 Hz, 1H), 7.34 (dd, J = 8.4, 2.4 Hz, 1H), 7.45-7.60 (m, 9H); ^{13}C NMR ($CDCl_3$) Γ 110.7, 112.5, 121.0, 122.1, 124.3, 125.3, 127.1, 127.7, 127.8, 128.3, 128.8, 128.9, 138.2, 139.4, 154.7, 157.1; IR (CH_2Cl_2)

3061, 3032, 1444, 1400, 1199, 1243 cm^{-1}; HRMS *m/z* 278.0501 (calcd for $C_{18}H_{11}ClO$, 278.0498).



11

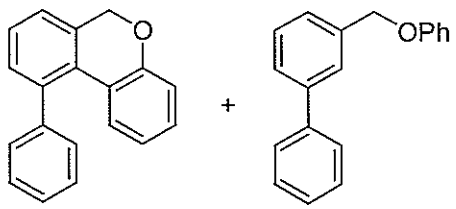
10-Phenyl-6*H*-isoindolo[2,1-*a*]indole (11). Compound **10** (0.102 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 49.2 mg (70 %) of the indicated compound **11** as a white solid: mp 139-140 °C; ^{1}H NMR ($CDCl_3$) Γ 5.08 (s, 2H), 6.16 (s, 1H), 7.03-7.07 (m, 1H), 7.14-7.18 (m, 1H), 7.32-7.54 (m, 8H), 7.64-7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 48.2, 94.3, 109.1, 119.7, 121.7, 122.4, 127.3, 128.0, 128.5, 128.8, 129.3, 131.0, 132.4, 133.7, 137.0, 139.9, 142.5, 143.2 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3053, 2916, 2850, 1471, 1551, 1446 cm^{-1}; HRMS *m/z* 281.1210 (calcd for $C_{21}H_{15}N$, 281.1204).



13

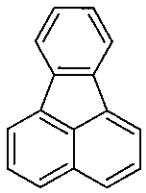
2-Methyl-10-phenyl-6*H*-isoindolo[2,1-*a*]indole (13). Compound **12** (0.106 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 52.4 mg (71 %) of the indicated compound **13** as a white solid: mp 143-145 °C (decomposes); ^{1}H NMR ($CDCl_3$) Γ 1.41 (s, 3H), 5.06 (s, 2H), 7.03-7.07 (m, 1H), 7.16-7.20 (m, 1H), 7.23-7.31 (m,

3H), 7.40-7.50 (m, 7H); ^{13}C NMR ($CDCl_3$) Γ 9.5, 48.1, 104.2, 109.0, 119.1, 120.0, 122.0, 122.4, 126.5, 127.9, 128.7, 129.9, 130.2, 132.6, 133.8, 134.0, 137.0, 140.0, 142.6, 142.8; IR (CH_2Cl_2) 3048, 2976, 2853, 1469, 2976, 2853, 1469, 1411 cm^{-1}; HRMS *m/z* 295.1369 (calcd for $C_{22}H_{17}N$, 295.1361).



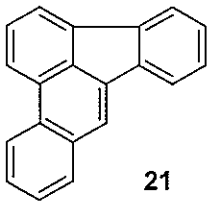
15 **16**

10-Phenyl-6*H*-benzo[*c*]chromene (15) and phenyl 3-phenylbenzyl ether (16). Compound **14** (96.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 120 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 47.8 mg (75 %) of a 60:40 inseparable mixture of compounds **15** and **16** respectively. Major isomer **15**: ^{1}H NMR ($CDCl_3$) Γ 5.02 (s, 2H) as a characteristic peak; HRMS *m/z* 258.1050 (calcd for $C_{19}H_{14}O$, 258.1045). Minor isomer **16**: ^{1}H NMR ($CDCl_3$) Γ 5.11 (s, 2H) as a characteristic peak; HRMS *m/z* 260.1206 (calcd for $C_{19}H_{16}O$, 260.1201). Mixture: ^{13}C NMR ($CDCl_3$) Γ 69.9, 70.2, 115.1, 117.6, 121.3, 121.3, 123.6, 124.1, 126.6, 126.7, 127.1, 127.4, 127.4, 127.5, 127.5, 127.7, 128.4, 128.9, 128.9, 128.9, 129.1, 129.1, 129.3, 129.4, 129.4, 129.8, 132.0, 135.5, 137.8, 139.3, 141.2, 141.9, 142.5, 156.6, 159.0; IR (neat) 3058, 3029, 1599, 1495, 1453, 1243 cm^{-1}.



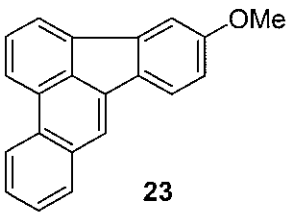
18

Fluoranthene (18). Compound **17** (82.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 1 d. The reaction mixture was chromatographed using 50:1 hexane/EtOAc to afford 41.0 mg (81 %) of the indicated compound **6** as a white solid: mp 107-108 °C (lit[25] mp 106-108 °C). The other spectral properties were identical to those previously reported.[26]



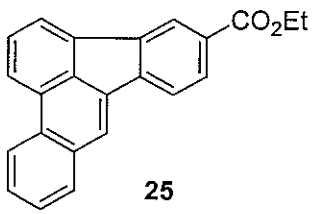
21

Benzo[*e*]acephenanthrylene (21). Compound **20**[13] (95.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexane/EtOAc to afford 49.2 mg (78 %) of the indicated compound **8** as a white solid: mp 166-167 °C (lit[27] mp 165-166 °C). The other spectral properties were identical to those previously reported.[28]



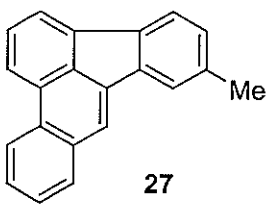
23

5-Methoxybenzo[*e*]acephenanthrylene (23). Compound **22** (0.103 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 50.1 mg (71 %) of the indicated compound **23** as a white solid: mp 188-189 °C (lit[28] mp 189-190 °C). The other spectral properties were identical to those previously reported.[28]



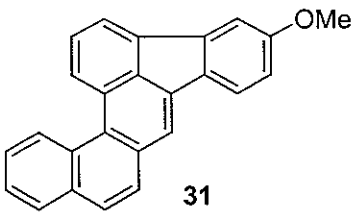
25

Ethyl benzo[*e*]acephenanthrylene-5-carboxylate (25). Compound **24** (0.113 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 40.5 mg (50 %) of the indicated compound **25** as a white solid: mp 153-154 °C; ^{1}H NMR ($CDCl_3$) Γ 1.46 (t, J = 7.2 Hz, 3H), 4.45 (q, J = 7.2 Hz, 2H), 7.63-7.65 (m, 1H), 7.68-7.70 (m, 1H), 7.74-7.78 (m, 1H), 7.98-8.04 (m, 3H), 8.09 (dd, J = 7.6, 1.6 Hz, 1H), 8.24 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.54 (d, J = 0.8 Hz, 1H), 8.64 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 14.5, 61.2, 120.1, 121.5, 122.1, 122.5, 123.2, 123.3, 127.0, 127.6, 127.7, 128.5, 129.0, 129.9, 130.6, 131.1, 132.4, 133.8, 134.0, 136.2, 140.7, 142.6, 166.9; IR (CH_2Cl_2) 2979, 1710, 1240, 1290 cm^{-1}; HRMS *m/z* 324.1157 (calcd for $C_{23}H_{16}O_2$, 324.1150).



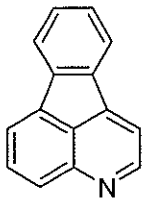
27

6-Methylbenzo[*e*]acephenanthrylene (27). Compound **26** (98.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexane/EtOAc to afford 37.2 mg (56 %) of the indicated compound **27** as a white solid: mp 149-151 °C; ^{1}H NMR ($CDCl_3$) Γ 2.50 (s, 3H), 7.22 (d, J = 7.6 Hz, 1H), 7.59-7.80 (m, 5H), 7.91 (d, J = 7.2 Hz, 1H), 8.01-8.02 (m, 1H), 8.17 (s, 1H), 8.40 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 21.9, 119.2, 121.2, 121.3, 121.3, 122.8, 123.2, 126.8, 127.0, 127.6, 128.3, 129.0, 130.2, 130.8, 132.4, 134.1, 135.3, 137.2, 137.5, 138.2, 138.9; IR (CH_2Cl_2) 2921, 2852, 1460, 1600, 1374 cm^{-1}; HRMS *m/z* 266.1099 (calcd for $C_{21}H_{14}$, 266.1096).



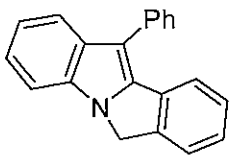
31

10-Methoxydibenz[*e,l*]acephenanthrylene (31). Compound **30** (0.115 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 54.0 mg (65 %) of the indicated compound **31** as a white solid: mp 178-179 °C; ^{1}H NMR ($CDCl_3$) Γ 3.95 (s, 3H), 6.93 (dd, J = 8.1, 2.4 Hz, 1H), 7.46 (d, J = 2.1 Hz, 1H), 7.60-7.66 (m, 1H), 7.70-8.03 (m, 7H), 8.11 (s, 1H), 8.98 (d, J = 8.4 Hz, 1H), 9.19 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 55.9, 107.4, 113.4, 119.6, 121.0, 122.8, 122.8, 126.0, 126.8, 127.3, 127.5, 127.8, 128.3, 128.4, 128.6, 128.7, 129.0, 131.5, 131.5, 133.8, 133.8, 136.1, 137.4, 142.6, 160.6; IR (CH_2Cl_2) 2921, 2849, 1608, 1461, 1285, 1213 cm^{-1}; HRMS *m/z* 332.1209 (calcd for $C_{25}H_{16}O$, 332.1201).



35

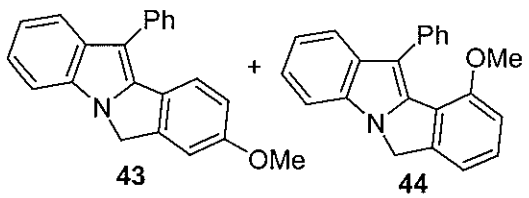
Indeno[1,2,3-*de*]quinoline (35). Compound **34** (82.8 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2.5 d. The reaction mixture was chromatographed using 3:2 hexanes/ethyl acetate to afford 27.4 mg (54 %) of the indicated compound **35** as a white solid: mp 100-101 °C (lit[29] mp 102-103 °C); ^{1}H NMR ($CDCl_3$) Γ 7.35-7.51 (m, 2H), 7.72-7.77 (m, 2H), 7.84-7.91 (m, 3H), 7.99 (d, J = 8.4 Hz, 1H), 9.07 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 114.4, 121.0, 122.2, 123.7, 128.2, 128.4, 130.4, 131.7, 135.4, 138.2, 138.2, 140.5, 145.1, 145.7, 152.9. The other spectral properties were identical to those previously reported.[30]



41

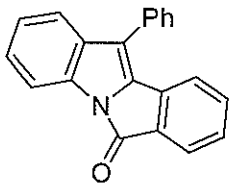
11-Phenyl-6*H*-isoindolo[2,1-*a*]indole (41). Compound **40** (103 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d affording a 92 % yield of the indicated compound **41**, which is unstable on silica gel, as determined by ^{1}H NMR spectroscopy. To obtained pure compound **41**, the crude product was recrystallized (hexane/EtOAc) to afford a pale purple solid: mp 148-151 °C; ^{1}H NMR (DMSO-d_6) Γ 5.27 (s, 2H), 7.09-7.13 (m, 1H), 7.21-7.25 (m, 1H), 7.36-7.39 (m, 3H), 7.51-7.58 (m, 3H), 7.63-7.65 (m, 1H), 7.68-7.70 (m, 3H), 7.74-7.76 (m, 1H); ^{13}C NMR (DMSO-d_6) Γ 48.2, 108.0,

110.2, 119.5, 120.0, 120.2, 122.0, 124.2, 126.2, 127.6, 128.0, 128.7, 128.9, 130.4, 131.9, 133.5, 134.4, 139.3, 142.7; IR (CH_2Cl_2) 3053, 2985, 1616, 1603, 1497 cm^{-1}; HRMS *m/z* 281.1209 (calcd for $C_{21}H_{15}N$, 281.1205).



43 **44**

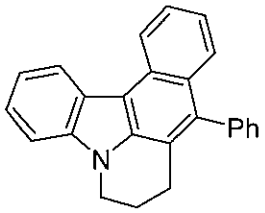
8-Methoxy-11-phenyl-6*H*-isoindolo[2,1-*a*]indole (43) and 10-methoxy-11-phenyl-6*H*-isoindolo[2,1-*a*]indole (44). Compound **42** (0.110 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 12 h. The reaction mixture was chromatographed using 9:1 hexane/EtOAc to afford 61 mg (78 %) of the compound **43** as a yellow solid and 9 mg (12 %) of the compound **44**. Compound **43**: mp 196-198 °C; ^{1}H NMR (DMSO-d_6) Γ 3.83 (s, 3H), 5.23 (s, 2H), 6.97 (d, J = 8.4 Hz, 1H), 7.07-7.10 (m, 1H), 7.17-7.21 (m, 1H), 7.27 (s, 1H), 7.34-7.37 (m, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.53-7.57 (m, 2H), 7.66-7.68 (m, 4H); ^{13}C NMR (DMSO-d_6) Γ 48.4, 55.8, 108.1, 109.3, 109.8, 113.7, 120.0, 120.3, 121.9, 122.1, 126.0, 126.2, 128.9, 129.3, 131.6, 134.1, 135.4, 140.3, 144.2, 159.7; IR (CH_2Cl_2) 3051, 1686, 1450 cm^{-1}; HRMS *m/z* 311.1316 (calcd for $C_{22}H_{17}ON$, 311.1310).



46

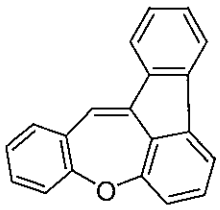
11-Phenyl-6*H*-isoindolo[2,1-*a*]indol-6-one (46). Compound **45** (0.106 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture

was chromatographed using 10:1 hexane/EtOAc to afford 24 mg (33 %) of the indicated compound **46** as a yellow solid: mp 222-223 °C; ^{1}H NMR ($CDCl_3$) Γ 7.17-7.21 (m, 1H), 7.31-7.36 (m, 2H), 7.40-7.44 (m, 1H), 7.45-7.49 (m, 1H), 7.54-7.60 (m, 4H), 7.70-7.72 (m, 2H), 7.79 (d, J = 7.6 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 113.8, 120.8, 121.4, 121.5, 124.3, 125.6, 127.0, 128.6, 129.0, 129.2, 129.3, 132.4, 133.9, 134.0, 134.1, 134.2, 134.4, 134.9, 162.8; IR (CH_2Cl_2) 3053, 2987, 1731, 1264 cm^{-1}; HRMS *m/z* 295.1003 (calcd for $C_{21}H_{13}ON$, 295.0997).



48

9-Phenyl-7,8-dihydro-6*H*-benzo[*c*]pyrido[1,2,3-*lm*]carbazole (48). Compound **47** (116 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 12 h. The reaction mixture was chromatographed using 20:1 hexane/EtOAc to afford 54 mg (65 %) of the indicated compound **48** as a yellow solid: mp 239-241 °C; ^{1}H NMR ($CDCl_3$) Γ 2.21-2.29 (m, 2H), 2.87 (t, J = 6.0 Hz, 2H), 4.31 (t, J = 5.7 Hz, 2H), 7.28-7.34 (m, 1H), 7.35-7.55 (m, 8H), 7.61-7.65 (m, 2H), 8.58 (d, J = 7.8 Hz, 1H), 8.74-8.77 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.8, 24.8, 41.3, 109.1, 112.5, 119.9, 121.1, 122.3, 122.6, 123.2, 123.7, 123.9, 125.9, 127.4, 127.9, 128.5, 129.1, 129.2, 130.8, 135.3, 135.7, 139.1, 139.2; IR (CH_2Cl_2) 3053, 2986, 1421, 1265 cm^{-1}; HRMS *m/z* 333.1523 (calcd for $C_{25}H_{19}N$, 333.1518). Anal. Calcd for $C_{25}H_{19}N$: C, 90.06; H, 5.74; N, 4.20. Found: C, 90.27; H, 5.44; N, 4.17.



50

Benzo[*f*]fluoreno[1,9-*bc*]oxepine (50). Compound **49** (99.1 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 18:1 hexanes/ethyl acetate to afford 53.6 mg (80 %) of the indicated compound **50** as a white solid: mp 106-107 °C; ^{1}H NMR ($CDCl_3$) Γ 6.69 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.83 (s, 1H), 6.93-6.95 (m, 1H), 6.97-6.99 (m, 1H), 7.05-7.07 (m, 1H), 7.16-7.30 (m, 5H), 7.58-7.59 (m, 1H), 7.62-7.64 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 115.4, 117.2, 120.4, 120.6, 122.3, 124.8, 126.0, 127.2, 128.3, 128.7, 129.1, 131.3, 131.4, 132.4, 137.1, 137.6, 139.9, 141.0, 154.8, 155.6; IR (CH_2Cl_2) 3050, 1580, 1238, 1450, 1426 cm^{-1}; HRMS *m/z* 268.0892 (calcd for $C_{20}H_{12}O$, 268.0888).

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CHAPTER 5. SYNTHESIS OF CYCLOPROPANES BY A NOVEL PALLADUM-CATALYZED ACTIVATION OF ALKYL C-H BONDS

A Paper submitted to the *Journal of Organic Chemistry*

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Abstract

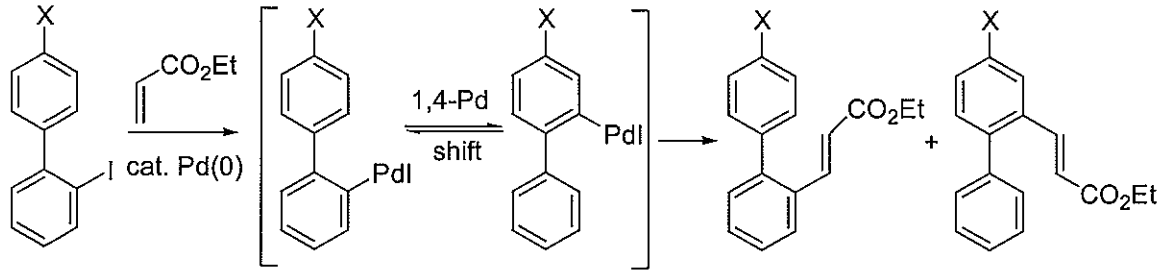
An efficient synthesis of cyclopropanes has been developed using palladium-catalyzed C-H activation in which two new carbon-carbon bonds are formed in a single step. This method involves the palladium-catalyzed activation of unreactive alkyl C-H bonds and provides an efficient way to synthesize cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics.

Introduction

The ability of palladium to activate C-H bonds has been used extensively in organic synthesis.[1] In recent years, palladium-catalyzed C-H activation has received considerable attention due to the wide variety of reactions this metal will catalyze. For instance, catalytic amounts of Pd salts have been used to effect the addition of C-H bonds of electron-rich arenes to alkenes and alkynes, and to effect carbonylation.[2] We have previously reported the synthesis of 9-benzylidene-9*H*-fluorenes by Pd-catalyzed intramolecular C-H activation involving the rearrangement of organopalladium intermediates derived from aryl halides and internal alkynes.[3] Similarly, intramolecular C-H activation in organopalladium intermediates derived from *o*-halobiaryls leads to a 1,4-palladium migration (Scheme 1).[4] We have already

shown that such intermediates can be trapped by Heck, Suzuki, and alkyne annulation reactions,[4,5] and intramolecular arylation.[6] Herein, we wish to report a novel C-H activation using palladium chemistry to synthesize cyclopropanes,[7] especially cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics.[8]

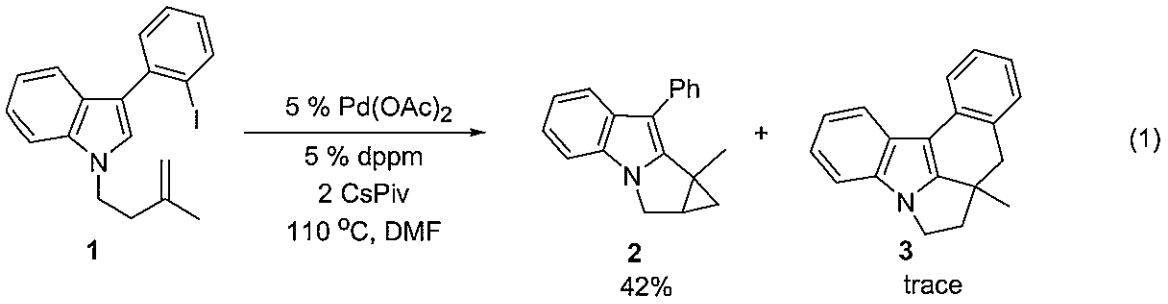
Scheme 1



Results and Discussion

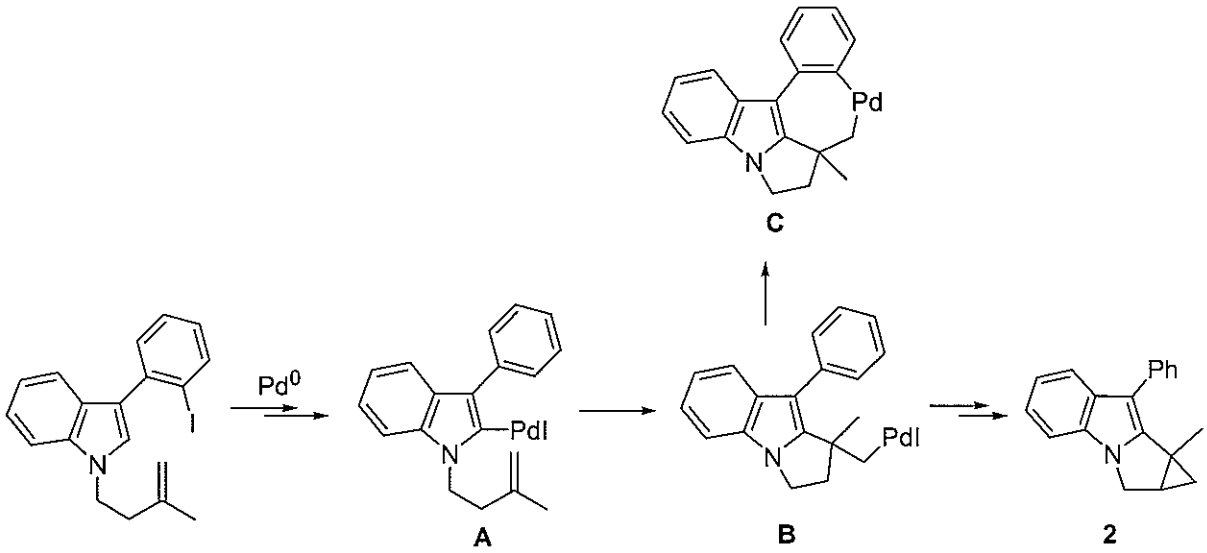
During our investigation of Pd-catalyzed aryl to aryl migration chemistry,[6] iodoindole **1** was allowed to react under our standard palladium migration conditions, but only trace amounts of the desired migration/arylation product **3** were detected (eq 1). Surprisely, compound **2** was isolated in a 42 % yield. As shown in Scheme 2, the indolylpalladium iodide **A**, formed by palladium migration from the 2 position of the phenyl group to the 2 position of the indole ring, apparently reacts with the carbon-carbon double bond to generate an alkyl intermediate **B**. Instead of forming a new carbon-carbon bond at the 2 position of the phenyl group by a seven-membered palladacycle **C**, the alkylpalladium iodide apparently forms a cyclopropane ring by activating a relatively unreactive alkyl C-H bond. Due to our interest in the novel palladium-catalyzed activation of alkyl C-H bonds and the substantial biological activity of cyclopropapyrrolo[1,2-*a*]indoles,[9] we have investigated this novel

palladium-catalyzed C-H activation and have examined its scope by employing various substrates.

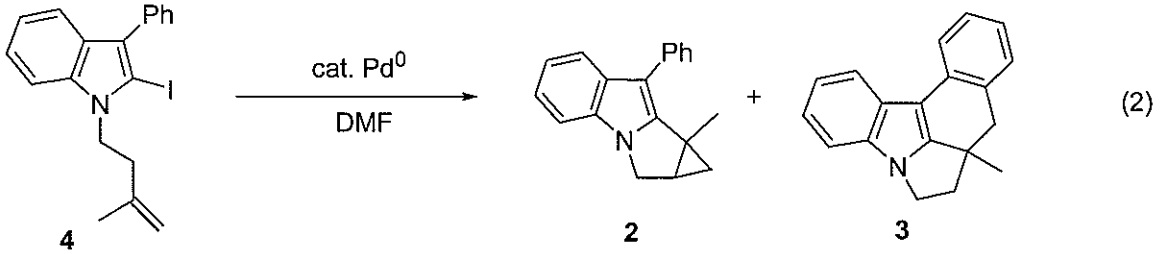


(1)

Scheme 2



Our initial studies focused on achieving optimal reaction conditions for this novel palladium-catalyzed C-H activation process employing the isomeric iodoindole **4** (eq 2).



(2)

While the reaction of compound **1** generated a 42 % yield of the desired cyclopropane **2** (eq 1), the reaction of compound **4** under the same reaction conditions [5 % $Pd(OAc)_2$, 5 mol % *bis*(diphenylphosphino)methane (dppm), 2 equiv of CsO_2CCMe_3 (CsPiv) and DMF as the

Table 1. Optimization reactions for the synthesis of compound **2**.[a,b]

entry	catalyst	ligand	base	temperature (^{0}C)	time (h)	% yield of **2**[c]
1	5 % $Pd(OAc)_2$	5 % dppm	2 CsPiv	110	6	62[d]
2		--	2 CsPiv	110	12	37
3		--	2 Bu_3N	110	72	15
4		5 % dppm	2 CsPiv	100	24	55[e]
5		5 % dcpm	2 CsPiv	110	1.5	47[e]
6		5 % dppm	2 NaOAc	115	24	36[e]
7		5 % dppm	2 Na_2CO_3	110	72	26[e]
8		5 % dppm	2 Cs_2CO_3	115	48	52[e]
9		5 % dppm	2 KO-*t*-Bu	115	0.5	trace
10	5 % $Pd(PPh_3)_4$	5 % dppm	2 Na_2CO_3	110	72	30[e]
11	5 % $Pd(PPh_3)_4$	--	2 Na_2CO_3	110	72	27[e]

[a] All reactions were carried out under the following reaction conditions: 0.25 mmol of compound **4**, 5 mol % $Pd(OAc)_2$, 5 mol % dppm, 2 equiv of CsPiv in 4 mL of DMF at the indicated temperature under an Ar atmosphere. [b] Along with cyclopropane **2**, another cyclopropane product, generated by having the palladium intermediate close onto the methyl group, has been obtained in a 5-10 % yield. [c] Isolated yield. [d] Compound **3** was isolated in a 15 % yield. [e] The yield is based on gas chromatographic analysis.

solvent] afforded cyclopropane **2** in a 62 % yield and compound **3** in a 15 % yield (entry 1, Table 1). Omitting dppm as the ligand, the yield dropped from 62 % (entry 1) to 37 % (entry 2). When Bu_3N was employed as the base, cyclopropane **2** was isolated in only a 15 % yield (entry 3). When the reaction was carried out at 100 °C, the yield dropped to 55 % (entry 4), and a longer reaction time was required to reach completion. Compared to the reaction using dppm as the ligand (entry 4), when *bis*(dicyclohexylphosphino)methane (dcpm), a more electron-donating ligand, was employed, the C-H activation process was much faster and reached completion in 1.5 h (entry 5). However, the yield decreased to 47 % from 55 % (entry 4). There was no reaction when NaOAc was employed as a base even at 110 °C. However, the reaction did proceed when the reaction temperature was increased to 115 °C, although the yield of cyclopropane **2** was low (entry 6). The bases Na_2CO_3, Cs_2CO_3, and KO-*t*-Bu have also been employed and the desired cyclopropane **2** has been obtained in a yield of 26 %, 52 %, and a trace amount, respectively (entries 7-9). When $Pd(PPh_3)_4$ was employed as the catalyst with and without the addition of dppm, compound **2** was produced in 30 % and 27 % yields, respectively (entries 10 and 11). Thus, we chose the following conditions as our "optimal" reaction conditions: 0.50 mmol of the substrate, 5 mol % $Pd(OAc)_2$, 5 mol % dppm, 2 equiv of CsPiv in DMF (4 mL) stirred at 110 °C under an Ar atmosphere.

Using our optimal reaction conditions, the scope of this novel Pd-catalyzed C-H activation process has been explored using a variety of substrates carefully selected in order to establish the generality of the process and its applicability to commonly encountered synthetic problems (Table 2). While the reaction of compound **4** afforded cyclopropane **2** in

Table 2. Synthesis of cyclopropanes by Pd-catalyzed activation of unreactive C-H bonds[a,b]

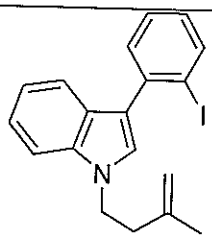
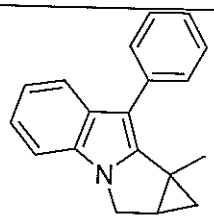
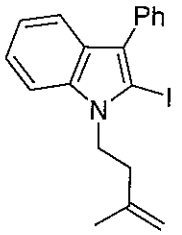
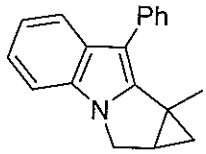
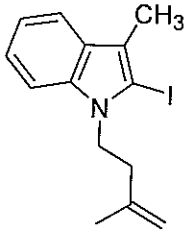
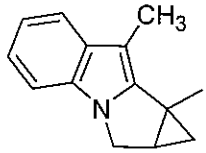
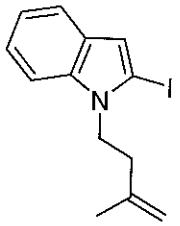
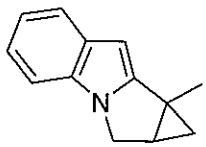
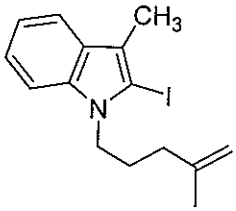
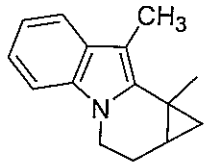
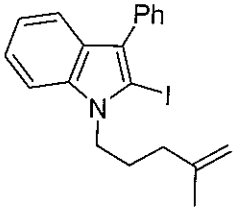
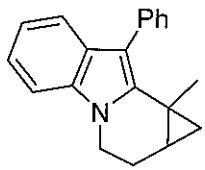
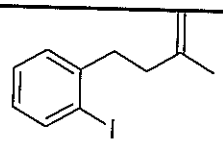
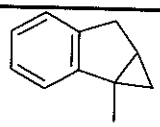
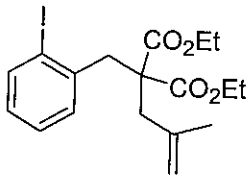
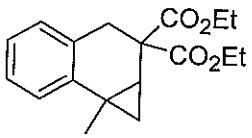
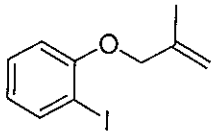
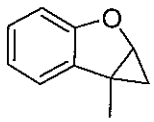
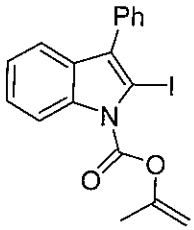
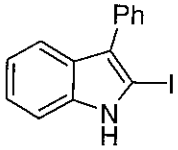
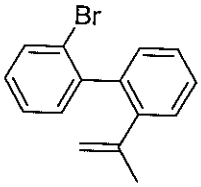
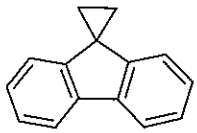
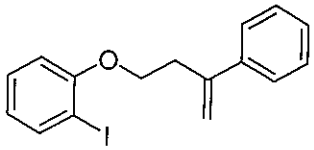
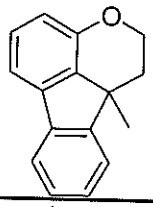
entry	aryl iodide		time (h)	product		% yield[c]
1		**1**	8		**2**	42
2		**4**	6		**2**	62
3		**5**	12		**6**	40 (46[d])
4		**7**	12		**8**	trace
5		**9**	16		**10**	31[d]
6		**11**	18		**12**	42

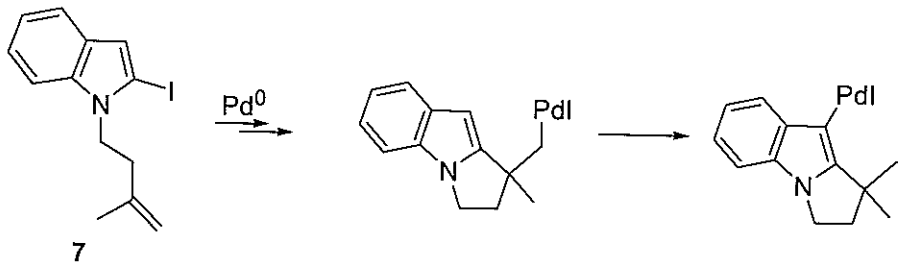
Table 2 continued

7		**13**	3		**14**	< 5 %
8		**15**	12		**16**	trace
9		**17**	12		**18**	0
10		**19**	12		**20**	72
11		**21**	24		**22**	trace
12		**23**	12		**24**	88[e]

[a] All reactions were carried out under the following reaction conditions, unless otherwise specified: 0.5 mmol of the substrate, 5 mol % $Pd(OAc)_2$, 5 mol % dppm, 2 equiv of CsPiv in 4 mL of DMF at 110 °C under an Ar atmosphere. [b] For entries 1-3, 5 and 6, along with the desired cyclopropane derivative, another cyclopropane product has been detected in 5-10 % yields, in which the palladium closes onto the methyl group. [c] Isolated yield. [d] The yield was determined by gas chromatographic analysis. [e] The reaction was carried out at 100 °C.

a 62 % yield (entry 2), the reaction of iodoindole **5** generated cyclopropane **6** in a 46 % yield (entry 3). Iodoindole **7**, with no substituent in the 3 position of the indole ring, has been allowed to react under our optimal reaction conditions, but only a trace amount of the desired product was detected. It is quite possible that the alkylpalladium intermediate first produced undergoes palladium migration to the 3 position of the indole ring cirumventing cyclopropane formation, although we failed to isolate any recognizable products (Scheme 3). This type of alkyl to aryl palladium migration has been observed previously in our research group under these same reaction conditions.[10]

Scheme 3



7

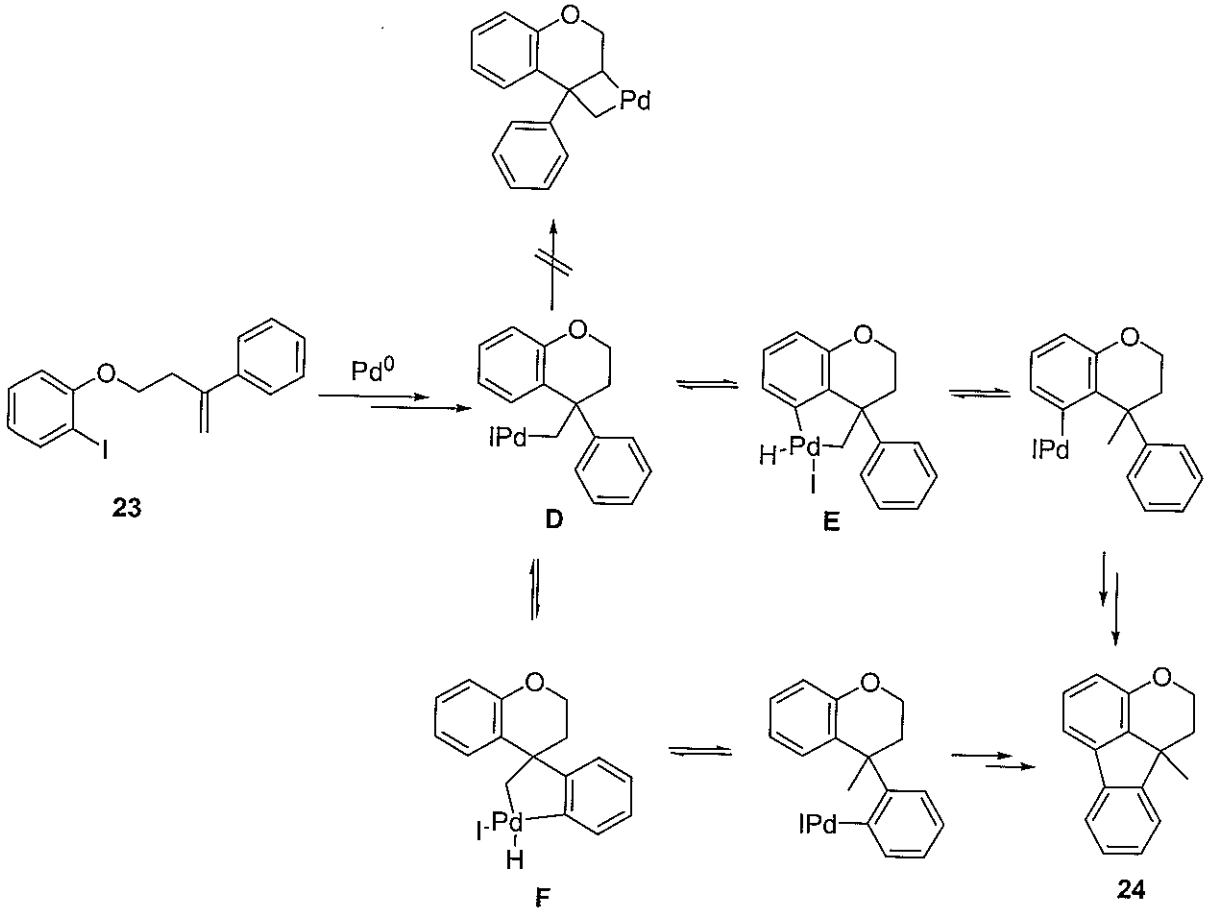
To test if the C-H activation process occurs when forming a new 6-membered ring, we have prepared compounds **9** and **11** and carried out the corresponding reactions under our optimal reaction conditions (entries 5 and 6). Although the yields are a little lower, those new fused 6-membered ring systems can be generated by this palladium-catalyzed alkyl C-H activation chemistry.

Is the indole nitrogen essential to this C-H activation process? To clarify this question, compounds **13** and **15** were employed under our optimal reaction conditions. Unfortunately, only trace amounts of the desired cyclopropane products **14** and **16** were detected by GC

analysis (entries 7 and 8). It appears that the indole ring system is critical to the formation of the cyclopropanes by this Pd-catalyzed C-H activation prcocess. Consistent with this observation is the fact that the reaction of compound **17** afforded none of the desired cyclopropane product. It is quite possible that compound **17** under our reaction conditions may generate a π-allylpalladium intermediate, which circumvents cyclopropane formation. When compound **19** was employed, the reaction again failed to produce any cyclopropane product. However, 2-iodo-3-phenylindole was isolated in a 72 % yield (entry 10). This product probably arises by simple decomposition of the *N*-(alkoxycarbonyl)indole. When, aryl bromide **21** was allowed to react under our optimal reaction conditions, none of the desired cyclopropane product was detected (entry 11).

When compound **23** was allowed to react under our optimal conditions, instead of obtaining the expected cyclopropane product, compound **24** was isolated in an 88 % yield after 12 h at 100 °C (entry 12). Possible mechanisms for the formation of ether **24** are shown in Scheme 4. Under our reaction conditions, the initial arylpalladium iodide is expected to react with the carbon-carbon double bond to form an alkylpalladium intermediate **D**. Instead of activating a relatively unreactive alkyl C-H bond, the palladium intermediate is more likely to react with a neighboring aromatic C-H bond to generate intermediate **E** or **F**. These species may arise not only because the aromatic C-H bonds are more acidic and thus more reactive, but also because formation of five-membered ring palladacycles is more favorable than formation of four-membered ring palladacycles. Intermediate **E** or **F** can then undergo reductive elimination, followed by intramolecular arylation, to afford the observed product, compound **24,** in a good yield. Thus, this process is another example of an alkyl to aryl palladium migration, similar to others observed recently in our research group.

Scheme 4



Conclusion

A novel palladium-catalyzed activation of simple alkyl C-H bonds has been investigated as a unique new way to form polycyclic cyclopropanes. Our experiments indicate that the indole ring is apparently critical to this activation process. This method provides an efficient synthesis of cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics.[8]

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise noted. All reagents were used directly as obtained commercially unless otherwise noted. (2-Iodophenyl)acetaldehyde,[11] 2-iodo-3-phenylindole[12] and compounds **13**,[13] **15**,[14] and **17**[14] were prepared according to literature procedures.

3-(2-Iodophenyl)indole. To a solution of (2-iodophenyl)acetaldehyde[11] (0.738 g, 3.0 mmol) in 15 mL of absolute ethanol was added 0.356 g of $PhNHNH_2$ (3.3 mmol) and 57.6 mg of CH_3SO_3H (0.6 mmol). The resulting yellow solution was stirred at 25 °C for 1 h. Another 0.519 g of CH_3SO_3H (5.4 mmol) was then added to the reaction mixture and the reaction was stirred at 85 °C for 2 d. The reaction was then allowed to cool to 25 °C. The ethanol was removed under reduced pressure and the residue was diluted with Et_2O (30 mL), washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (5:1 hexane/EtOAc) to afford 0.41 g of the indicated compound (43 % yield) as an yellow oil: ^{1}H NMR ($CDCl_3$) Γ 7.01-7.05 (m, 1H), 7.14-7.18 (m, 1H), 7.23-7.27 (m, 1H), 7.38-7.49 (m, 4H), 7.54 (d, J = 8.0 Hz, 1H), 8.01 (dd, J = 1.2, 8.0 Hz, 1H), 8.27 (br s, 1H); ^{13}C NMR ($CDCl_3$) Γ 101.0, 111.5, 120.3,

120.4, 122.6, 123.8, 126.8, 128.2, 128.5, 131.6, 135.8, 140.0, 140.1 (one sp^2 carbon missing due to overlap).

3-Methyl-3-butenyl tosylate.[15] To a mixture of Et_3N (2.026 g, 20 mmol) and 3-methyl-3-buten-1-ol (0.862 g, 10 mmol) in CH_2Cl_2 at 0 °C was slowly added *p*-tosyl chloride (1.909 g, 10 mmol). The reaction mixture was stirred at 0 °C for 3 h, then diluted with CH_2Cl_2, washed with 10 % aq HCl, 10 % aq $NaHCO_3$, and water and then concentrated, and dried over anhydrous Na_2SO_4 to afford the indicated compound (2.015 g, 84 %) as a yellow oil, which was used without further purification.

***N*-(3-Methyl-3-butenyl)-3-(2-iodophenyl)indole (1).** To a suspension of NaH (0.75 mmol, 60 % in mineral oil) in dry DMF (2 mL) was added dropwise a solution of 3-(2-iodophenyl)indole (0.16 g, 0.50 mmol) in dry DMF (2.5 mL) at 0 °C under an Ar atmosphere. Lots of bubbles were generated. The resulting deep yellow suspension was stirred at 0 °C for 30 min. A solution of 3-methyl-3-butenyl tosylate (0.24 g, 1.0 mmol) in dry DMF (2.5 mL) was added dropwise and the resulting yellow solution was stirred at 0 °C for 14 h. The reaction was diluted with Et_2O (25 mL), washed with brine (30 mL), and the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was chromatographed (15:1 hexane/EtOAc) to afford 0.137 g of the indicated compound in a 71 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.79 (s, 3H), 2.58 (t, J = 7.2 Hz, 2H), 4.27-4.32 (m, 2H), 4.74 (d, J = 0.6 Hz, 1H), 4.82-4.83 (m, 1H), 6.96-7.02 (m, 1H), 7.11-7.16 (m, 1H), 7.22-7.29 (m, 1H), 7.29 (s, 1H), 7.35-7.48 (m, 3H), 7.52-7.55 (m, 1H), 7.99 (dd, J = 1.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.9, 38.4, 45.3, 100.9, 109.7, 113.0, 118.6, 119.8, 120.5, 122.0, 127.3, 127.5, 128.2, 128.3, 131.6, 135.8, 140.0, 140.2, 142.2; IR

(neat, cm^{-1}) 3048, 2966, 2933, 1649, 1585, 1458; HRMS Calcd for $C_{19}H_{18}NI$: 387.0484. Found: 387.0490.

***N*-(3-Methyl-3-butenyl)-2-iodo-3-phenylindole (4).** Using the procedure used to prepare compound **1**, but employing 2-iodo-3-phenylindole[12] and 3-methyl-3-butenyl tosylate, afforded compound **4** in an 88 % yield as a yellow oil: ^1H NMR ($CDCl_3$) Γ 1.87 (s, 3H), 2.44-2.49 (m, 2H), 4.34-4.39 (m, 2H), 4.84 (d, J = 0.9 Hz, 1H), 4.88 (d, J = 0.9 Hz, 1H), 7.06-7.11 (m, 1H), 7.17-7.22 (m, 1H), 7.35-7.40 (m, 2H), 7.47-7.50 (m, 2H), 7.56-7.61 (m, 3H); ^{13}C NMR ($CDCl_3$) Γ 23.1, 38.0, 46.8, 85.8, 109.8, 112.7, 119.4, 120.3, 122.5, 123.4, 127.0, 128.2, 128.6, 130.3, 135.4, 137.9, 142.4; IR (neat, cm^{-1}) 3072, 2963, 2936, 1649, 1603, 1530, 1446; HRMS Calcd for $C_{19}H_{18}NI$: 387.0484. Found: 387.0491.

2-Iodo-3-methylindole. This compound was prepared by modifying a reported procedure.[16] To a solution of 3-methylindole (2.64 g, 20 mmol) in dry THF (55 mL) was added dropwise *n*-BuLi (2.5 M in hexane, 8.4 mL, 21 mmol) at -78 °C under an Ar atmosphere. The resulting suspension was stirred at -78 °C for 20 min. Carbon dioxide was bubbled through the reaction mixture for 30 min. The resulting clear yellow solution was then warmed to 25 °C. Lots of bubbles were generated. The solvent was removed under reduced pressure at 25 °C. To the residue was added dry THF (50 mL) and the reaction mixture was allowed to cool to -78 °C. To the yellow solution was added slowly *t*-BuLi (1.7 M in pentane, 12.5 mL, 21.3 mmol) and the resulting orange solution was stirred at -78 °C for 1 h. A solution of ICH_2CH_2I (recrystallized from MeOH) (5.64 g, 20 mmol) in dry THF (15 mL) was added at -78 °C. The resulting yellow solution was stirred at -78 °C for another 1 hour and was then warmed to 25 °C. The reaction mixture was washed with satd aq NH_4Cl (50 mL). The organic layer was dried over Na_2SO_4 and the residue was chromatographed

(5:1 hexane/EtOAc) to afford 5.15 g of the indicated compound in a 97 % yield with spectra identical to those previously reported.[16]

***N*-(3-Methyl-3-butenyl)-2-iodo-3-methylindole (5).** Using the procedure used to prepare compound **1**, but employing 2-iodo-3-methylindole and 3-methyl-3-butenyl tosylate, afforded compound **5** in a 71 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.84 (s, 3H), 2.31 (s, 3H), 2.36-2.40 (m, 2H), 4.23-4.27 (m, 2H), 4.79 (d, J = 0.8 Hz, 1H), 4.84 (d, J = 0.8 Hz, 1H), 7.05-7.09 (m, 1H), 7.12-7.16 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.51 (dd, J = 0.4, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 12.6, 23.1, 38.1, 46.4, 86.3, 109.6, 112.5, 117.3, 118.6, 119.3, 121.9, 128.7, 137.7, 142.5; IR ($CDCl_3$, cm^{-1}) 3074, 3055, 2968, 2912, 1649, 1456; HRMS Calcd for $C_{14}H_{16}NI$: 325.0328. Found: 325.0334.

***N*-(3-Methyl-3-butenyl)-2-iodoindole (7).** Using the procedure used to prepare compound **1**, but employing 2-iodoindole and 3-methyl-3-butenyl tosylate, afforded compound **7** in a 68 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.83 (s, 3H), 2.38-2.42 (m, 2H), 4.23-4.27 (m, 2H), 4.77-4.78 (m, 1H), 4.84-4.85 (m, 1H), 6.77 (d, J = 0.8 Hz, 1H), 7.04-7.08 (m, 1H), 7.12-7.16 (m, 1H), 7.31-7.33 (dd, J = 0.8, 8.0 Hz, 1H), 7.51-7.54 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.1, 38.0, 46.3, 82.9, 109.7, 112.3, 112.7, 119.8, 120.0, 121.9, 130.0, 137.3, 142.3; IR (neat, cm^{-1}) 3061, 2962, 1649, 1455; HRMS Calcd for $C_{13}H_{14}NI$: 311.0171. Found: 311.0178.

4-Methyl-4-penten-1-ol. To 25 mL of dry THF was added slowly *t*-BuLi (1.7 M in pentane, 24.7 mL, 42 mmol) at -78 °C under an Ar atmosphere. The resulting yellow solution was stirred at -78 °C for 5 min, 2-bromopropene (1.86 mL, 21 mmol) was added dropwise, and the resulting suspension was stirred at -78 °C for 30 min. Oxetane (1.30 mL, 20 mmol) was added slowly and the reaction mixture was stirred at -78 °C for another 30

min. Then $BF_3 \cdot OEt_2$ (2.52 mL, 20 mmol) was added dropwise, and the clear yellow solution was further stirred at -78 °C for 30 min. The reaction was quenched with brine (25 mL) and allowed to warm to 25 °C. 10 Ml of 10 % aq HCl was added to the reaction mixture and the organic layer was dried over $NaSO_4$, and concentrated under reduced pressure. The residue was chromatographed (3:1 hexane/EtOAc) to afford 0.72 g of the indicated compound in a 36 % yield as an yellow oil with spectra identical to those previously reported.[17]

4-Methyl-4-pentenyl tosylate. To a mixture of pyridine (2.3 mL, 28.4 mmol) and 4-methyl-4-penten-1-ol (0.71 g, 7.1 mmol) in CH_2Cl_2 (10 mL) at 0 °C was slowly added *p*-tosyl chloride (1.36 g, 7.1 mmol). The reaction mixture was stirred at 0 °C for 12 h, then diluted with CH_2Cl_2, washed with 10 % aq HCl (20 mL), 10 % aq $NaHCO_3$ (20 mL), and water (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed (9:1 hexane/EtOAc) to afford 1.30 g of the indicated compound in a 72 % yield as a colorless oil: ^{1}H NMR ($CDCl_3$) Γ 1.66 (s, 3H), 1.74-1.83 (m, 2H), 2.03 (t, J = 7.5 Hz, 2H), 2.45 (s, 3H), 4.03 (t, J = 6.6 Hz, 2H), 4.59 (d, J = 0.6 Hz, 1H), 4.69 (d, J = 0.6 Hz, 1H), 7.35 (d, J = 7.5 Hz, 2H), 7.78-7.80 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 21.8, 22.4, 26.9, 33.5, 70.3, 111.1, 128.1, 130.0, 133.4, 144.0, 144.9.

***N*-(4-Methyl-4-pentenyl)-2-iodo-3-methylindole (9).** Using the procedure used to prepare compound **1**, but employing 2-iodo-3-methylindole and 4-methyl-4-pentenyl tosylate, afforded compound **9** in an 82 % yield as a yellow oil: ^{1}H NMR ($CDCl_3$) Γ 1.75 (s, 3H), 1.84-1.91 (m, 2H), 2.10 (t, J = 8.0 Hz, 2H), 2.31 (s, 3H), 4.13-4.16 (m, 2H), 4.74 (s, 1H), 4.78 (s, 1H), 7.04-7.08 (m, 1H), 7.11-7.16 (m, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.50-7.52 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 12.6, 22.7, 27.9, 35.0, 47.0, 86.5, 109.6, 110.7, 117.2, 118.5,

119.2, 121.8, 128.6, 137.9, 144.7. IR (neat, cm^{-1}) 3074, 3054, 2964, 1648, 1454; HRMS Calcd for $C_{15}H_{18}NI$: 339.0484. Found: 339.0491.

***N*-(Isopropenyloxycarbonyl)-2-iodo-3-phenylindole (19).** Using the procedure used to prepare compound **1**, but employing 2-iodo-3-phenylindole and isopropenyl chloroformate, afforded compound **11** in a 77 % yield as a yellow solid: mp 85-87 °C; ^1H NMR ($CDCl_3$) Γ 2.18 (d, J = 0.4 Hz, 3H), 4.92-4.93 (m, 1H), 5.02 (d, J = 1.6 Hz, 1H), 7.20-7.24 (m, 1H), 7.28-7.33 (m, 1H), 7.40-7.46 (m, 2H), 7.48-7.53 (m, 4H), 8.15 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 19.9, 77.9, 103.6, 115.8, 119.7, 123.8, 125.3, 128.3, 128.8, 130.5, 133.3, 134.2, 138.4, 148.9, 152.6 (one sp^2 carbon missing due to overlap); IR ($CHCl_3$, cm^{-1}) 3019, 1746, 1677, 1445; HRMS Calcd for $C_{18}H_{14}O_2NI$: 403.0069. Found: 403.0076.

2'-(2-Bromophenyl)acetophenone. To a stirred mixture of $PdCl_2(PPh_3)_2$ (0.702 g, 0.15 mmol), K_2CO_3 (4.15 g, 30 mmol), 2'-iodoacetophenone (2.46 g, 10 mmol), DMF (80 mL) and H_2O (18 mL) was added slowly a solution of 2-bromoboronic acid (3.01 g, 15 mmol) in DMF (10 mL) at 25 °C under an Ar atmosphere. The resulting mixture was stirred at 80 °C for 6 h and then allowed to cool to 25 °C, diluted with Et_2O (50 mL), and washed with brine (2 x 50 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chormatographed (10:1 hexane/EtOAc) to afford 1.4 g of the indicated compound in a 52 % yield as a pale red oil: ^1H NMR ($CDCl_3$) 2.02 (d, J = 0.8 Hz, 3H), 7.23-7.28 (m, 3H), 7.35-7.37 (m, 1H), 7.45-7.50 (m, 1H), 7.52-7.56 (m, 1H), 7.64-7.66 (m, 1H), 7.73-7.76 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 29.4, 123.1, 127.6, 128.3, 128.5, 129.4, 131.1, 131.3, 131.3, 132.9, 139.5, 140.3, 142.3, 201.7.

2-Bromo-2'-isopropenylbiphenyl (21). To a suspension of triphenylmethylphosphonium bromide (1.77 g, 4.95 mmol) in dry THF (25 mL) was added

slowly *n*-BuLi (2.5 M in hexane, 2.0 mL, 4.95 mmol) at 0 °C under an Ar atmosphere. The resulting yellow suspension was stirred at 0 °C for 30 min. A solution of 2'-(2-bromophenyl)acetophenone (3.3 mmol) in dry THF (5 mL) was added dropwise and the reaction mixture was stirred at 0 °C for 30 min. The solvent was removed under reduced pressure and hexane (40 mL) was added to the residue. The mixture was stirred at 25 °C for 30 min and the phosphonium salt was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was chromatographed (30:1 hexane/EtOAc) to afford 0.90 g of the indicated compound in a 50 % yield as a white solid: mp 58-60 °C; ^{1}H NMR ($CDCl_3$) Γ 1.77 (s, 3H), 4.82-4.83 (m, 1H), 4.95-4.97 (m, 1H), 7.15-7.23 (m, 2H), 7.24-7.39 (m, 5H), 7.61-7.64 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 23.7, 116.5, 123.9, 126.7, 127.0, 128.0, 128.5, 128.7, 130.7, 131.8, 132.8, 139.0, 142.9, 143.0, 145.1; IR ($CHCl_3$, cm^{-1}) 3058, 3011, 2969, 1632, 1463; HRMS Calcd for $C_{15}H_{13}{}^{79}Br$: 272.0201. Found: 272.0207.

3-Phenyl-3-butenyl tosylate. To a solution of TsCl (0.80 g, 4.2 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of 3-bromo-3-buten-1-ol (0.302 g, 2.0 mmol) in CH_2Cl_2 (4 mL) at 0 °C under an Ar atmosphere. Pyridine (2.56 mL) was added slowly and the reaction mixture was stirred at 25 °C for 3 h. The reaction was diluted with Et_2O (20 mL), washed with 1N HCl (2 x 20 mL) and brine (20 mL), and the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude 3-bromo-3-butenyl tosylate was subjected to the following reaction without further purification. To a mixture of $PdCl_2(PPh_3)_2$ (70.1 mg, 0.1 mmol), K_2CO_3 (0.83 g, 6.0 mmol), 3-bromo-3-butenyl tosylate (crude, 2.0 mmol), DMF (5 mL) and H_2O (3 mL) was added a solution of $PhB(OH)_2$ (0.36 g, 3.0 mmol) in DMF (10 mL) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at 25 °C for 12 h. The reaction was diluted with Et_2O (20 mL) and washed with brine

(2 x 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed (5:1 hexane/EtOAc) to afford 0.29 g of the indicated compound in a 48 % overall yield as a brown oil: ^{1}H NMR ($CDCl_3$) Γ 2.44 (s, 3H), 2.86 (dt, J = 0.8, 7.2 Hz, 2H), 4.10 (t, J = 7.2 Hz, 2H), 5.08 (s, 1H), 5.34 (s, 1H), 7.25-7.31 (m, 7H), 7.72-7.74 (m, 2H); ^{13}C NMR ($CDCl_3$) Γ 21.8, 35.0, 68.9, 115.5, 126.2, 128.0, 128.1, 128.7, 130.0, 133.3, 139.9, 143.0, 144.9.

2-Iodophenyl 3-phenyl-3-butenyl ether (23). To a suspension of NaH (60 % in mineral oil, 44 mg, 1.12 mmol) in dry DMF (1.5 mL) was added a solution of 2-iodophenol (0.23 g, 1.02 mmol) in dry DMF (2 mL) at 0 °C under an Ar atmosphere. Lots of bubbles were generated. After 20 min, a solution of 3-phenyl-3-butenyl tosylate (0.28 g, 0.93 mmol) in dry DMF (2 mL) was added slowly. The reaction mixture was allowed to warm and stirred at 25 °C for 1 d to reach completion. The reaction was diluted with Et_2O (20 mL) and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduce pressure. The residue was chromatographed (35:1 hexane/EtOAc) to afford 0.15 g of the indicated compound in a 46 % yield as an yellow oil: ^{1}H NMR ($CDCl_3$) Γ 3.07 (dt, J = 0.9, 6.9 Hz, 2H), 4.10 (t, J = 6.9 Hz, 2H), 5.25-5.27 (m, 1H), 5.43 (d, J = 1.2 Hz, 1H), 6.65-6.71 (m, 1H), 6.73 (dd, J = 1.2, 8.4 Hz, 1H), 7.21-7.37 (m, 4H), 7.45-7.48 (m, 2H), 7.76 (dd, J = 2.0, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 35.3, 68.2, 86.9, 112.5, 115.2, 122.7, 126.4, 127.9, 128.7, 129.6, 139.7, 140.8, 144.5, 157.6; IR (neat, cm^{-1}) 3080, 3056, 2946, 1581, 1464; HRMS Calcd for $C_{16}H_{15}IO$: 350.0168. Found: 350.0171.

General procedure for the synthesis of cyclopropanes by Pd-catalyzed C-H activation. To a 6 dram vial was added $Pd(OAc)_2$ (6.0 mg, 0.025 mmol), dppm (9.2 mg, 0.025 mmol), CsPiv (234 mg, 1.0 mmol), the substrate (0.50 mmol), and dry DMF (4 mL).

The reaction mixture was stirred at 25 °C under an Ar atmosphere for 5 min, and was then stirred at 110 °C. Completion of the reaction was monitored by thin-layer chromatography and GC-mass spectral analysis. When the reaction was complete, the reaction mixture was allowed to cool to 25 °C, diluted with Et_2O (20 mL), and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to purification by chromatography or gas chromatographic analysis.

8b-Methyl-8-phenyl-1,1a,2,8b-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]indole (1). White solid: mp 158-160 °C; ^{1}H NMR ($CDCl_3$) Γ 1.01-1.03 (m, 1H), 1.28 (dd, J = 4.8, 8.0 Hz, 1H), 1.46 (s, 3H), 2.08-2.10 (m, 1H), 4.05 (d, J = 6.4 Hz, 1H), 4.24 (dd, J = 5.6, 10.4 Hz, 1H), 7.06-7.17 (m, 3H), 7.25-7.29 (m, 1H), 7.42-7.46 (m, 2H), 7.61 (dd, J = 0.8, 8.0 Hz,1H), 7.71 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 17.5, 23.6, 24.2, 28.8, 46.5, 108.4, 109.2, 119.3, 119.7, 121.2, 125.6, 128.4, 129.5, 131.3, 132.8, 135.2, 145.7; IR ($CHCl_3$, cm^{-1}) 3018, 2930, 1602, 1478, 1460, 1216; HRMS Calcd for $C_{19}H_{17}N$: 259.1361. Found: 259.1365.

7a-Methyl-6,7,7a,7b,8,12b-hexahydrobenzo[*c*]pyrrolo[1,2,3-*lm*]carbazole (3). White solid: mp 154-157 °C; ^{1}H NMR ($CDCl_3$) Γ 1.37 (s, 3H), 2.61-2.65 (m, 2H), 2.96-3.05 (m, 2H), 4.14-4.19 (m, 1H), 4.33-4.40 (m, 1H), 7.01-7.05 (m, 1H), 7.15-7.17 (m, 2H), 7.20-7.22 (m, 1H), 7.25-7.30 (m, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.85-7.87 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 22.5, 35.9, 45.6, 45.9, 46.9, 104.1, 110.6, 119.8, 120.2, 120.7, 122.7, 124.3, 127.4, 129.0, 129.7, 134.2, 135.0, 136.0, 154.9; IR ($CHCl_3$, cm^{-1}) 3017, 2959, 1631, 1492, 1433, 1215; HRMS Calcd for $C_{19}H_{17}N$: 259.1361. Found: 259.1366.

8,8b-Dimethyl-1,1a,2,8b-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]indole (6). White solid: mp 53-55 °C; ^{1}H NMR ($CDCl_3$) Γ 0.77-0.80 (m, 1H), 1.15 (dd, J = 0.8, 8.0 Hz, 1H), 1.66 (s, 3H), 1.98-2.01 (m, 1H), 2.34 (s, 3H), 3.94 (d, J = 10.0 Hz, 1H), 4.08-4.12 (m, 1H),

7.00-7.06 (m, 3H), 7.44 (d, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) Γ 8.48, 17.8, 23.2, 23.9, 28.5, 46.4, 100.7, 108.7, 118.3, 118.5, 120.5, 132.7, 133.4, 145.1; IR ($CHCl_3$, cm^{-1}) 3051, 3007, 2962, 2924, 1619, 1478, 1463; HRMS Calcd for $C_{14}H_{15}N$: 197.1205. Found: 197.1208.

10b-Methyl-1,10b-dihydro-2*H*-indeno[1,2,3-*de*]chromene (24). White solid: mp 51-53 °C; ^{1}H NMR ($CDCl_3$) Γ 1.46 (s, 3H), 1.63-1.70 (ddd, J = 8.0, 11.2, 11.2 Hz, 1H), 2.29-2.33 (ddd, J = 0.8, 8.0, 11.2 Hz, 1H), 4.56 (ddd, J = 0.8, 8.0, 13.2 Hz, 1H), 4.65 (ddd, J = 8.0, 11.2, 13.2 Hz, 1H), 6.71-6.75 (m, 1H), 7.22-7.26 (m, 2H), 7.29 (dd, J = 1.2, 7.2 Hz, 1H), 7.33-7.37 (m, 1H), 7.42-7.44 (m, 1H), 7.69-7.72 (m, 1H); ^{13}C NMR ($CDCl_3$) Γ 25.7, 31.0, 42.6, 65.7, 112.5, 113.8, 121.3, 123.2, 127.1, 127.5, 129.5, 134.9, 140.4, 140.6, 153.0, 153.9; IR ($CHCl_3$, cm^{-1}) 3053, 3010, 2963, 2919, 1614, 1592, 1486, 1447; HRMS Calcd for $C_{16}H_{14}O$: 222.1045. Found: 222.1048.

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GENERAL CONCLUSIONS

In this dissertation, the scope and limitations of iodocyclization and several palladium-catalyzed processes have been presented. A wide variety of isoquinolines, naphthyridines, naphthalenes, carbazoles, cyclopropanes and other heterocycles and carbocycles have been synthesized using these new methods.

Chapter 1 describes an efficient synthesis of a wide variety of halo-, selenium-, sulfur-containing substituted isoquinolines and naphthyridines, which employs very mild reaction conditions. This methodology accommodates a variety of iminoalkynes and affords the anticipated substituted isoquinolines and naphthyridines in moderate to excellent yields.

Chapter 2 describes an efficient and straightforward route to synthesize 4-(1-alkenyl)isoquinolines and 4-alkyl-3-arylisoquinolines containing a ketone group, using a palladium(II)-catalyzed cyclization, followed by olefination (Heck reaction). To form isoquinolines in high yields, both electronic effects and facilitation by an *ortho*-methoxy group are necessary.

Chapter 3 describes an efficient palladium-catalyzed synthesis of highly substituted naphthalenes and carbazoles, in which two new carbon-carbon bonds are formed in a single step under relatively mild reaction conditions. This method accommodates a variety of functional groups and generally affords the anticipated highly substituted naphthalenes and carbazoles in good to excellent yields.

Chapter 4 presents a novel method for the synthesis of complex fused polycycles employing two sequential Pd-catalyzed intramolecular processes involving C-H activation. This methodology exploits relatively facile aryl to aryl and vinylic to aryl palladium

migrations, followed by intramolecular arylation to prepare a wide variety of carbocycles and heterocycles.

Chapter 5 presents a novel palladium-catalyzed activation of relatively unreactive alkyl C-H bonds for the synthesis of cyclopropapyrrolo[1,2-*a*]indoles, analogues of the mitomycin antibiotics. Our experiments have shown that the indole ring is critical to this activation process.

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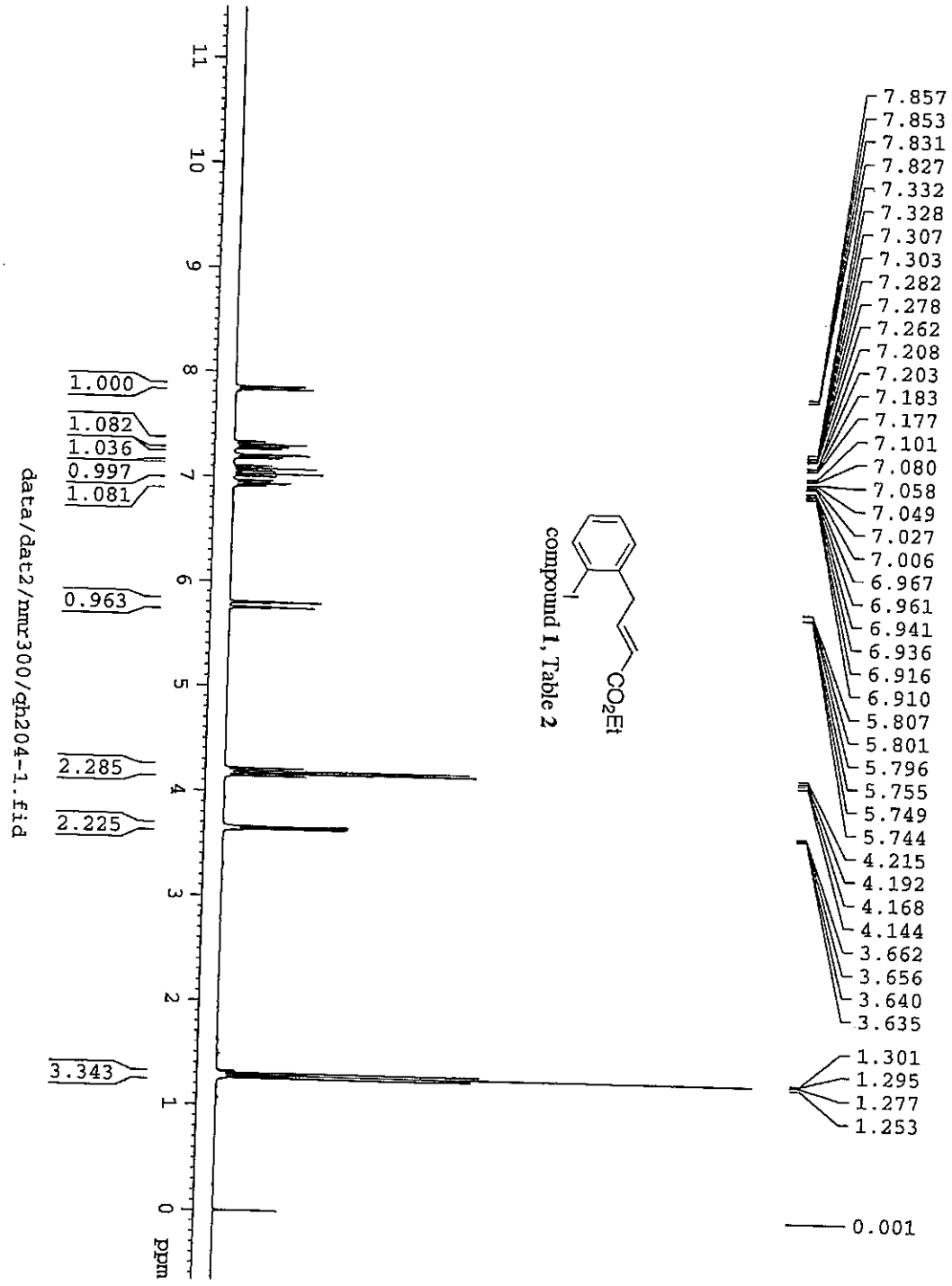
I have met so many great professors and students in the past few years at Iowa State University who have helped me through a number of things. I have to thank all the professors who have taught me fascinating chemistry. I also want to thank my program of study committee members for providing me both academic and personal help. I want to thank the past members of the Larock group that I have worked with: Dr. Fengkui Li, Dr. Alex Pletnev, Dr. Dmitry Kadnikov, Dr. Marino Campo, Dr. Haiming Zhang, Dr. Guangxiu Dai, and Daohua Zhang. I can't allow myself to forget to thank the current members of the Larock group: Dr. Dawei Yue, Roman Rozhkov, Xiaoxia Zhang, Tuanli Yao, Chengxiang Zhou, Zhijian Liu, Jian Zhao, Nicola Della Ca, Jesse Waldo, Shipa Worlikar, Tanay Kesharwani, especially Dr. Alessia Fazio, with whom I worked on the same project. Some of you guys really helped me a lot in the laboratory. It has been my great pleasure being with all of you guys.

Finally, I want to thank my lovely wife, Chunrong Pan, for her loving support, patience, understanding, and incredible sacrifices during my five years at Iowa State University.

APPENDIX C. CHAPTER 3 ^{1}H AND ^{13}C NMR SPECTRA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1.081
0.963
2.285
2.225
3.343
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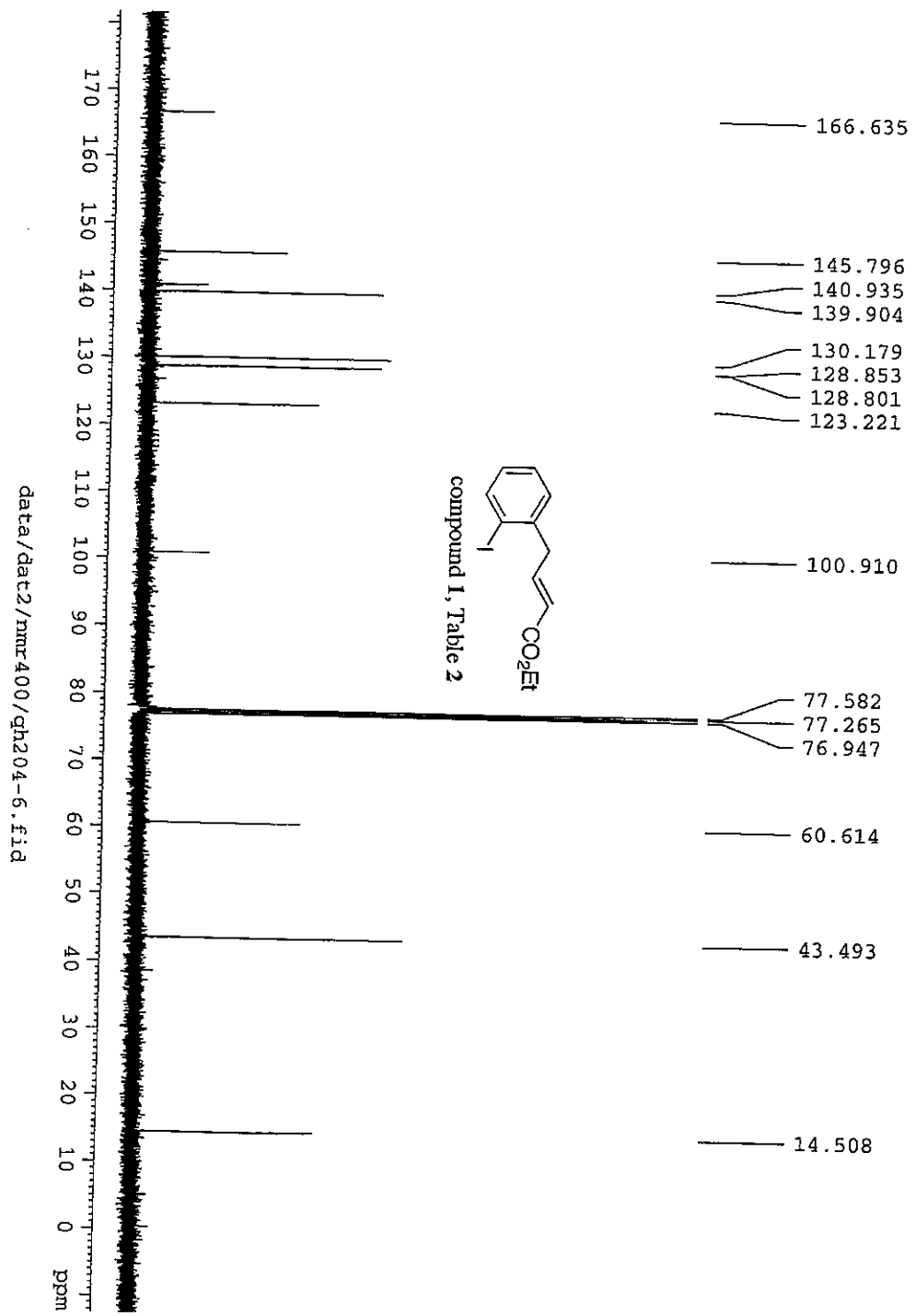
CO2Et
7.857
7.853
7.831
7.827
7.332
7.328
7.307
7.303
7.282
7.278
7.262
7.208
7.203
7.183
7.177
7.101
7.080
7.058
7.049
7.027
7.006
6.967
6.961
6.941
6.936
6.916
6.910
5.807
5.801
5.796
5.755
5.749
5.744
4.215
4.192
4.168
4.144
3.662
3.656
3.640
3.635
1.301
1.295
1.277
1.253
0.001
ppm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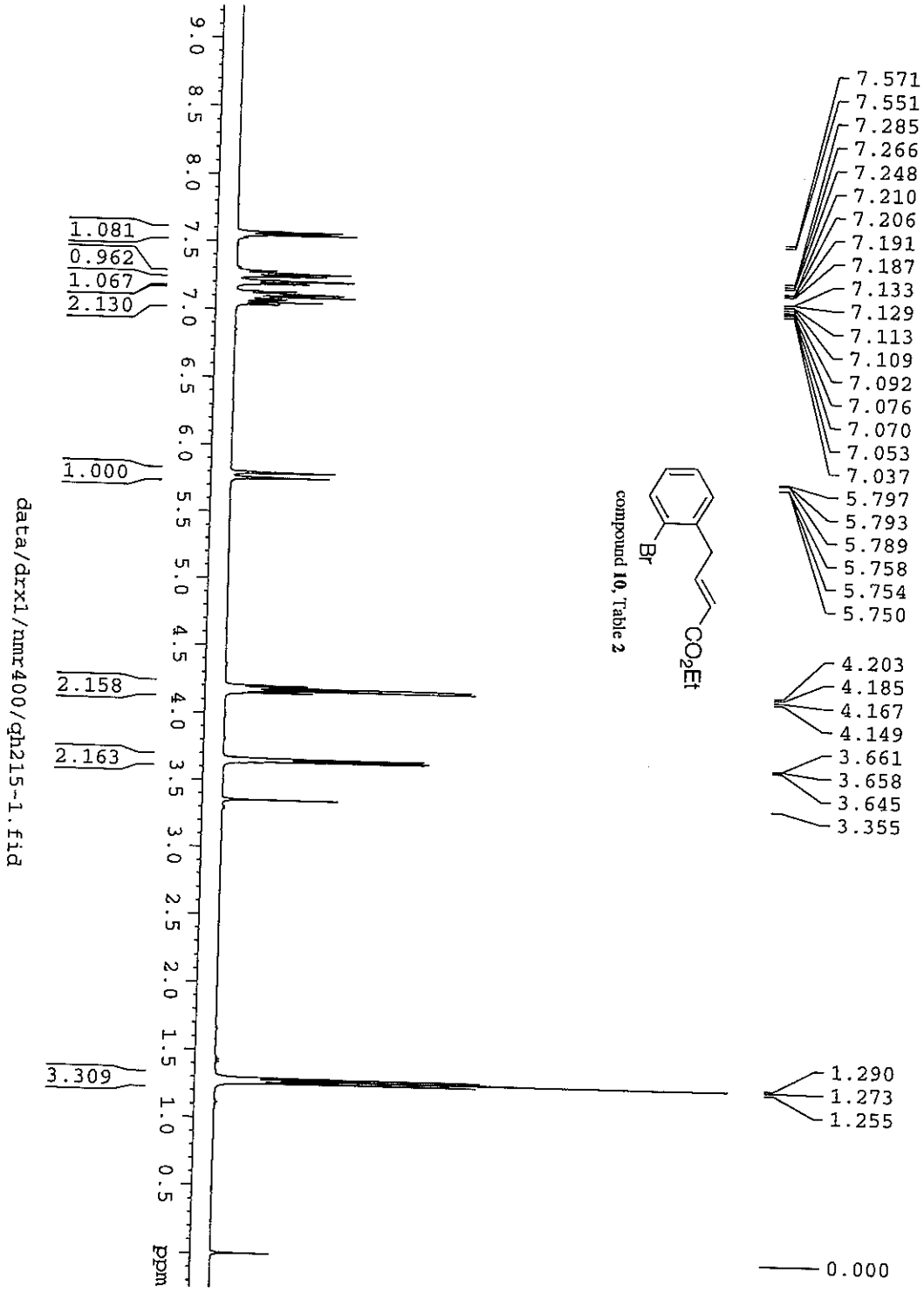
145.796
140.935
139.904
130.179
128.853
128.801
123.221
100.910
77.582
77.265
76.947
60.614
43.493
14.508
compound 1, Table 2
CO2Et
I
data/dat2/nmr400/gh204-6.fid
ppm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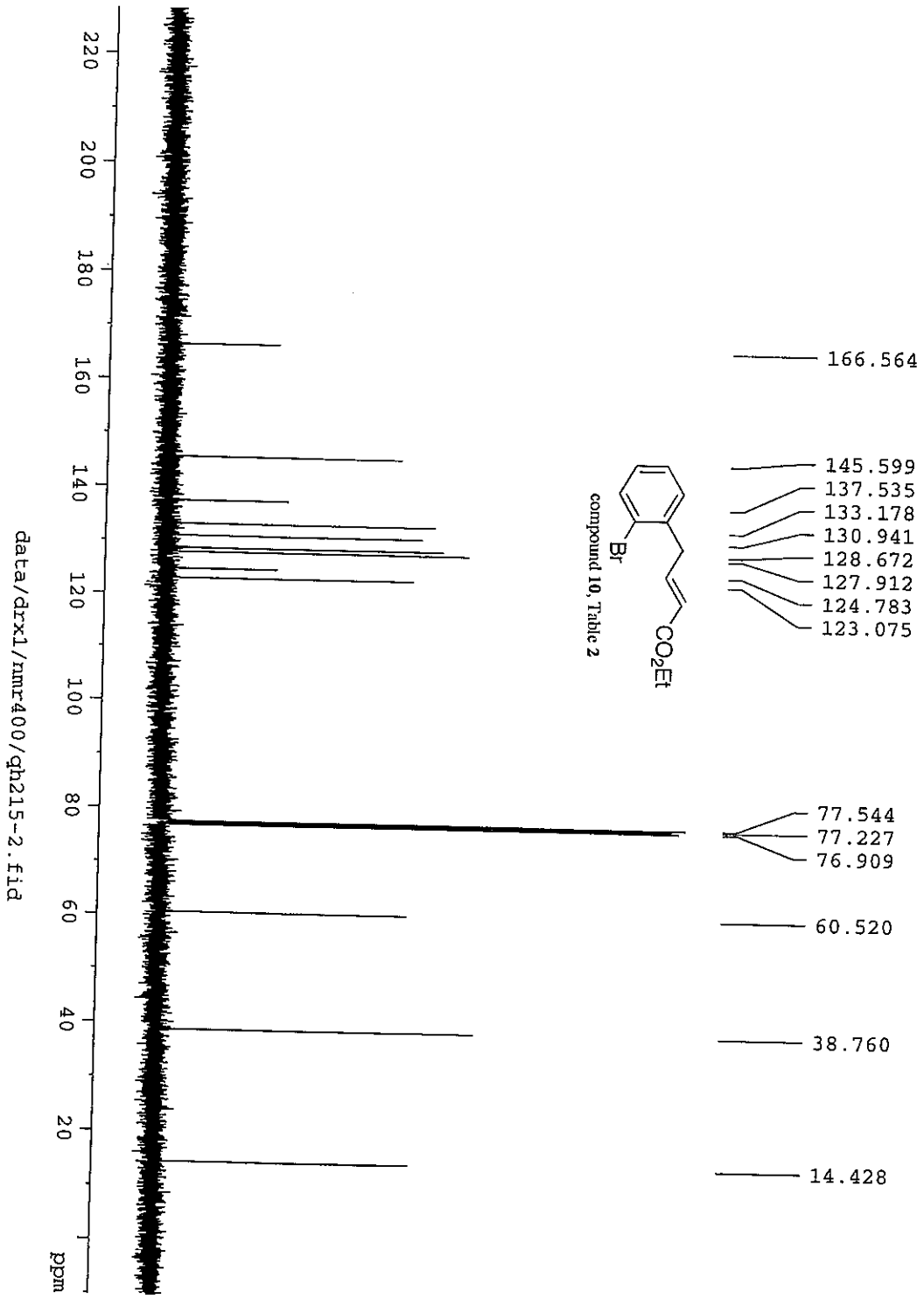
1.000
2.158
2.163
3.309
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
7.571
7.551
7.285
7.266
7.248
7.210
7.206
7.191
7.187
7.133
7.129
7.113
7.109
7.092
7.076
7.070
7.053
7.037
5.797
5.793
5.789
5.758
5.754
5.750
4.203
4.185
4.167
4.149
3.661
3.658
3.645
3.355
1.290
1.273
1.255
0.000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133.178
130.941
128.672
127.912
124.783
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77.544
77.227
76.909
60.520
38.760
14.428
Br
CO2Et
compound 10, Table 2
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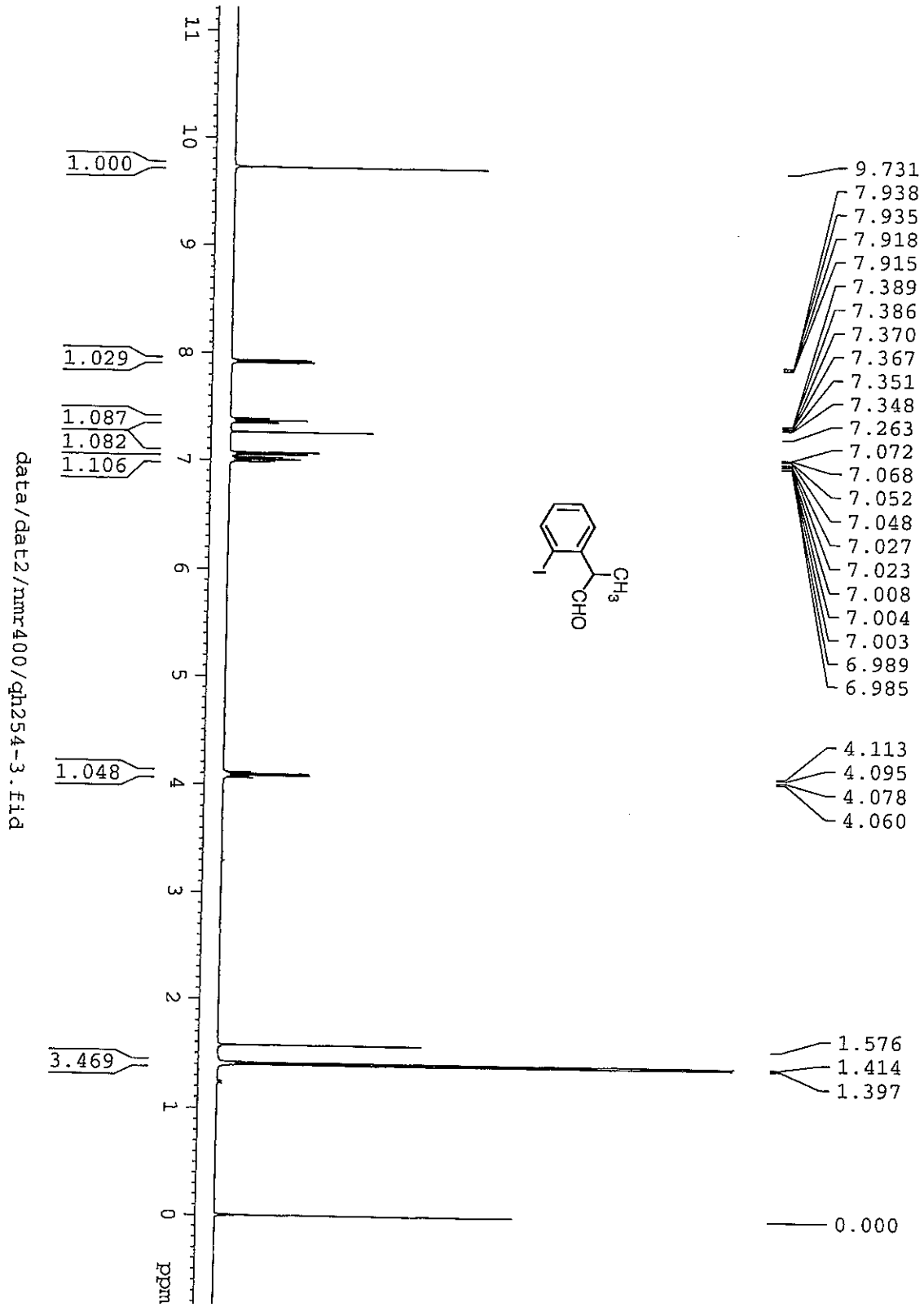
180
160
140
120
100
80
60
40
20
ppm
data/drx1/nmr400/qh215-2.fid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3.469
ppm
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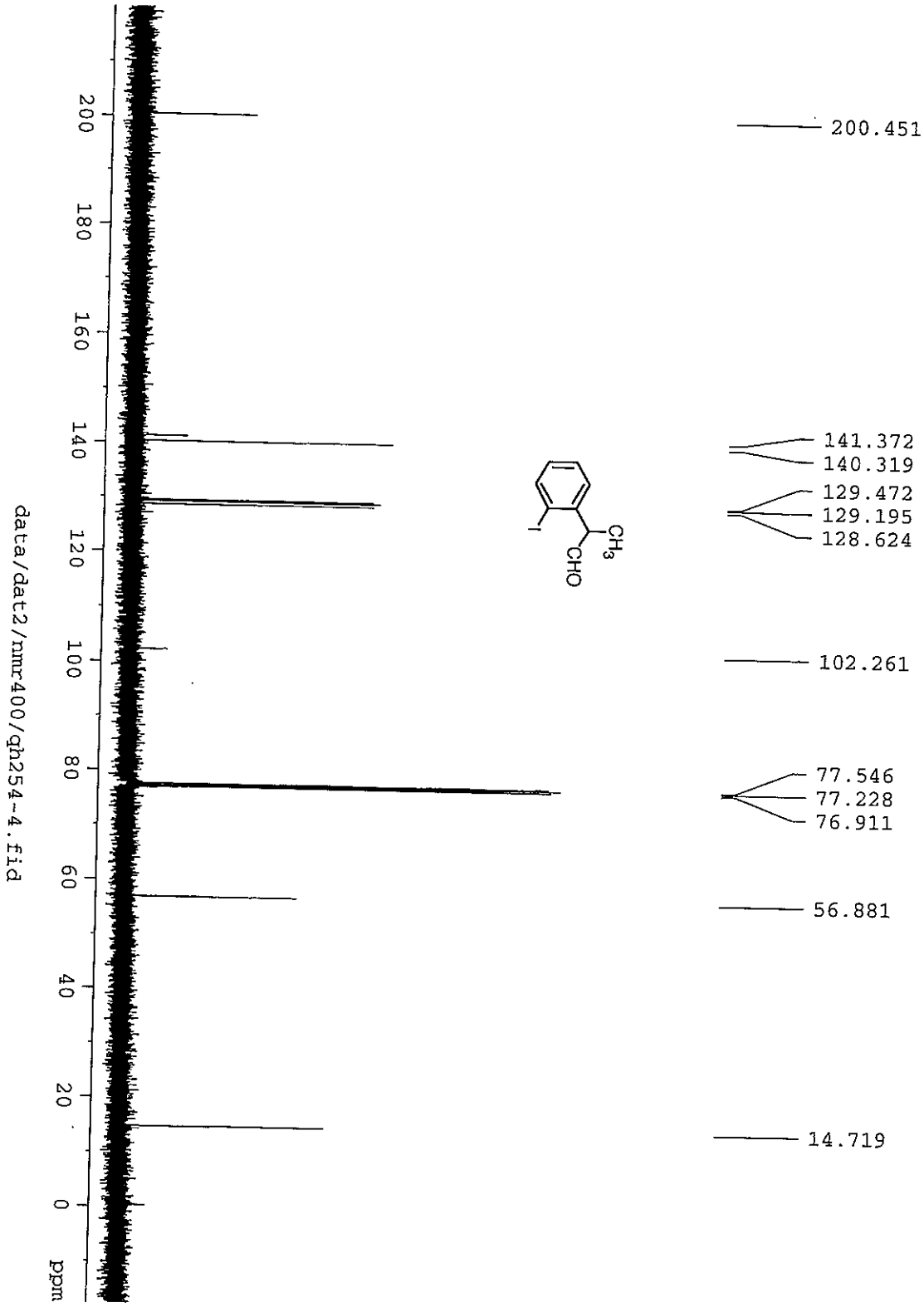
7.938
7.935
7.918
7.915
7.389
7.386
7.370
7.367
7.351
7.348
7.263
7.072
7.068
7.052
7.048
7.027
7.023
7.008
7.004
7.003
6.989
6.985
4.113
4.095
4.078
4.060
1.576
1.414
1.397
0.000
CH3
CHO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140.319
129.472
129.195
128.624
102.261
77.546
77.228
76.911
56.881
14.719
CH3
CHO
200
180
160
140
120
100
80
60
40
20
0
ppm
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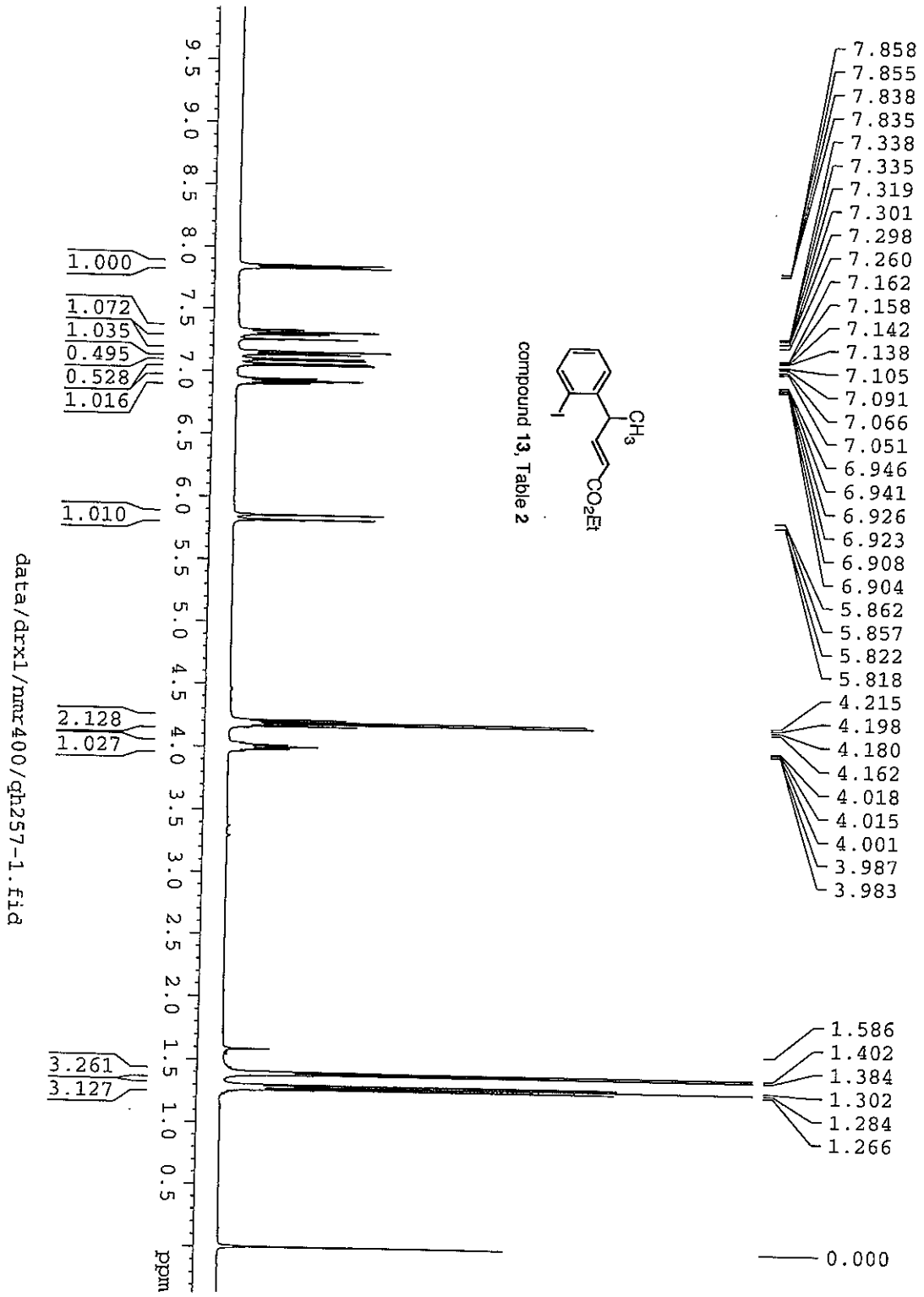
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7.335
7.319
7.301
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7.162
7.158
7.142
7.138
7.105
7.091
7.066
7.051
6.946
6.941
6.926
6.923
6.908
6.904
5.862
5.857
5.822
5.818
4.215
4.198
4.180
4.162
4.018
4.015
4.001
3.987
3.983
1.586
1.402
1.384
1.302
1.284
1.266
0.000
1.000
1.072
1.035
0.495
0.528
1.016
1.010
2.128
1.027
3.261
3.127
compound 13, Table 2
CH3
CO2Et
I
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
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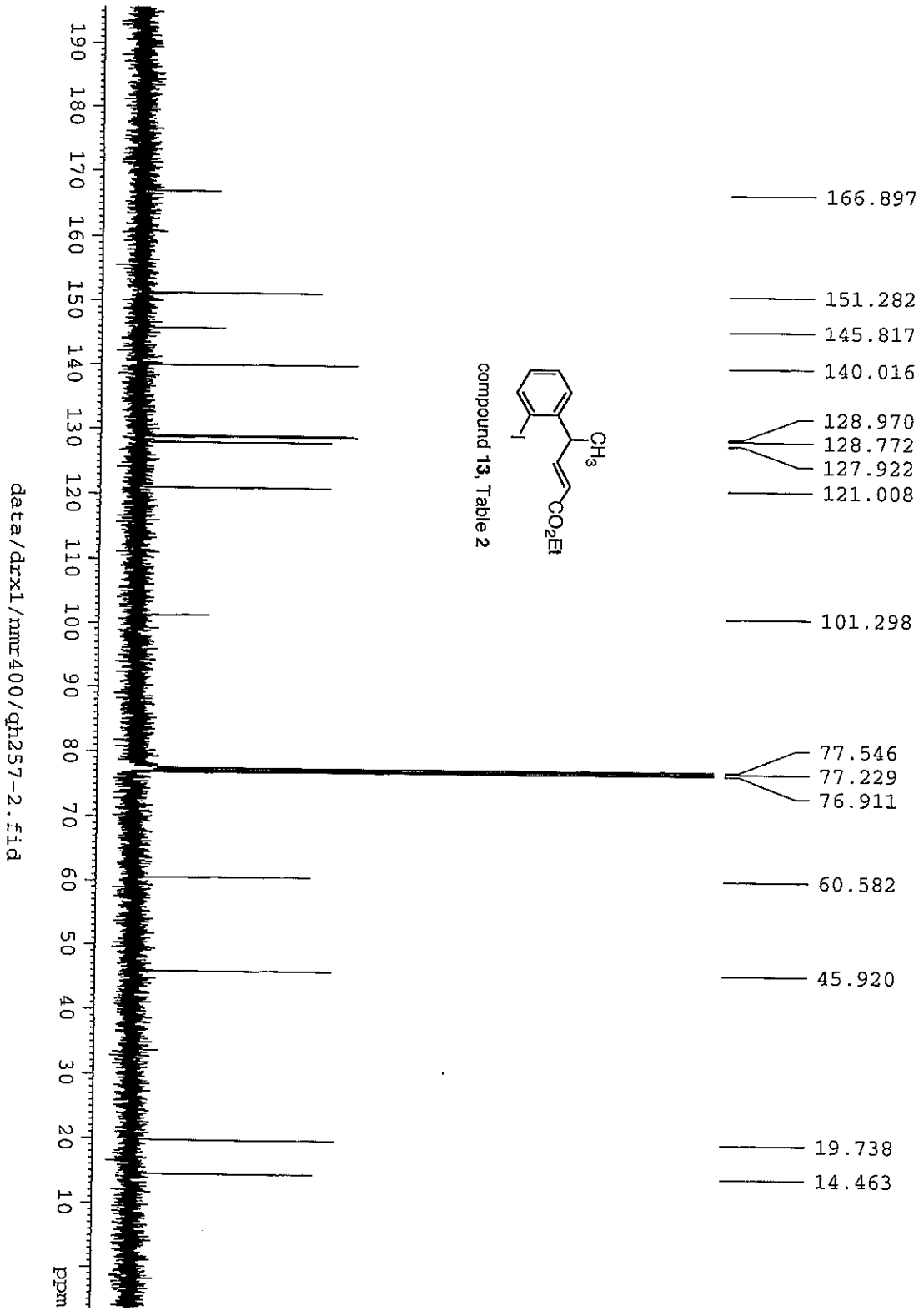
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140.016
128.970
128.772
127.922
121.008
101.298
77.546
77.229
76.911
60.582
45.920
19.738
14.463
CH3
CO2Et
compound 13, Table 2
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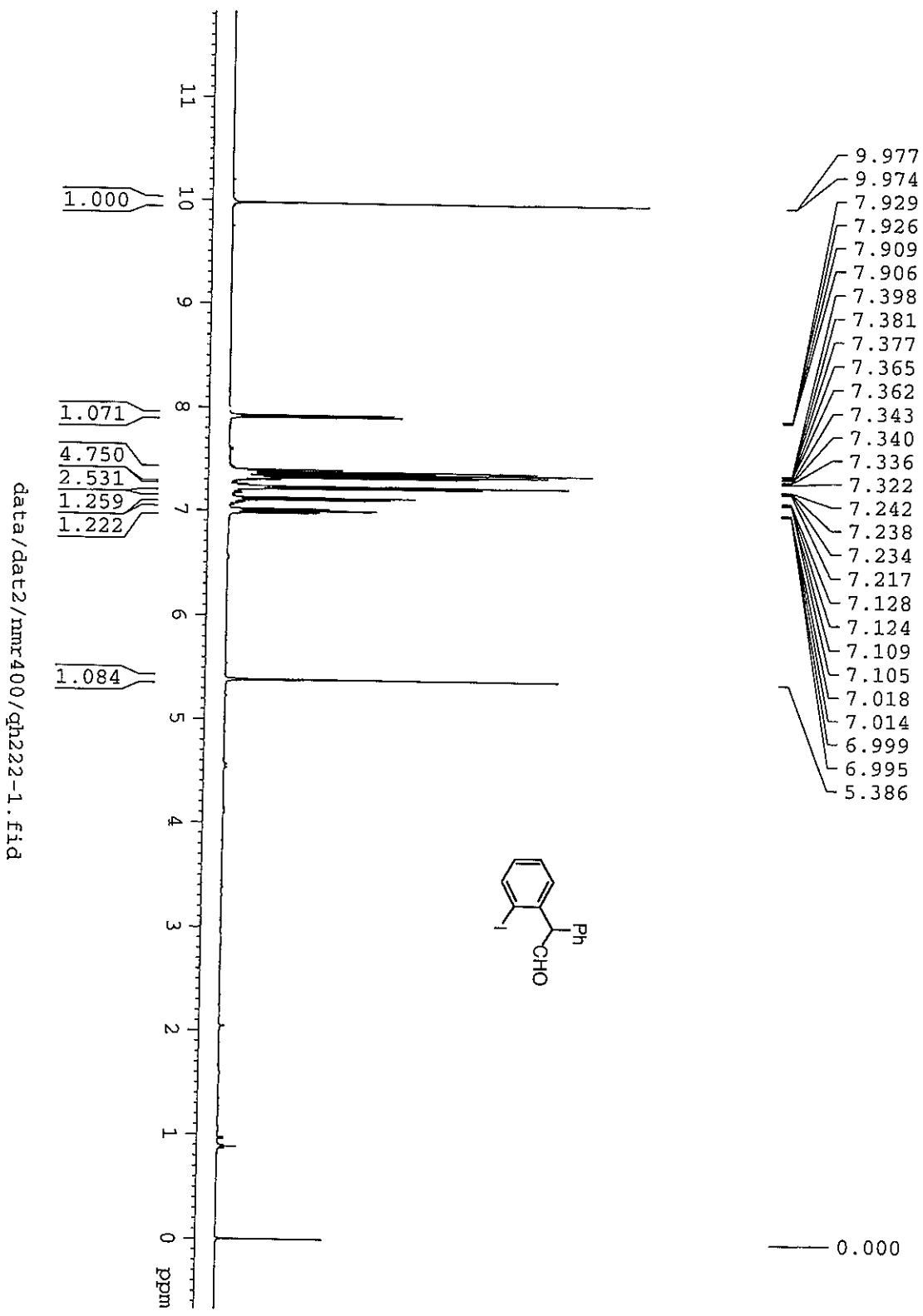
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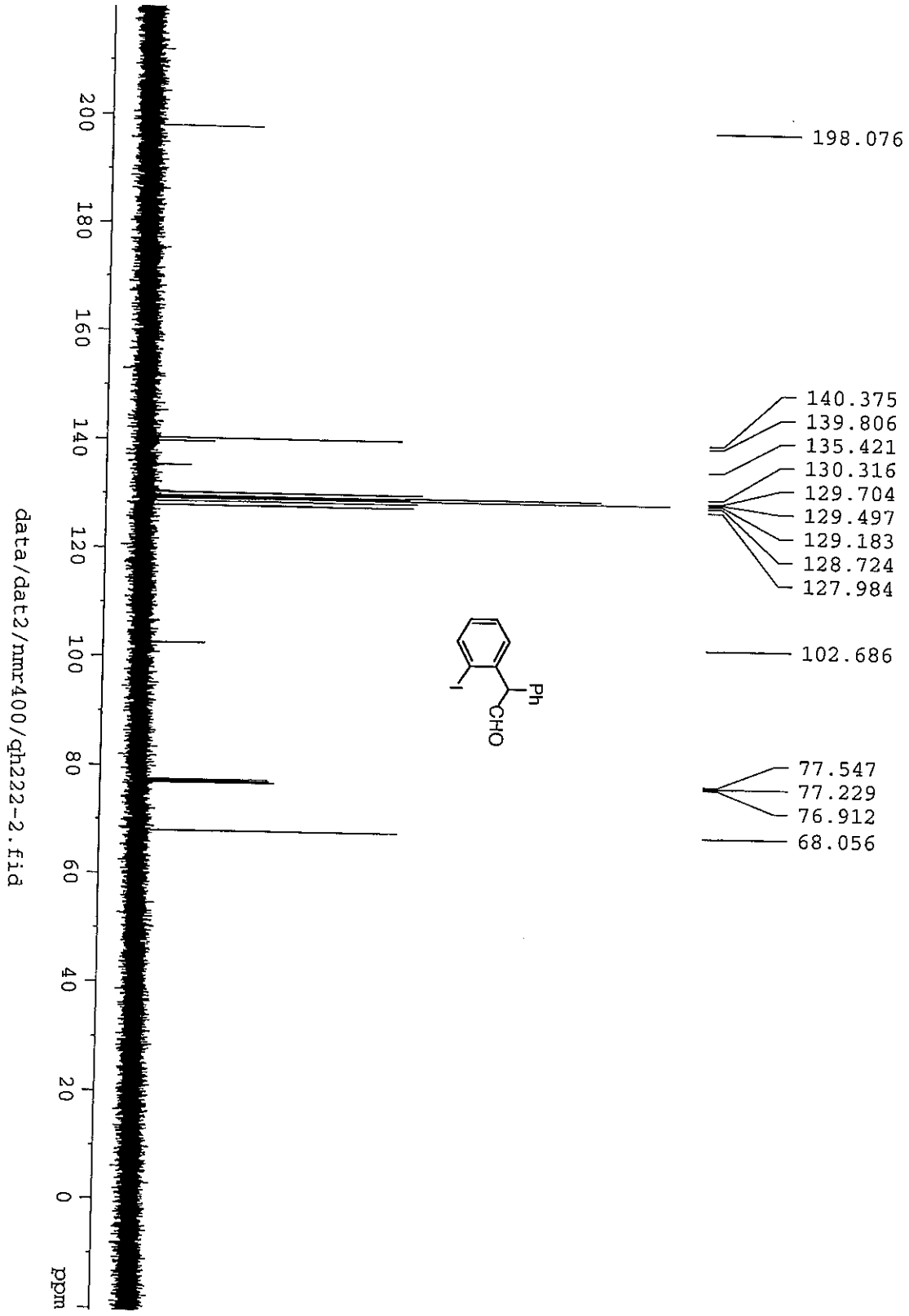
7.929
7.926
7.909
7.906
7.398
7.381
7.377
7.365
7.362
7.343
7.340
7.336
7.322
7.242
7.238
7.234
7.217
7.128
7.124
7.109
7.105
7.018
7.014
6.999
6.995
5.386
1.000
1.071
4.750
2.531
1.259
1.222
1.084
0.000
Ph
CHO
I
ppm
data/dat2/nmr400/qh222-1.fid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139.806
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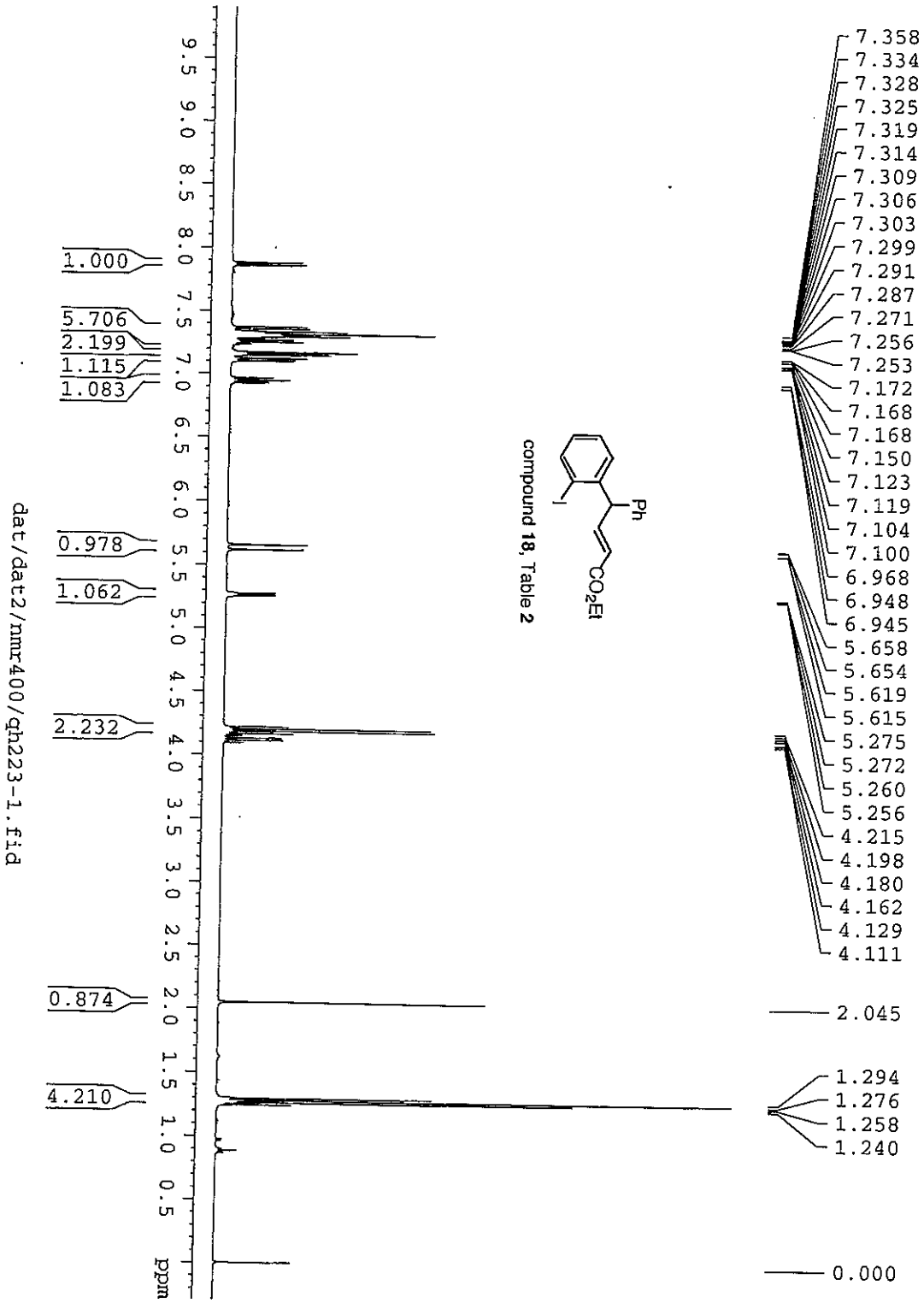
130.316
129.704
129.497
129.183
128.724
127.984
102.686
77.547
77.229
76.912
68.056
I
Ph
CHO
200
180
160
140
120
100
80
60
40
20
0
ppm
data/dat2/nmr400/qh222-2.fid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7.319
7.314
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7.306
7.303
7.299
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7.287
7.271
7.256
7.253
7.172
7.168
7.168
7.150
7.123
7.119
7.104
7.100
6.968
6.948
6.945
5.658
5.654
5.619
5.615
5.275
5.272
5.260
5.256
4.215
4.198
4.180
4.162
4.129
4.111
2.045
1.294
1.276
1.258
1.240
0.000
Ph
CO2Et
compound 18, Table 2
1.000
5.706
2.199
1.115
1.083
0.978
1.062
2.232
0.874
4.210
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
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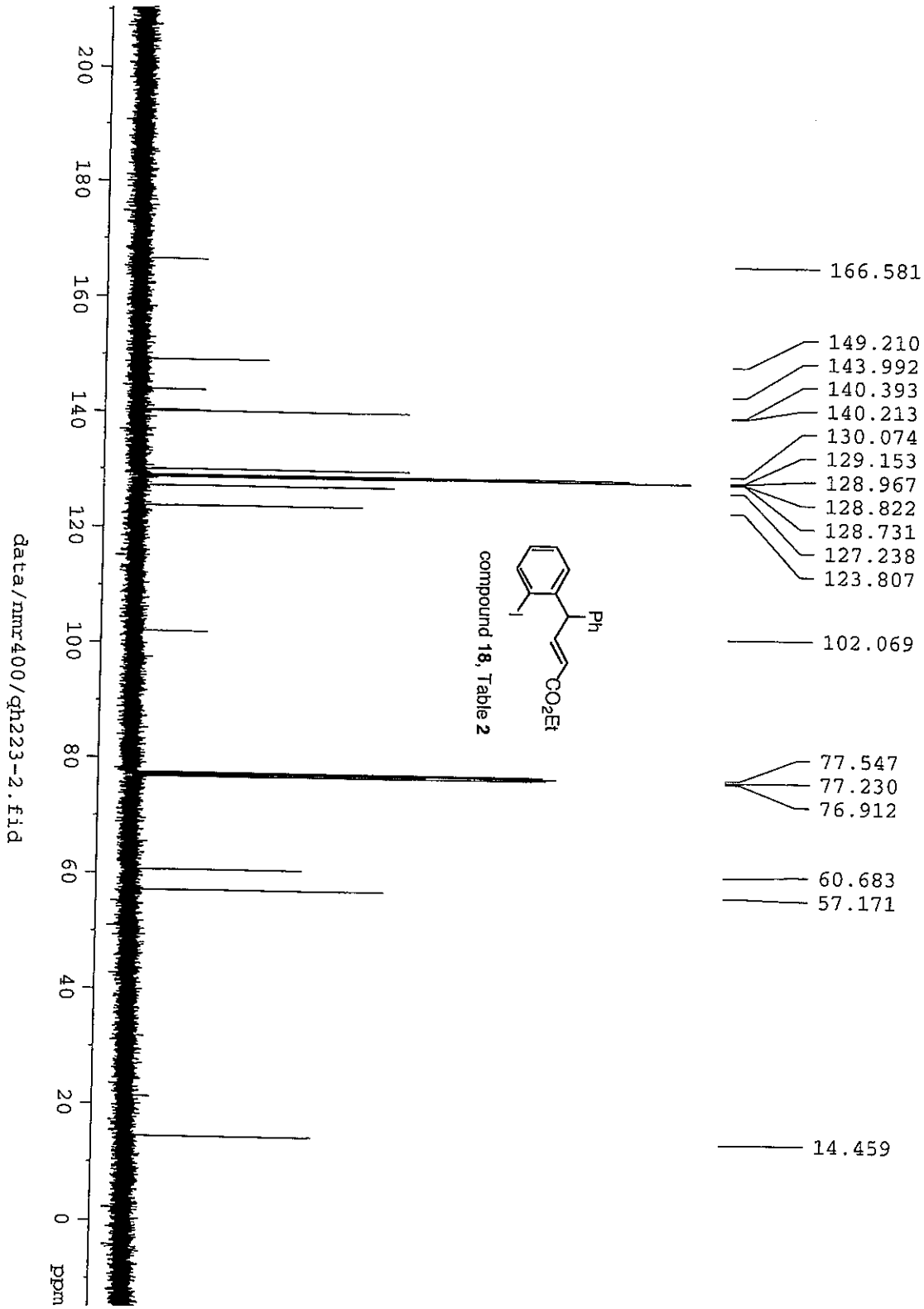
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140.393
140.213
130.074
129.153
128.967
128.822
128.731
127.238
123.807
102.069
77.547
77.230
76.912
60.683
57.171
14.459
Ph
CO2Et
compound 18, Table 2
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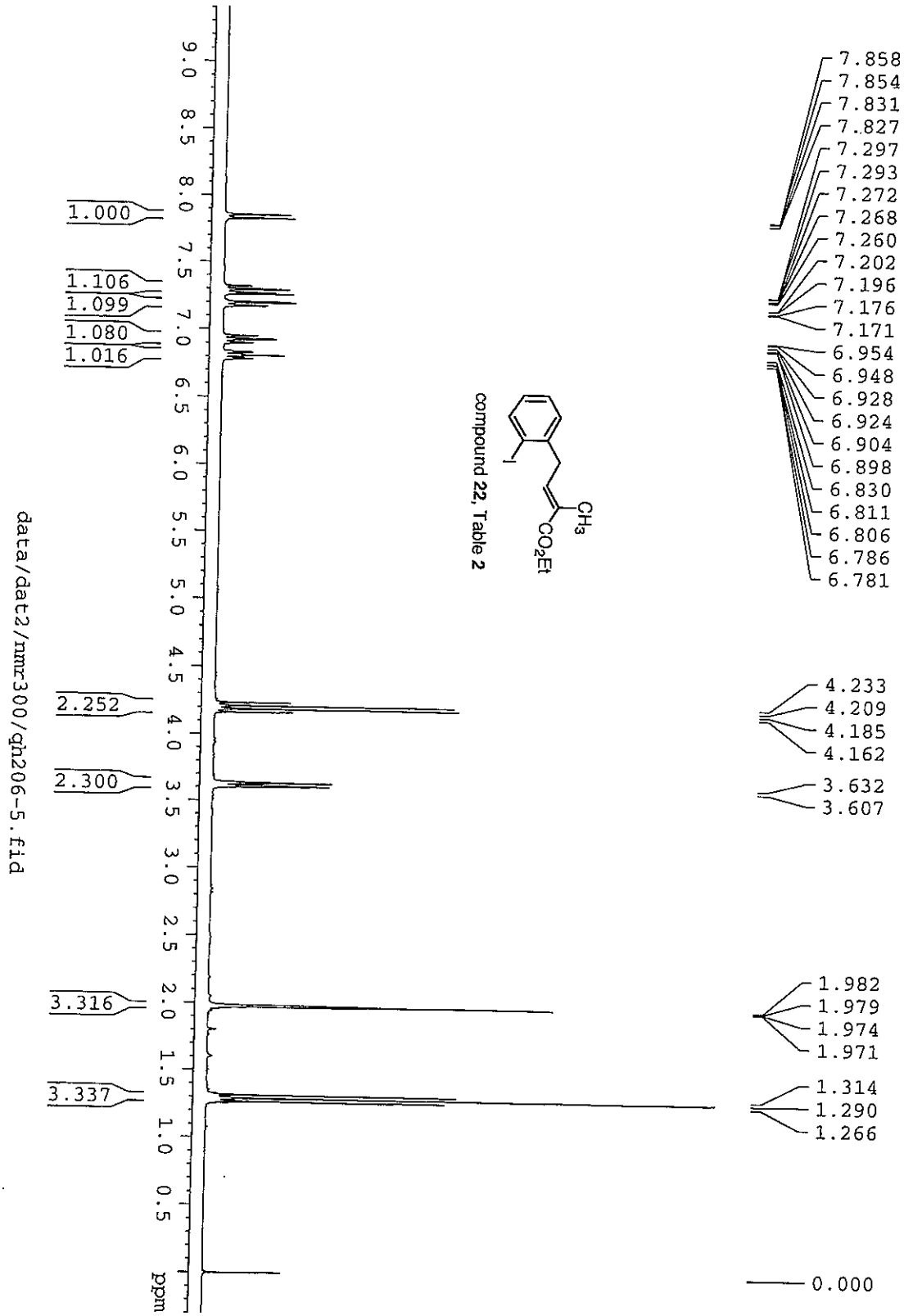
180
160
140
120
100
80
60
40
20
0
ppm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CO2Et
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7.831
7.827
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7.293
7.272
7.268
7.260
7.202
7.196
7.176
7.171
6.954
6.948
6.928
6.924
6.904
6.898
6.830
6.811
6.806
6.786
6.781
4.233
4.209
4.185
4.162
3.632
3.607
1.982
1.979
1.974
1.971
1.314
1.290
1.266
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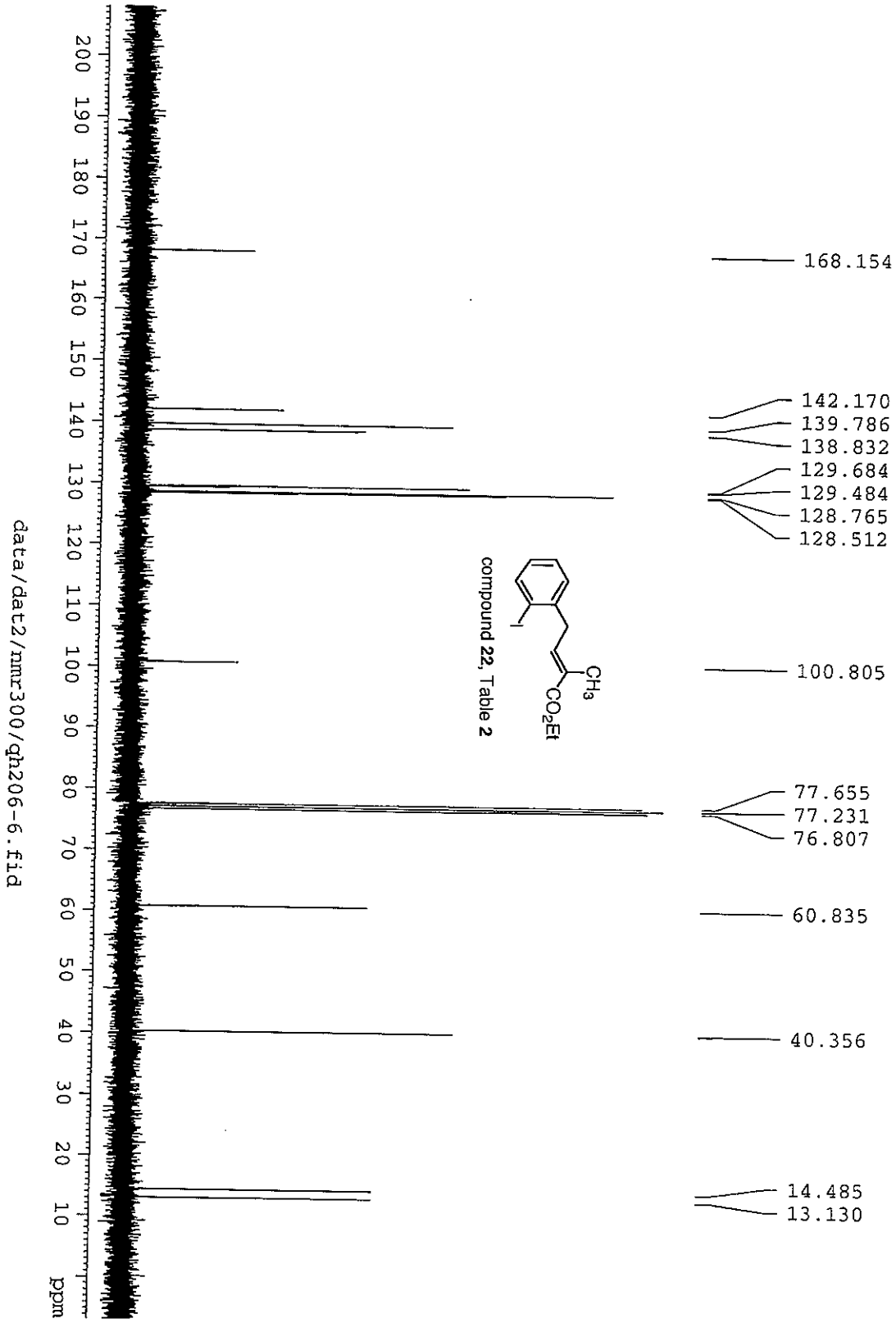
1.000
1.106
1.099
1.080
1.016
2.252
2.300
3.316
3.337
ppm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129.484
128.765
128.512
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77.655
77.231
76.807
60.835
40.356
14.485
13.130
compound 22, Table 2
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CO2Et
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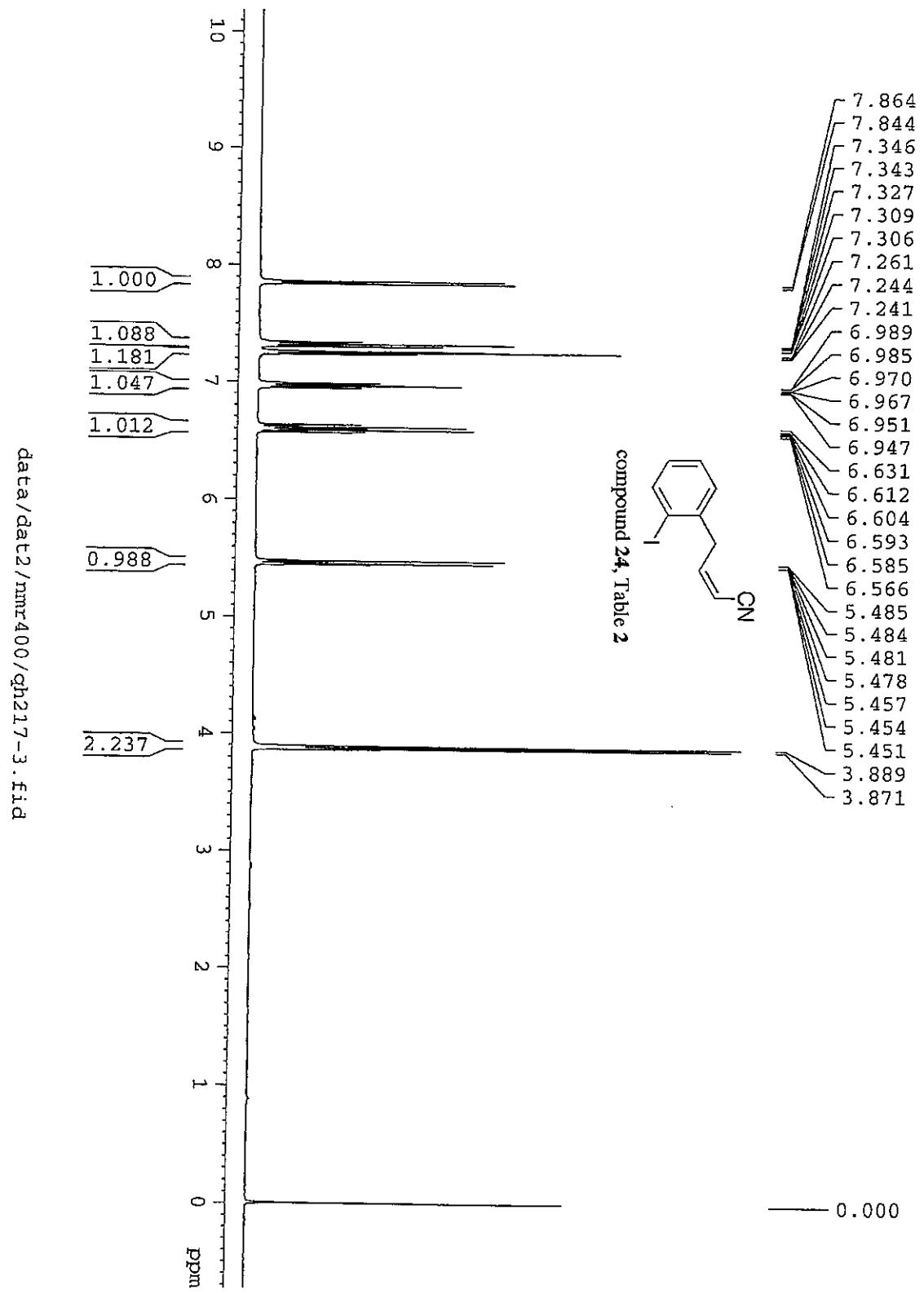
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7.309
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7.261
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7.241
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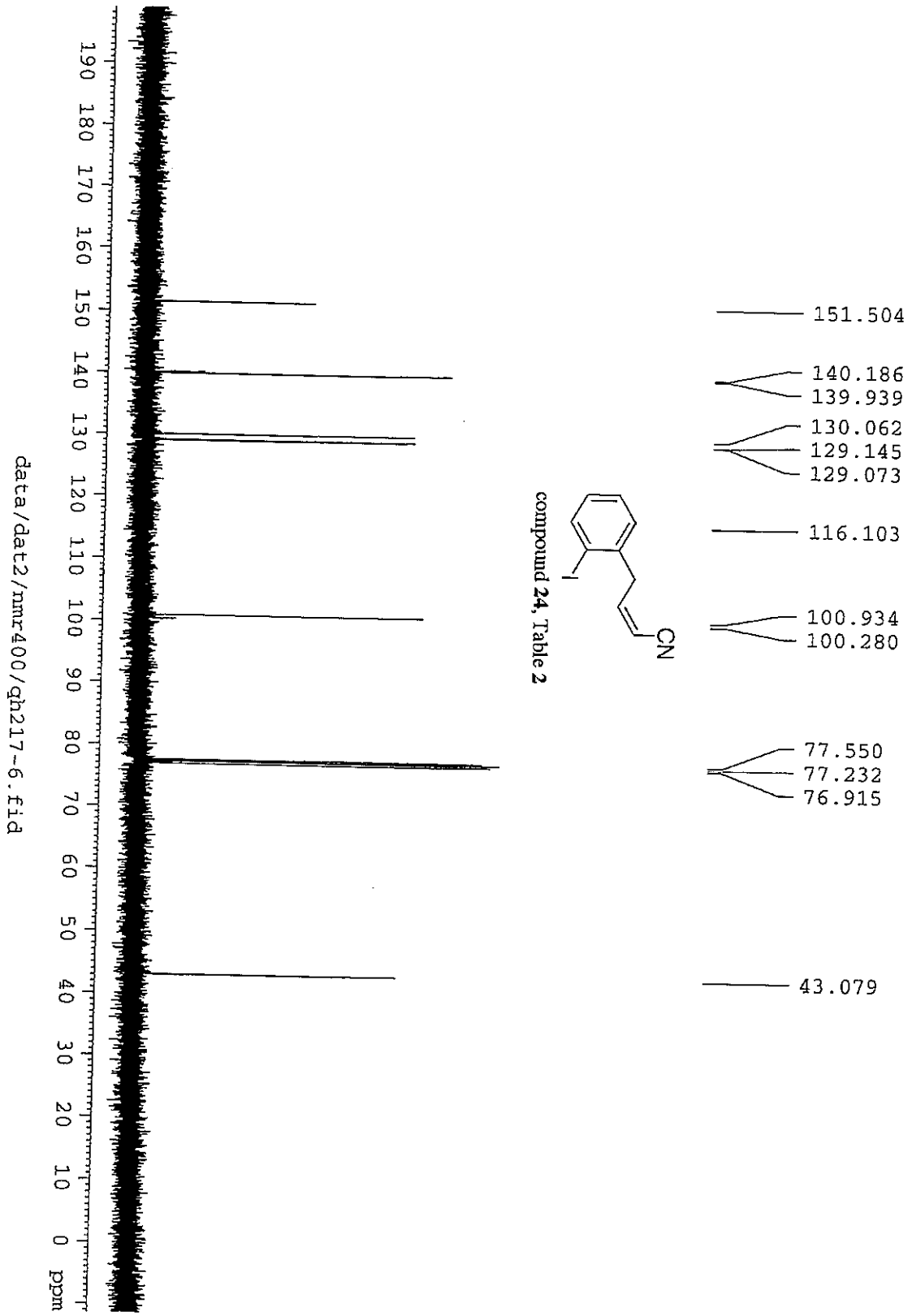
6.970
6.967
6.951
6.947
6.631
6.612
6.604
6.593
6.585
6.566
5.485
5.484
5.481
5.478
5.457
5.454
5.451
3.889
3.871
1.000
1.088
1.181
1.047
1.012
0.988
2.237
0.000
ppm
compound 24, Table 2
CN
data/dat2/nmr400/qh217-3.fid


151.504
140.186
139.939
130.062
129.145
129.073
116.103
100.934
100.280
77.550
77.232
76.915
43.079
CN
I
compound 24, Table 2
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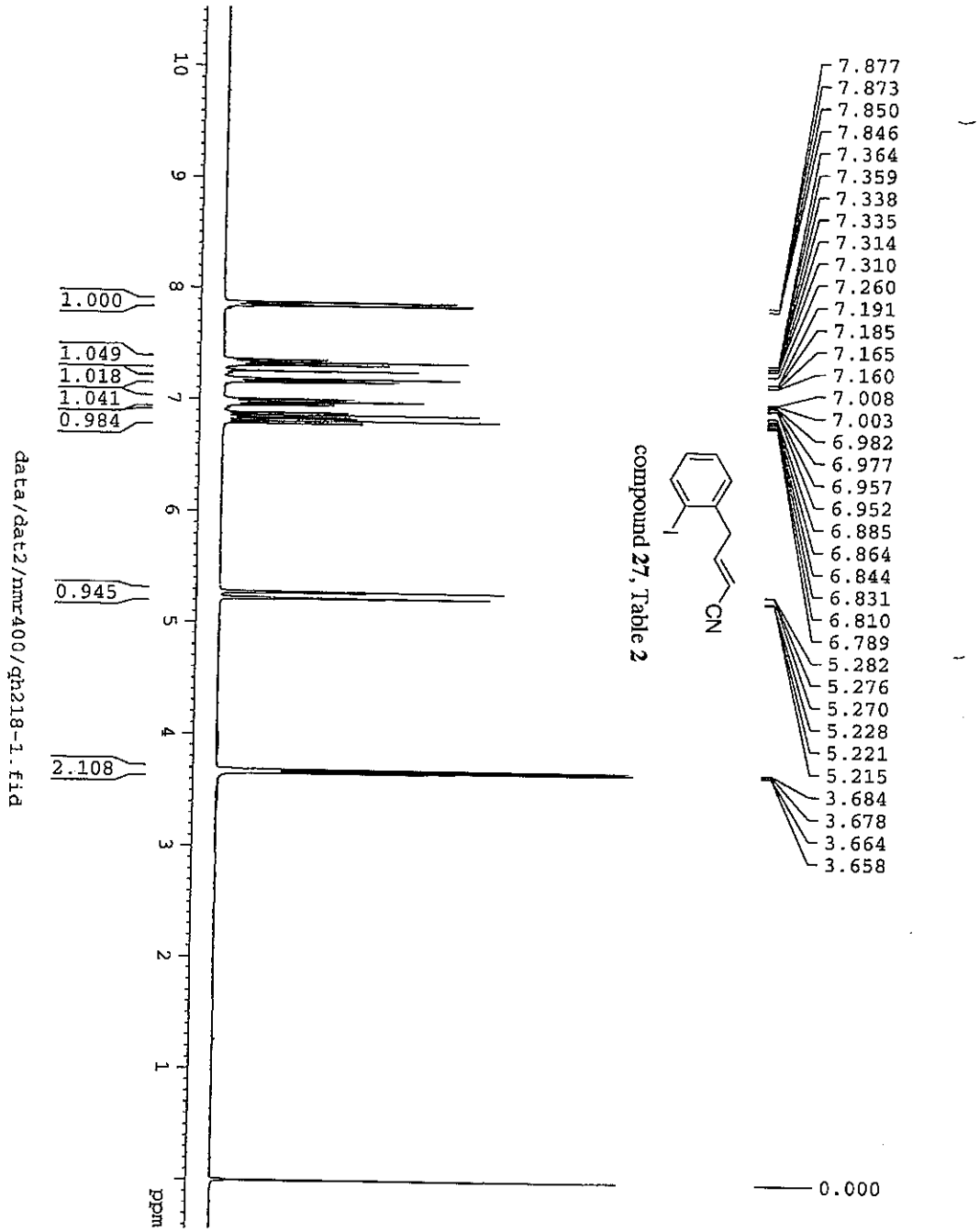
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1.018
1.041
0.984
0.945
2.108
ppm
compound 27, Table 2
CN
7.877
7.873
7.850
7.846
7.364
7.359
7.338
7.335
7.314
7.310
7.260
7.191
7.185
7.165
7.160
7.008
7.003
6.982
6.977
6.957
6.952
6.885
6.864
6.844
6.831
6.810
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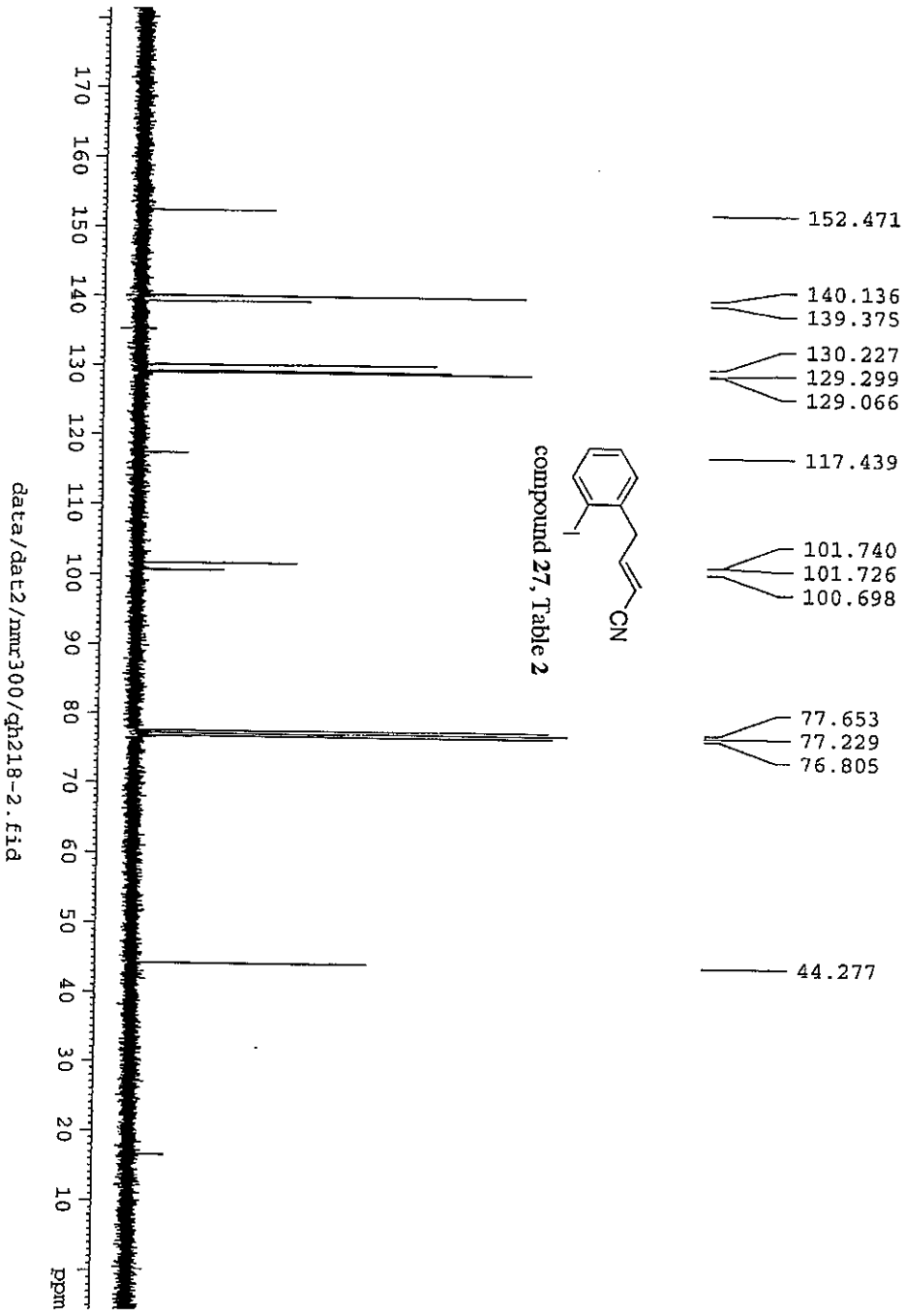
0.000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130.227
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129.066
117.439
101.740
101.726
100.698
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77.229
76.805
44.277
CN
compound 27, Table 2
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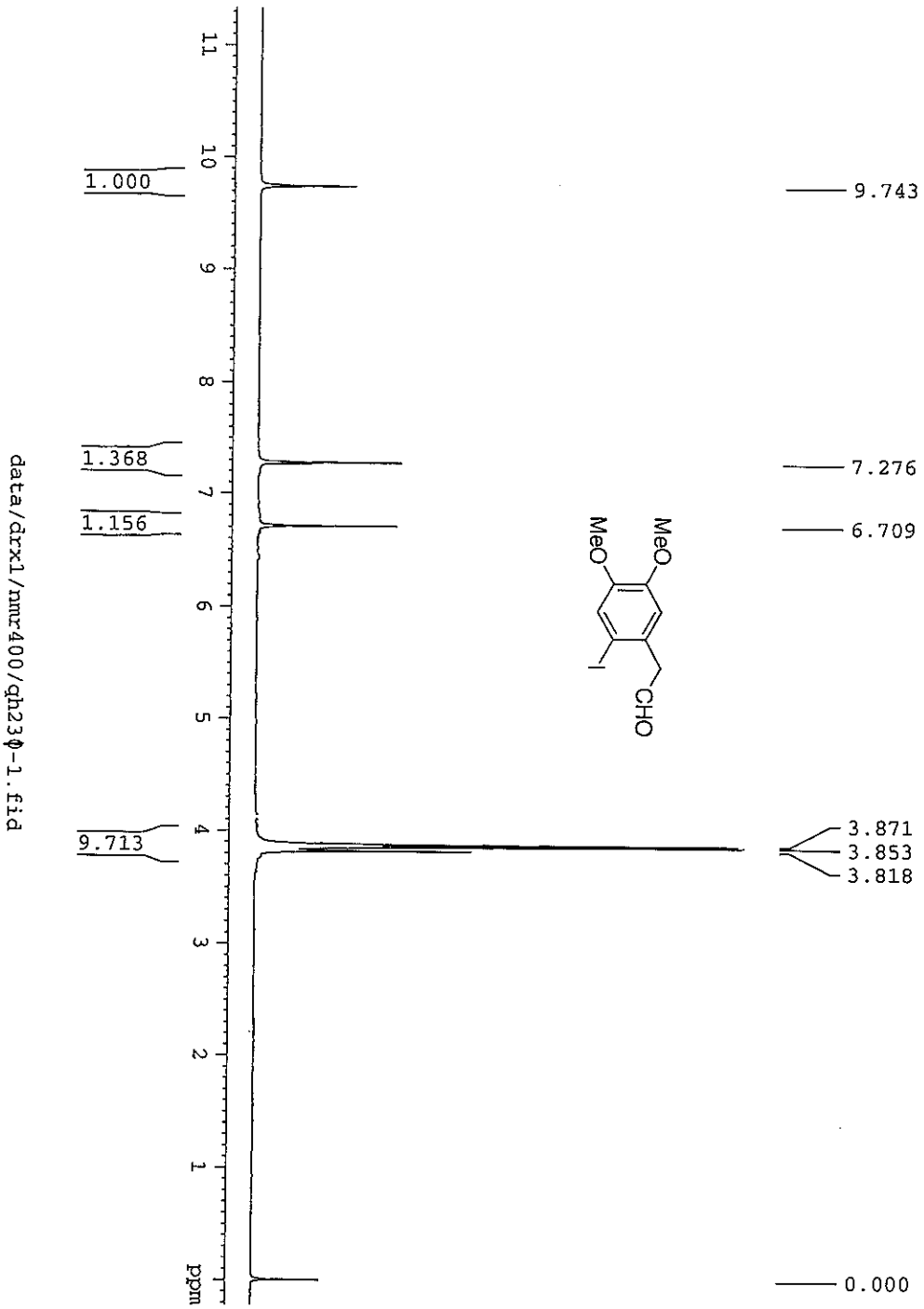
ppm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6.709
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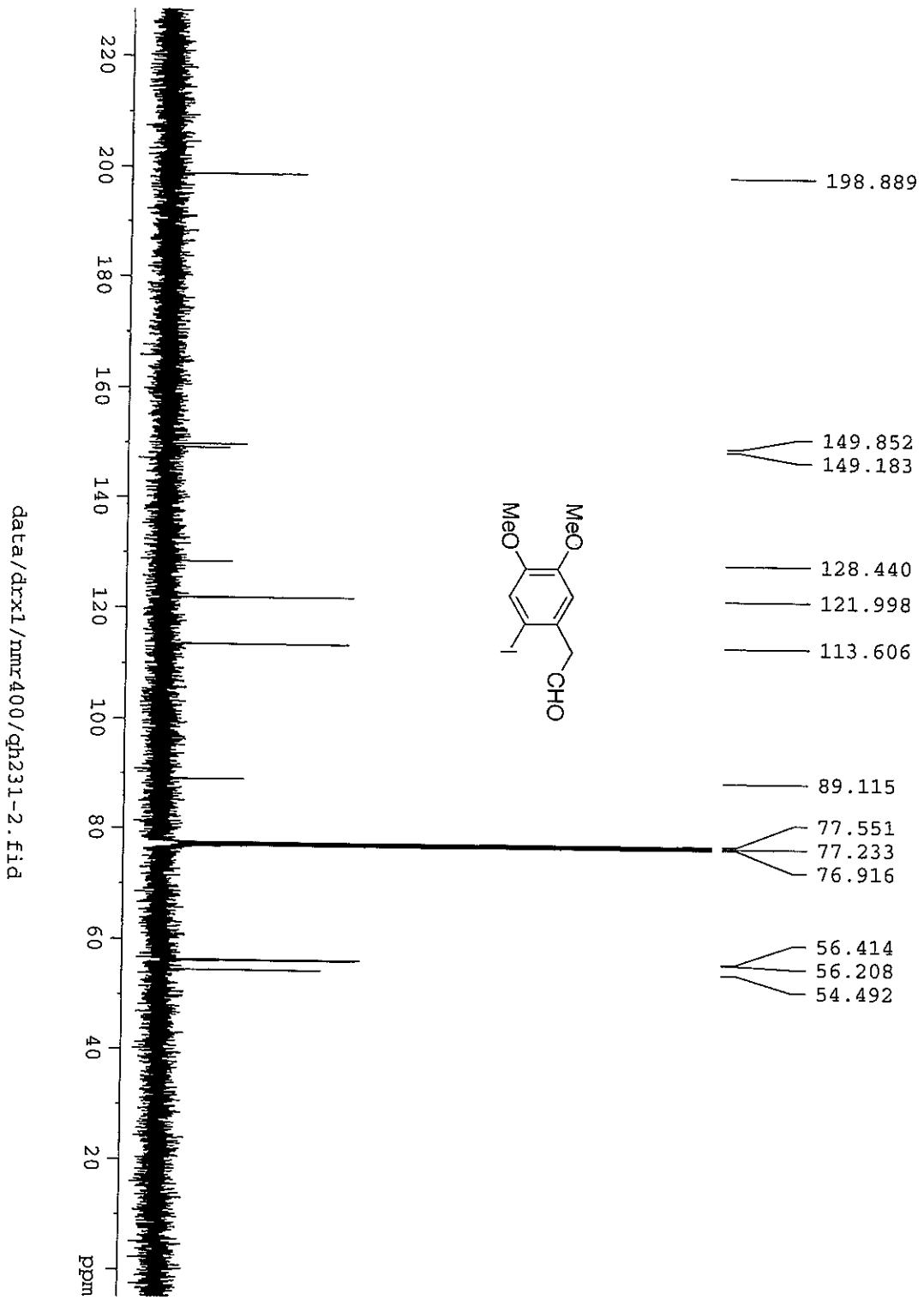
3.818
0.000
MeO
MeO
CHO
ppm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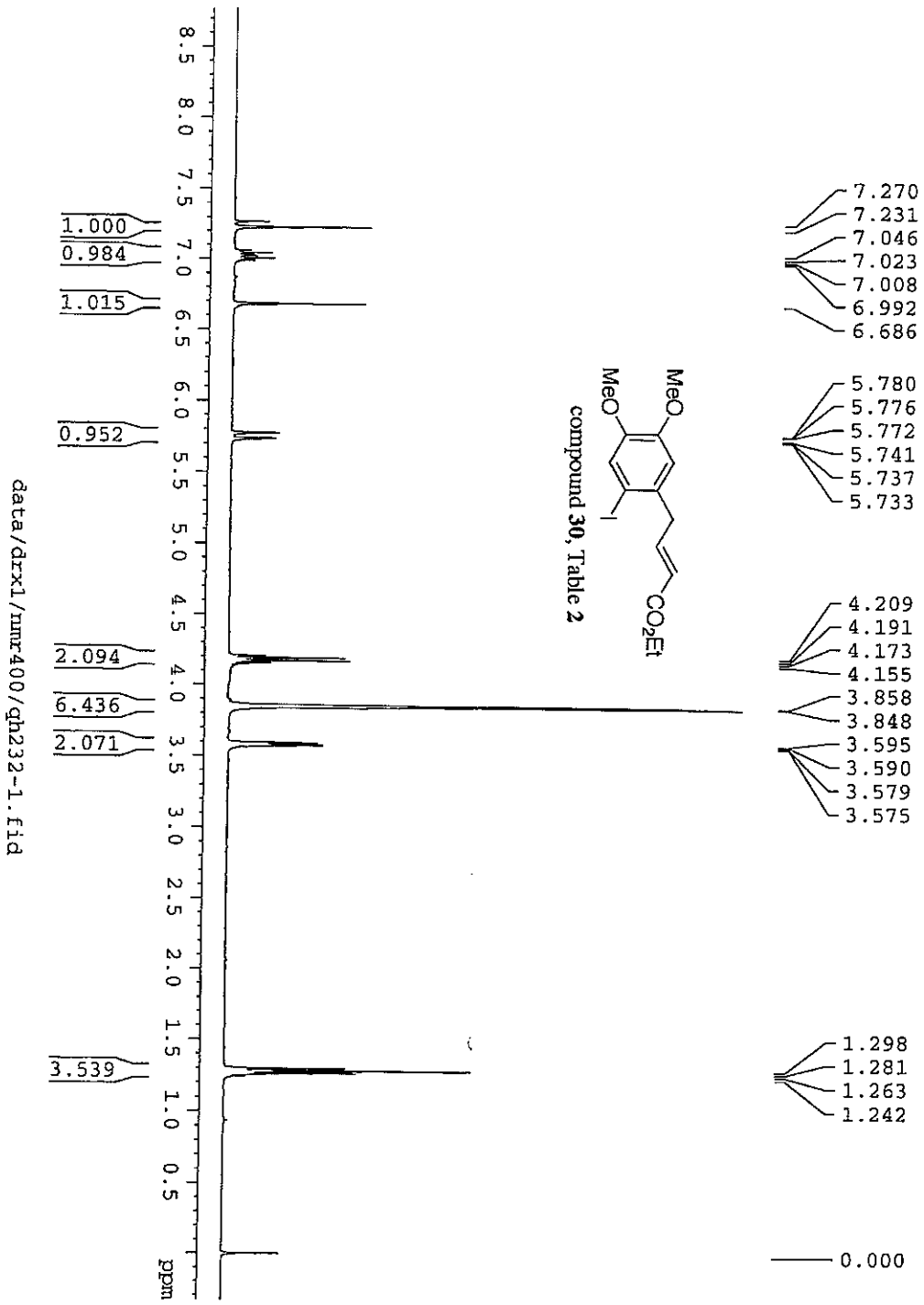
149.852
149.183
128.440
121.998
113.606
89.115
77.551
77.233
76.916
56.414
56.208
54.492
MeO
MeO
I
CHO
220
200
180
160
140
120
100
80
60
40
20
ppm
data/drx1/nmr400/qh231-2.fid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5.780
5.776
5.772
5.741
5.737
5.733
4.209
4.191
4.173
4.155
3.858
3.848
3.595
3.590
3.579
3.575
1.298
1.281
1.263
1.242
0.000
1.000
0.984
1.015
0.952
2.094
6.436
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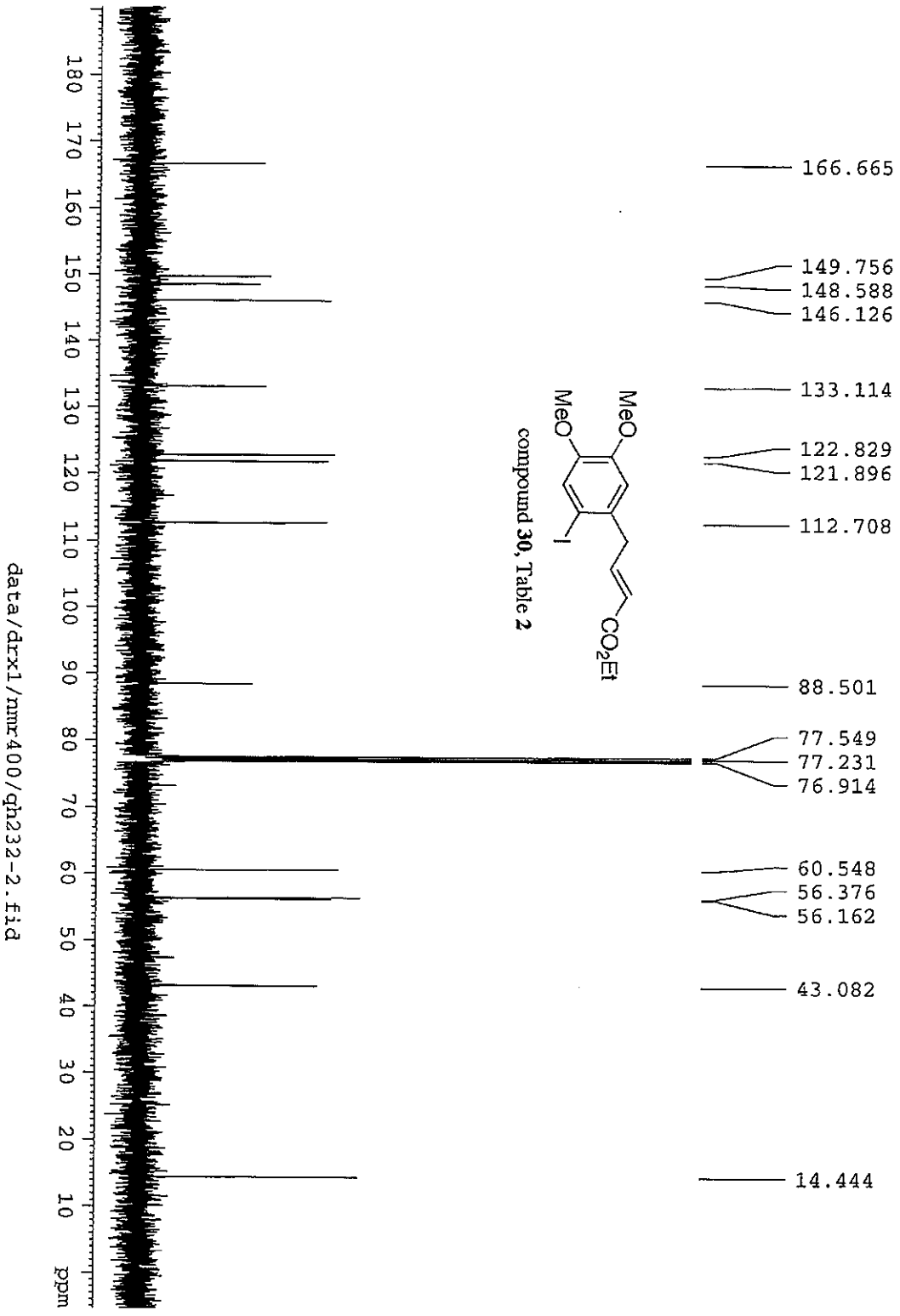
3.539
MeO
MeO
I
CO2Et
compound 30, Table 2
data/drx1/nmr400/qh232-1.fid
ppm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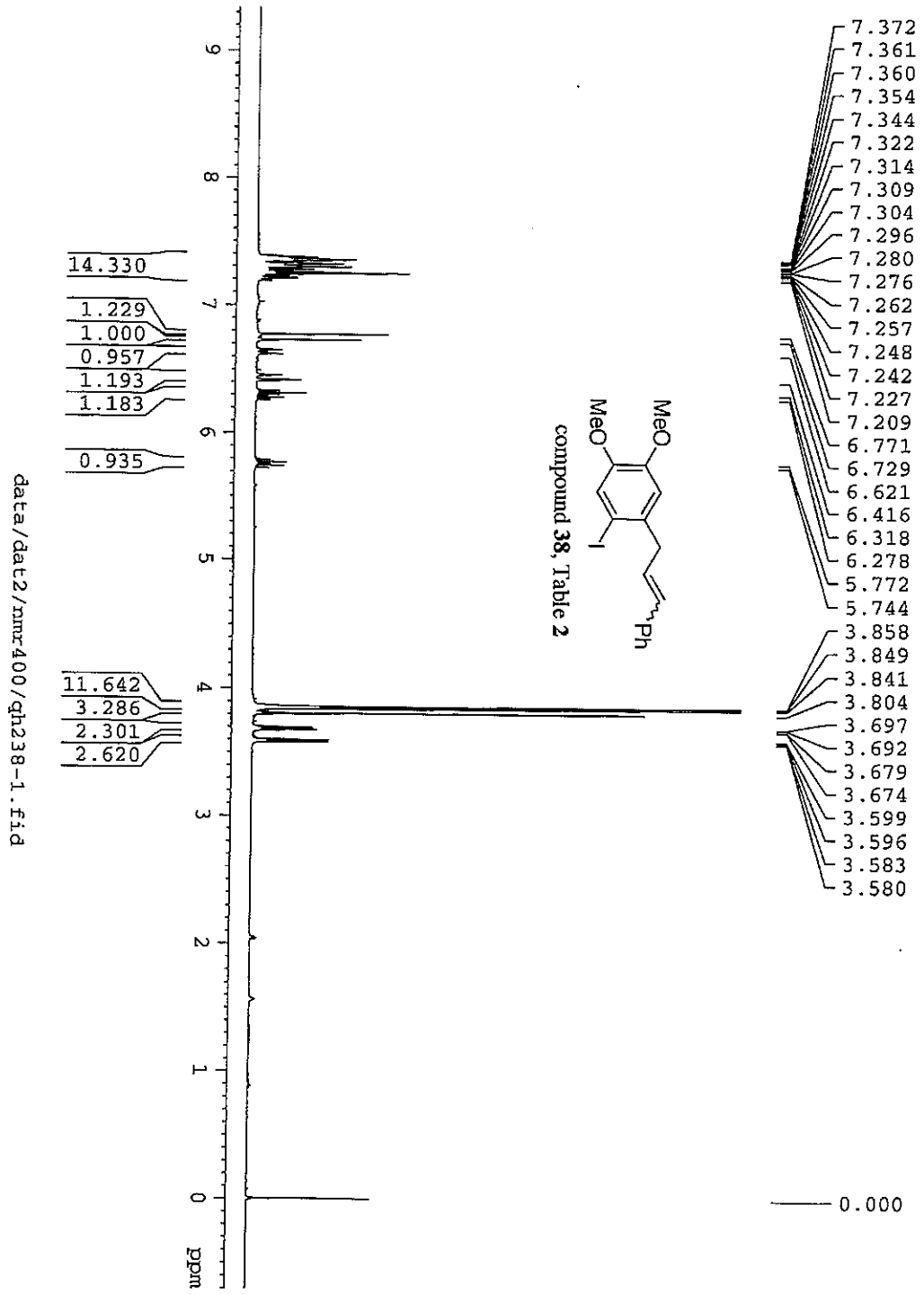
148.588
146.126
133.114
122.829
121.896
112.708
88.501
77.549
77.231
76.914
60.548
56.376
56.162
43.082
14.444
MeO
MeO
I
CO2Et
compound 30, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh232-2.fid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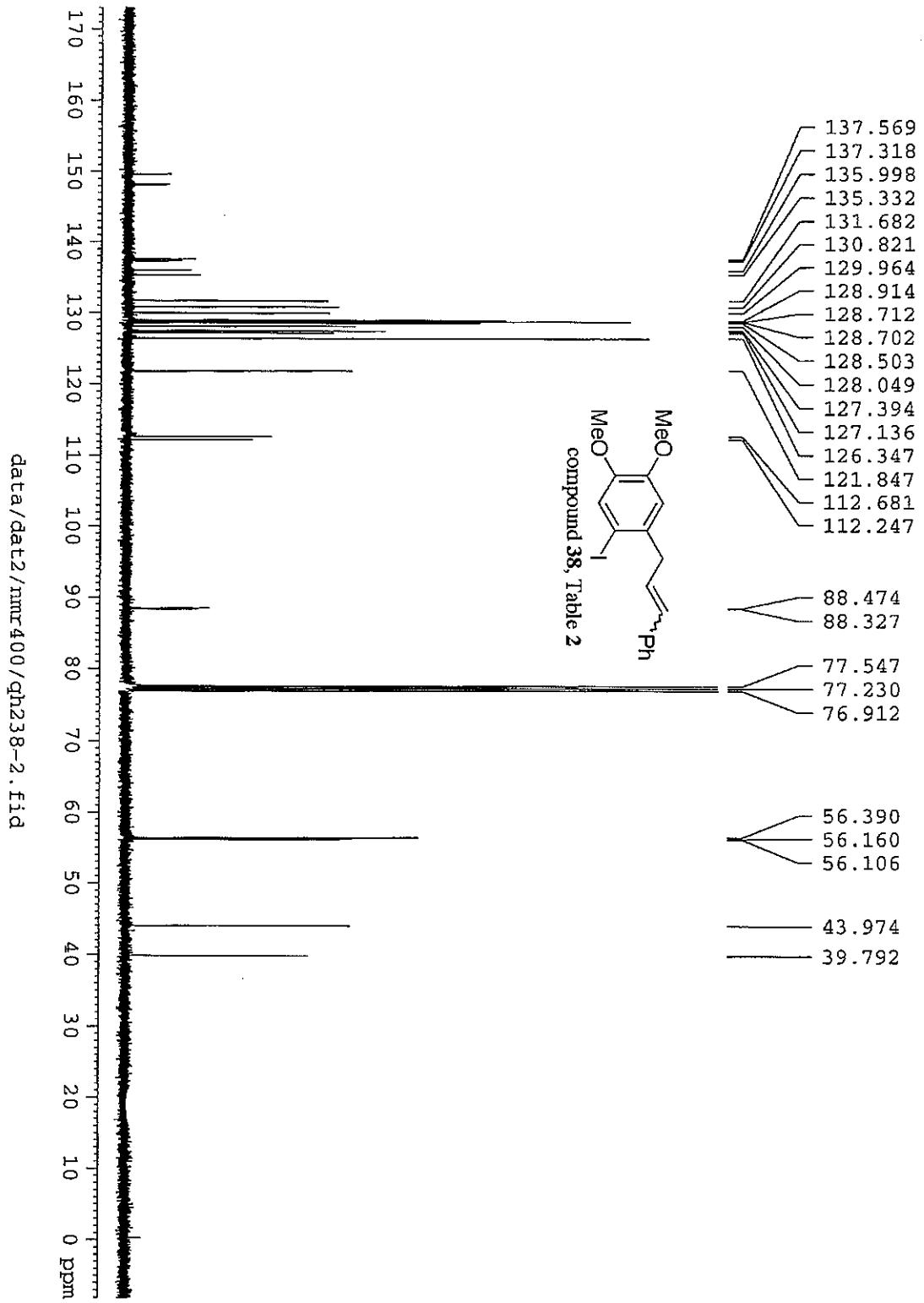
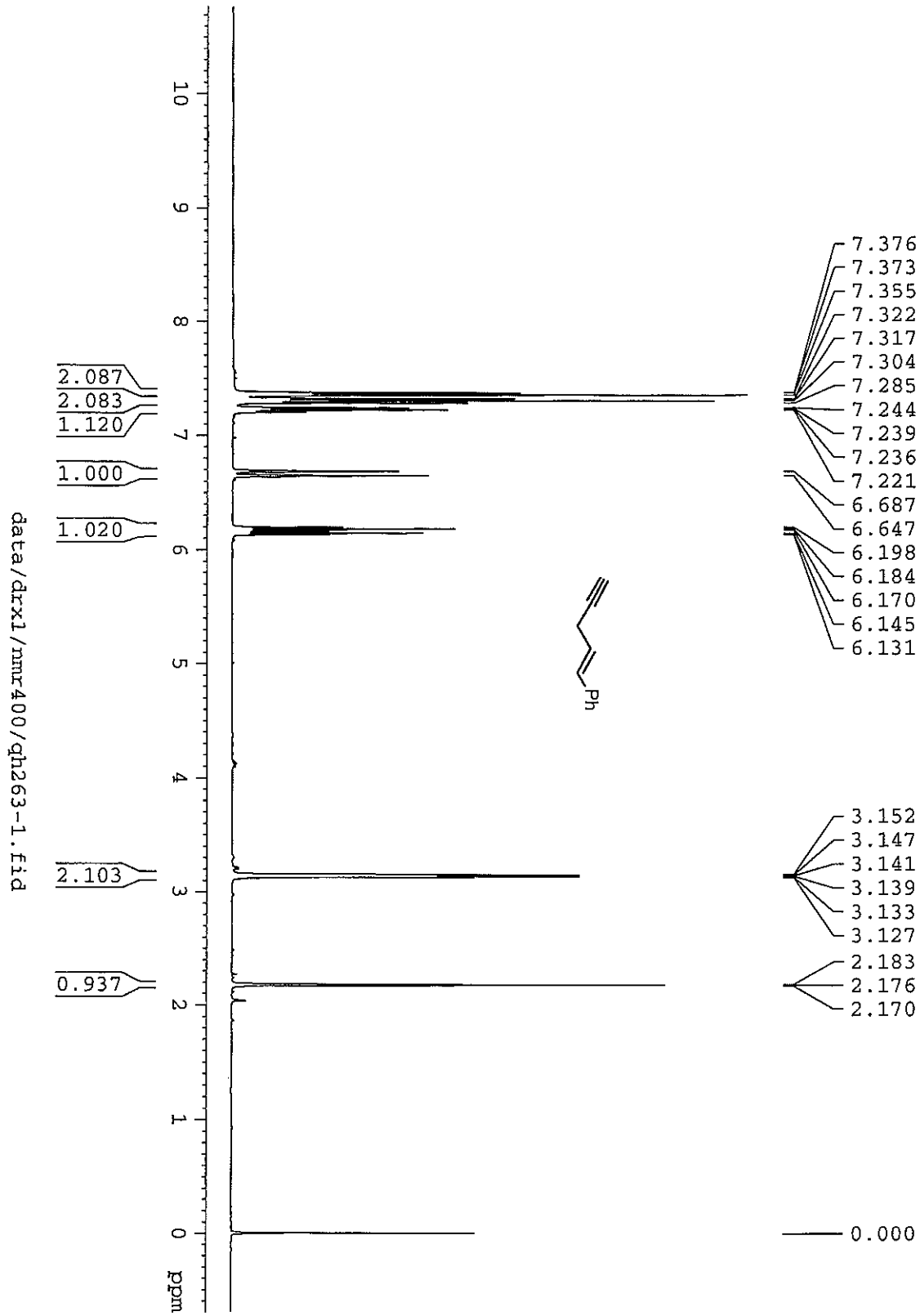
7.361
7.360
7.354
7.344
7.322
7.314
7.309
7.304
7.296
7.280
7.276
7.262
7.257
7.248
7.242
7.227
7.209
6.771
6.729
6.621
6.416
6.318
6.278
5.772
5.744
3.858
3.849
3.841
3.804
3.697
3.692
3.679
3.674
3.599
3.596
3.583
3.580
14.330
1.229
1.000
0.957
1.193
1.183
0.935
11.642
3.286
2.301
2.620
MeO
MeO
Ph
I
compound 38, Table 2
0.000
ppm
data/dat2/nmr400/qh238-1.fid


137.569
137.318
135.998
135.332
131.682
130.821
129.964
128.914
128.712
128.702
128.503
128.049
127.394
127.136
126.347
121.847
112.681
112.247
88.474
88.327
77.547
77.230
76.912
56.390
56.160
56.106
43.974
39.792
MeO
MeO
Ph
compound 38, Table 2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh238-2.fid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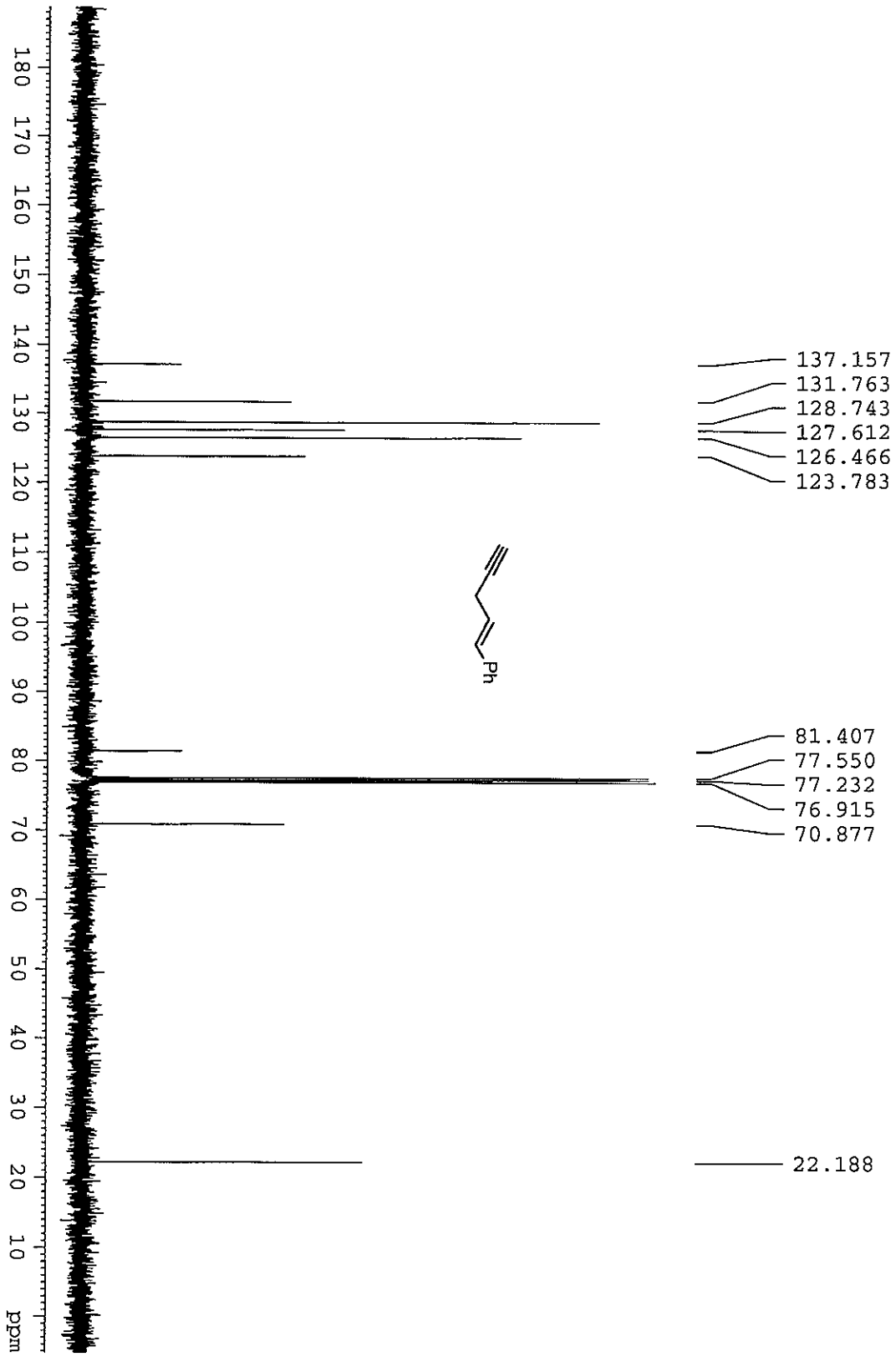
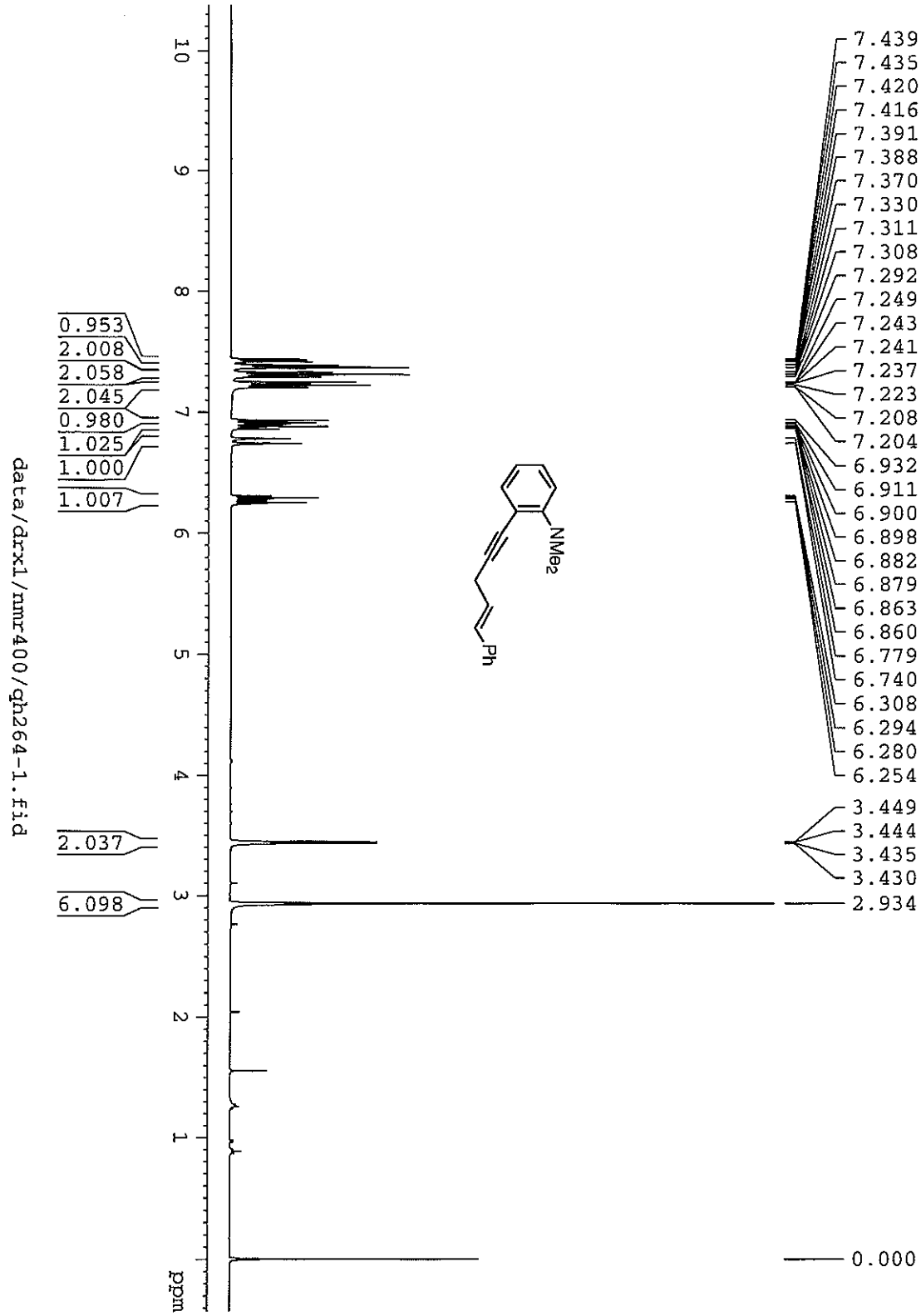
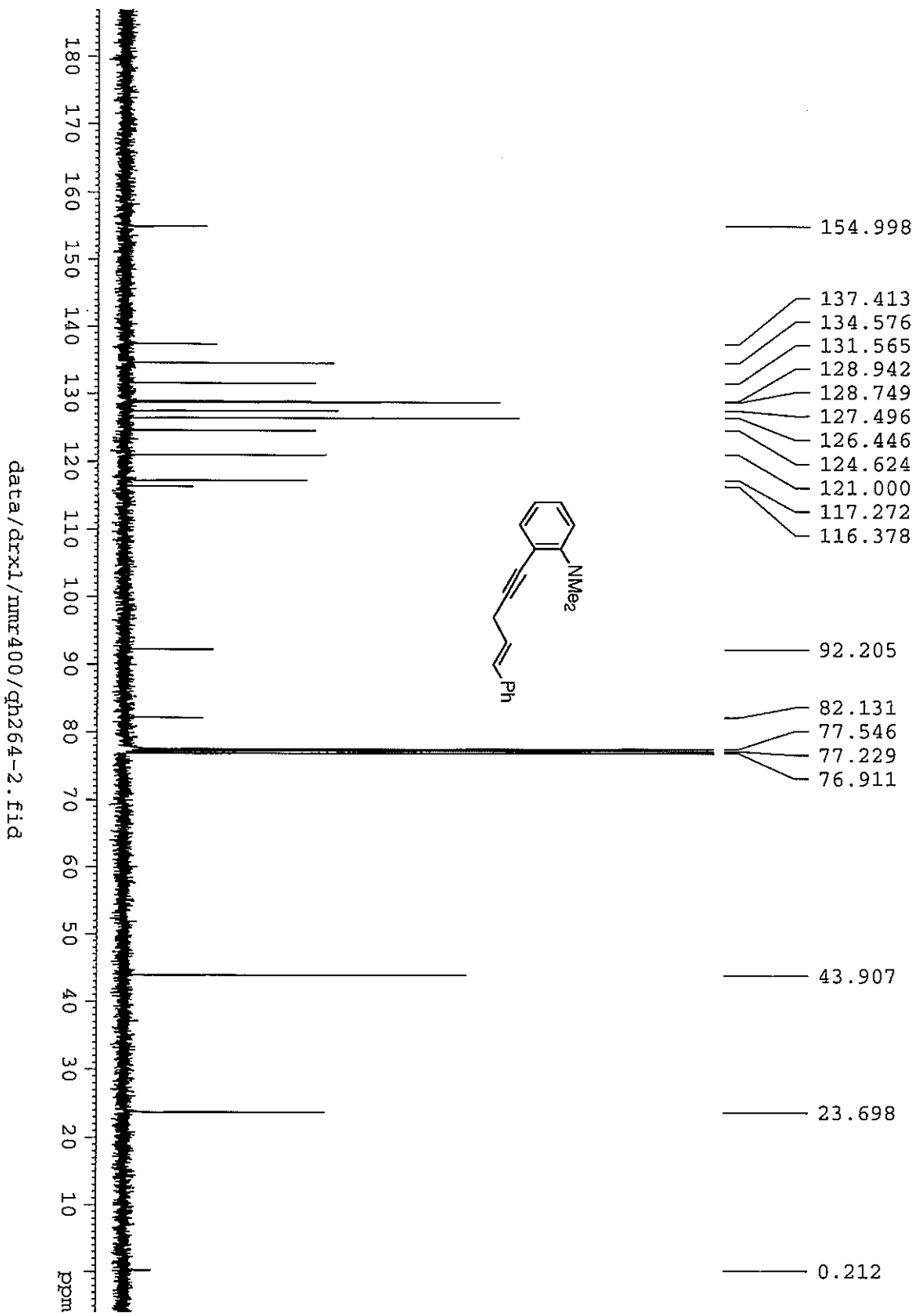
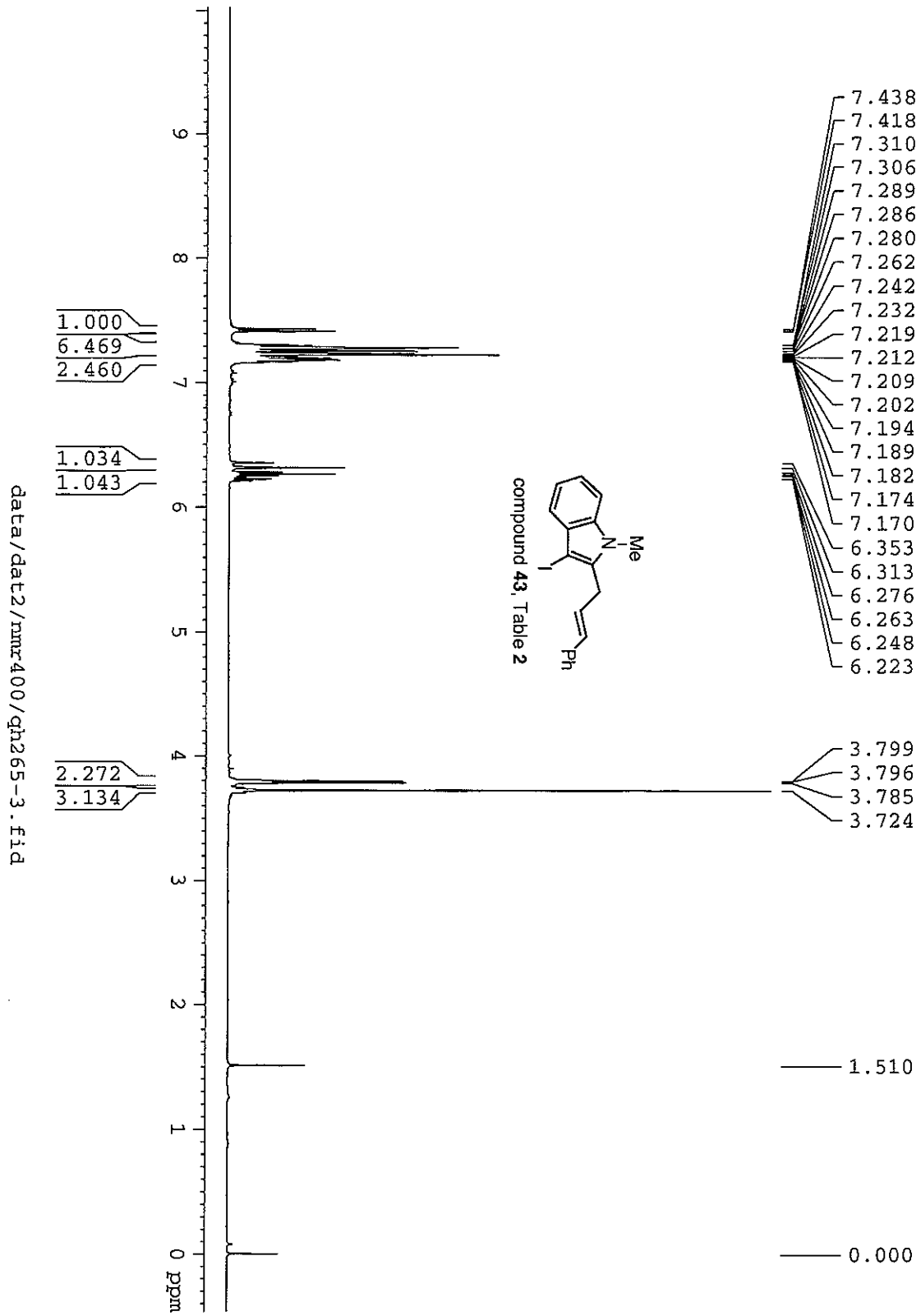
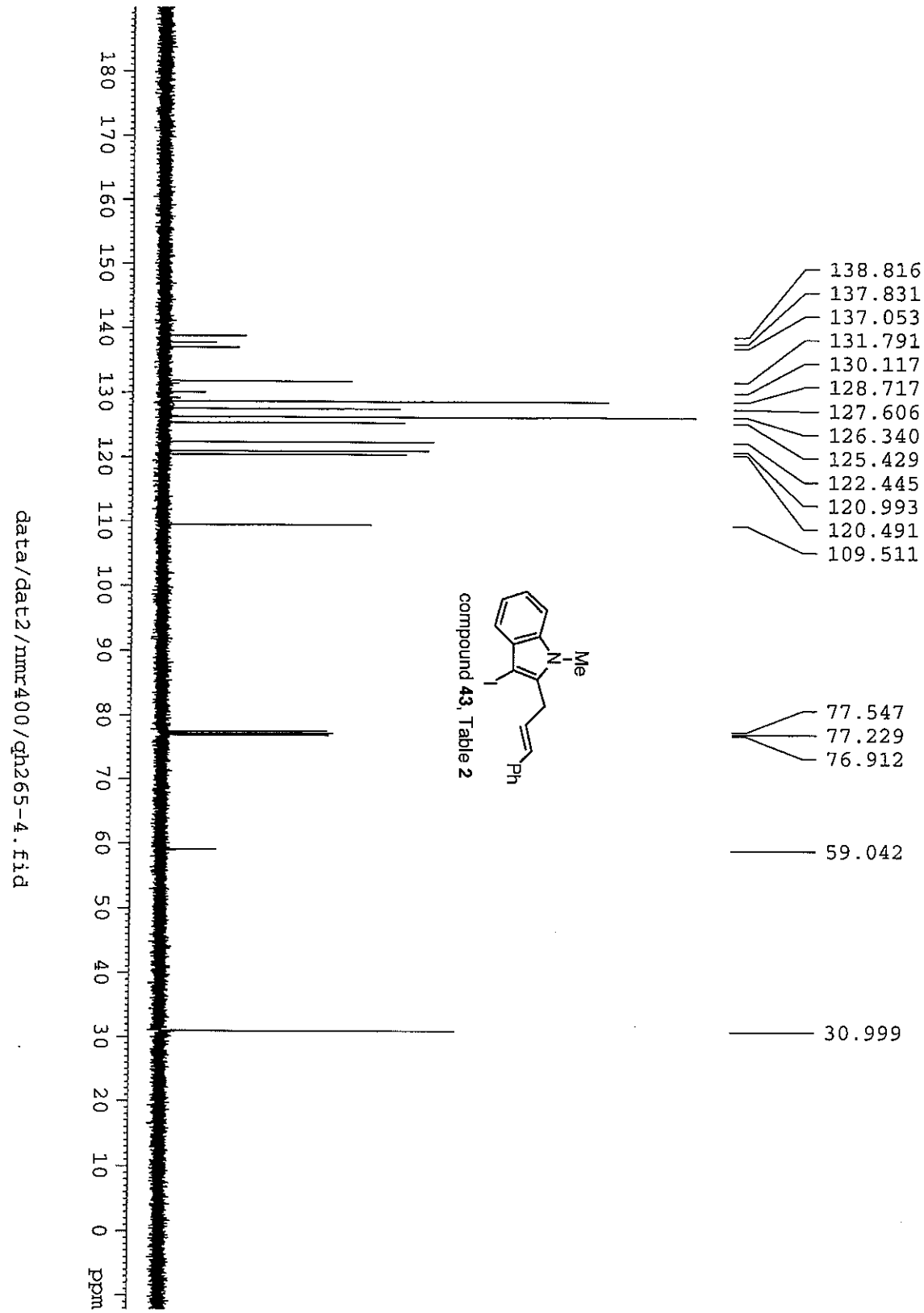
2.087
2.083
1.120
1.000
1.020
2.103
0.937
7.376
7.373
7.355
7.322
7.317
7.304
7.285
7.244
7.239
7.236
7.221
6.687
6.647
6.198
6.184
6.170
6.145
6.131
Ph
3.152
3.147
3.141
3.139
3.133
3.127
2.183
2.176
2.170
0.000
10
9
8
7
6
5
4
3
2
1
0
ppm

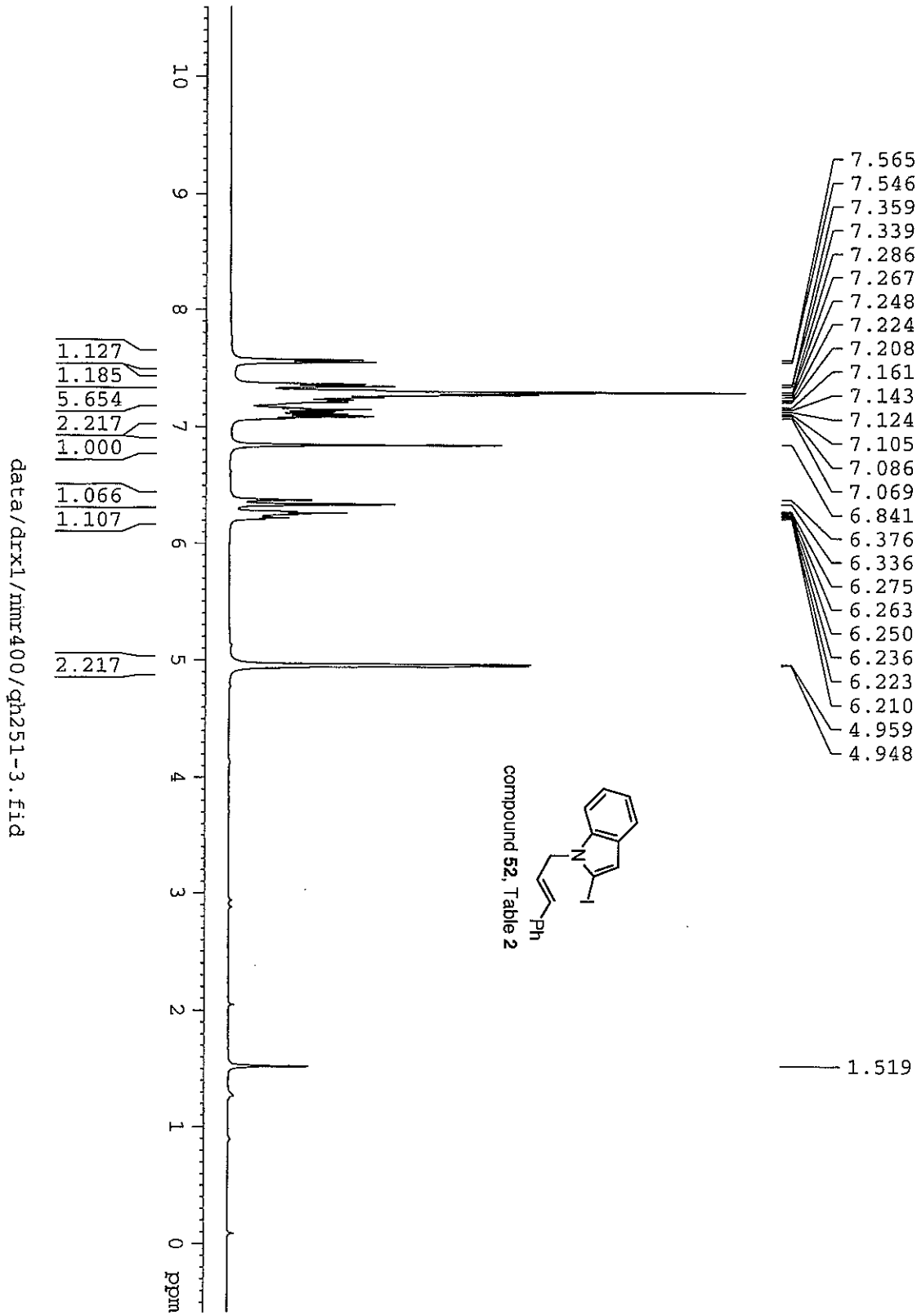

137.157
131.763
128.743
127.612
126.466
123.783
Ph
81.407
77.550
77.232
76.915
70.877
22.188
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

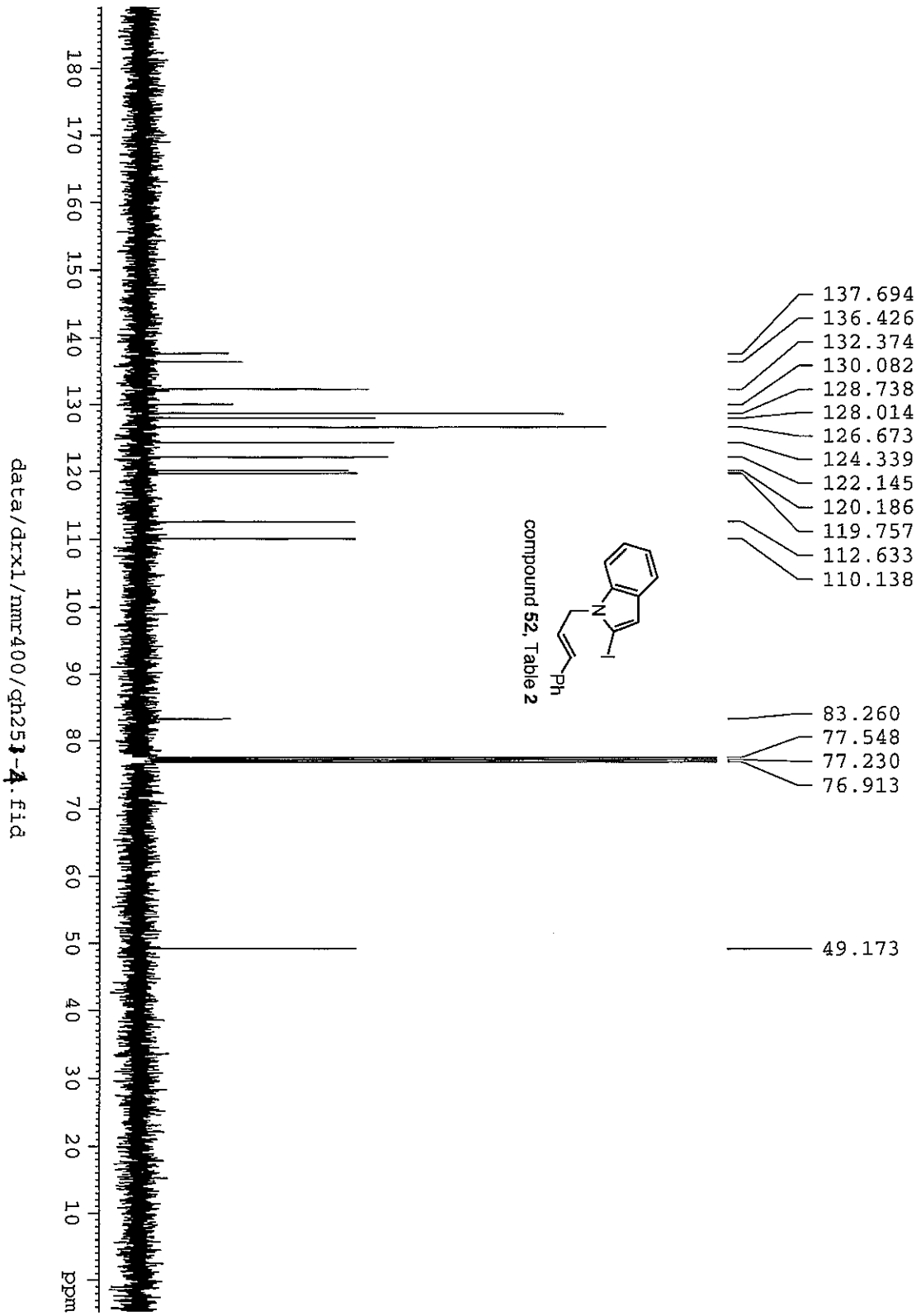

data/drx1/nmr400/qh264-1.fid
0.953
2.008
2.058
2.045
0.980
1.025
1.000
1.007
2.037
6.098
NMe2
Ph
7.439
7.435
7.420
7.416
7.391
7.388
7.370
7.330
7.311
7.308
7.292
7.249
7.243
7.241
7.237
7.223
7.208
7.204
6.932
6.911
6.900
6.898
6.882
6.879
6.863
6.860
6.779
6.740
6.308
6.294
6.280
6.254
3.449
3.444
3.435
3.430
2.934
0.000
ppm

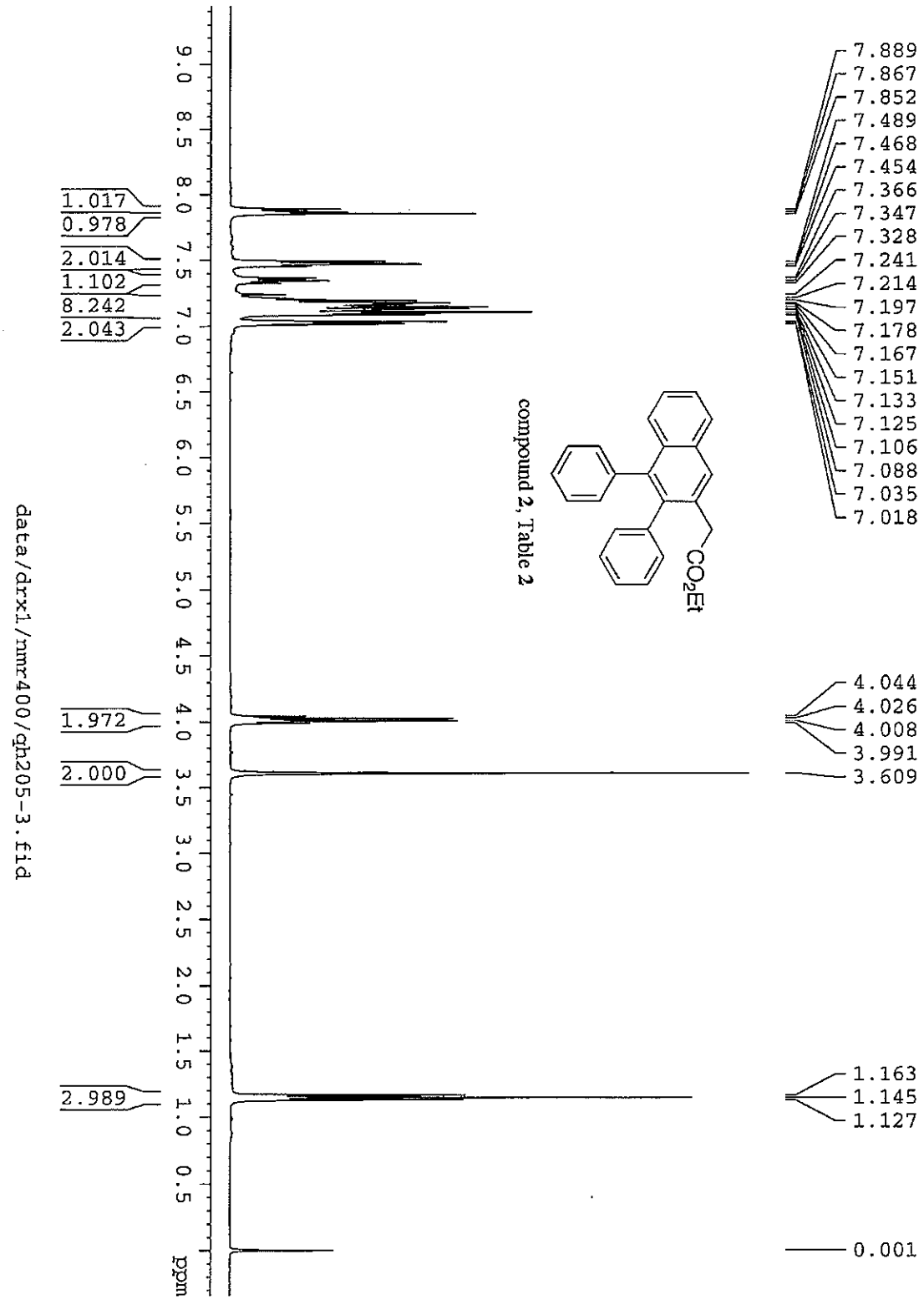

154.998
137.413
134.576
131.565
128.942
128.749
127.496
126.446
124.624
121.000
117.272
116.378
92.205
82.131
77.546
77.229
76.911
43.907
23.698
0.212
NMe2
Ph
ppm
data/drx1/nmr400/qh264-2.fid

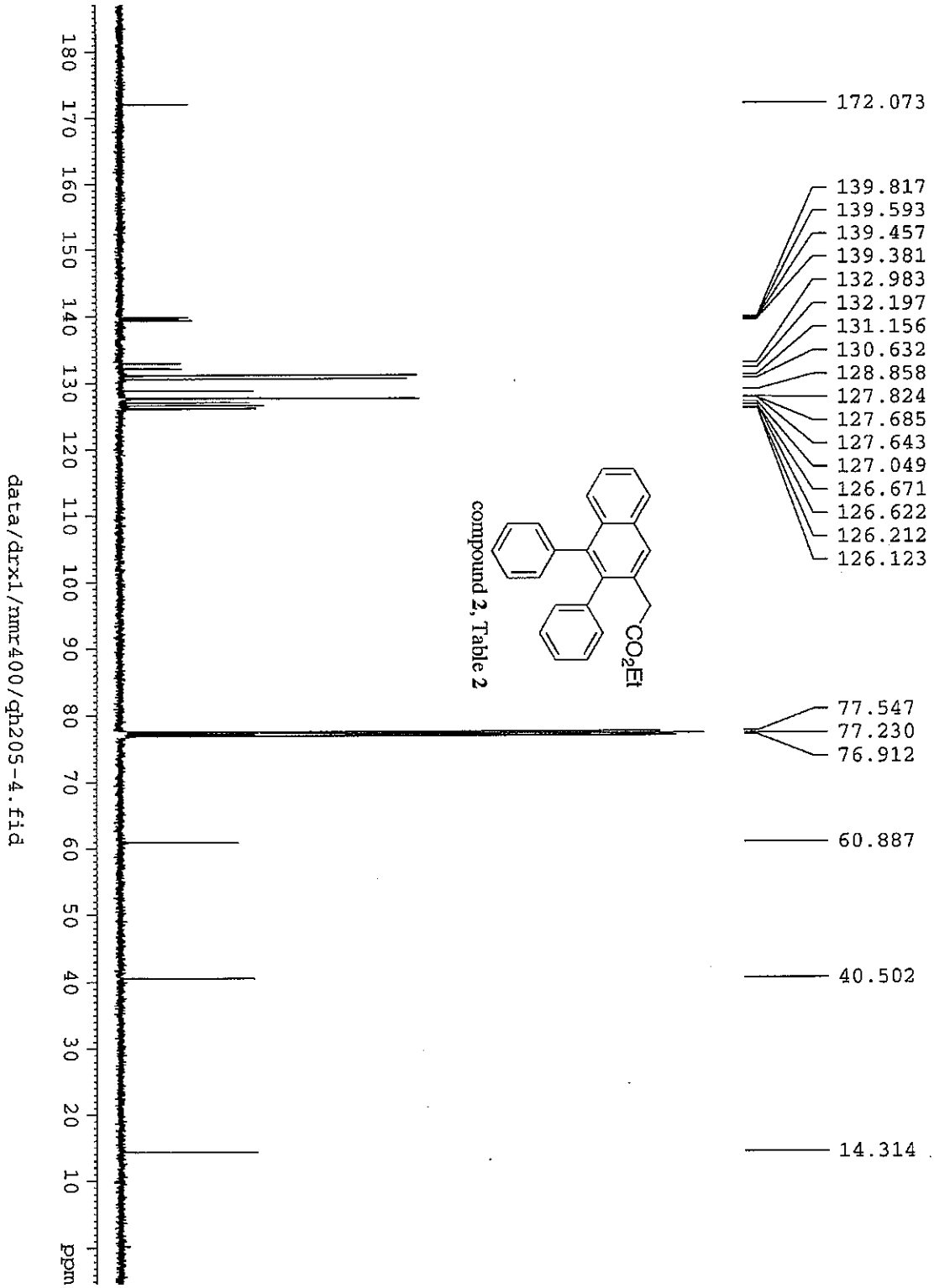

data/dat2/nmr400/qh265-3.fid
compound 43, Table 2
Me
I
Ph
1.000
6.469
2.460
1.034
1.043
2.272
3.134
7.438
7.418
7.310
7.306
7.289
7.286
7.280
7.262
7.242
7.232
7.219
7.212
7.209
7.202
7.194
7.189
7.182
7.174
7.170
6.353
6.313
6.276
6.263
6.248
6.223
3.799
3.796
3.785
3.724
1.510
0.000
ppm

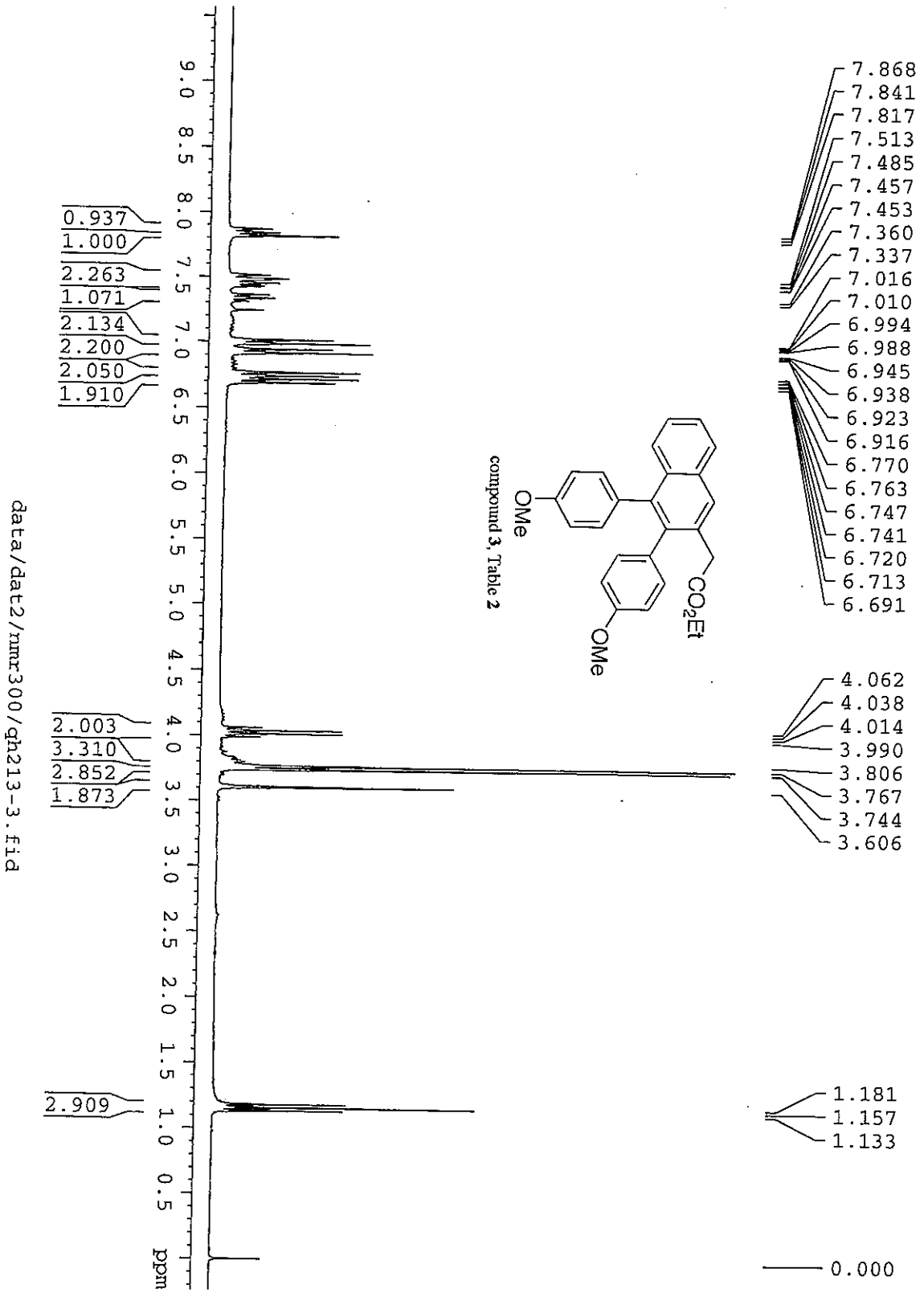

138.816
137.831
137.053
131.791
130.117
128.717
127.606
126.340
125.429
122.445
120.993
120.491
109.511
77.547
77.229
76.912
59.042
30.999
Me
N
I
Ph
compound 43, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh265-4.fid

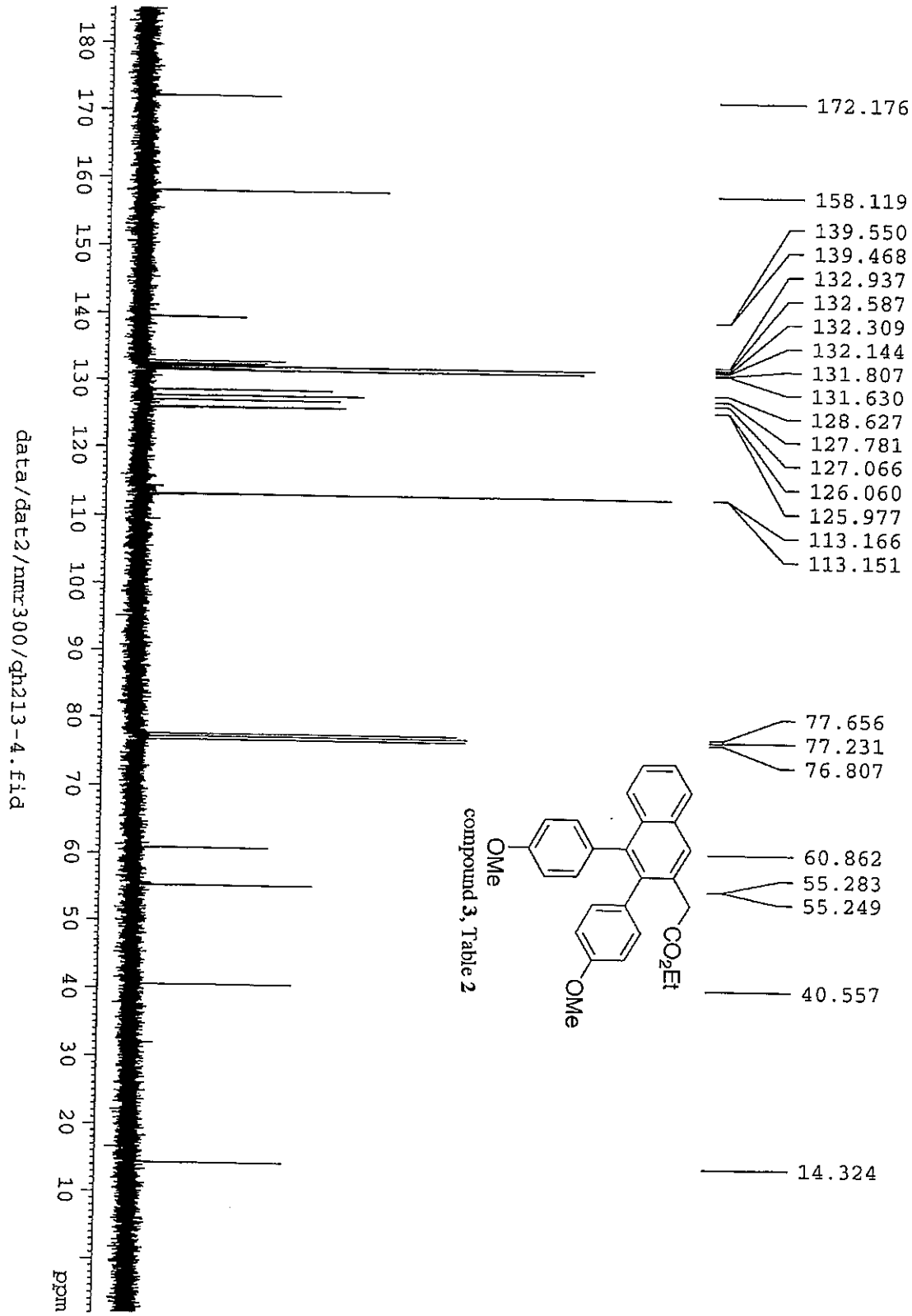

7.565
7.546
7.359
7.339
7.286
7.267
7.248
7.224
7.208
7.161
7.143
7.124
7.105
7.086
7.069
6.841
6.376
6.336
6.275
6.263
6.250
6.236
6.223
6.210
4.959
4.948
1.519
1.127
1.185
5.654
2.217
1.000
1.066
1.107
2.217
10
9
8
7
6
5
4
3
2
1
0
ppm
N
Ph
I
compound 52, Table 2
data/drx1/nmr400/qh251-3.fid

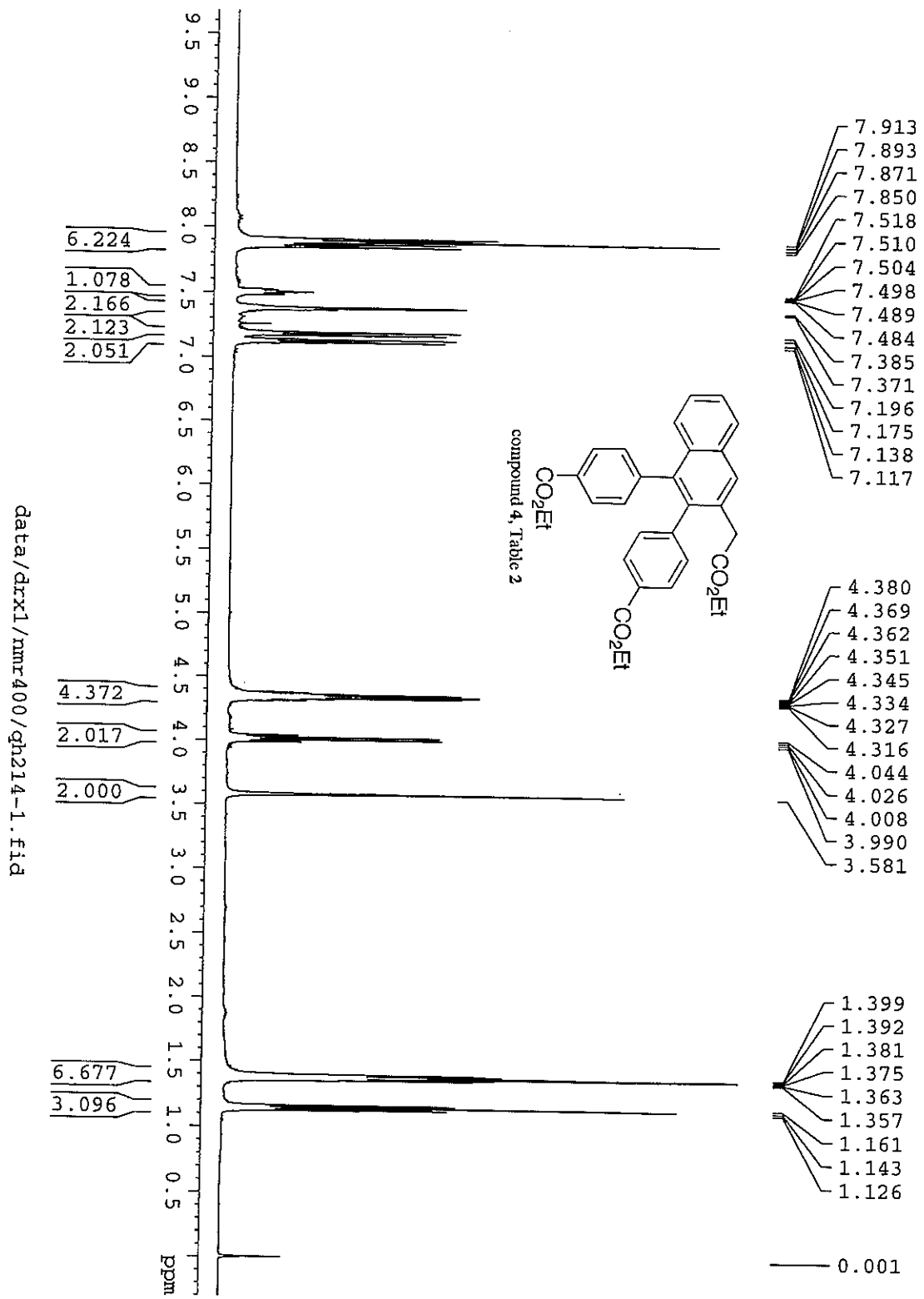

137.694
136.426
132.374
130.082
128.738
128.014
126.673
124.339
122.145
120.186
119.757
112.633
110.138
83.260
77.548
77.230
76.913
49.173
compound 52, Table 2
N
I
Ph
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drxl/nmr400/qh251-4.fid

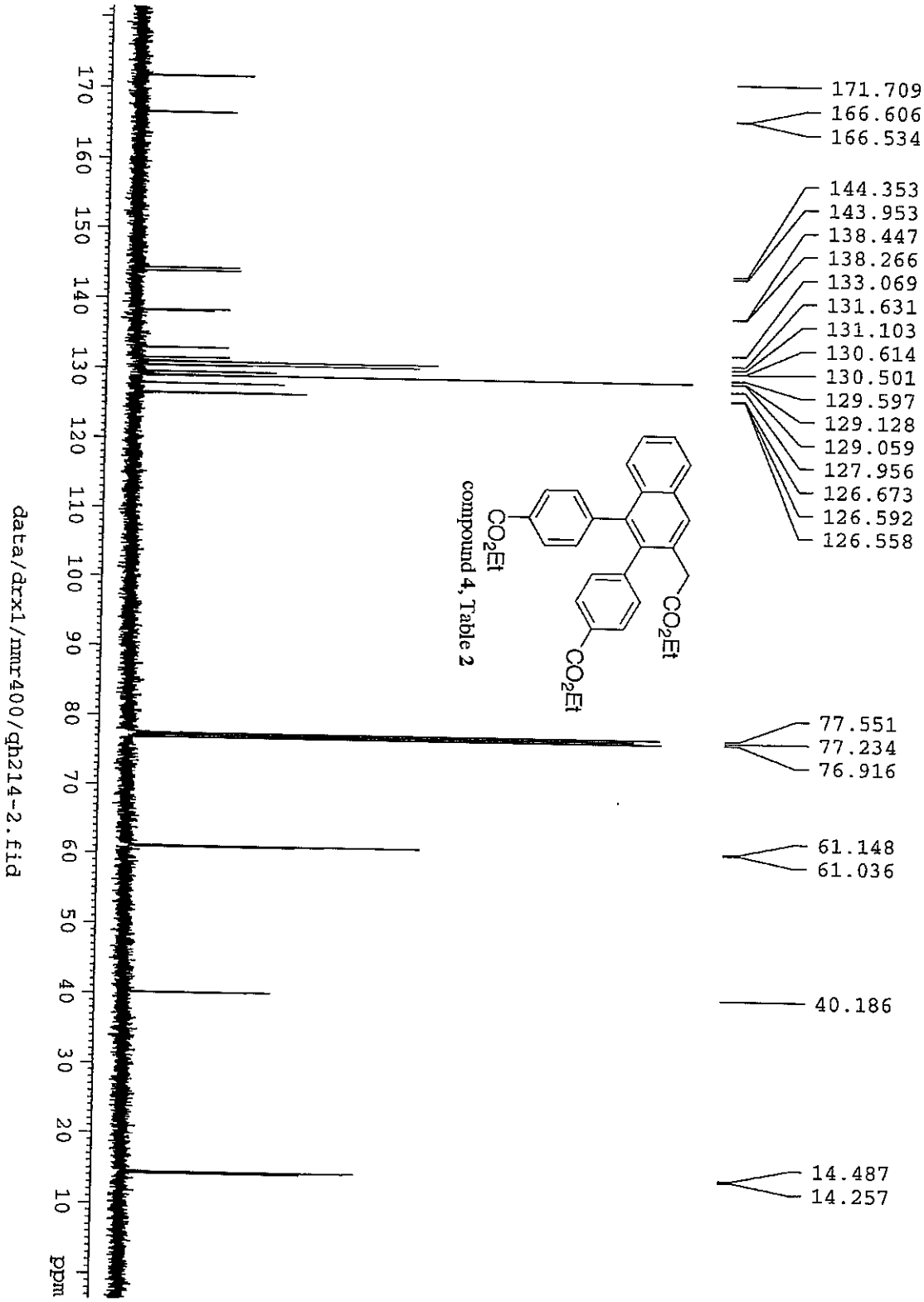

7.889
7.867
7.852
7.489
7.468
7.454
7.366
7.347
7.328
7.241
7.214
7.197
7.178
7.167
7.151
7.133
7.125
7.106
7.088
7.035
7.018
4.044
4.026
4.008
3.991
3.609
1.163
1.145
1.127
0.001
1.017
0.978
2.014
1.102
8.242
2.043
1.972
2.000
2.989
ppm
compound 2, Table 2
CO2Et
data/drx1/nmr400/qh205-3.fid

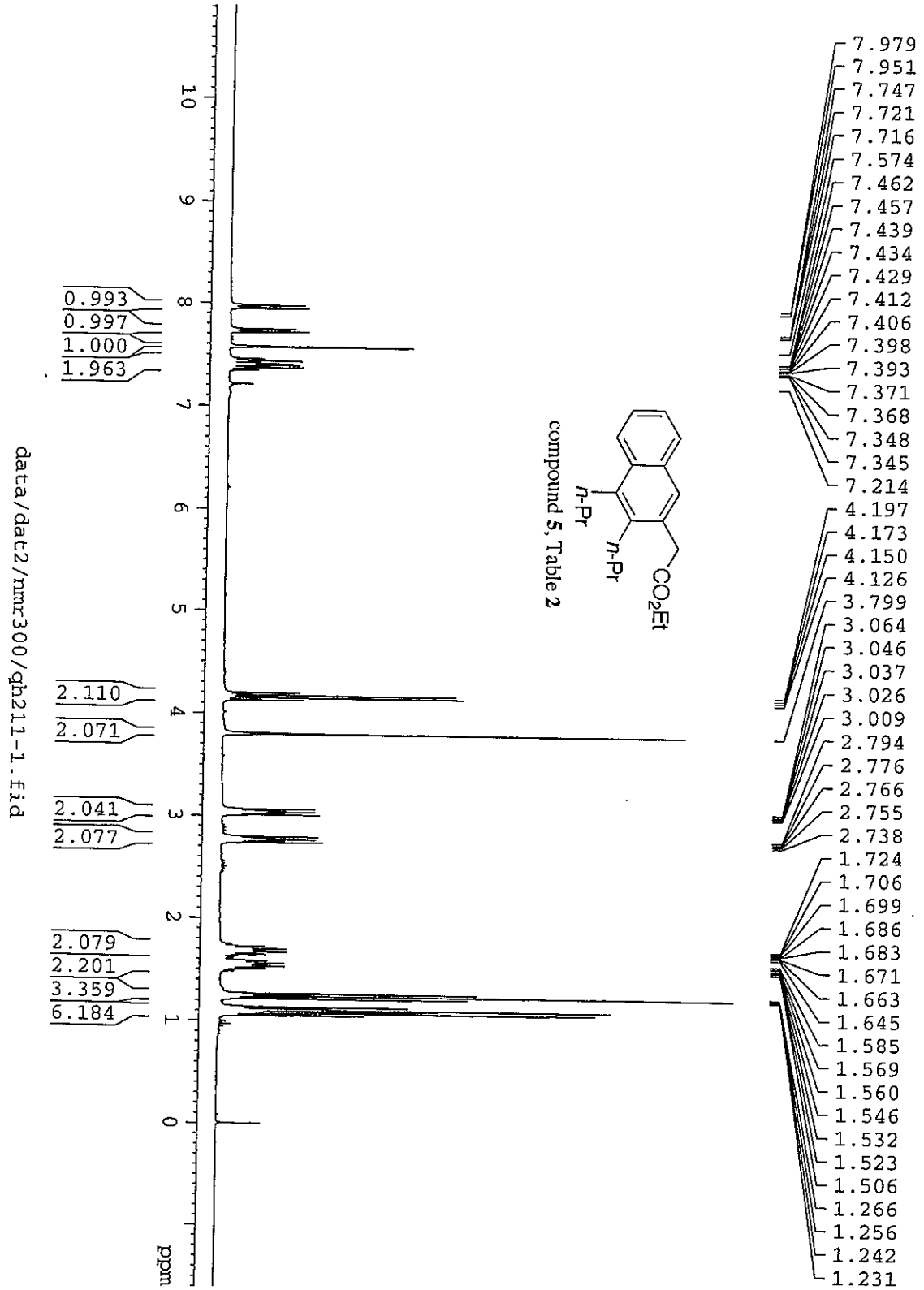

172.073
139.817
139.593
139.457
139.381
132.983
132.197
131.156
130.632
128.858
127.824
127.685
127.643
127.049
126.671
126.622
126.212
126.123
77.547
77.230
76.912
60.887
40.502
14.314
CO2Et
compound 2, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh205-4.fid

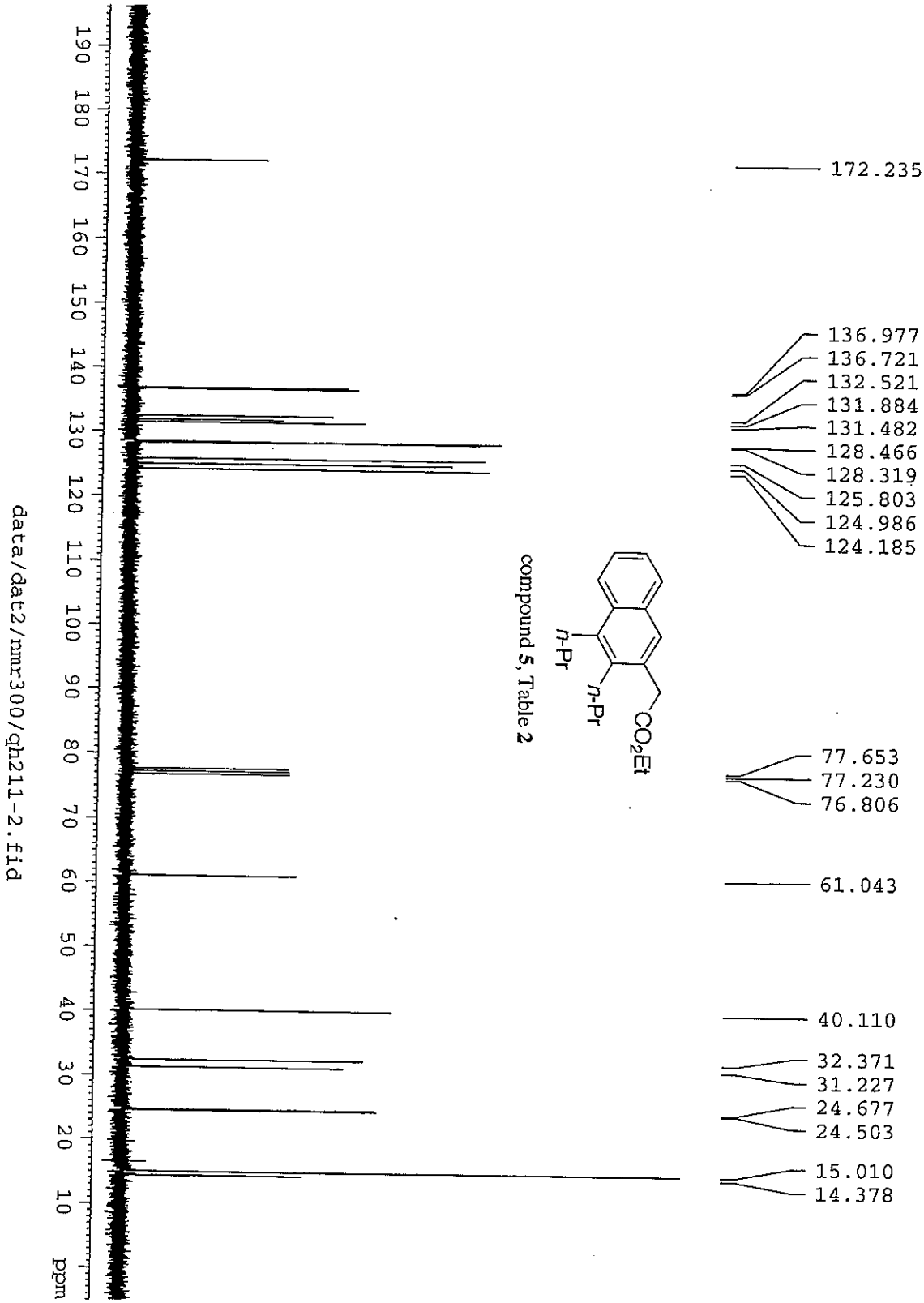

7.868
7.841
7.817
7.513
7.485
7.457
7.453
7.360
7.337
7.016
7.010
6.994
6.988
6.945
6.938
6.923
6.916
6.770
6.763
6.747
6.741
6.720
6.713
6.691
4.062
4.038
4.014
3.990
3.806
3.767
3.744
3.606
1.181
1.157
1.133
0.000
0.937
1.000
2.263
1.071
2.134
2.200
2.050
1.910
2.003
3.310
2.852
1.873
2.909
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
OMe
OMe
CO2Et
compound 3, Table 2
data/dat2/nmr300/qh213-3.fid

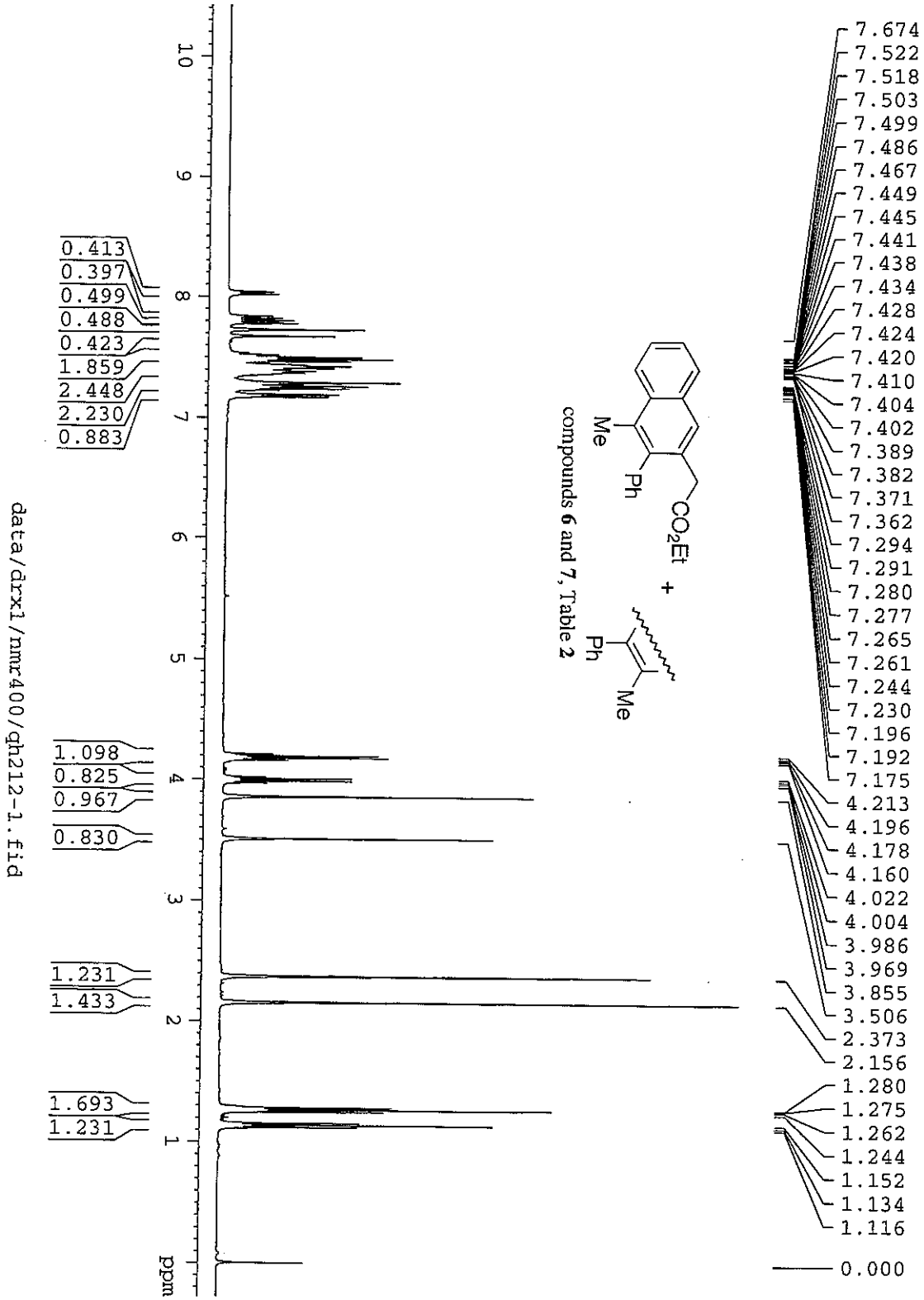

172.176
158.119
139.550
139.468
132.937
132.587
132.309
132.144
131.807
131.630
128.627
127.781
127.066
126.060
125.977
113.166
113.151
77.656
77.231
76.807
60.862
55.283
55.249
40.557
14.324
OMe
OMe
CO2Et
compound 3, Table 2
data/dat2/nmr300/qh213-4.fid
ppm

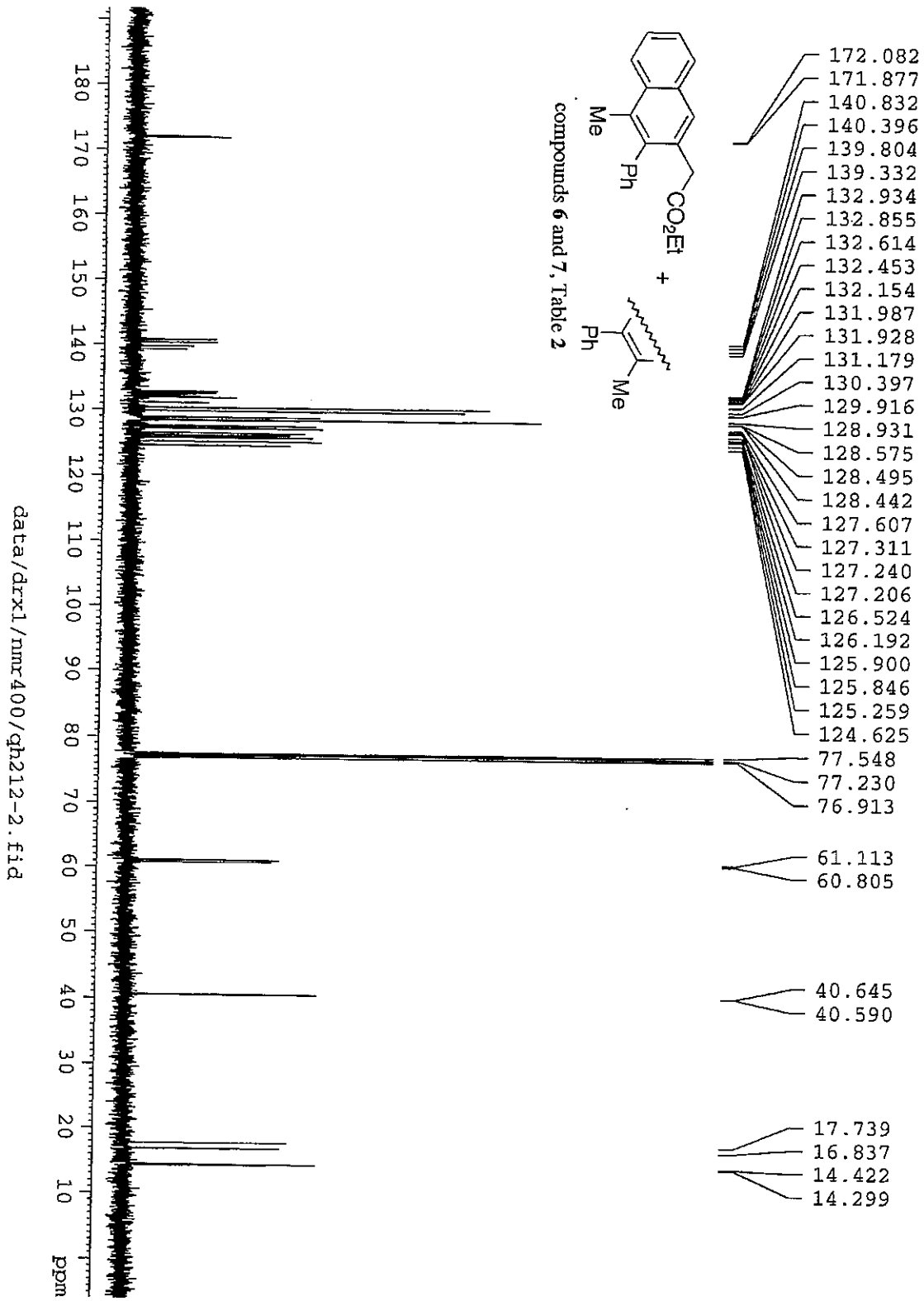

data/drx1/nmr400/qh214-1.fid
compound 4, Table 2
CO2Et
CO2Et
CO2Et
6.224
1.078
2.166
2.123
2.051
4.372
2.017
2.000
6.677
3.096
7.913
7.893
7.871
7.850
7.518
7.510
7.504
7.498
7.489
7.484
7.385
7.371
7.196
7.175
7.138
7.117
4.380
4.369
4.362
4.351
4.345
4.334
4.327
4.316
4.044
4.026
4.008
3.990
3.581
1.399
1.392
1.381
1.375
1.363
1.357
1.161
1.143
1.126
0.001
ppm

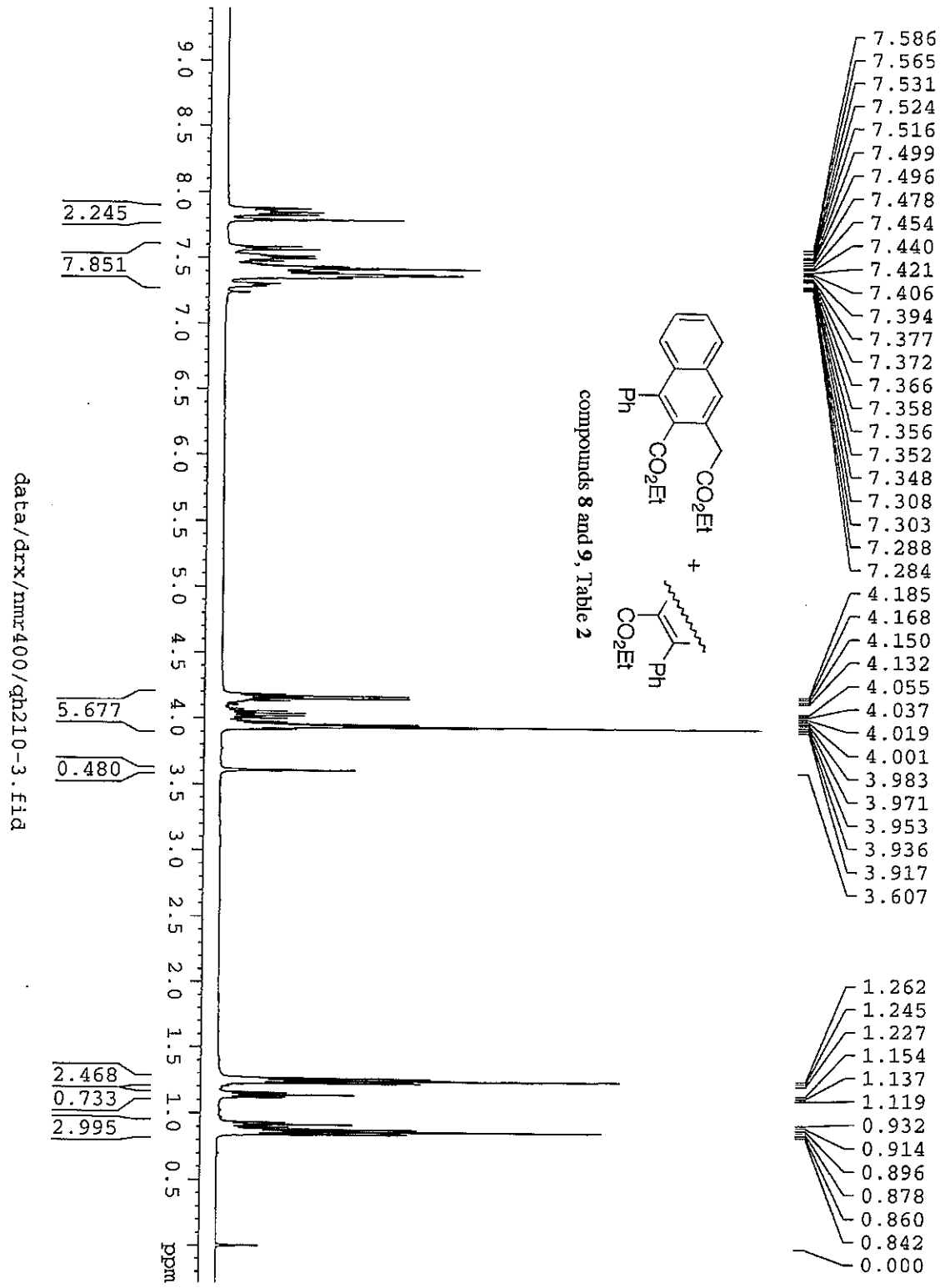

171.709
166.606
166.534
144.353
143.953
138.447
138.266
133.069
131.631
131.103
130.614
130.501
129.597
129.128
129.059
127.956
126.673
126.592
126.558
77.551
77.234
76.916
61.148
61.036
40.186
14.487
14.257
CO2Et
CO2Et
CO2Et
compound 4, Table 2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh214-2.fid


data/dat2/nmr300/qh211-1.fid
compound 5, Table 2
n-Pr
n-Pr
CO2Et
0.993
0.997
1.000
1.963
2.110
2.071
2.041
2.077
2.079
2.201
3.359
6.184
7.979
7.951
7.747
7.721
7.716
7.574
7.462
7.457
7.439
7.434
7.429
7.412
7.406
7.398
7.393
7.371
7.368
7.348
7.345
7.214
4.197
4.173
4.150
4.126
3.799
3.064
3.046
3.037
3.026
3.009
2.794
2.776
2.766
2.755
2.738
1.724
1.706
1.699
1.686
1.683
1.671
1.663
1.645
1.585
1.569
1.560
1.546
1.532
1.523
1.506
1.266
1.256
1.242
1.231
ppm

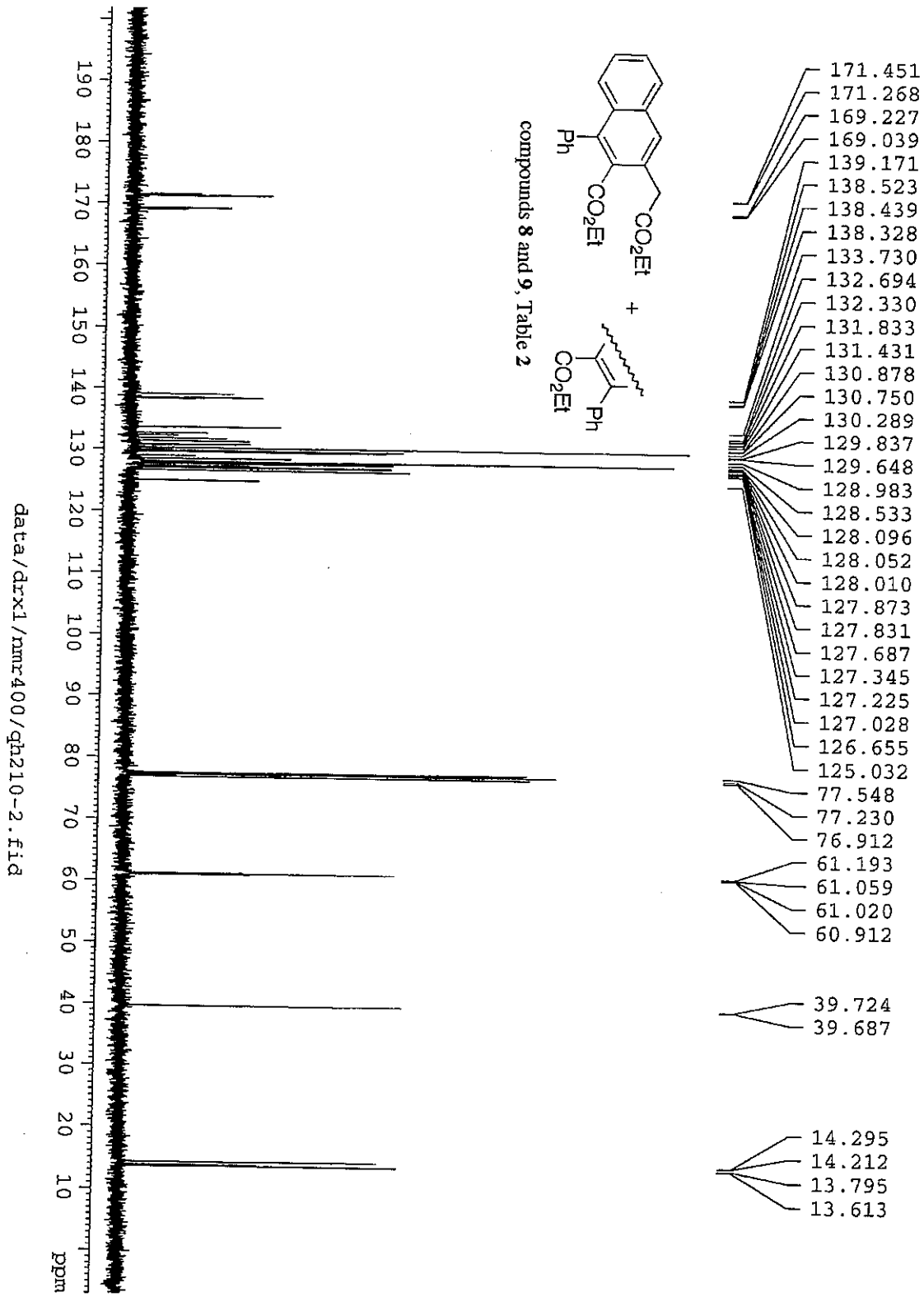

172.235
136.977
136.721
132.521
131.884
131.482
128.466
128.319
125.803
124.986
124.185
77.653
77.230
76.806
61.043
40.110
32.371
31.227
24.677
24.503
15.010
14.378
n-Pr
n-Pr
CO2Et
compound 5, Table 2
data/dat2/nmr300/qh211-2.fid
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

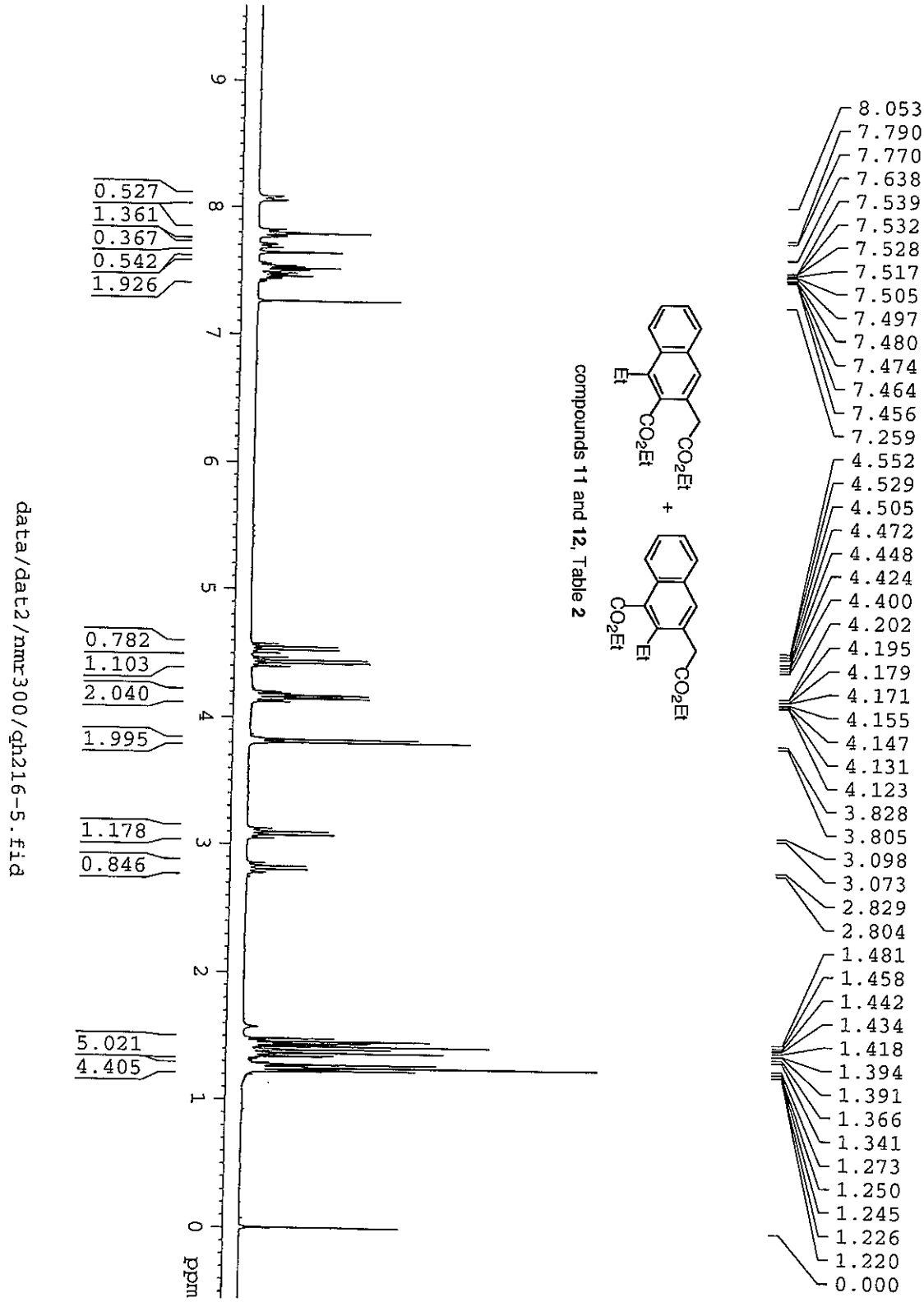

data/drx1/nmr400/qh212-1.fid
compounds 6 and 7, Table 2
Me
Ph
CO2Et
+
Ph
Me
0.413
0.397
0.499
0.488
0.423
1.859
2.448
2.230
0.883
1.098
0.825
0.967
0.830
1.231
1.433
1.693
1.231
ppm
7.674
7.522
7.518
7.503
7.499
7.486
7.467
7.449
7.445
7.441
7.438
7.434
7.428
7.424
7.420
7.410
7.404
7.402
7.389
7.382
7.371
7.362
7.294
7.291
7.280
7.277
7.265
7.261
7.244
7.230
7.196
7.192
7.175
4.213
4.196
4.178
4.160
4.022
4.004
3.986
3.969
3.855
3.506
2.373
2.156
1.280
1.275
1.262
1.244
1.152
1.134
1.116
0.000


Me
Ph
CO2Et
+
Ph
Me
compounds 6 and 7, Table 2
172.082
171.877
140.832
140.396
139.804
139.332
132.934
132.855
132.614
132.453
132.154
131.987
131.928
131.179
130.397
129.916
128.931
128.575
128.495
128.442
127.607
127.311
127.240
127.206
126.524
126.192
125.900
125.846
125.259
124.625
77.548
77.230
76.913
61.113
60.805
40.645
40.590
17.739
16.837
14.422
14.299
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drxl/nmr400/qh212-2.fid



compounds **8** and **9**, Table **2**


171.451
171.268
169.227
169.039
139.171
138.523
138.439
138.328
133.730
132.694
132.330
131.833
131.431
130.878
130.750
130.289
129.837
129.648
128.983
128.533
128.096
128.052
128.010
127.873
127.831
127.687
127.345
127.225
127.028
126.655
125.032
77.548
77.230
76.912
61.193
61.059
61.020
60.912
39.724
39.687
14.295
14.212
13.795
13.613
Ph
CO2Et
CO2Et
+
CO2Et
Ph
compounds 8 and 9, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh210-2.fid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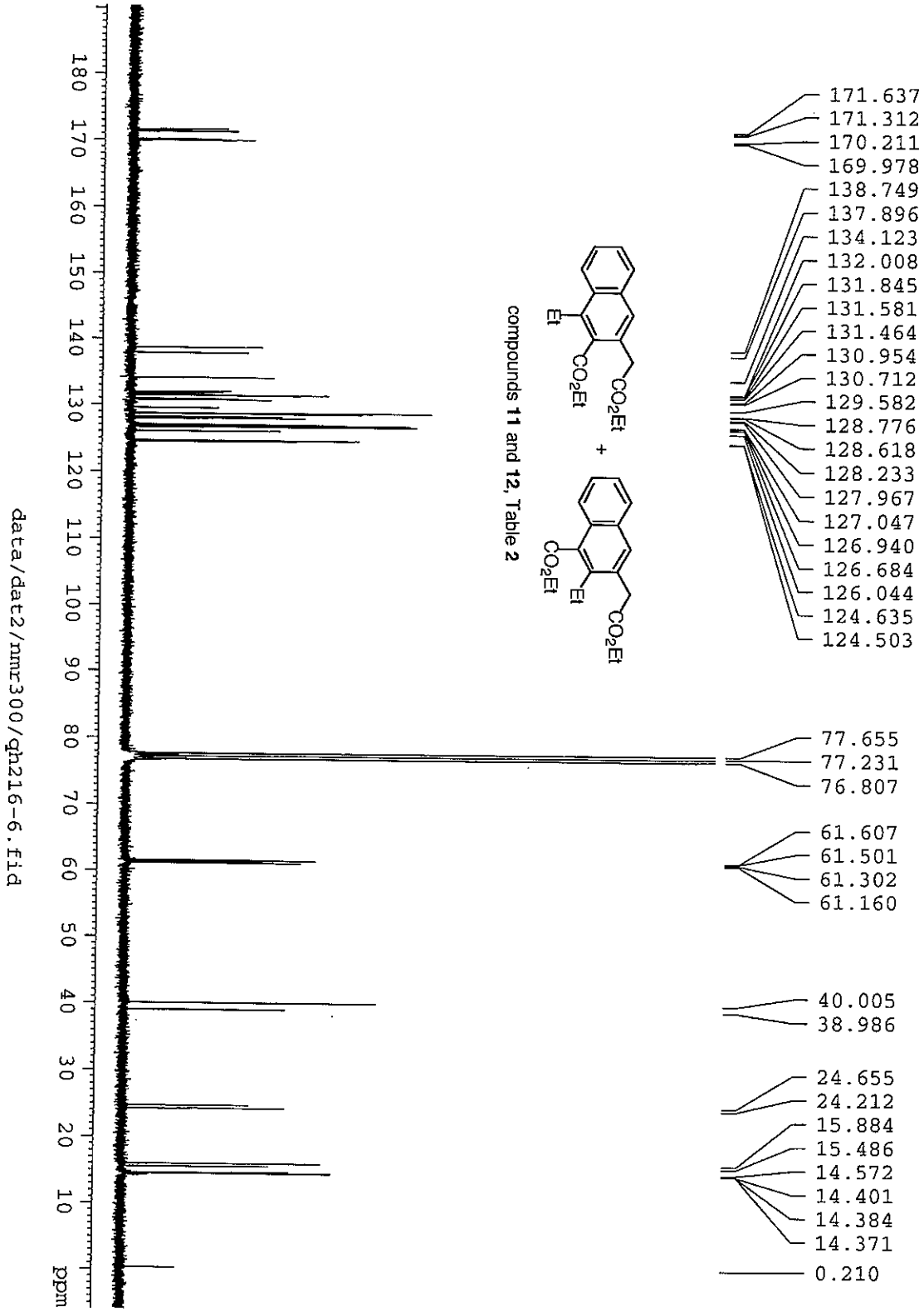
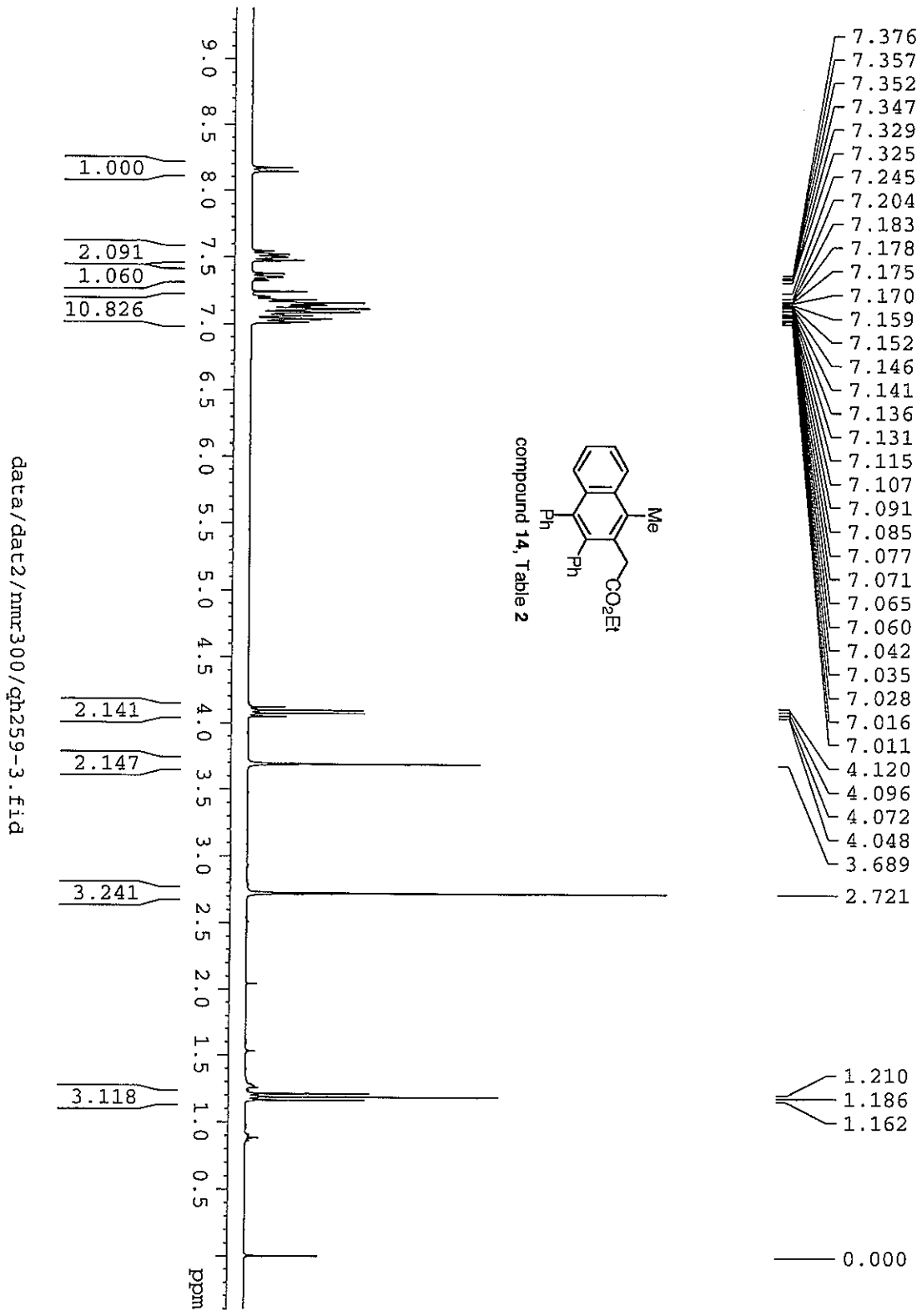
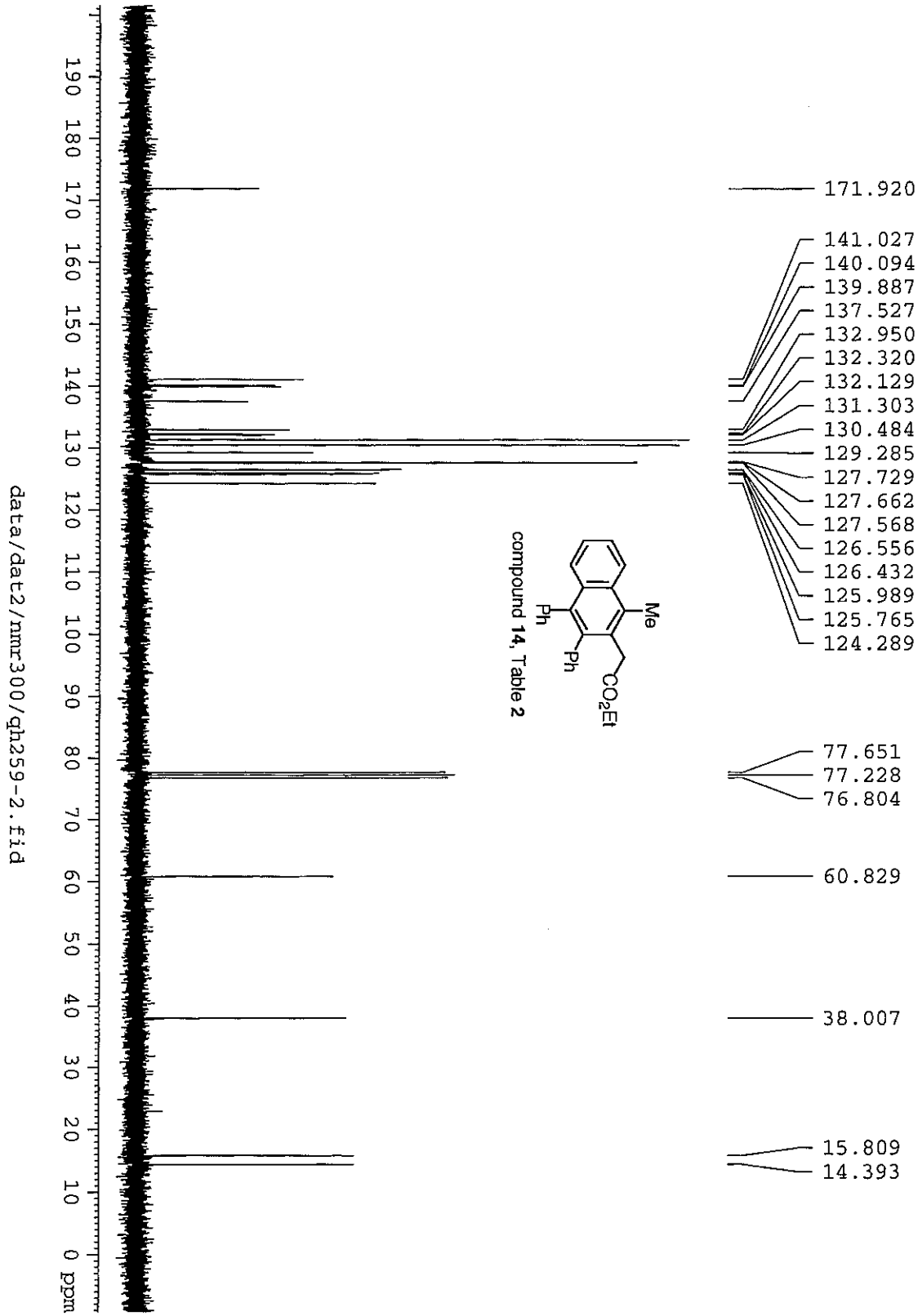
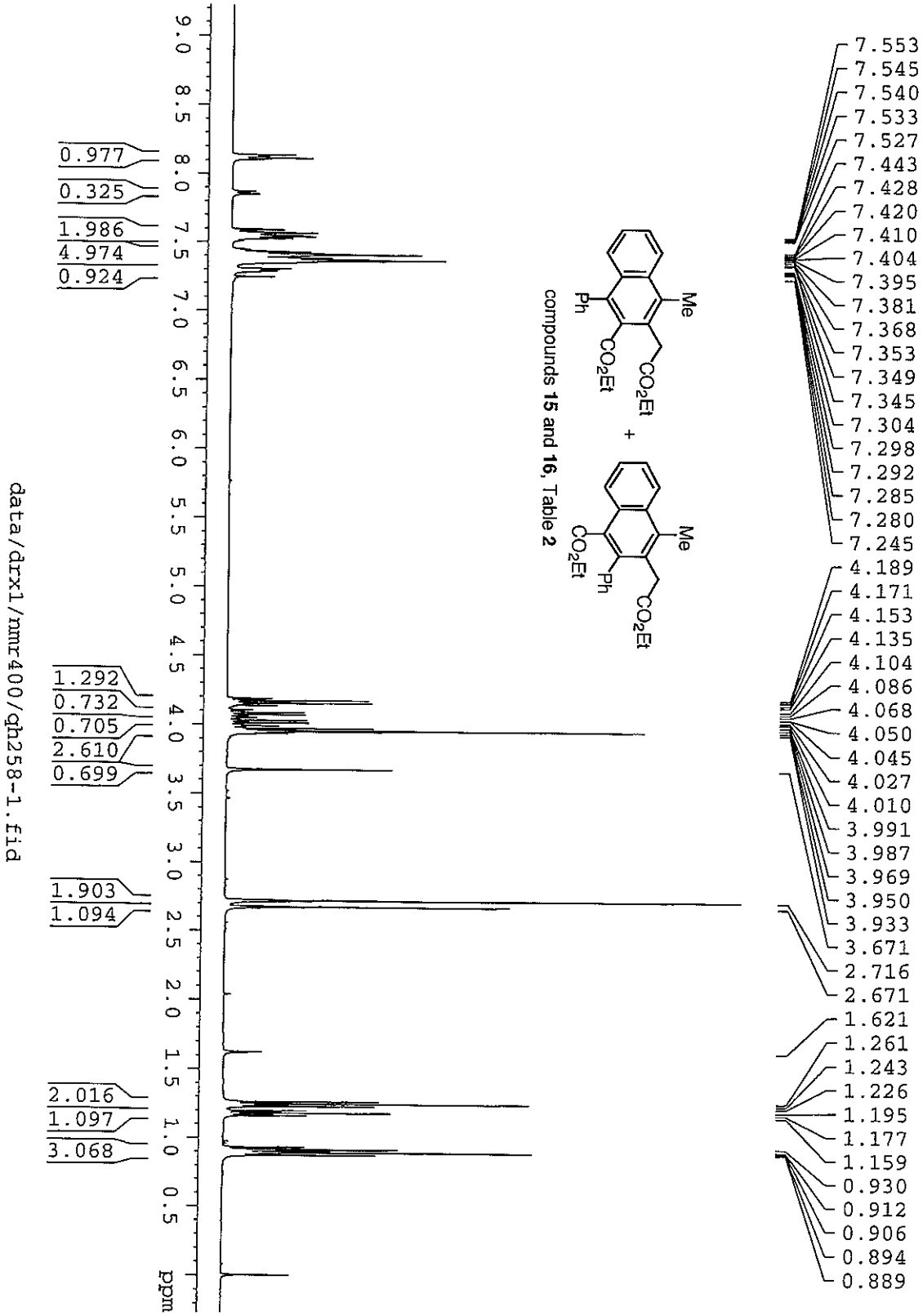
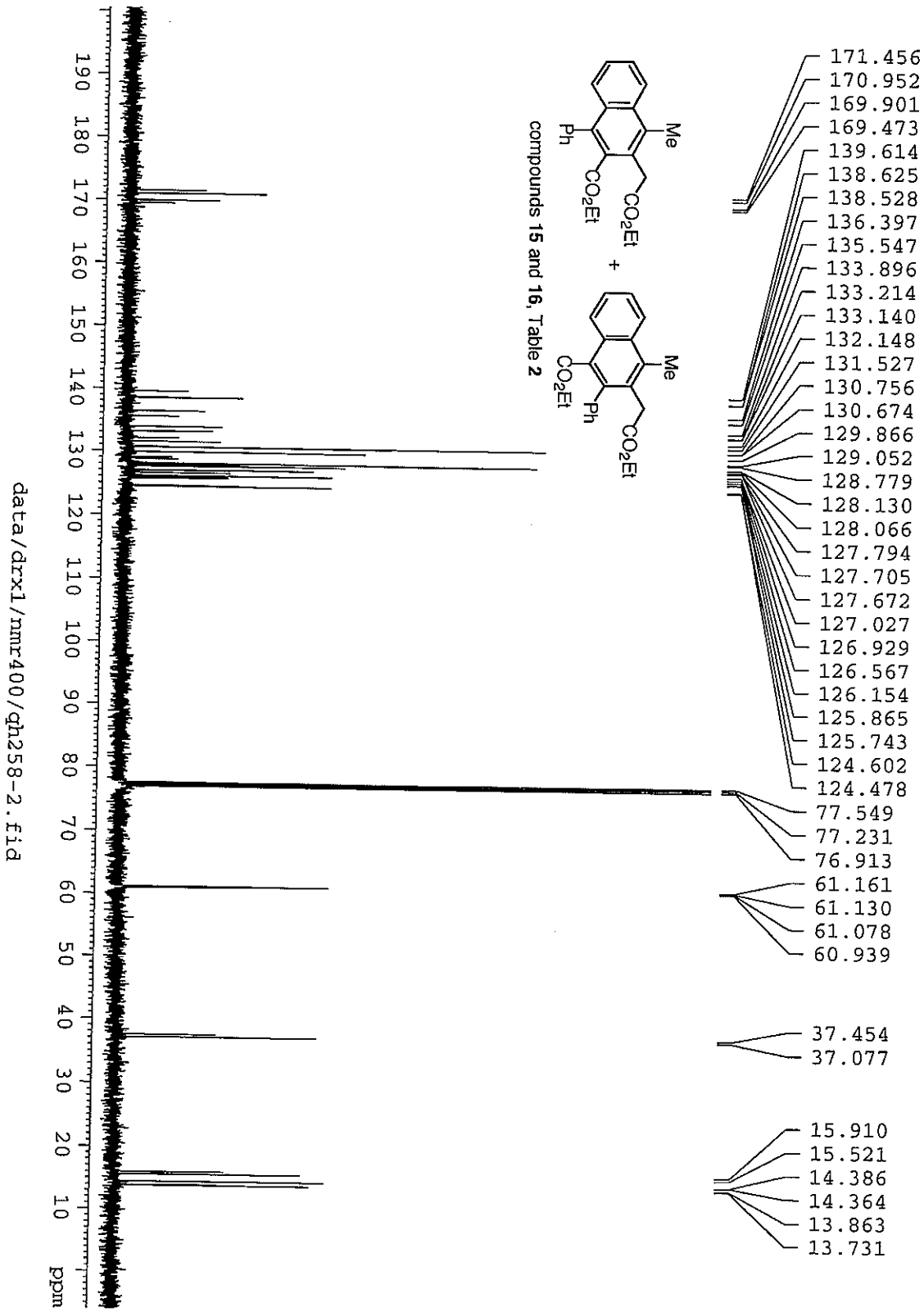
0.527
1.361
0.367
0.542
1.926
0.782
1.103
2.040
1.995
1.178
0.846
5.021
4.405
ppm
compounds 11 and 12, Table 2
Et
CO2Et
CO2Et
+
CO2Et
Et
CO2Et
8.053
7.790
7.770
7.638
7.539
7.532
7.528
7.517
7.505
7.497
7.480
7.474
7.464
7.456
7.259
4.552
4.529
4.505
4.472
4.448
4.424
4.400
4.202
4.195
4.179
4.171
4.155
4.147
4.131
4.123
3.828
3.805
3.098
3.073
2.829
2.804
1.481
1.458
1.442
1.434
1.418
1.394
1.391
1.366
1.341
1.273
1.250
1.245
1.226
1.220
0.000

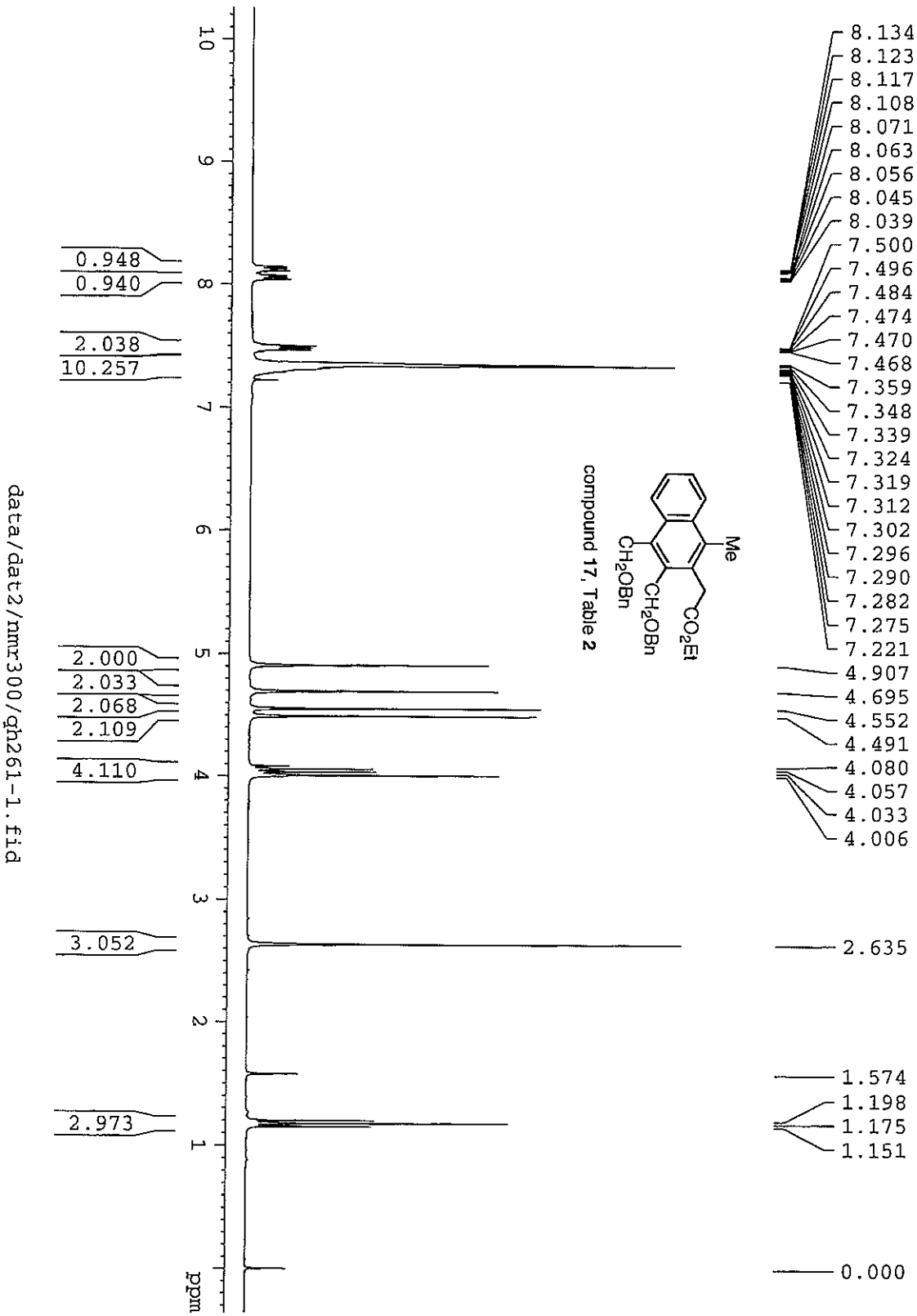

171.637
171.312
170.211
169.978
138.749
137.896
134.123
132.008
131.845
131.581
131.464
130.954
130.712
129.582
128.776
128.618
128.233
127.967
127.047
126.940
126.684
126.044
124.635
124.503
77.655
77.231
76.807
61.607
61.501
61.302
61.160
40.005
38.986
24.655
24.212
15.884
15.486
14.572
14.401
14.384
14.371
0.210
Et
CO2Et
CO2Et
+
CO2Et
Et
CO2Et
compounds 11 and 12, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh216-6.fid

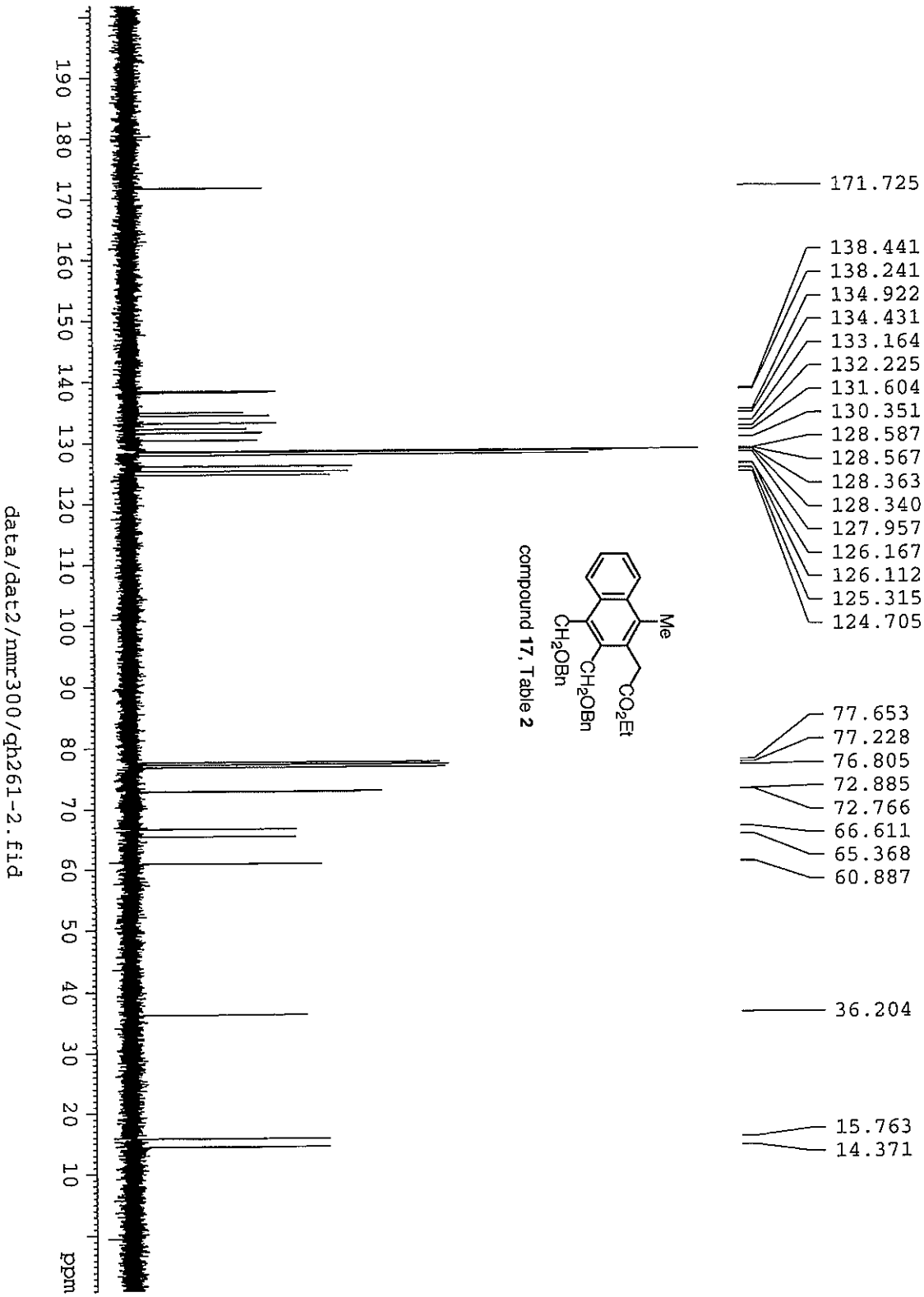

data/dat2/nmr300/qh259-3.fid
compound 14, Table 2
Me
Ph
Ph
CO2Et
1.000
2.091
1.060
10.826
2.141
2.147
3.241
3.118
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
7.376
7.357
7.352
7.347
7.329
7.325
7.245
7.204
7.183
7.178
7.175
7.170
7.159
7.152
7.146
7.141
7.136
7.131
7.115
7.107
7.091
7.085
7.077
7.071
7.065
7.060
7.042
7.035
7.028
7.016
7.011
4.120
4.096
4.072
4.048
3.689
2.721
1.210
1.186
1.162
0.000

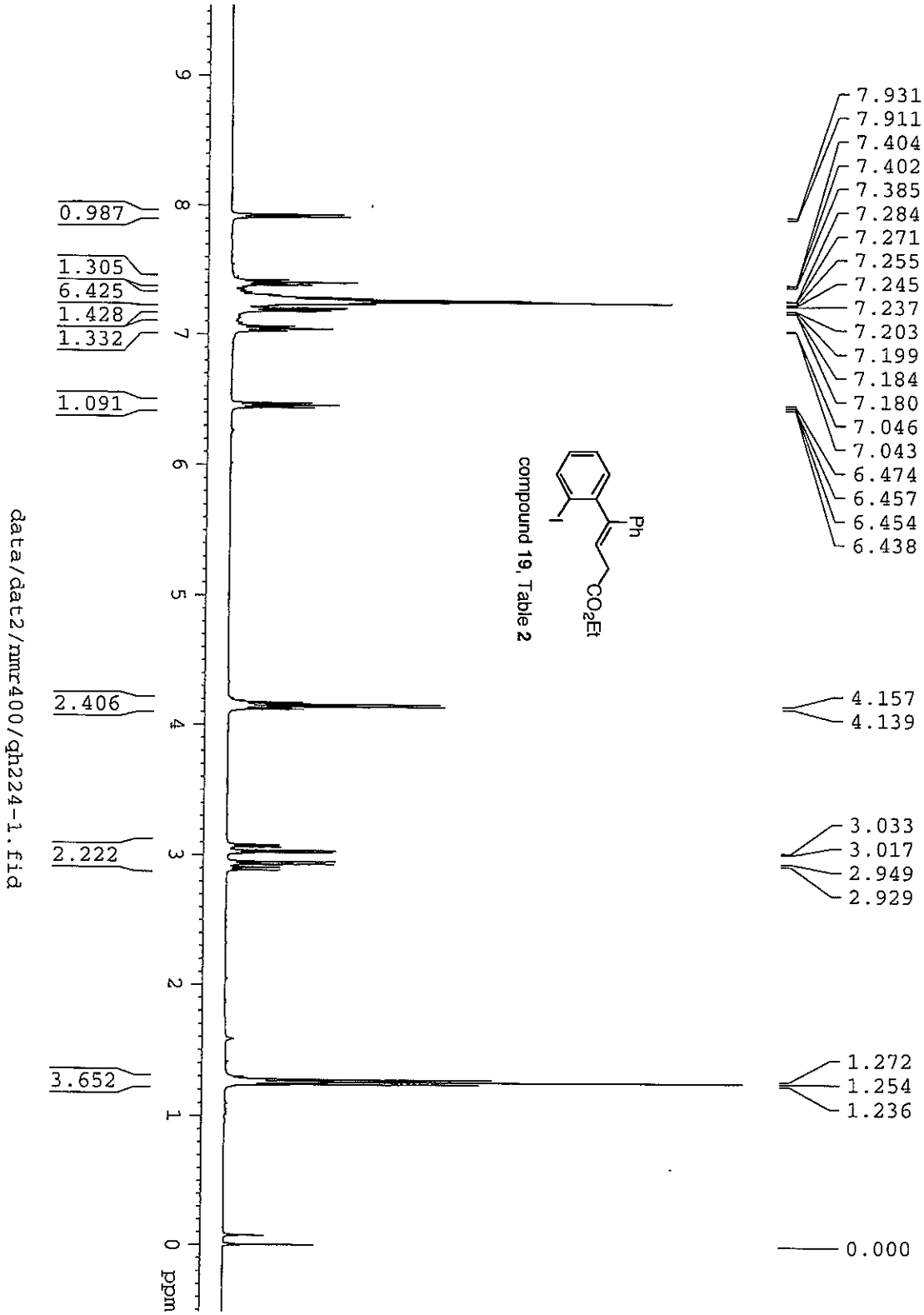

171.920
141.027
140.094
139.887
137.527
132.950
132.320
132.129
131.303
130.484
129.285
127.729
127.662
127.568
126.556
126.432
125.989
125.765
124.289
77.651
77.228
76.804
60.829
38.007
15.809
14.393
Me
Ph
Ph
CO2Et
compound 14, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr300/qh259-2.fid

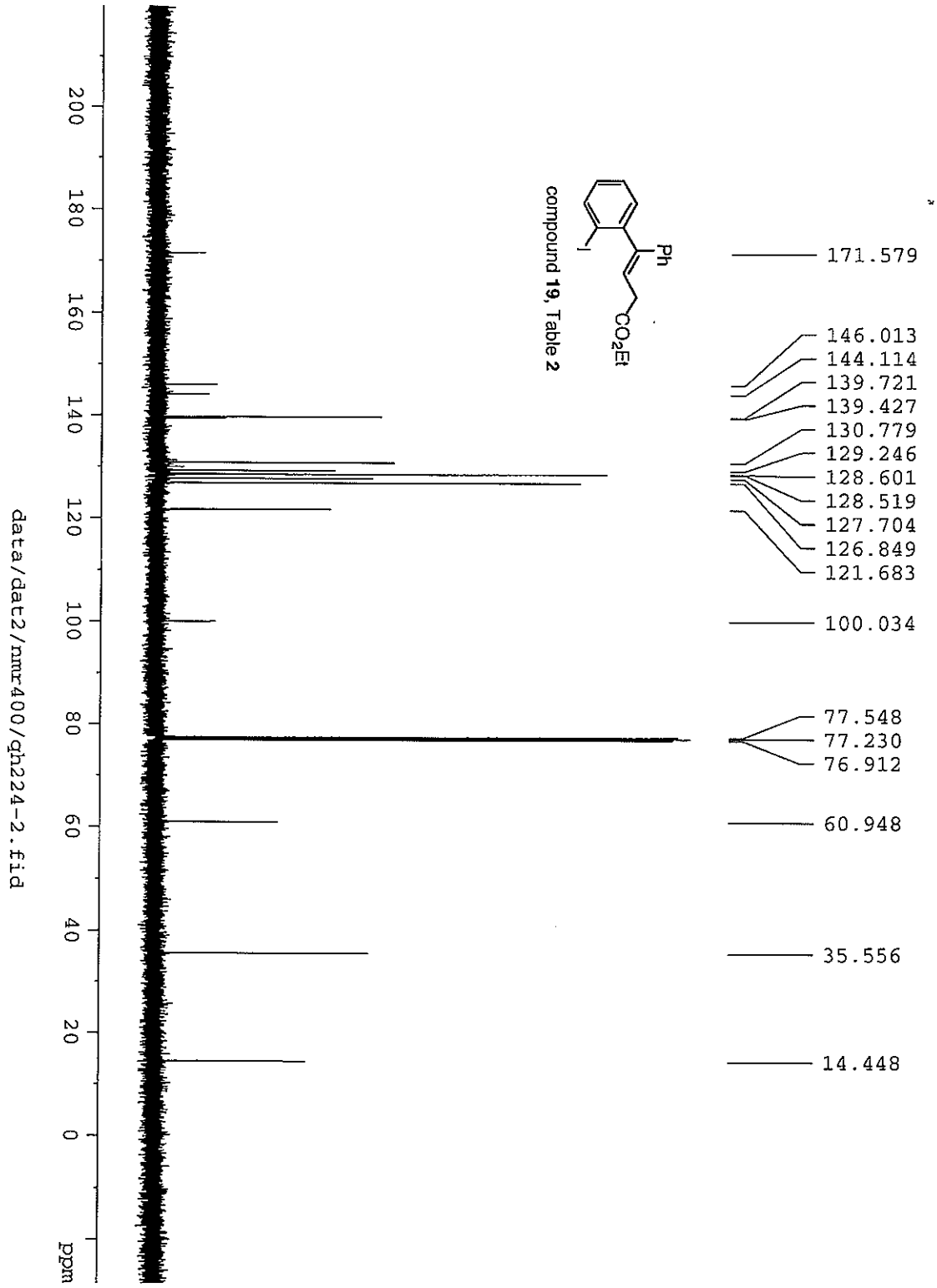

7.553
7.545
7.540
7.533
7.527
7.443
7.428
7.420
7.410
7.404
7.395
7.381
7.368
7.353
7.349
7.345
7.304
7.298
7.292
7.285
7.280
7.245
4.189
4.171
4.153
4.135
4.104
4.086
4.068
4.050
4.045
4.027
4.010
3.991
3.987
3.969
3.950
3.933
3.671
2.716
2.671
1.621
1.261
1.243
1.226
1.195
1.177
1.159
0.930
0.912
0.906
0.894
0.889
Me
Ph
CO2Et
CO2Et
+
Me
CO2Et
Ph
CO2Et
compounds 15 and 16, Table 2
0.977
0.325
1.986
4.974
0.924
1.292
0.732
0.705
2.610
0.699
1.903
1.094
2.016
1.097
3.068
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
data/drx1/nmr400/qh258-1.fid

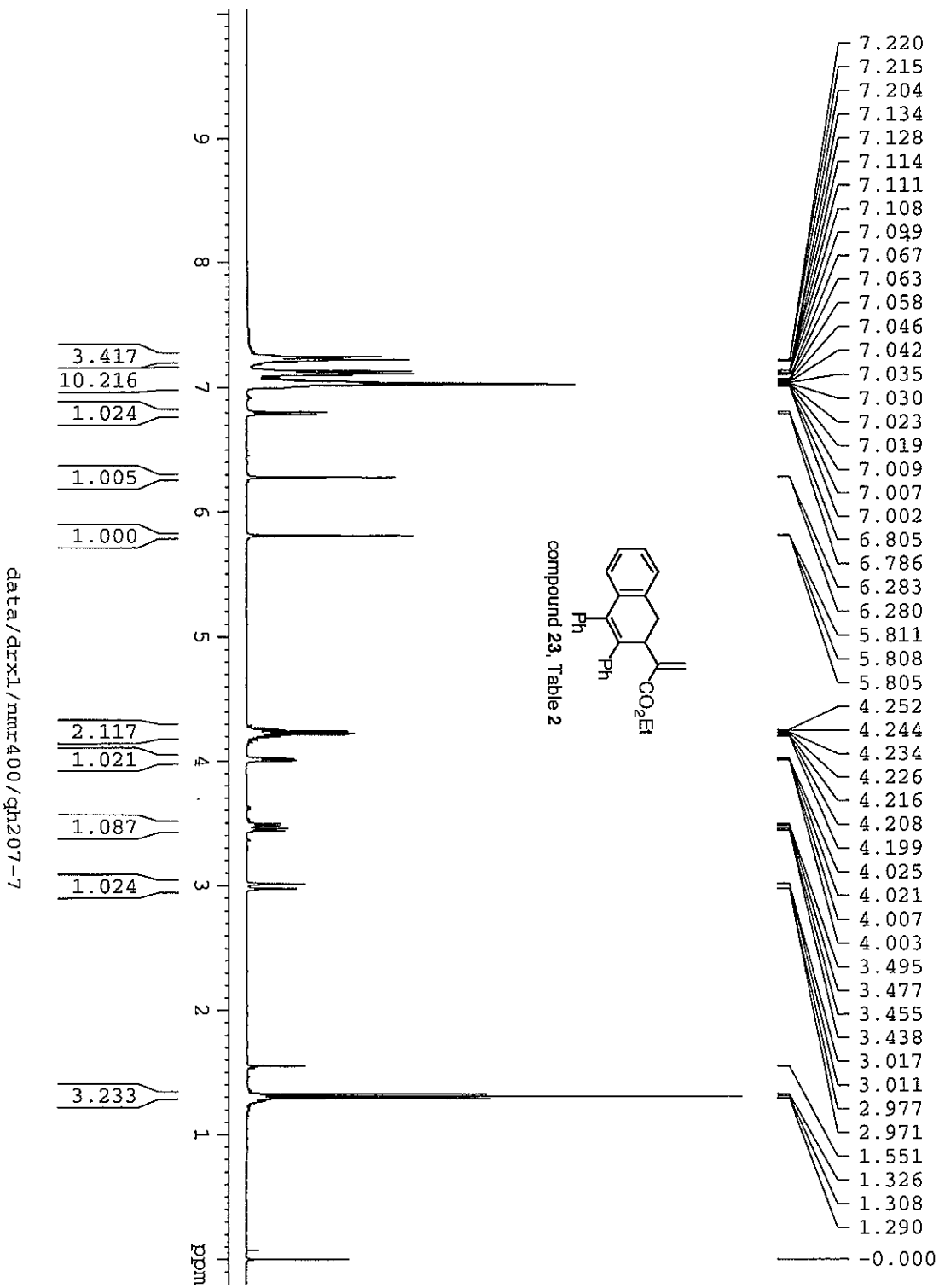

171.456
170.952
169.901
169.473
139.614
138.625
138.528
136.397
135.547
133.896
133.214
133.140
132.148
131.527
130.756
130.674
129.866
129.052
128.779
128.130
128.066
127.794
127.705
127.672
127.027
126.929
126.567
126.154
125.865
125.743
124.602
124.478
77.549
77.231
76.913
61.161
61.130
61.078
60.939
37.454
37.077
15.910
15.521
14.386
14.364
13.863
13.731
Me
Ph
CO2Et
CO2Et
+
Me
CO2Et
Ph
CO2Et
compounds 15 and 16, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh258-2.fid

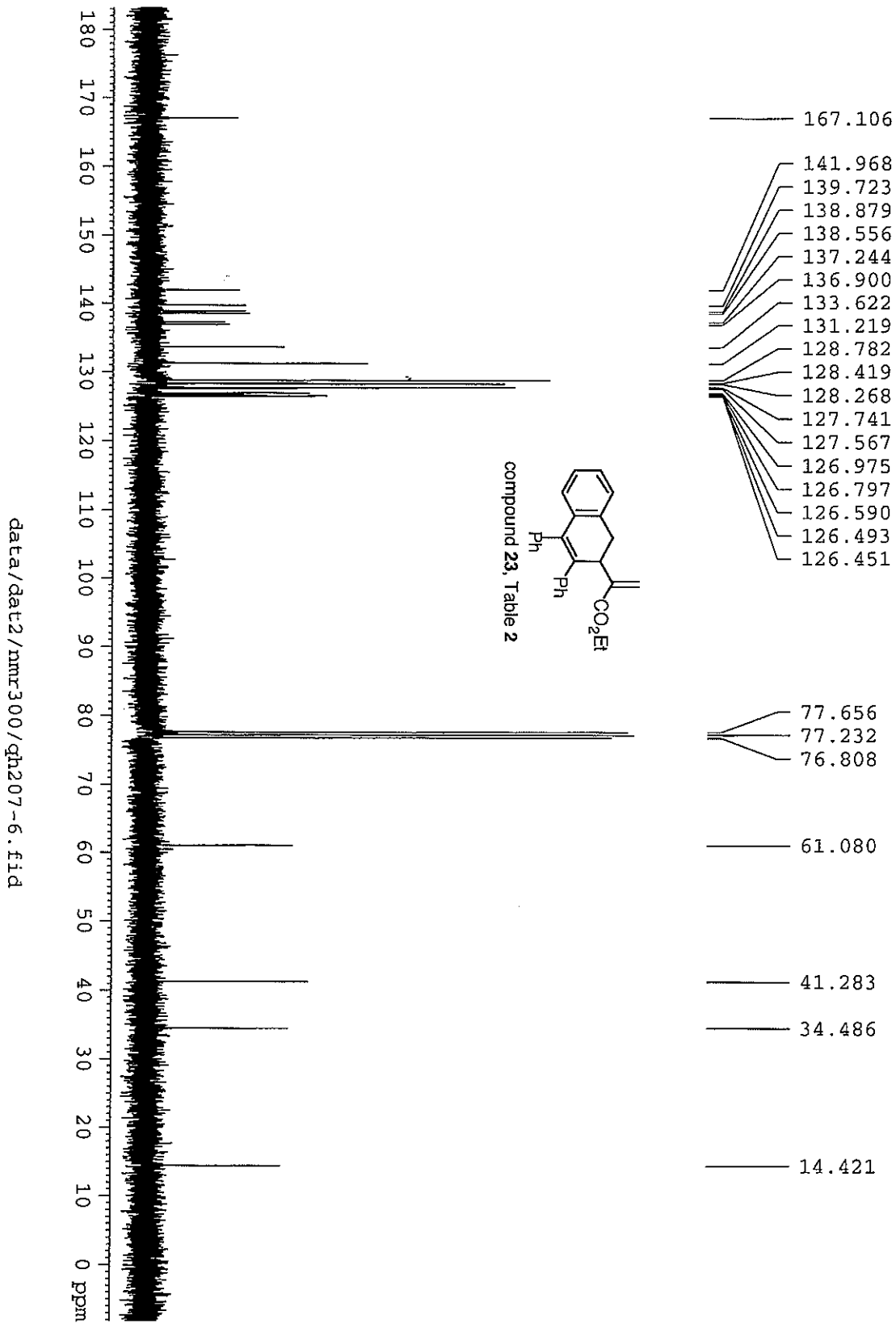

data/dat2/nmr300/qh261-1.fid
compound 17, Table 2
Me
CH2OBn
CH2OBn
CO2Et
0.948
0.940
2.038
10.257
2.000
2.033
2.068
2.109
4.110
3.052
2.973
8.134
8.123
8.117
8.108
8.071
8.063
8.056
8.045
8.039
7.500
7.496
7.484
7.474
7.470
7.468
7.359
7.348
7.339
7.324
7.319
7.312
7.302
7.296
7.290
7.282
7.275
7.221
4.907
4.695
4.552
4.491
4.080
4.057
4.033
4.006
2.635
1.574
1.198
1.175
1.151
0.000
ppm

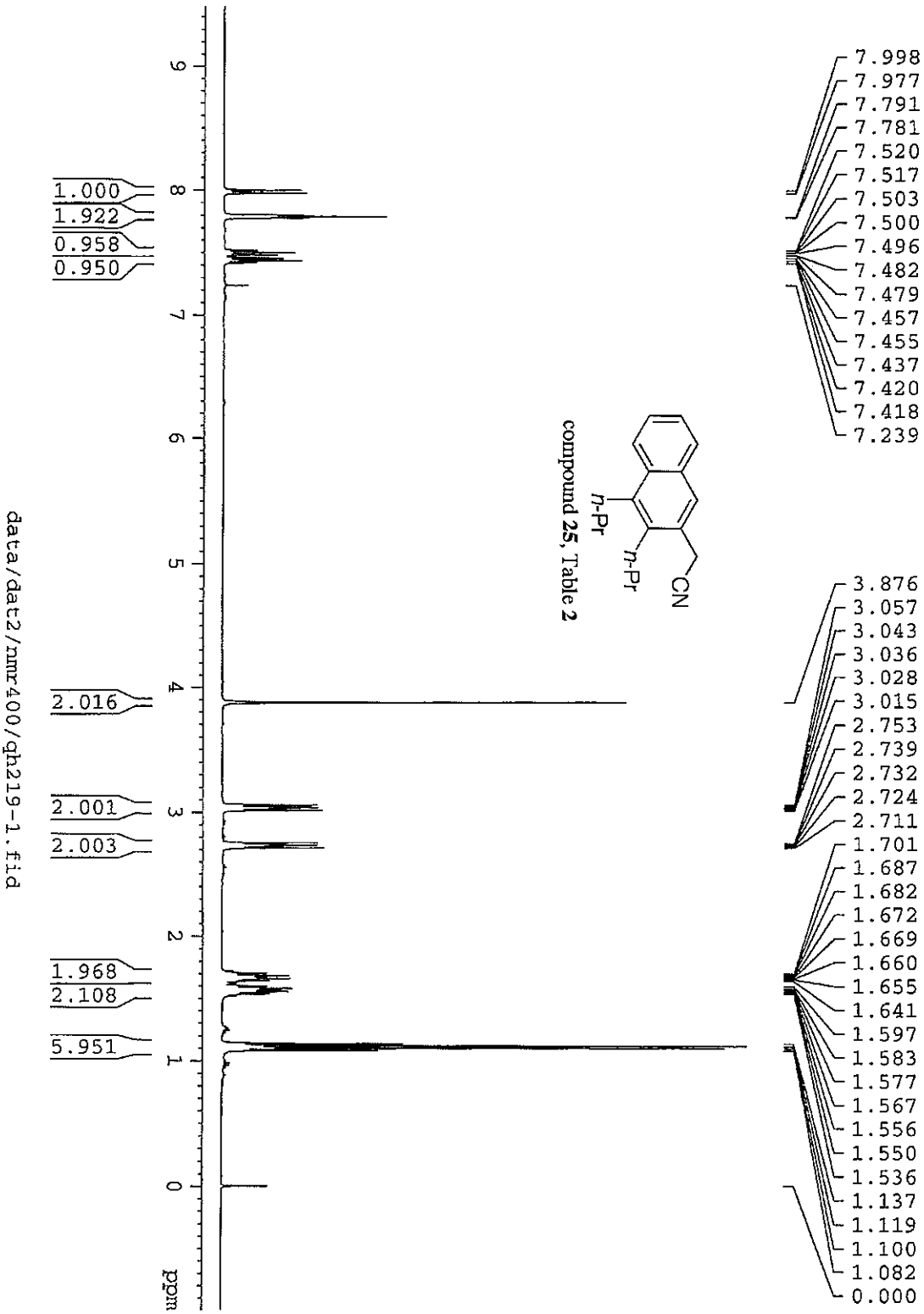

171.725
138.441
138.241
134.922
134.431
133.164
132.225
131.604
130.351
128.587
128.567
128.363
128.340
127.957
126.167
126.112
125.315
124.705
77.653
77.228
76.805
72.885
72.766
66.611
65.368
60.887
36.204
15.763
14.371
Me
CH2OBn
CH2OBn
CO2Et
compound 17, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh261-2.fid

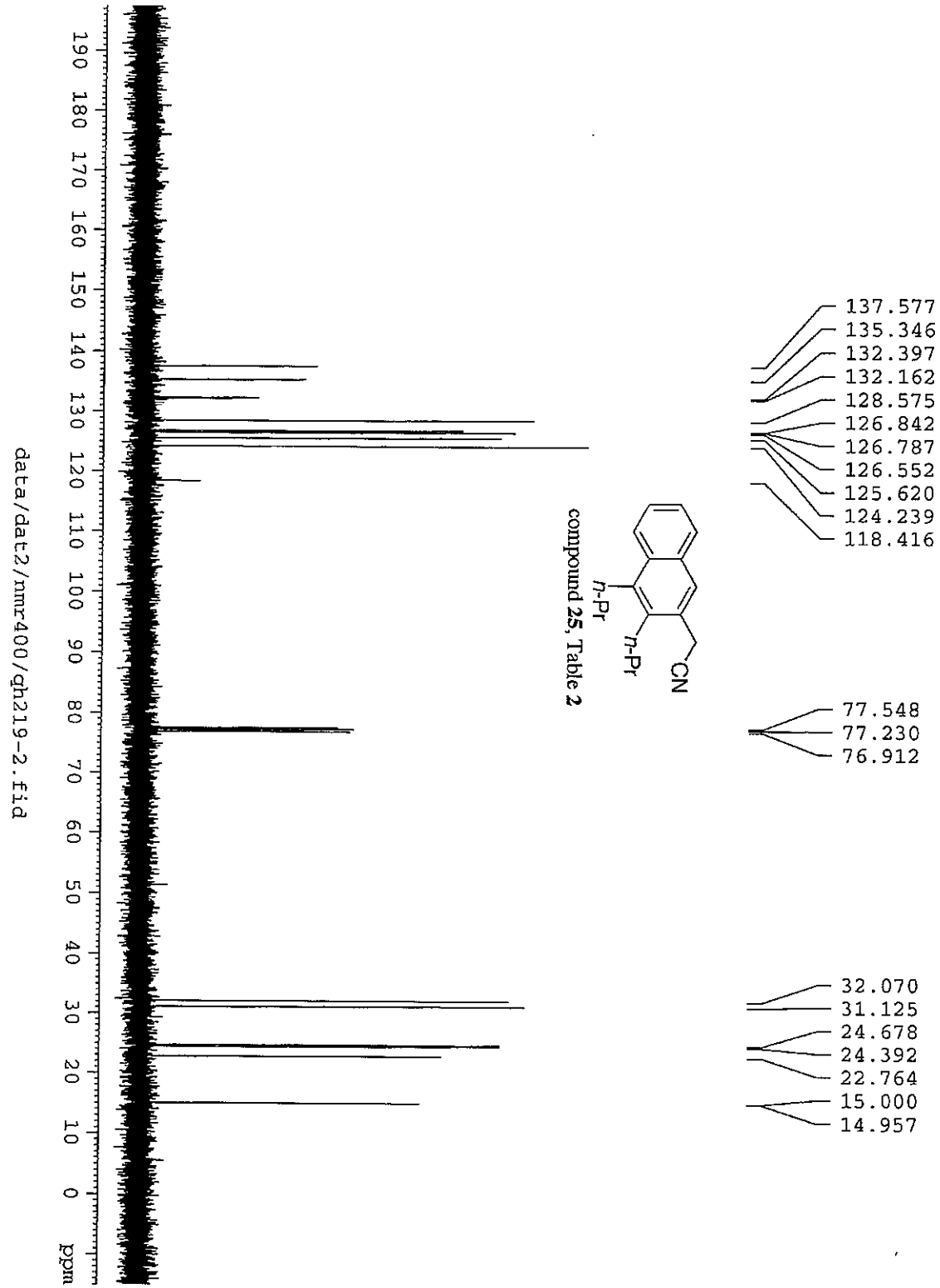

data/dat2/nmr400/qh224-1.fid
compound 19, Table 2
Ph
CO2Et
0.987
1.305
6.425
1.428
1.332
1.091
2.406
2.222
3.652
7.931
7.911
7.404
7.402
7.385
7.284
7.271
7.255
7.245
7.237
7.203
7.199
7.184
7.180
7.046
7.043
6.474
6.457
6.454
6.438
4.157
4.139
3.033
3.017
2.949
2.929
1.272
1.254
1.236
0.000
ppm

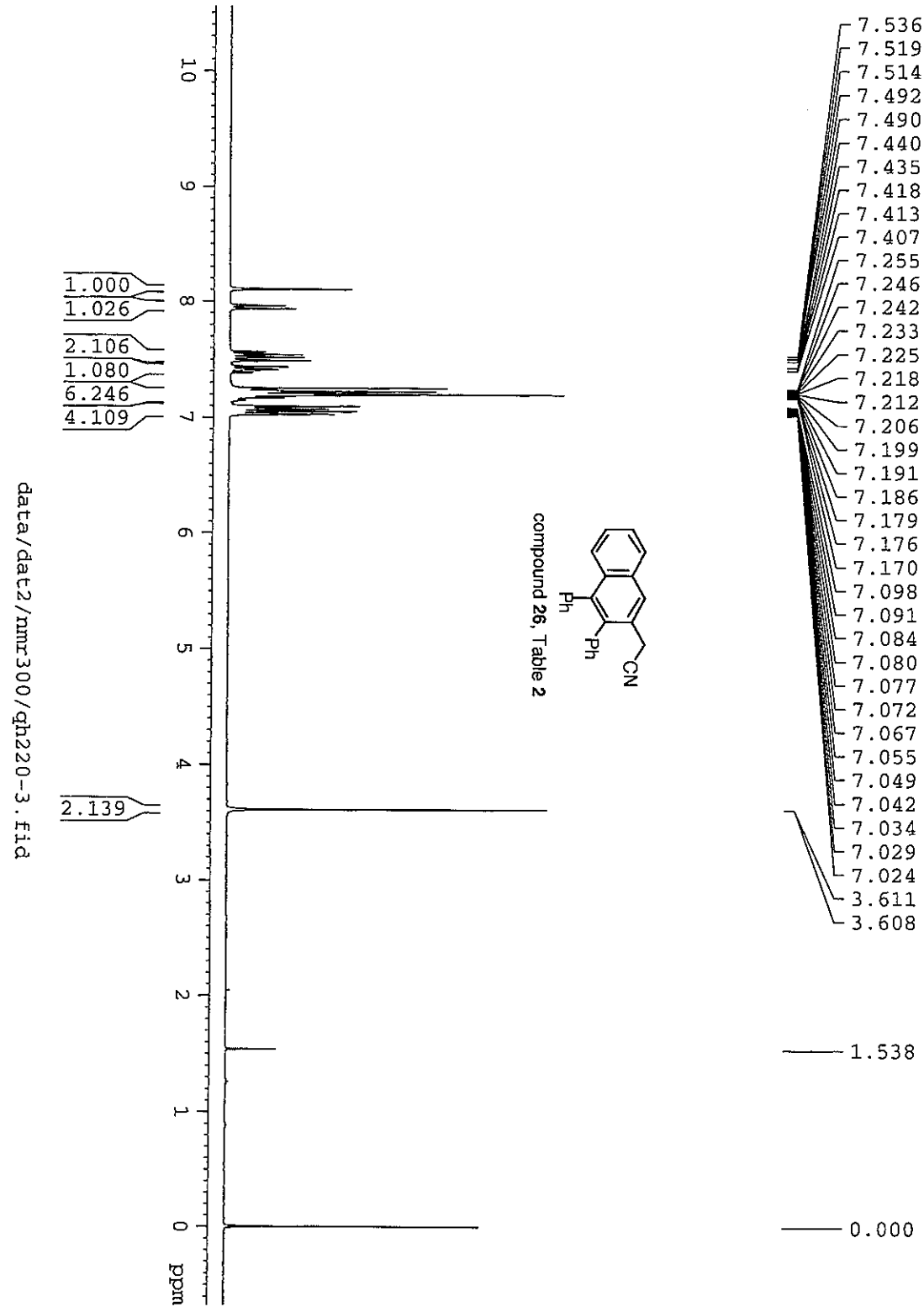

compound 19, Table 2
Ph
CO2Et
171.579
146.013
144.114
139.721
139.427
130.779
129.246
128.601
128.519
127.704
126.849
121.683
100.034
77.548
77.230
76.912
60.948
35.556
14.448
200
180
160
140
120
100
80
60
40
20
0
ppm
data/dat2/nmr400/qh224-2.fid

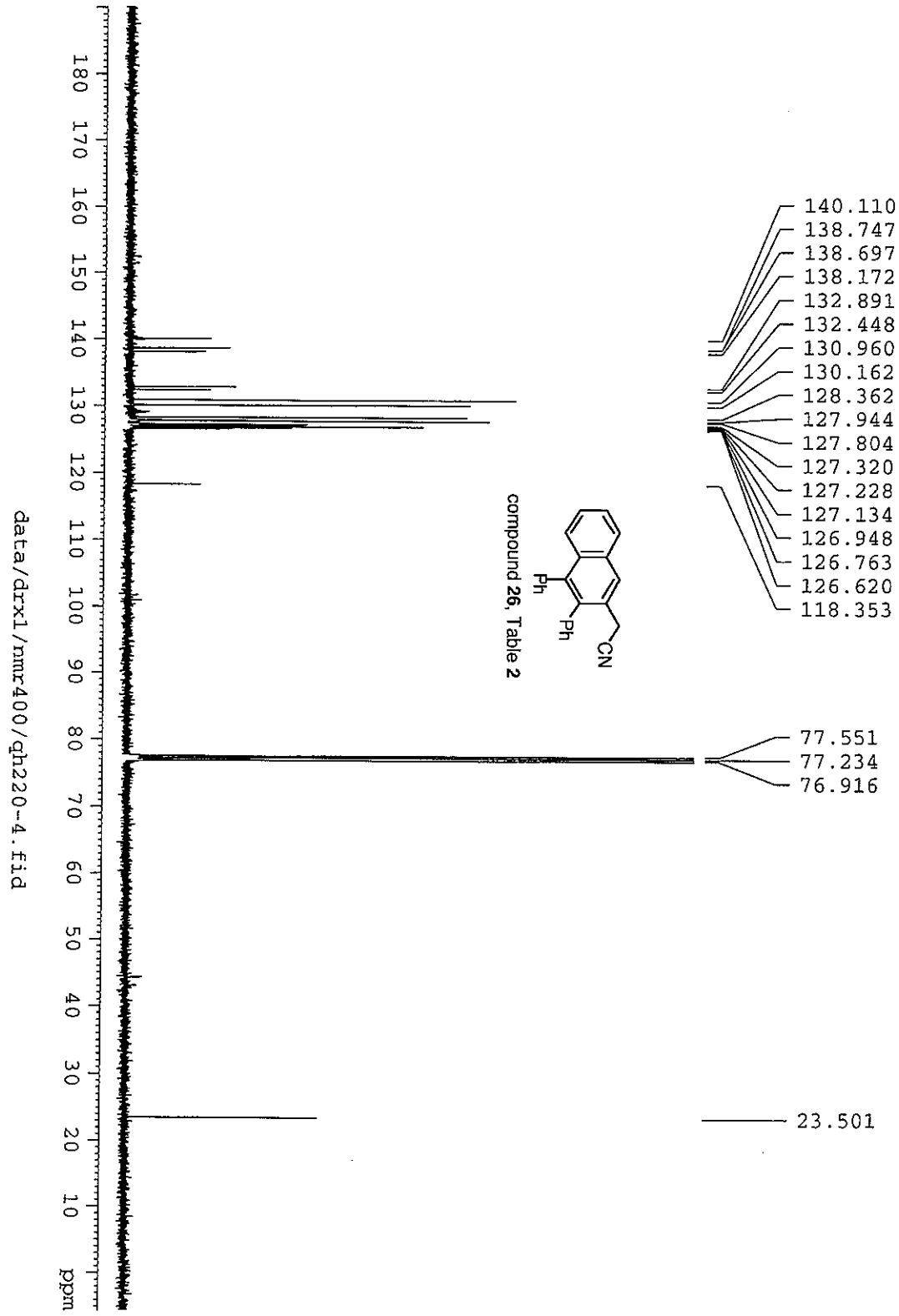

data/drx1/nmr400/qh207-7
compound 23, Table 2
Ph
Ph
CO2Et
3.417
10.216
1.024
1.005
1.000
2.117
1.021
1.087
1.024
3.233
ppm
7.220
7.215
7.204
7.134
7.128
7.114
7.111
7.108
7.099
7.067
7.063
7.058
7.046
7.042
7.035
7.030
7.023
7.019
7.009
7.007
7.002
6.805
6.786
6.283
6.280
5.811
5.808
5.805
4.252
4.244
4.234
4.226
4.216
4.208
4.199
4.025
4.021
4.007
4.003
3.495
3.477
3.455
3.438
3.017
3.011
2.977
2.971
1.551
1.326
1.308
1.290
-0.000

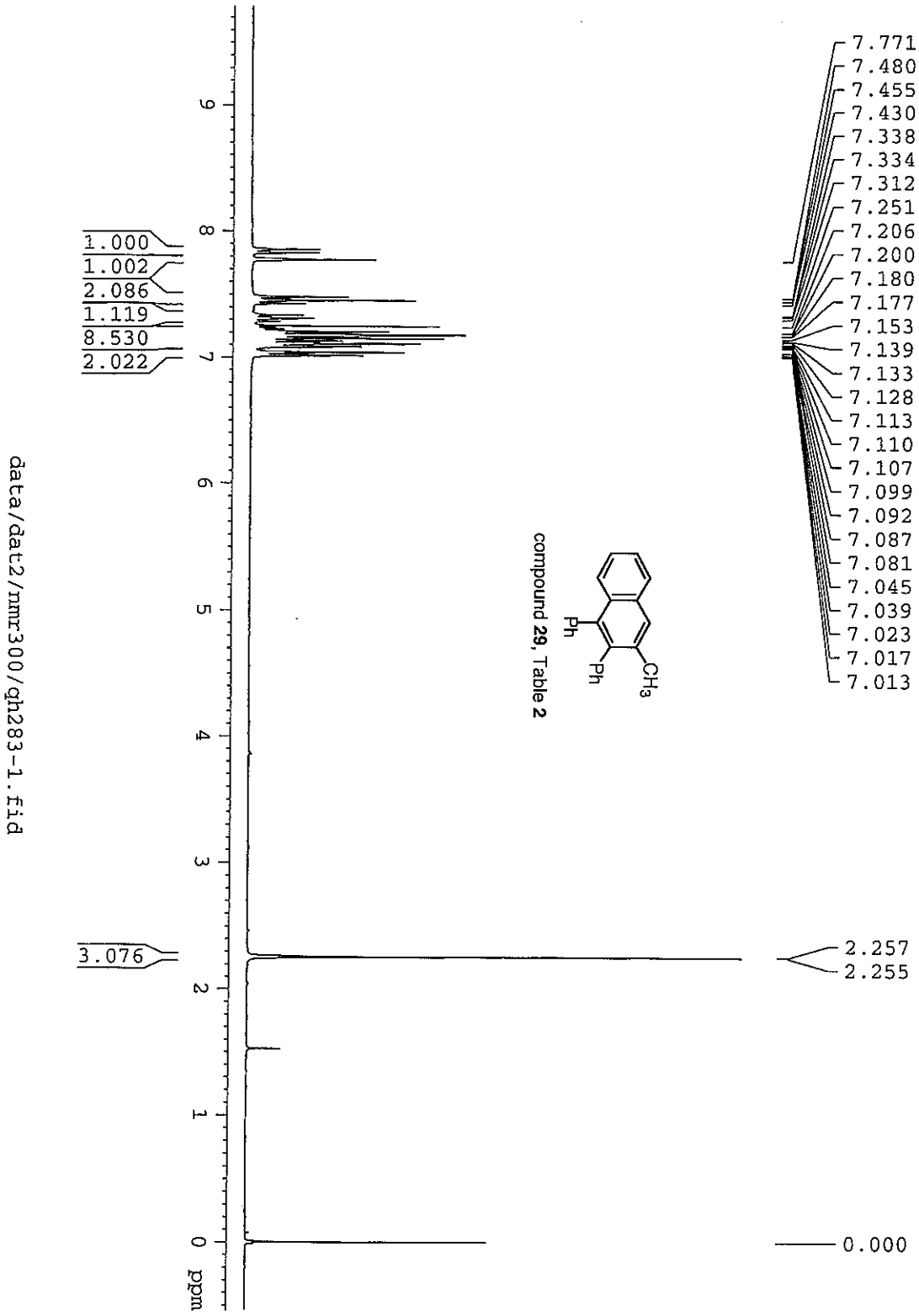

167.106
141.968
139.723
138.879
138.556
137.244
136.900
133.622
131.219
128.782
128.419
128.268
127.741
127.567
126.975
126.797
126.590
126.493
126.451
77.656
77.232
76.808
61.080
41.283
34.486
14.421
Ph
Ph
CO2Et
compound 23, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr300/qh207-6.fid

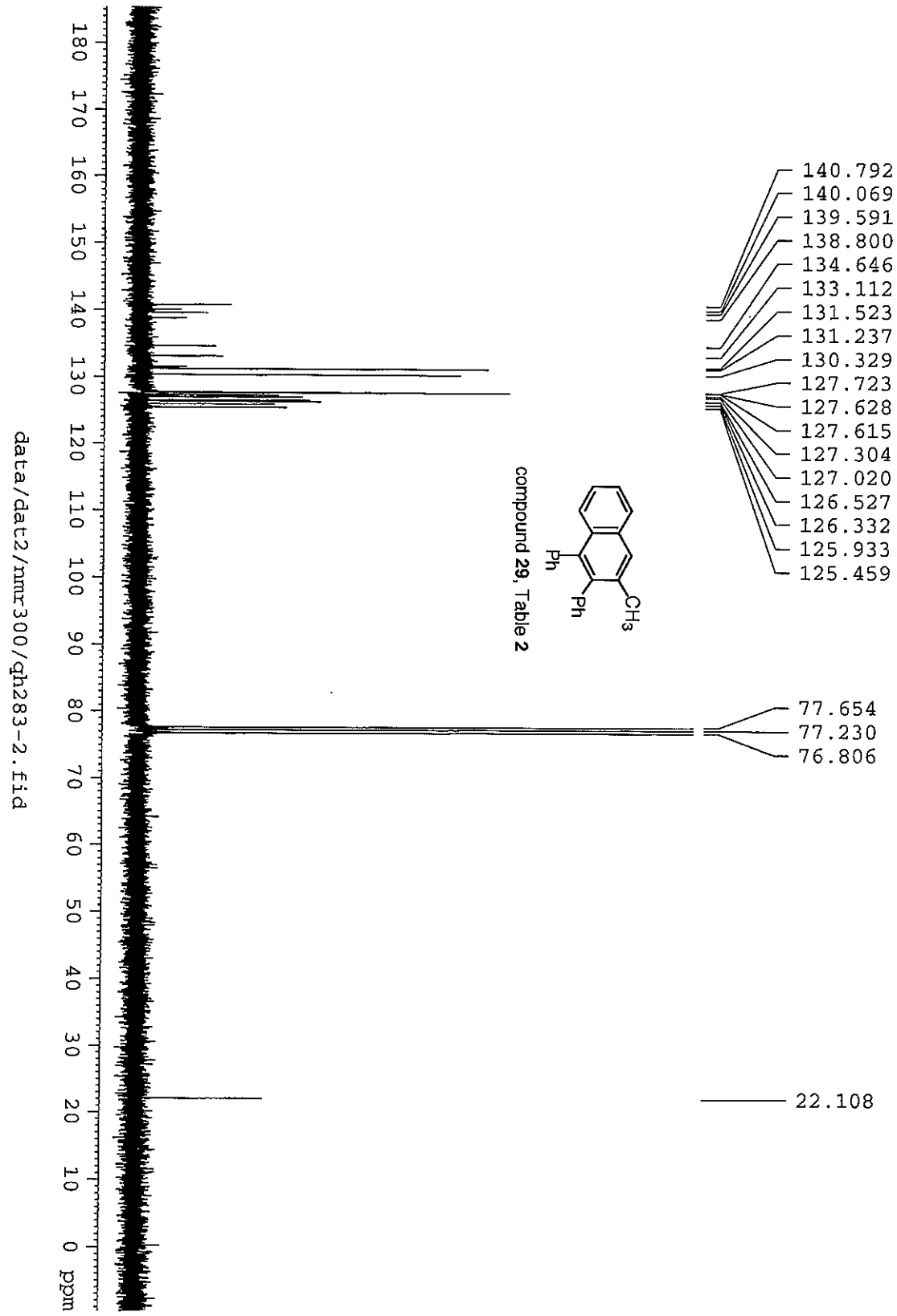

7.998
7.977
7.791
7.781
7.520
7.517
7.503
7.500
7.496
7.482
7.479
7.457
7.455
7.437
7.420
7.418
7.239
3.876
3.057
3.043
3.036
3.028
3.015
2.753
2.739
2.732
2.724
2.711
1.701
1.687
1.682
1.672
1.669
1.660
1.655
1.641
1.597
1.583
1.577
1.567
1.556
1.550
1.536
1.137
1.119
1.100
1.082
0.000
1.000
1.922
0.958
0.950
2.016
2.001
2.003
1.968
2.108
5.951
n-Pr
n-Pr
CN
compound 25, Table 2
data/dat2/nmr400/qh219-1.fid
ppm

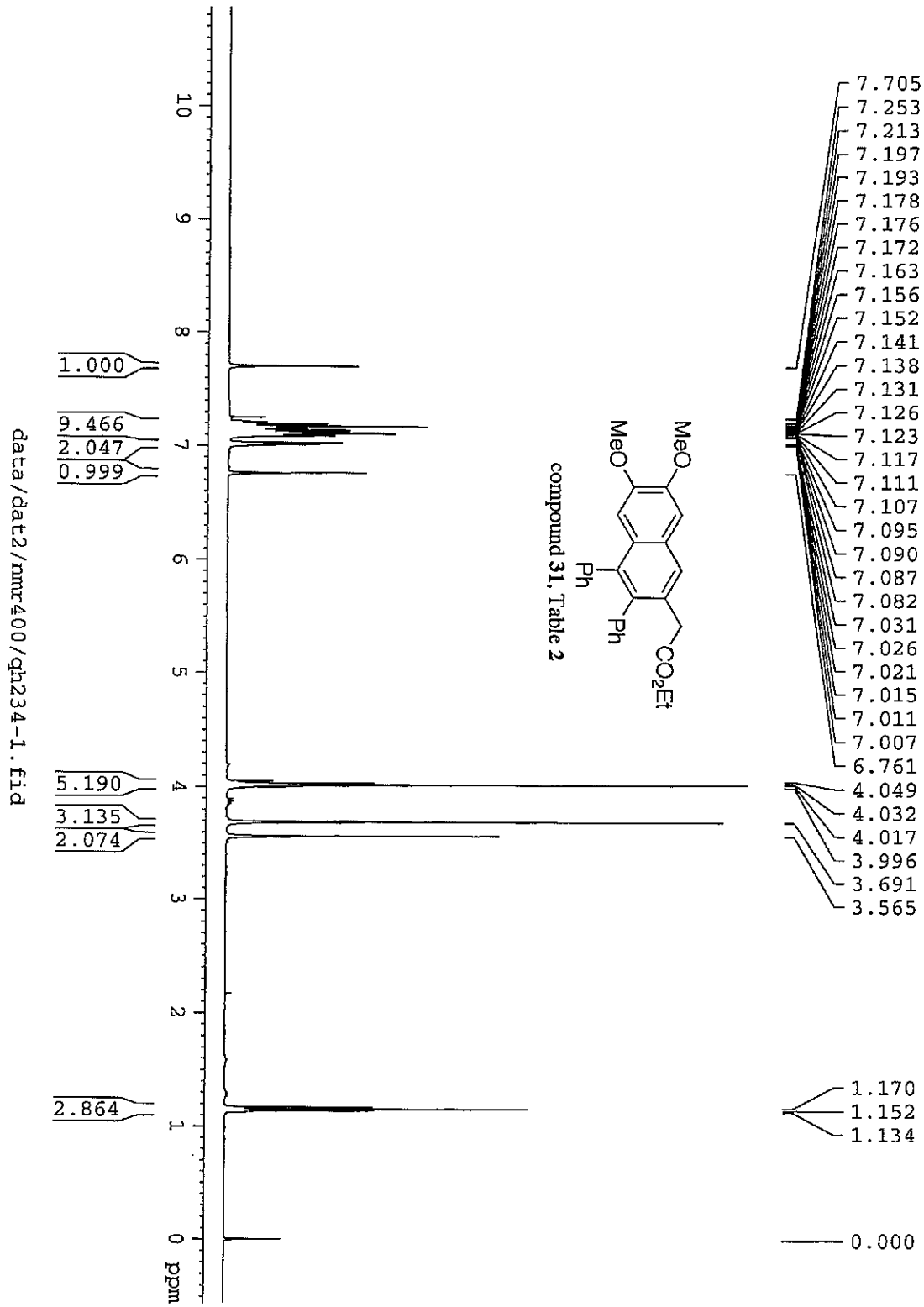

137.577
135.346
132.397
132.162
128.575
126.842
126.787
126.552
125.620
124.239
118.416
77.548
77.230
76.912
32.070
31.125
24.678
24.392
22.764
15.000
14.957
n-Pr
n-Pr
CN
compound 25, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh219-2.fid

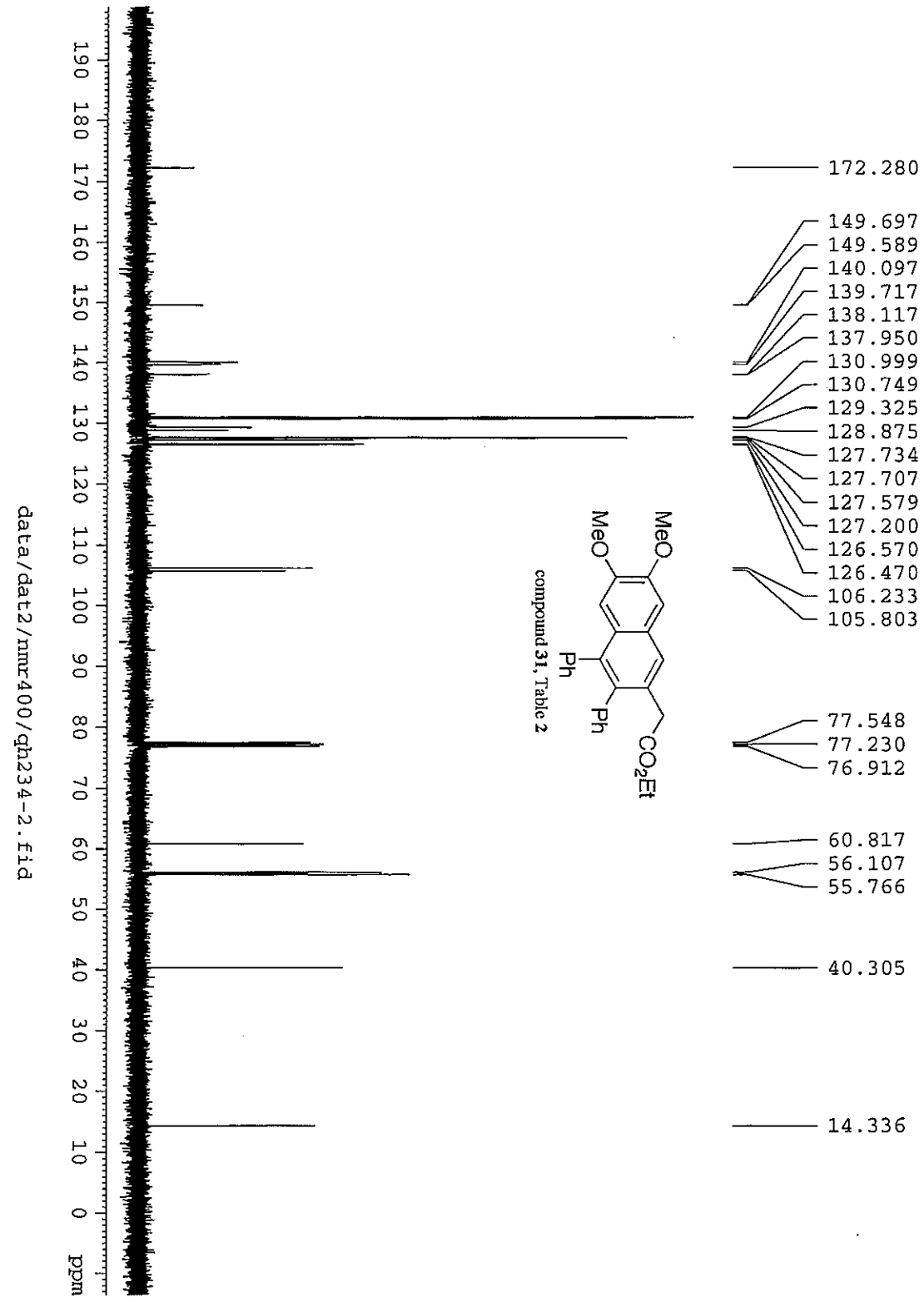

7.536
7.519
7.514
7.492
7.490
7.440
7.435
7.418
7.413
7.407
7.255
7.246
7.242
7.233
7.225
7.218
7.212
7.206
7.199
7.191
7.186
7.179
7.176
7.170
7.098
7.091
7.084
7.080
7.077
7.072
7.067
7.055
7.049
7.042
7.034
7.029
7.024
3.611
3.608
1.538
0.000
1.000
1.026
2.106
1.080
6.246
4.109
2.139
10
9
8
7
6
5
4
3
2
1
0
ppm
Ph
Ph
CN
compound 26, Table 2
data/dat2/nmr300/qh220-3.fid


140.110
138.747
138.697
138.172
132.891
132.448
130.960
130.162
128.362
127.944
127.804
127.320
127.228
127.134
126.948
126.763
126.620
118.353
77.551
77.234
76.916
23.501
compound 26, Table 2
Ph
Ph
CN
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh220-4.fid


7.771
7.480
7.455
7.430
7.338
7.334
7.312
7.251
7.206
7.200
7.180
7.177
7.153
7.139
7.133
7.128
7.113
7.110
7.107
7.099
7.092
7.087
7.081
7.045
7.039
7.023
7.017
7.013
2.257
2.255
0.000
1.000
1.002
2.086
1.119
8.530
2.022
3.076
compound 29, Table 2
Ph
Ph
CH3
data/dat2/nmr300/qh283-1.fid
ppm


140.792
140.069
139.591
138.800
134.646
133.112
131.523
131.237
130.329
127.723
127.628
127.615
127.304
127.020
126.527
126.332
125.933
125.459
77.654
77.230
76.806
22.108
Ph
Ph
CH3
compound 29, Table 2
data/dat2/nmr300/gh283-2.fid
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


data/dat2/nmr400/qh234-1.fid
compound 31, Table 2
MeO
MeO
Ph
Ph
CO2Et
1.000
9.466
2.047
0.999
5.190
3.135
2.074
2.864
7.705
7.253
7.213
7.197
7.193
7.178
7.176
7.172
7.163
7.156
7.152
7.141
7.138
7.131
7.126
7.123
7.117
7.111
7.107
7.095
7.090
7.087
7.082
7.031
7.026
7.021
7.015
7.011
7.007
6.761
4.049
4.032
4.017
3.996
3.691
3.565
1.170
1.152
1.134
0.000
ppm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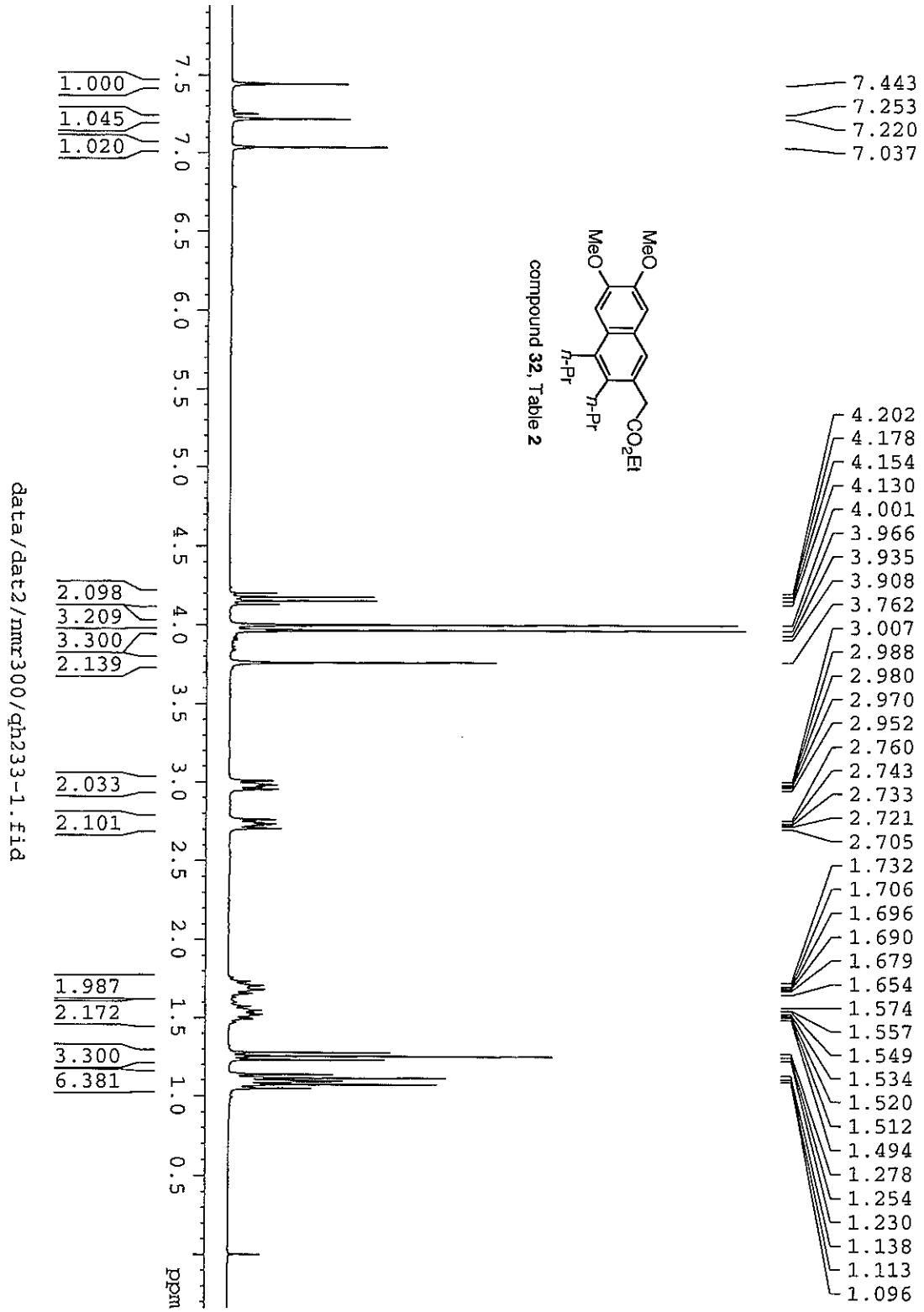
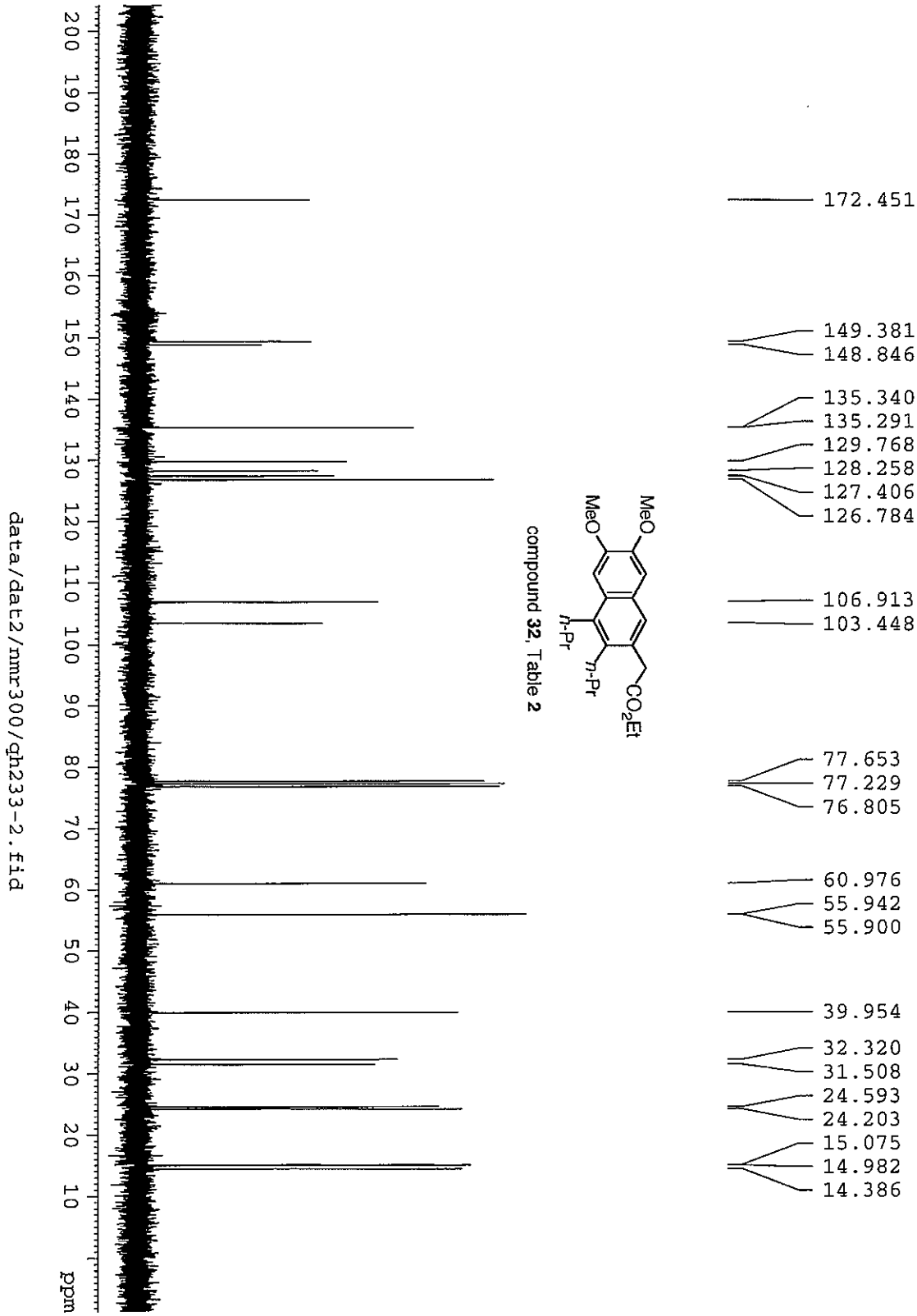
149.697
149.589
140.097
139.717
138.117
137.950
130.999
130.749
129.325
128.875
127.734
127.707
127.579
127.200
126.570
126.470
106.233
105.803
77.548
77.230
76.912
60.817
56.107
55.766
40.305
14.336
MeO
MeO
Ph
Ph
CO2Et
compound 31, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh234-2.fid


compound 32, Table 2
MeO
MeO
n-Pr
n-Pr
CO2Et
7.443
7.253
7.220
7.037
4.202
4.178
4.154
4.130
4.001
3.966
3.935
3.908
3.762
3.007
2.988
2.980
2.970
2.952
2.760
2.743
2.733
2.721
2.705
1.732
1.706
1.696
1.690
1.679
1.654
1.574
1.557
1.549
1.534
1.520
1.512
1.494
1.278
1.254
1.230
1.138
1.113
1.096
1.000
1.045
1.020
2.098
3.209
3.300
2.139
2.033
2.101
1.987
2.172
3.300
6.381
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
data/dat2/nmr300/qh233-1.fid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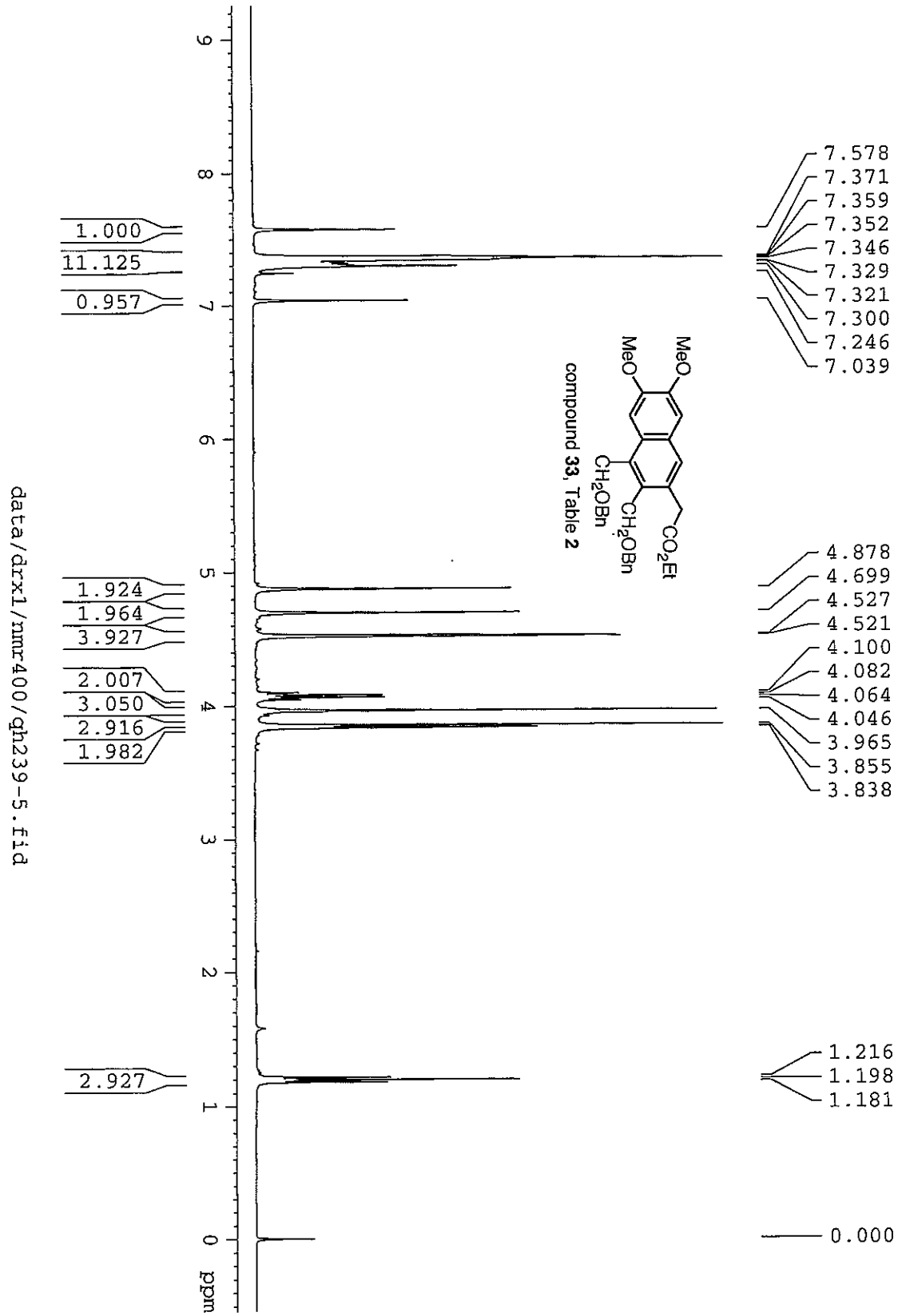
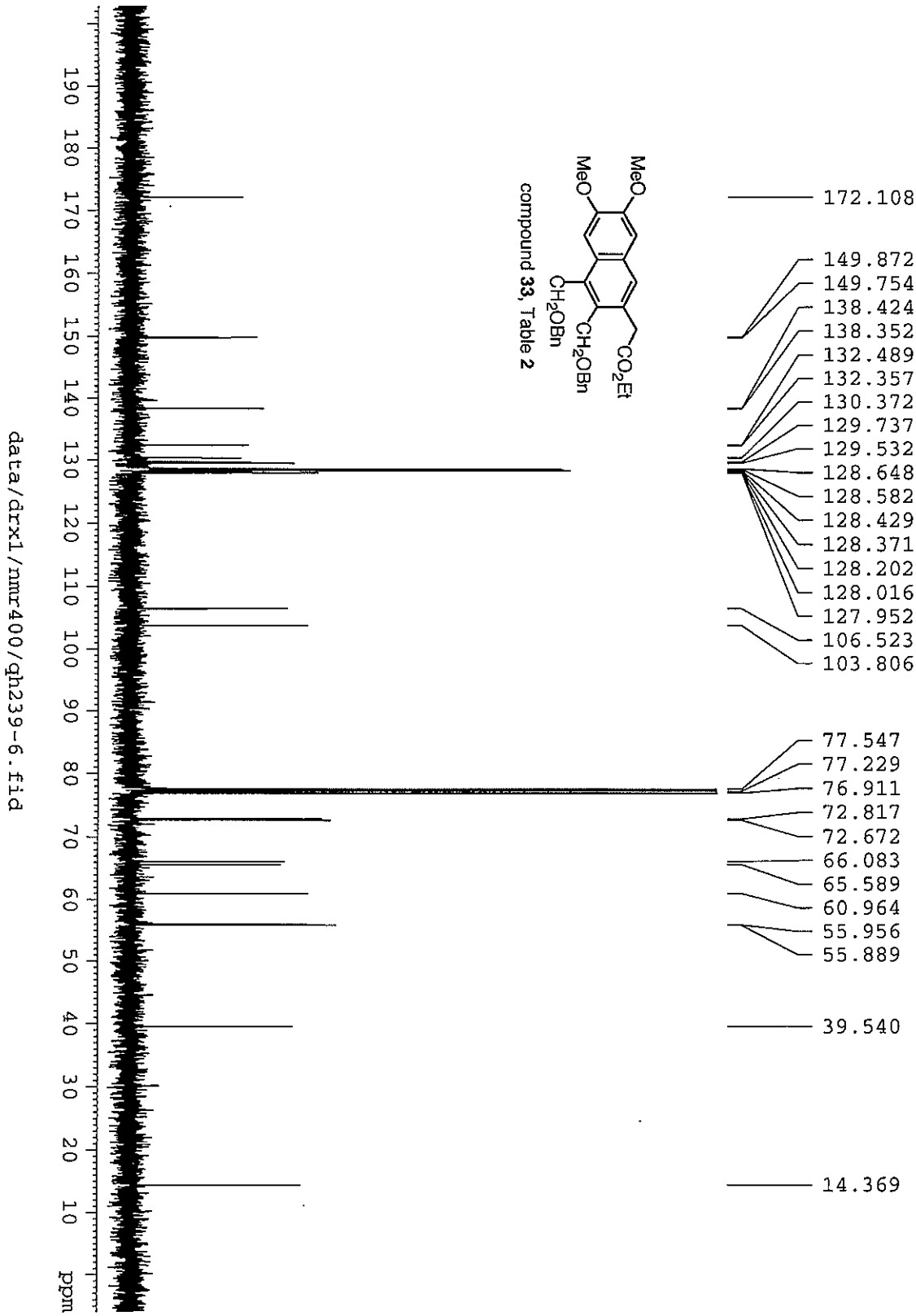
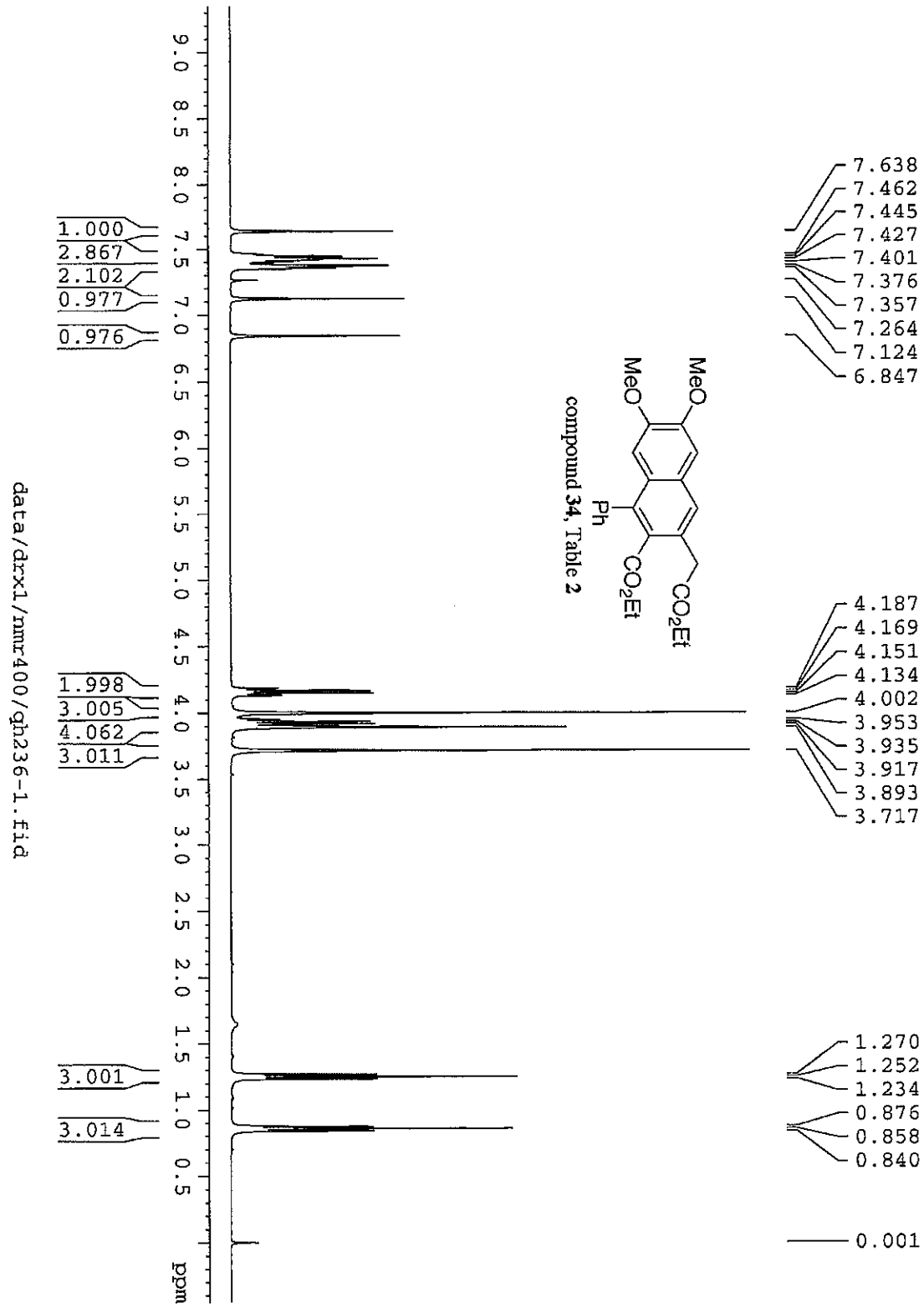
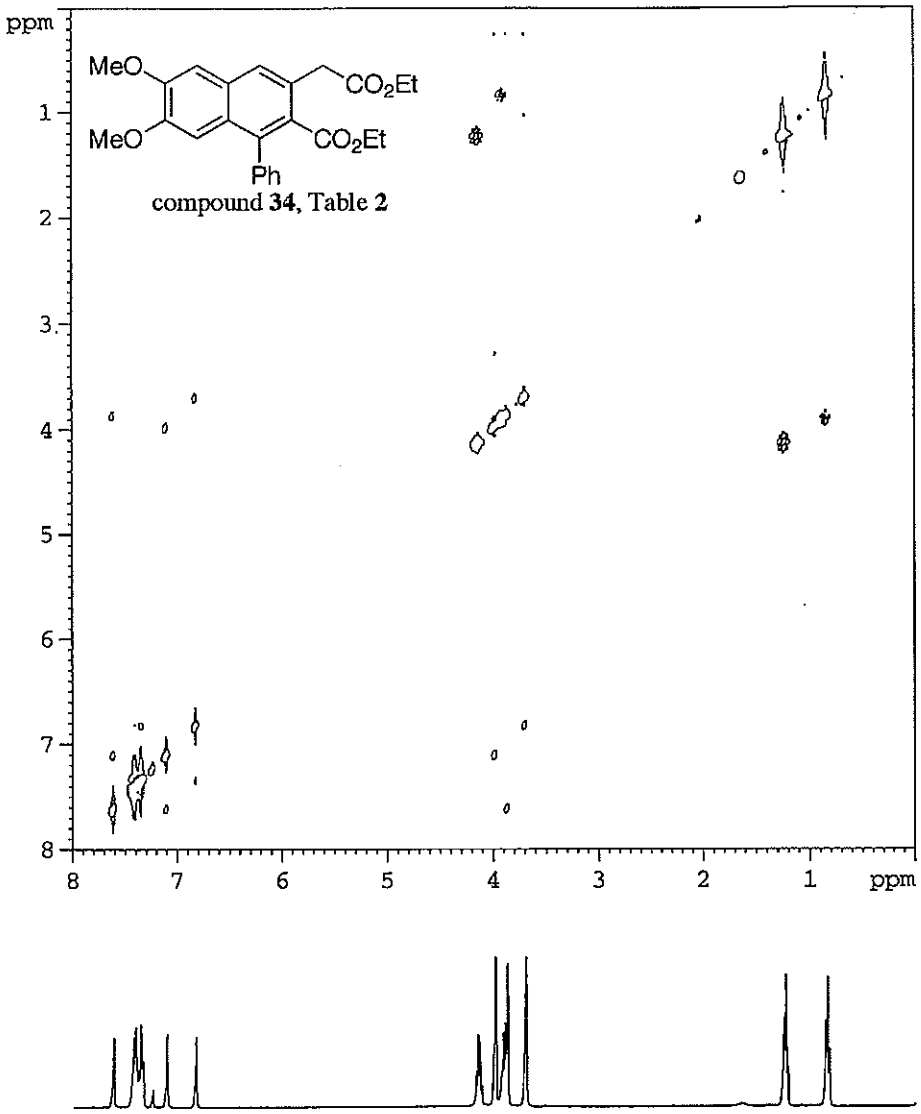
148.846
135.340
135.291
129.768
128.258
127.406
126.784
106.913
103.448
77.653
77.229
76.805
60.976
55.942
55.900
39.954
32.320
31.508
24.593
24.203
15.075
14.982
14.386
MeO
MeO
n-Pr
n-Pr
CO2Et
compound 32, Table 2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh233-2.fid


7.578
7.371
7.359
7.352
7.346
7.329
7.321
7.300
7.246
7.039
4.878
4.699
4.527
4.521
4.100
4.082
4.064
4.046
3.965
3.855
3.838
1.216
1.198
1.181
0.000
1.000
11.125
0.957
1.924
1.964
3.927
2.007
3.050
2.916
1.982
2.927
MeO
MeO
CH2OBn
CH2OBn
CO2Et
compound 33, Table 2
data/drx1/nmr400/qh239-5.fid
ppm


MeO
MeO
CH2OBn
CH2OBn
CO2Et
compound 33, Table 2
172.108
149.872
149.754
138.424
138.352
132.489
132.357
130.372
129.737
129.532
128.648
128.582
128.429
128.371
128.202
128.016
127.952
106.523
103.806
77.547
77.229
76.911
72.817
72.672
66.083
65.589
60.964
55.956
55.889
39.540
14.369
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh239-6.fid


data/drx1/nmr400/qh236-1.fid
compound 34, Table 2
MeO
MeO
Ph
CO2Et
CO2Et
1.000
2.867
2.102
0.977
0.976
1.998
3.005
4.062
3.011
3.001
3.014
7.638
7.462
7.445
7.427
7.401
7.376
7.357
7.264
7.124
6.847
4.187
4.169
4.151
4.134
4.002
3.953
3.935
3.917
3.893
3.717
1.270
1.252
1.234
0.876
0.858
0.840
0.001
ppm



500

```
Current Data Parameters
NAME                  qh236-2d-3
EXPNO                          1
PROCNO                         1

F2 - Acquisition Paramet
Date_                   20020318
Time                       14.01
INSTRUM                    spect
PROBHD     5 mm TXI 31P
PULPROG                 noesyst
TD                            2048
SOLVENT                    CDCl3
NS                             8
DS                             4
SWH                     3229.974
FIDRES                  1.577136
AQ                      0.3170804
RG                            64
DW                         154.800
DE                            4.50
TE                           300.0
d0                      0.00000300
D1                      7.96968794
D8                      0.69999999
d11                     0.03000000
IN0                     0.00030960
13                            45

============ CHANNEL f1
NUC1                          1H
P1                            7.70
PL1                           0.00
SFO1                400.1317249

F1 - Acquisition paramet
ND0                            1
TD                           275
SFO1                    400.1317
FIDRES                  11.745360
SW                          8.072

F2 - Processing paramete
SI                          1024
SF                  400.1300180
WDW                       QSINE
SSB                            2
LB                          0.00
GB                             0
PC                          1.00

F1 - Processing paramete
SI                          1024
MC2                States-TPPI
SF                  400.1300180
WDW                       QSINE
SSB                            2
LB                          0.00
GB                             0

2D NMR plot parameters
CX2                         20.00
CX1                         20.00
F2PLO                       8.302
F2LO                     3321.90
F2PHI                       0.230
F2HI                        91.93
F1PLO                       8.302
F1LO                     3321.90
F1PHI                       0.230
F1HI                        91.93
F2PPMCM                  0.40362
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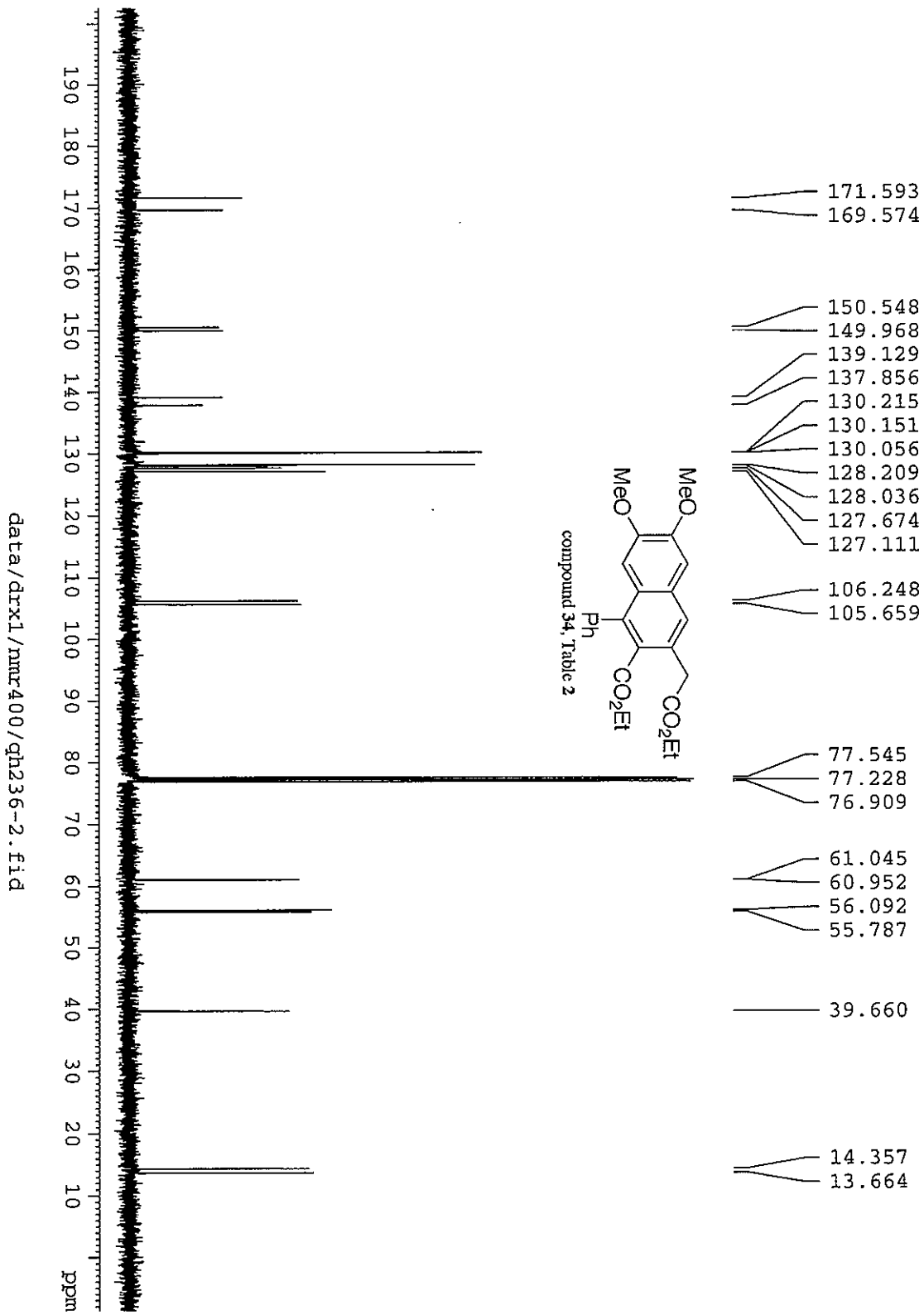
data/drx1/nmr400/qh236-3D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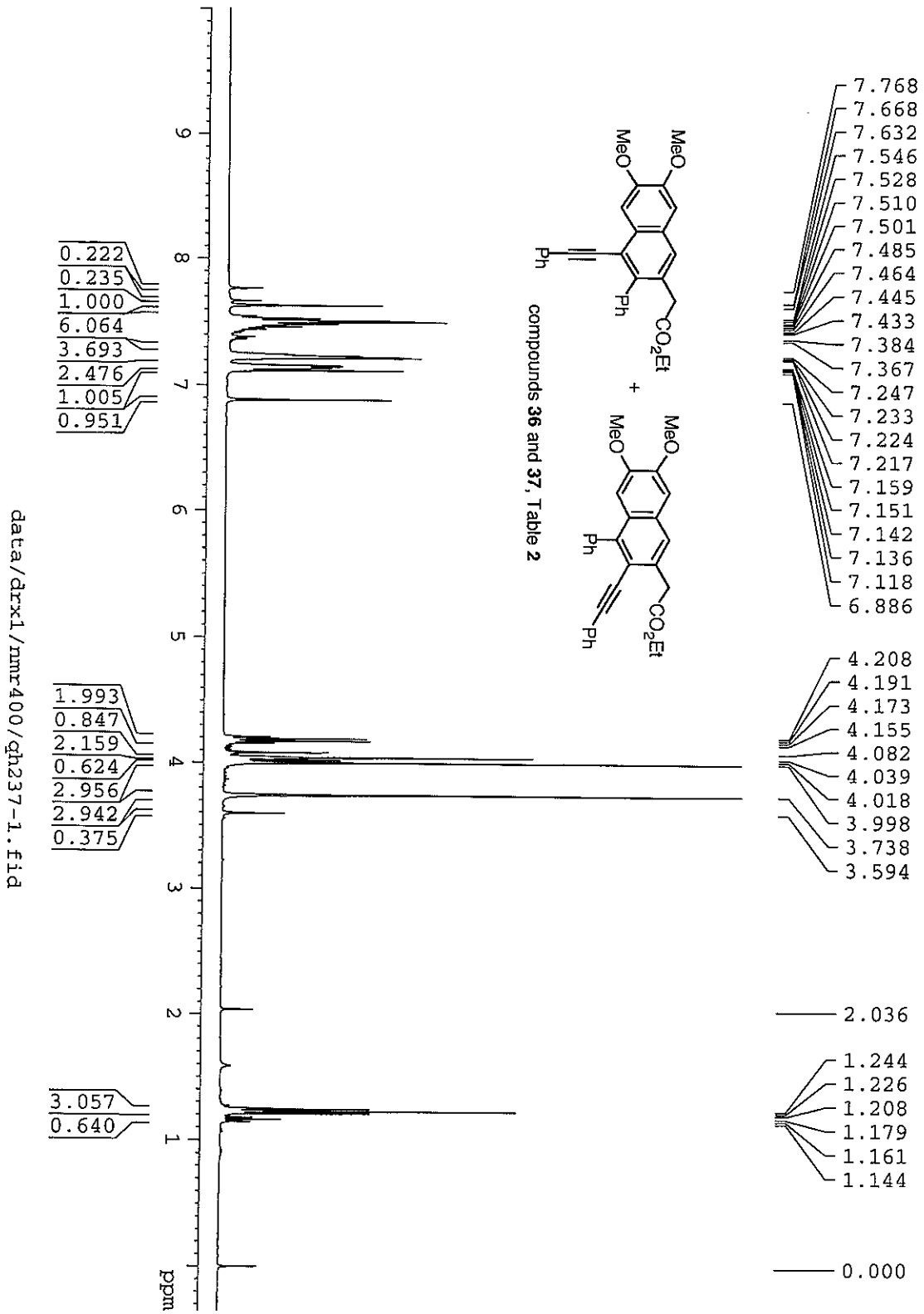
150.548
149.968
139.129
137.856
130.215
130.151
130.056
128.209
128.036
127.674
127.111
106.248
105.659
77.545
77.228
76.909
61.045
60.952
56.092
55.787
39.660
14.357
13.664
MeO
MeO
Ph
CO2Et
CO2Et
compound 34, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh236-2.fid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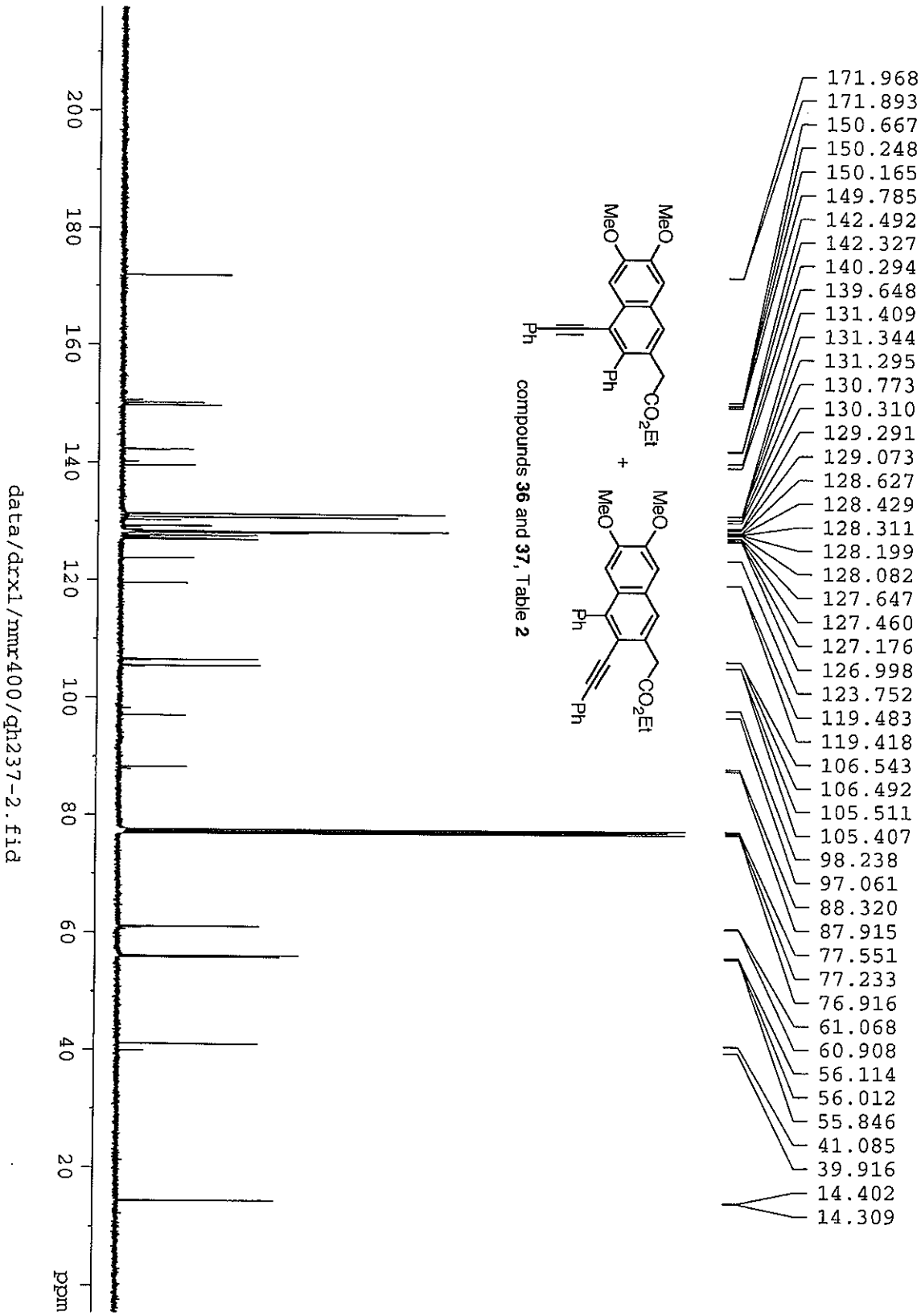
compounds 36 and 37, Table 2
MeO
MeO
Ph
Ph
CO2Et
+
ppm
0.222
0.235
1.000
6.064
3.693
2.476
1.005
0.951
1.993
0.847
2.159
0.624
2.956
2.942
0.375
3.057
0.640
7.768
7.668
7.632
7.546
7.528
7.510
7.501
7.485
7.464
7.445
7.433
7.384
7.367
7.247
7.233
7.224
7.217
7.159
7.151
7.142
7.136
7.118
6.886
4.208
4.191
4.173
4.155
4.082
4.039
4.018
3.998
3.738
3.594
2.036
1.244
1.226
1.208
1.179
1.161
1.144
0.000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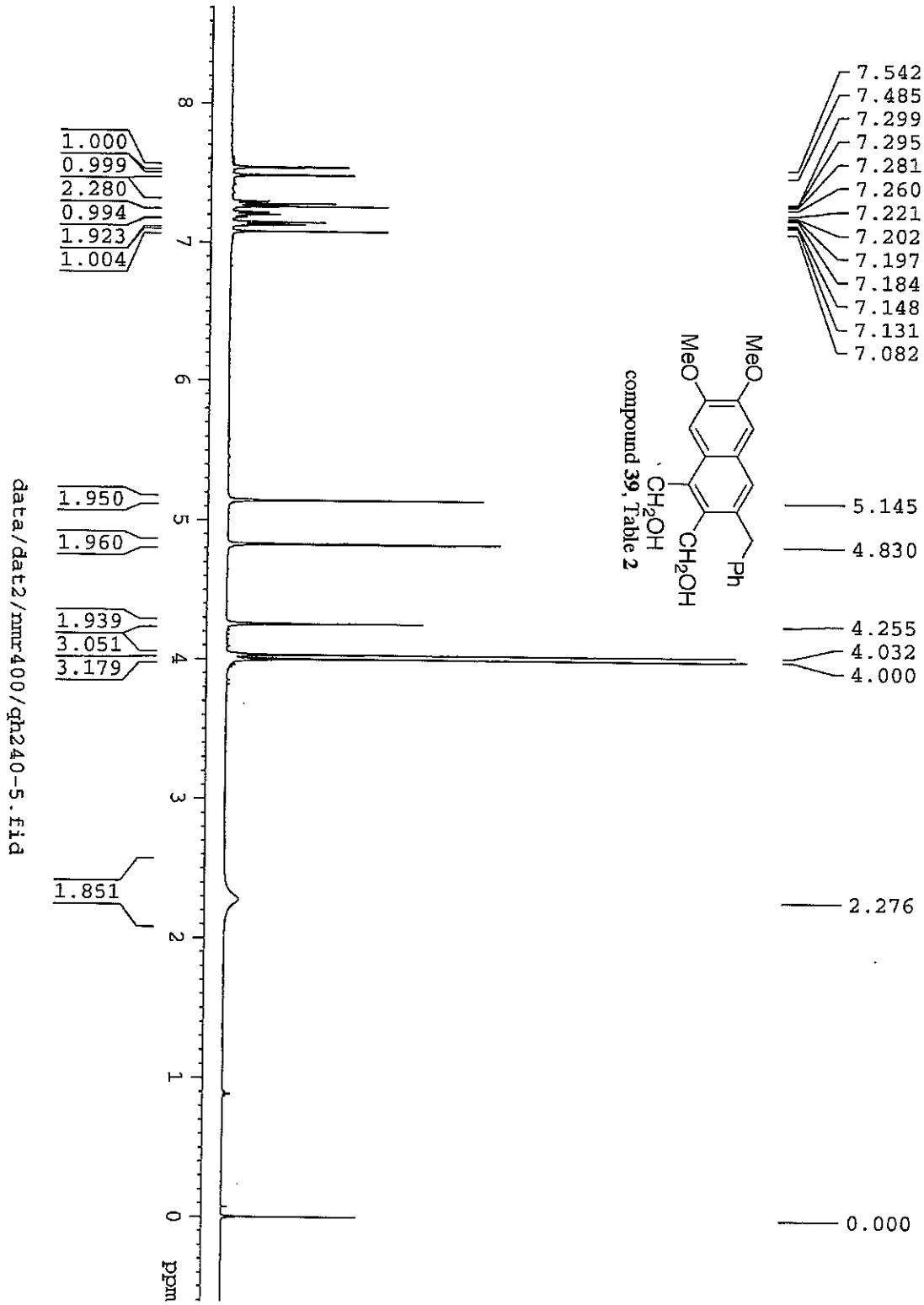
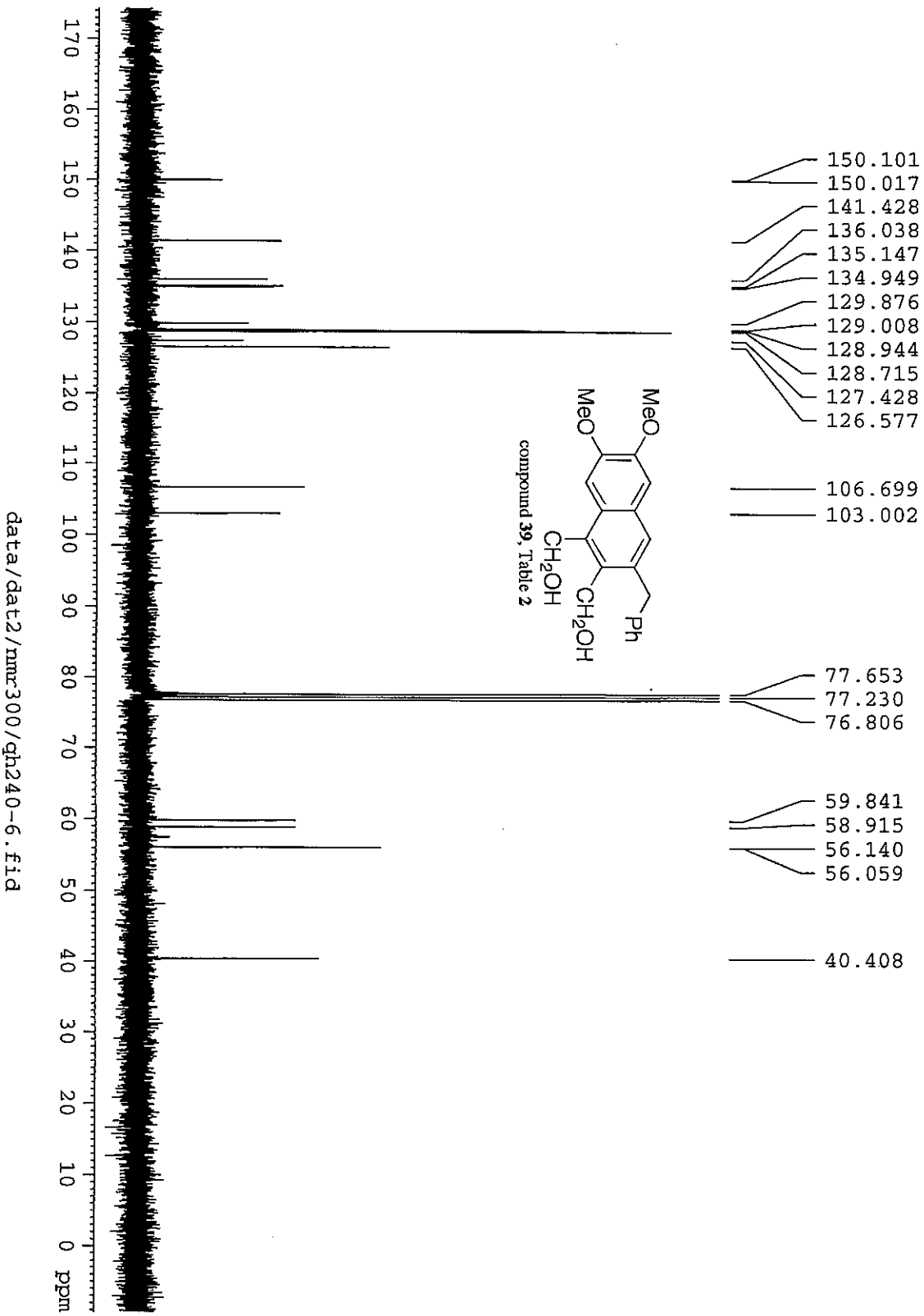
171.893
150.667
150.248
150.165
149.785
142.492
142.327
140.294
139.648
131.409
131.344
131.295
130.773
130.310
129.291
129.073
128.627
128.429
128.311
128.199
128.082
127.647
127.460
127.176
126.998
123.752
119.483
119.418
106.543
106.492
105.511
105.407
98.238
97.061
88.320
87.915
77.551
77.233
76.916
61.068
60.908
56.114
56.012
55.846
41.085
39.916
14.402
14.309
MeO
MeO
Ph
CO2Et
+
compounds 36 and 37, Table 2
200
180
160
140
120
100
80
60
40
20
ppm
data/drx1/nmr400/qh237-2.fid


7.542
7.485
7.299
7.295
7.281
7.260
7.221
7.202
7.197
7.184
7.148
7.131
7.082
5.145
4.830
4.255
4.032
4.000
2.276
0.000
1.000
0.999
2.280
0.994
1.923
1.004
1.950
1.960
1.939
3.051
3.179
1.851
MeO
MeO
CH2OH
CH2OH
Ph
compound 39, Table 2
ppm
data/dat2/nmr400/qh240-5.fid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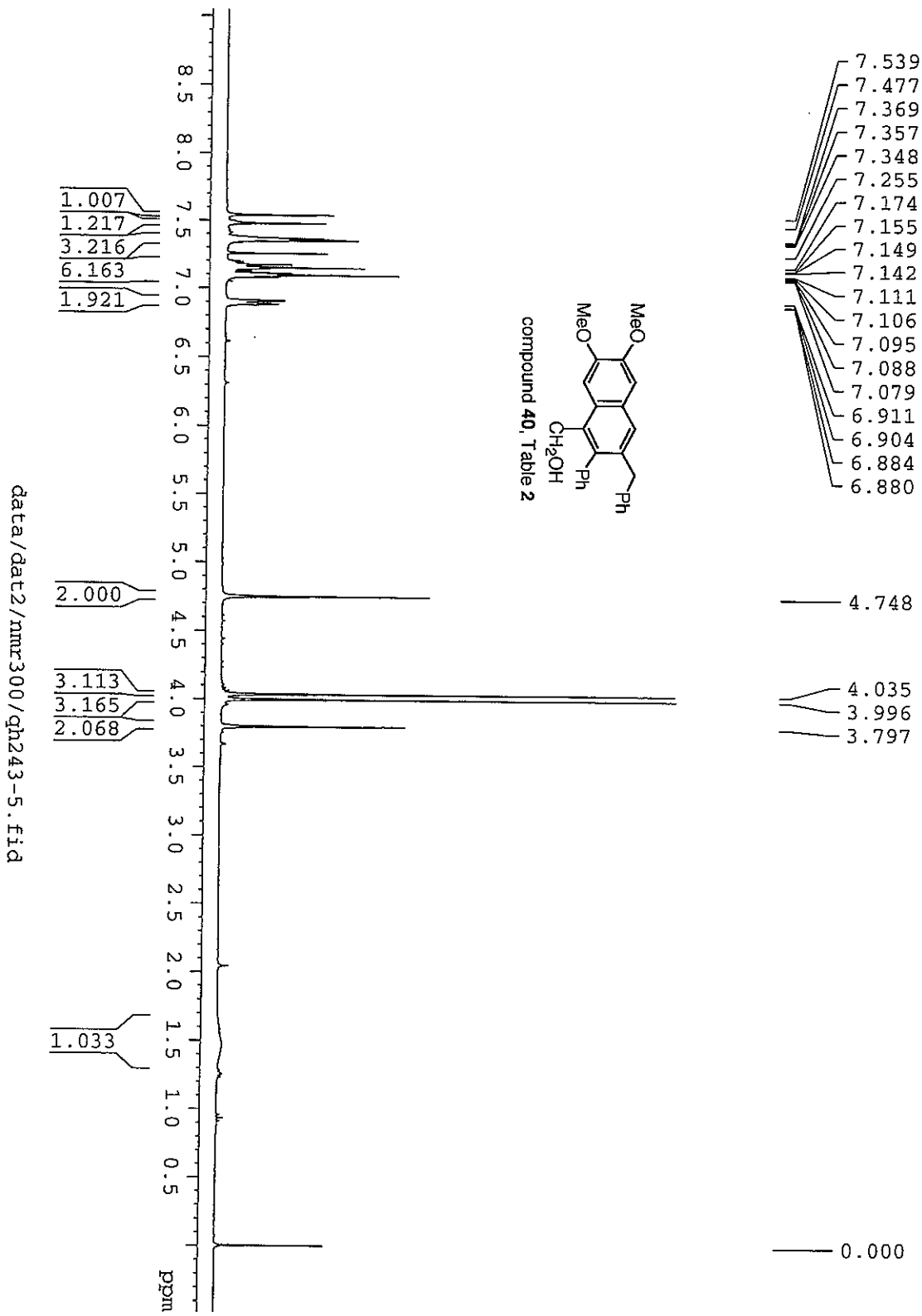
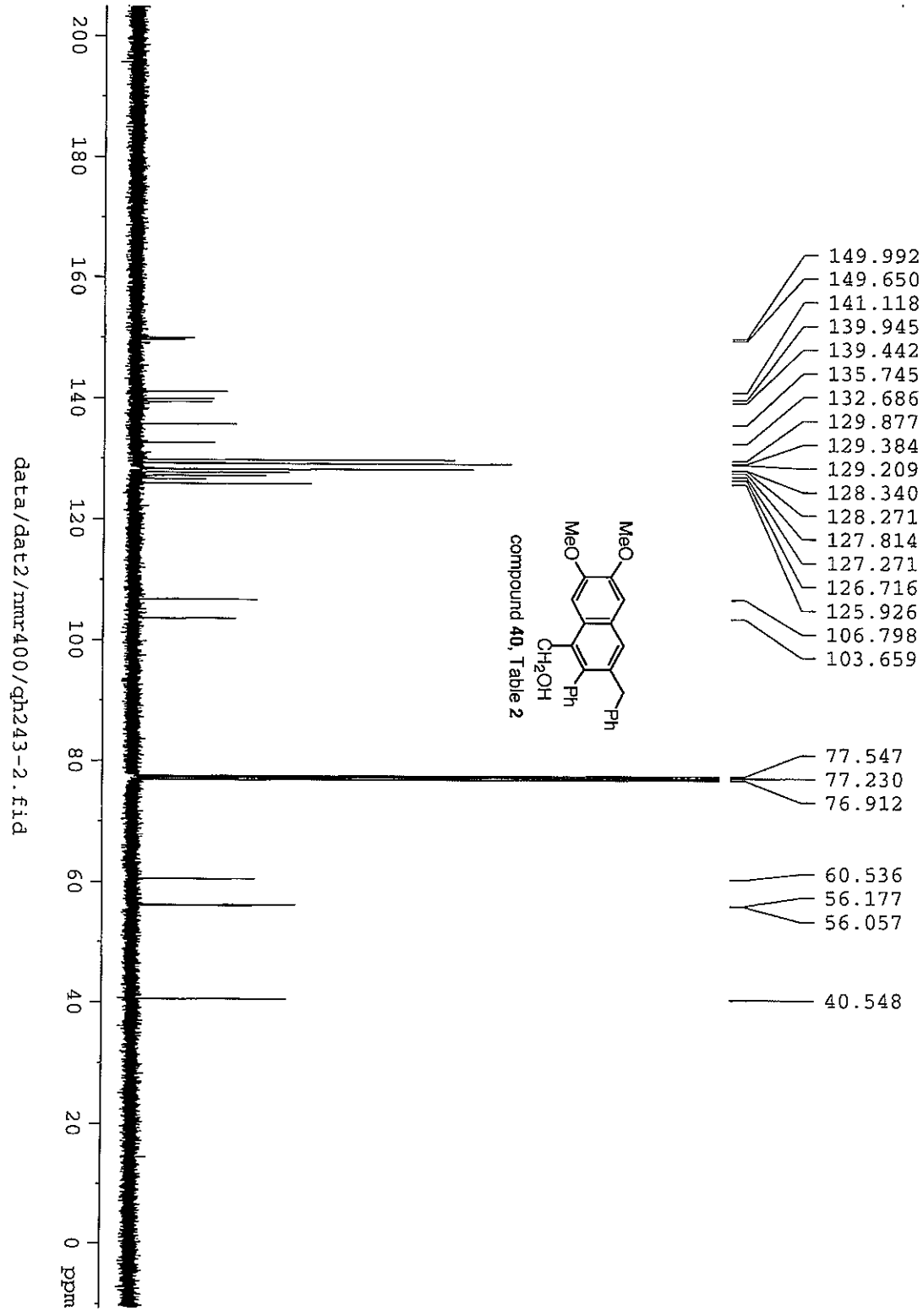
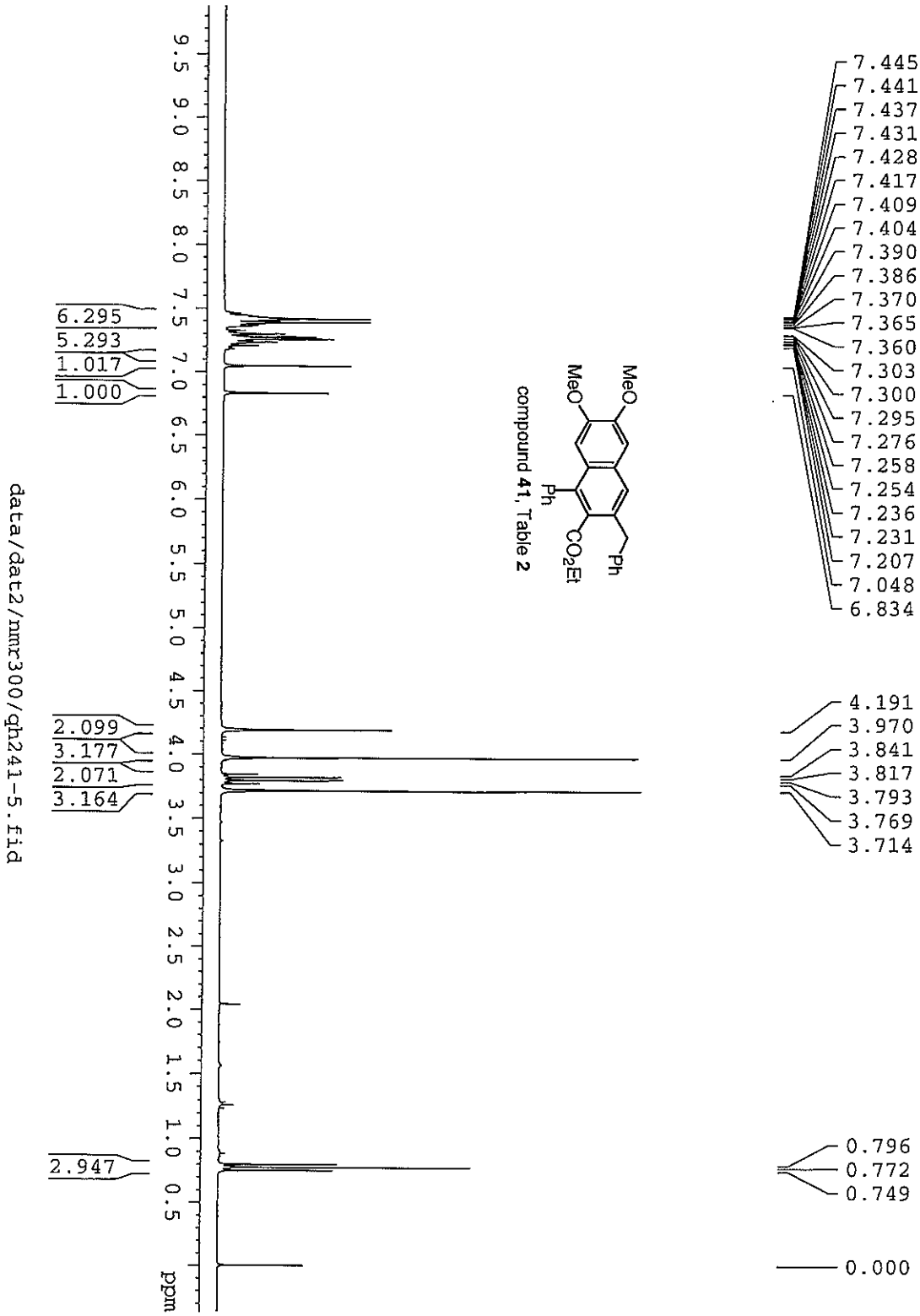
150.017
141.428
136.038
135.147
134.949
129.876
129.008
128.944
128.715
127.428
126.577
106.699
103.002
77.653
77.230
76.806
59.841
58.915
56.140
56.059
40.408
MeO
MeO
CH2OH
CH2OH
Ph
compound 39, Table 2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr300/qh240-6.fid


7.539
7.477
7.369
7.357
7.348
7.255
7.174
7.155
7.149
7.142
7.111
7.106
7.095
7.088
7.079
6.911
6.904
6.884
6.880
4.748
4.035
3.996
3.797
0.000
1.007
1.217
3.216
6.163
1.921
2.000
3.113
3.165
2.068
1.033
MeO
MeO
CH2OH
Ph
Ph
compound 40, Table 2
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/dat2/nmr300/qh243-5.fid


149.992
149.650
141.118
139.945
139.442
135.745
132.686
129.877
129.384
129.209
128.340
128.271
127.814
127.271
126.716
125.926
106.798
103.659
77.547
77.230
76.912
60.536
56.177
56.057
40.548
MeO
MeO
CH2OH
Ph
Ph
compound 40, Table 2
200
180
160
140
120
100
80
60
40
20
0 ppm
data/dat2/nmr400/qh243-2.fid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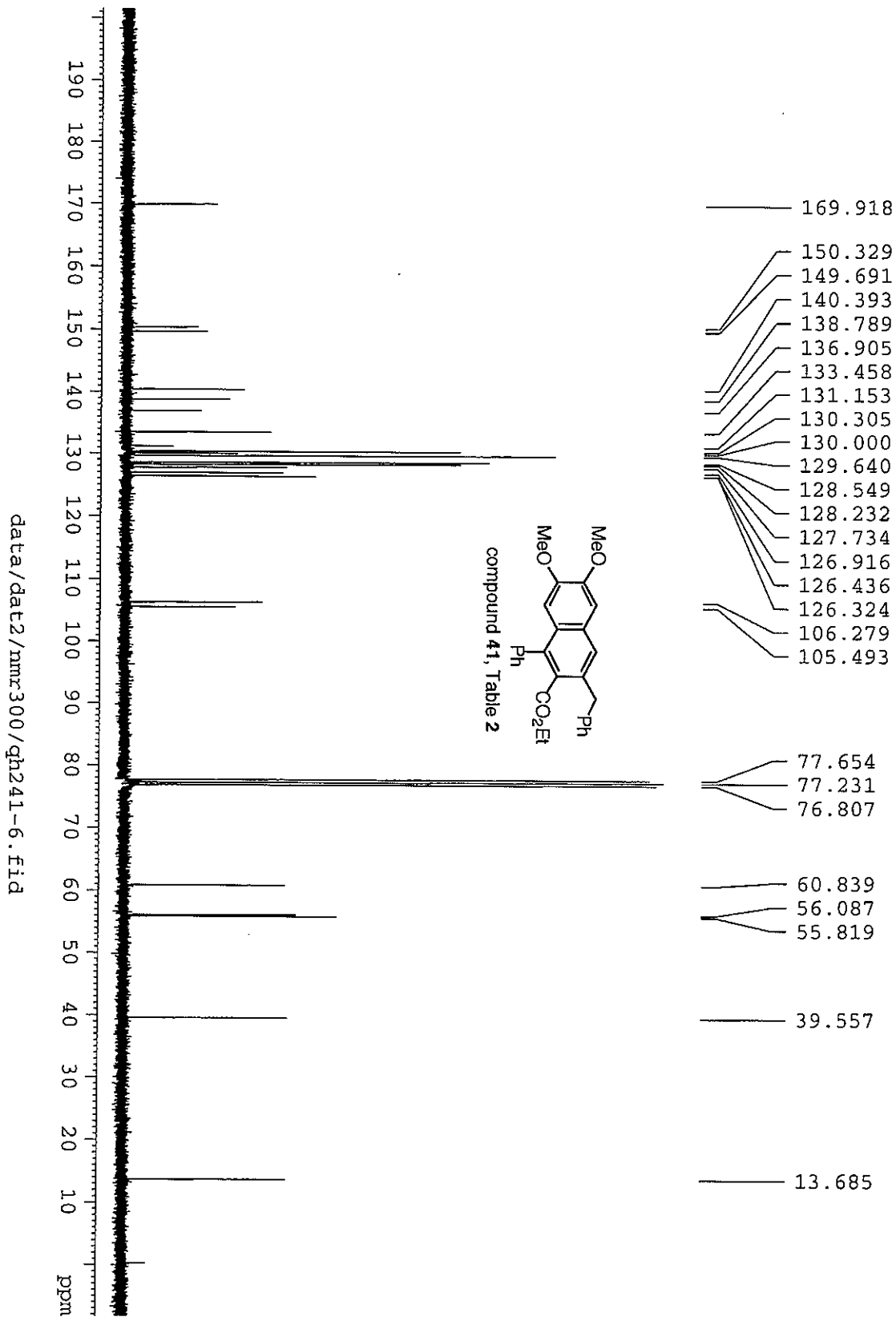
7.428
7.417
7.409
7.404
7.390
7.386
7.370
7.365
7.360
7.303
7.300
7.295
7.276
7.258
7.254
7.236
7.231
7.207
7.048
6.834
4.191
3.970
3.841
3.817
3.793
3.769
3.714
0.796
0.772
0.749
0.000
MeO
MeO
Ph
CO2Et
Ph
compound 41, Table 2
6.295
5.293
1.017
1.000
2.099
3.177
2.071
3.164
2.947
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/dat2/nmr300/qh241-5.fid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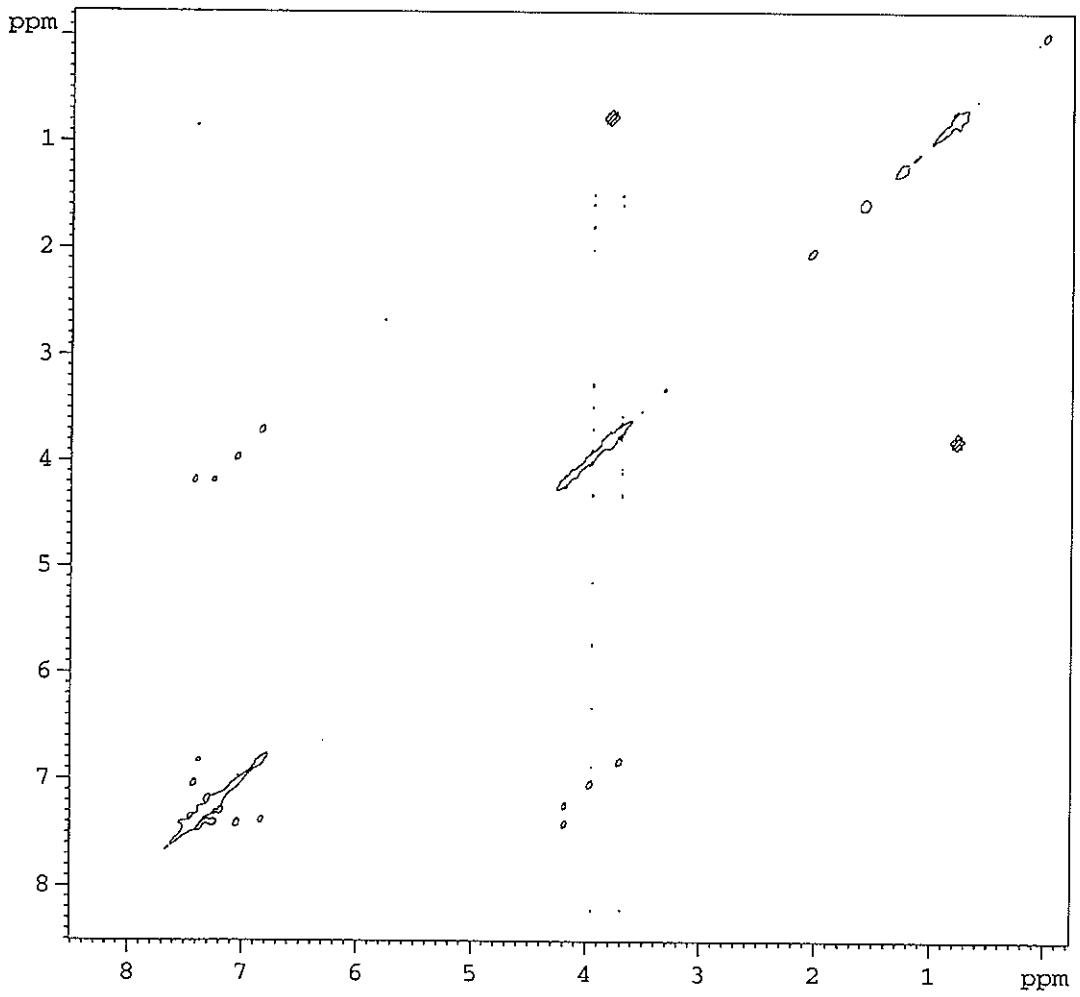
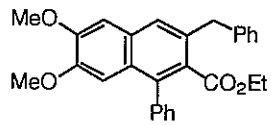
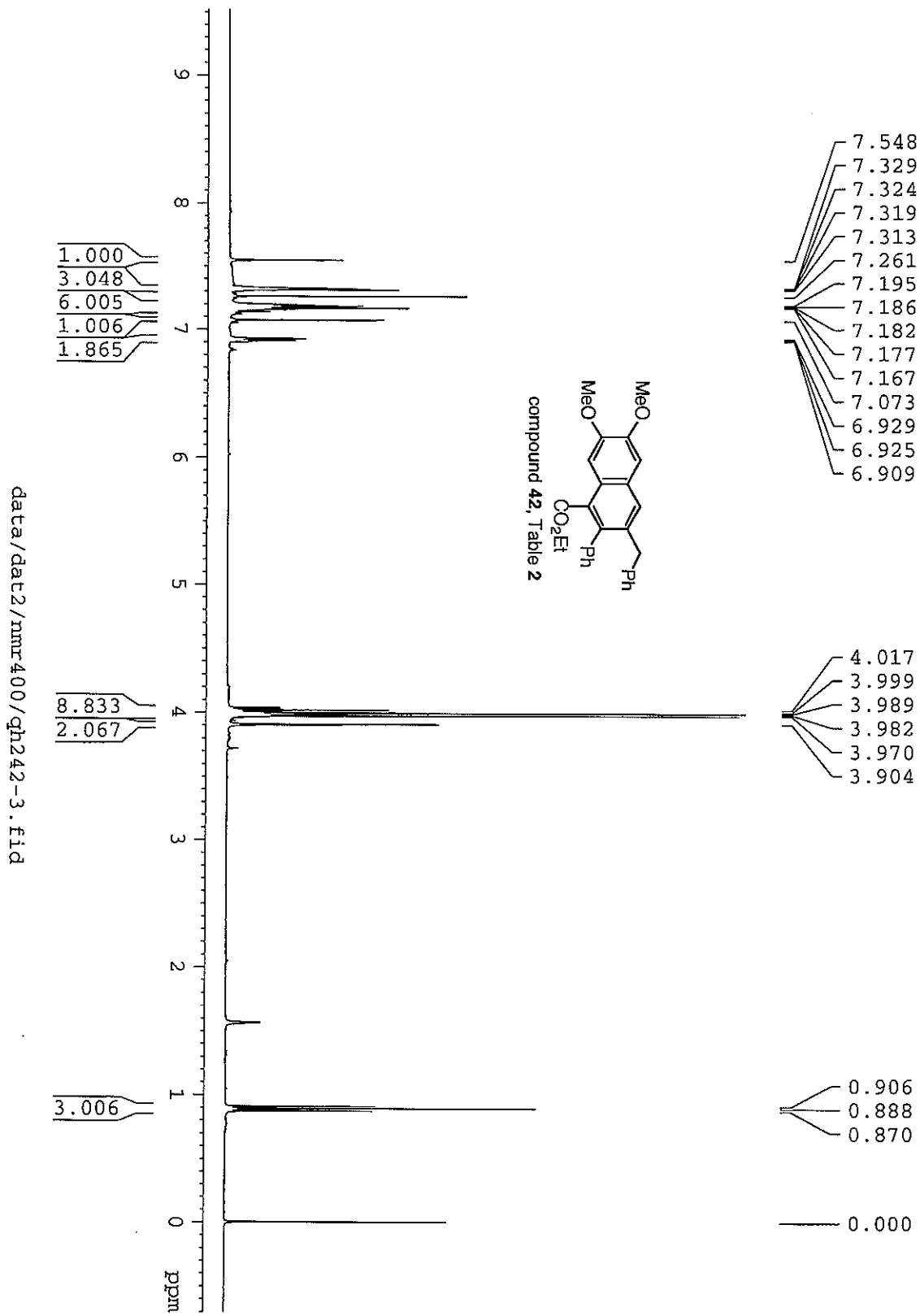
133.458
131.153
130.305
130.000
129.640
128.549
128.232
127.734
126.916
126.436
126.324
106.279
105.493
77.654
77.231
76.807
60.839
56.087
55.819
39.557
13.685
MeO
MeO
Ph
CO2Et
Ph
compound 41, Table 2
ppm
data/dat2/nmr300/qh241-6.fid



data/drx1/nmr400/qh241-4D



compound **41**, Table **2**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compound 42, Table 2
MeO
MeO
CO2Et
Ph
Ph
1.000
3.048
6.005
1.006
1.865
8.833
2.067
3.006
7.548
7.329
7.324
7.319
7.313
7.261
7.195
7.186
7.182
7.177
7.167
7.073
6.929
6.925
6.909
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3.999
3.989
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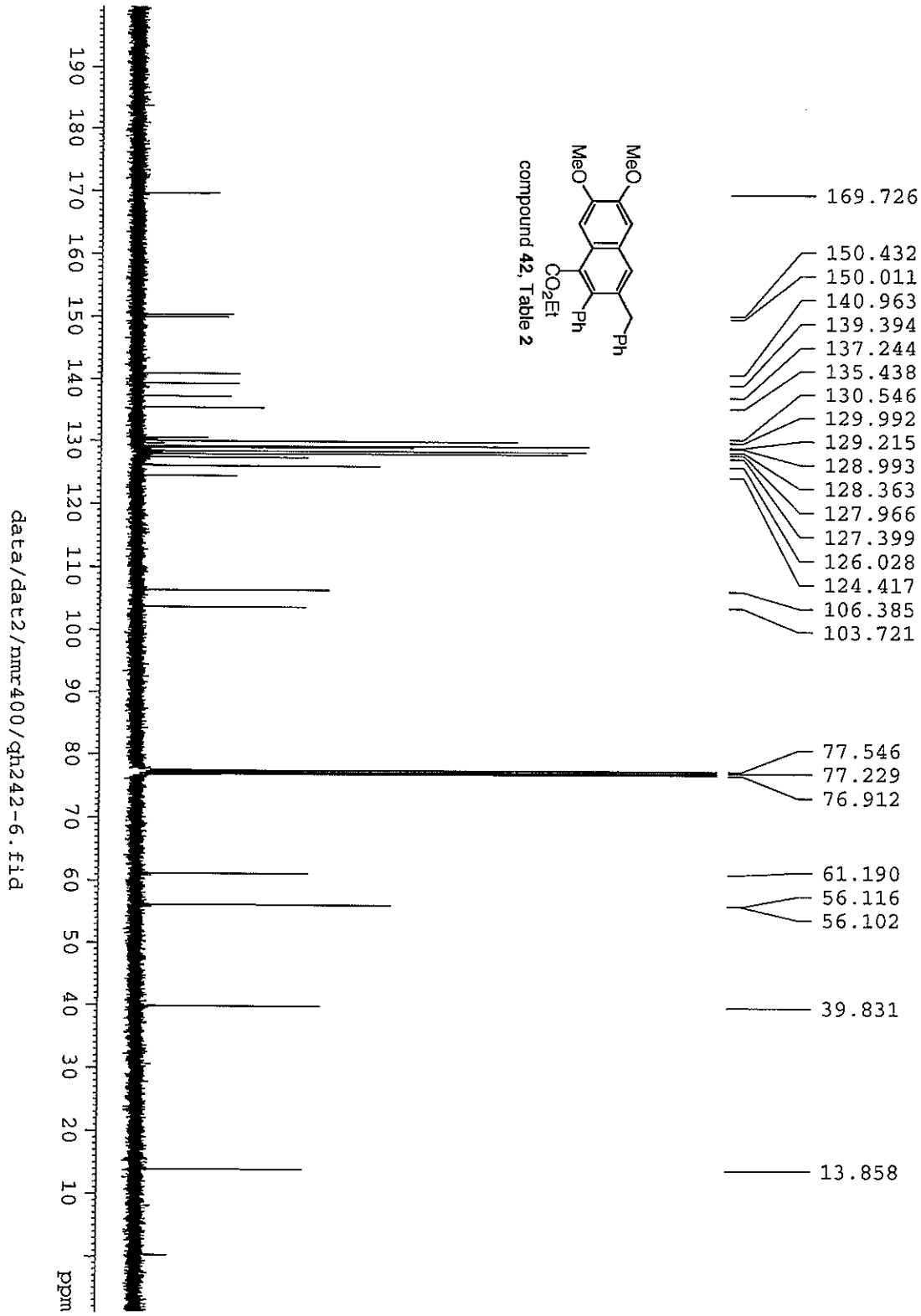
3.970
3.904
0.906
0.888
0.870
0.000
ppm


MeO
MeO
CO2Et
Ph
Ph
compound 42, Table 2
169.726
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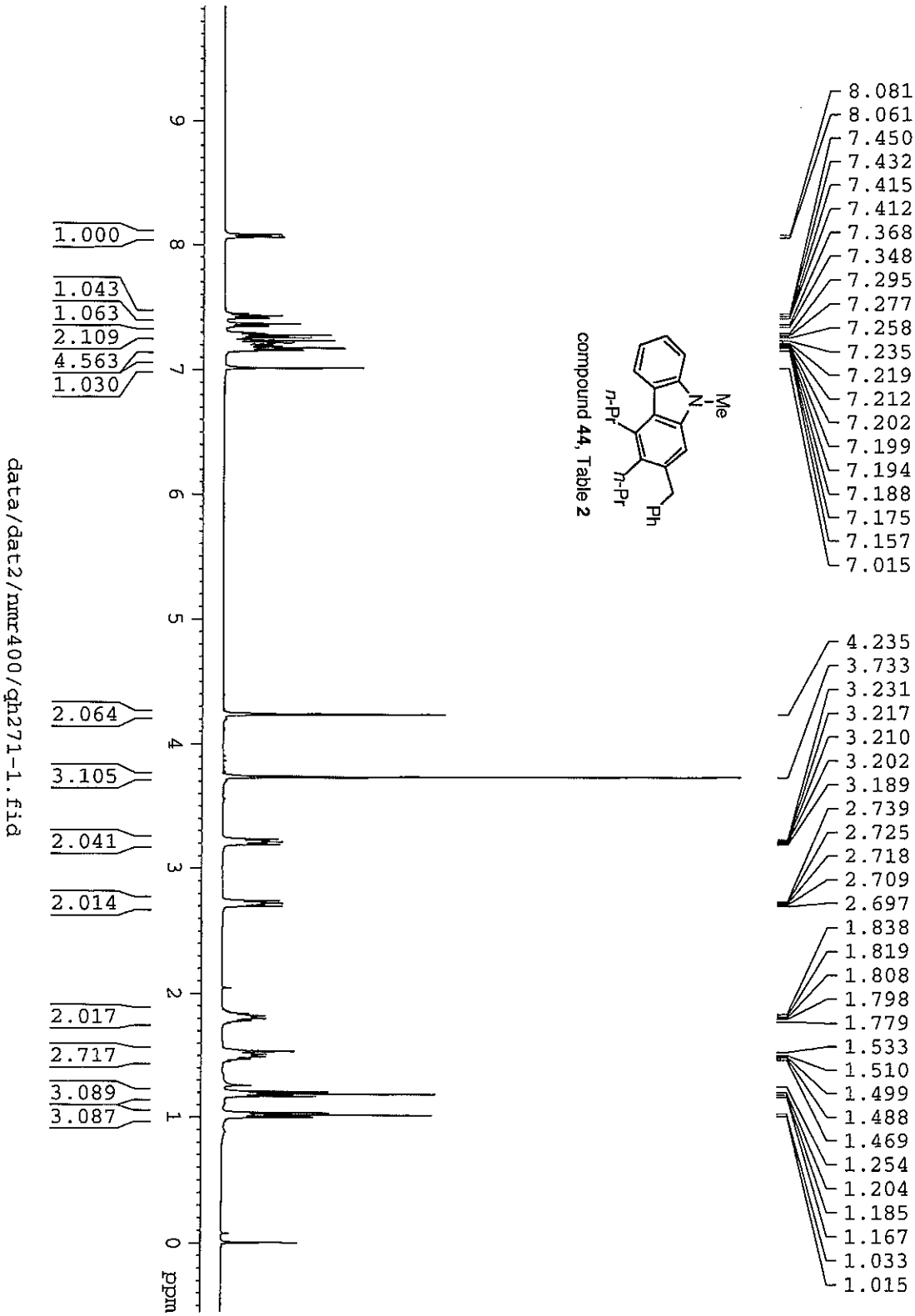
150.011
140.963
139.394
137.244
135.438
130.546
129.992
129.215
128.993
128.363
127.966
127.399
126.028
124.417
106.385
103.721
77.546
77.229
76.912
61.190
56.116
56.102
39.831
13.858
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm
data/dat2/nmr400/qh242-6.fid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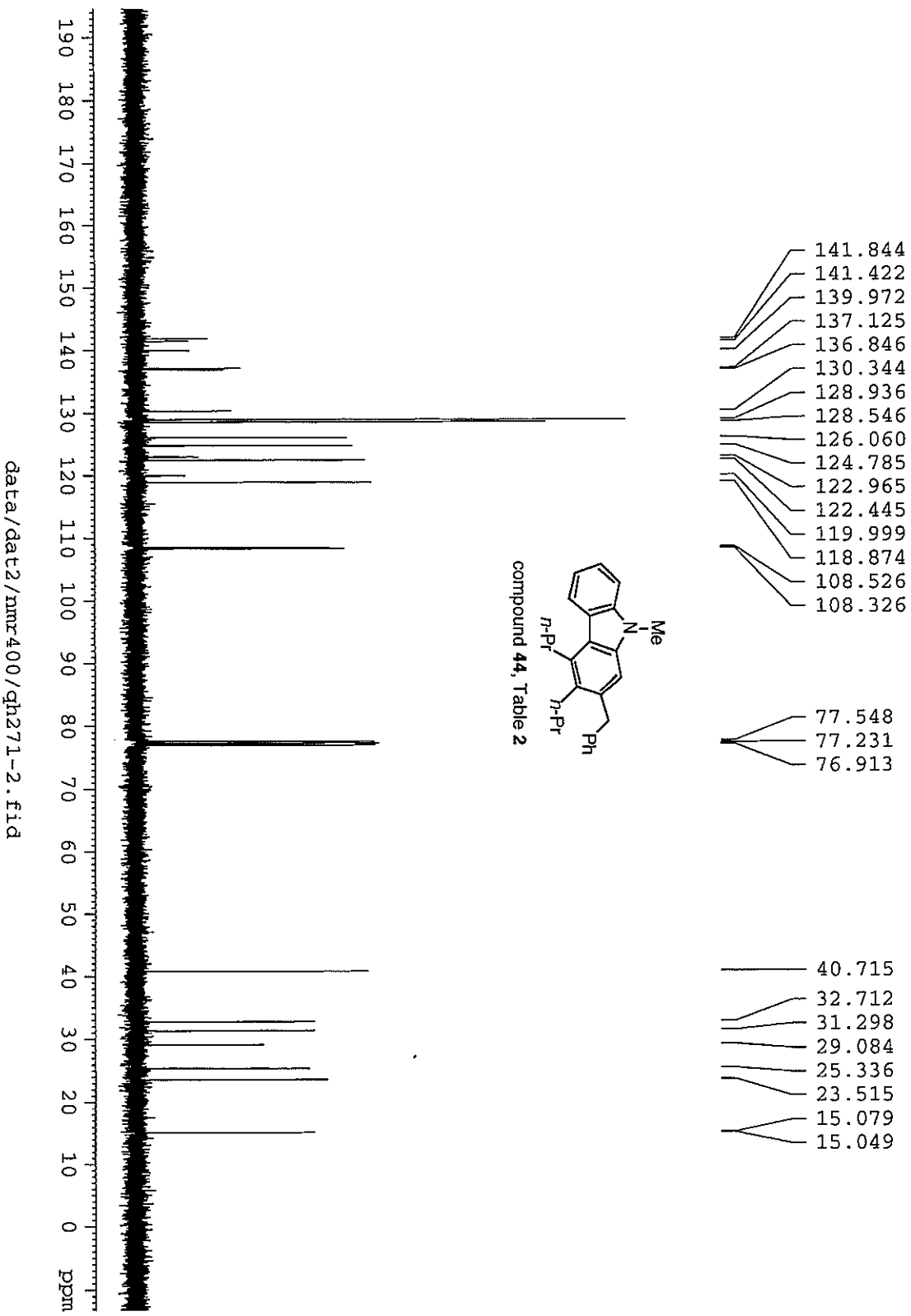
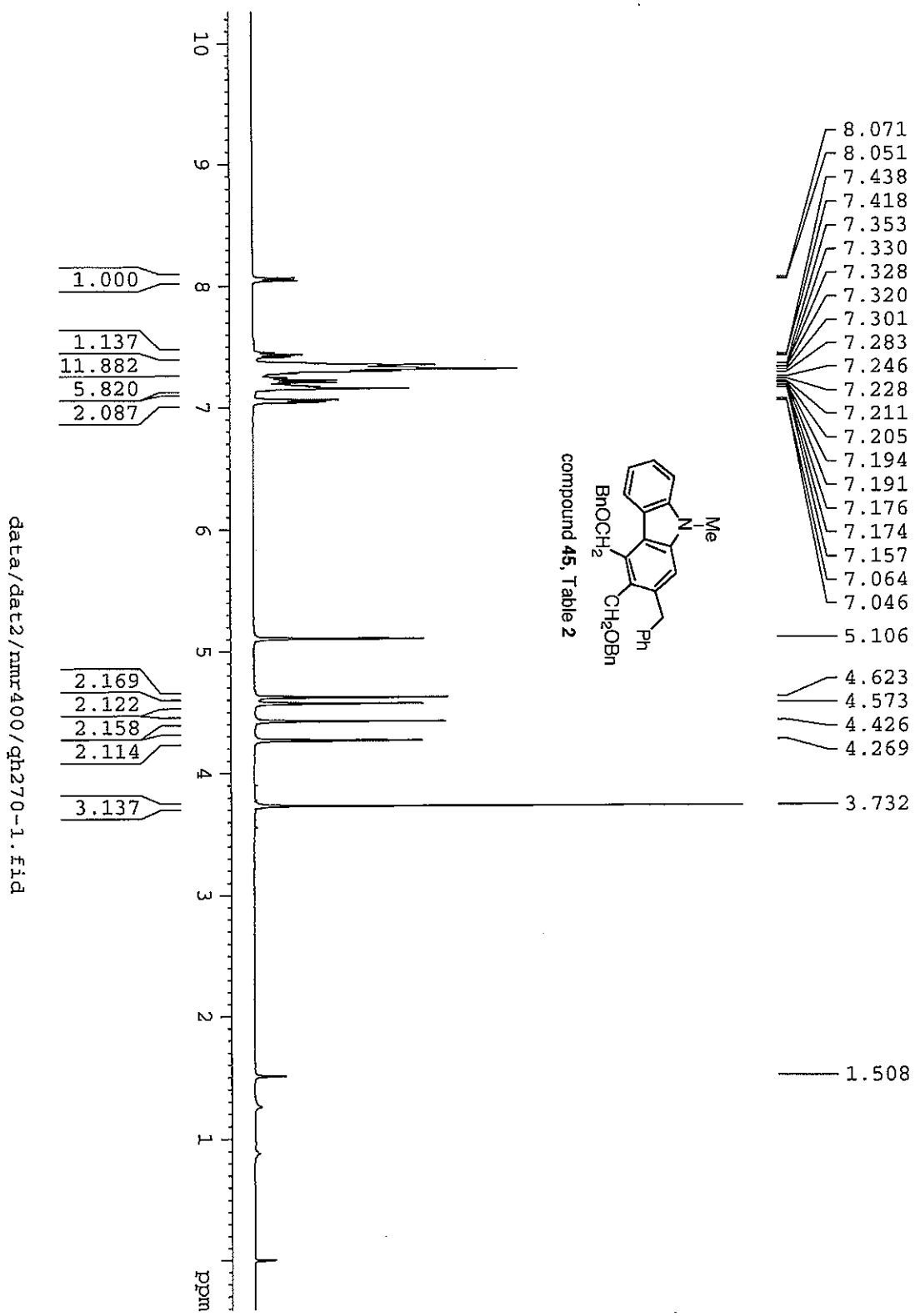
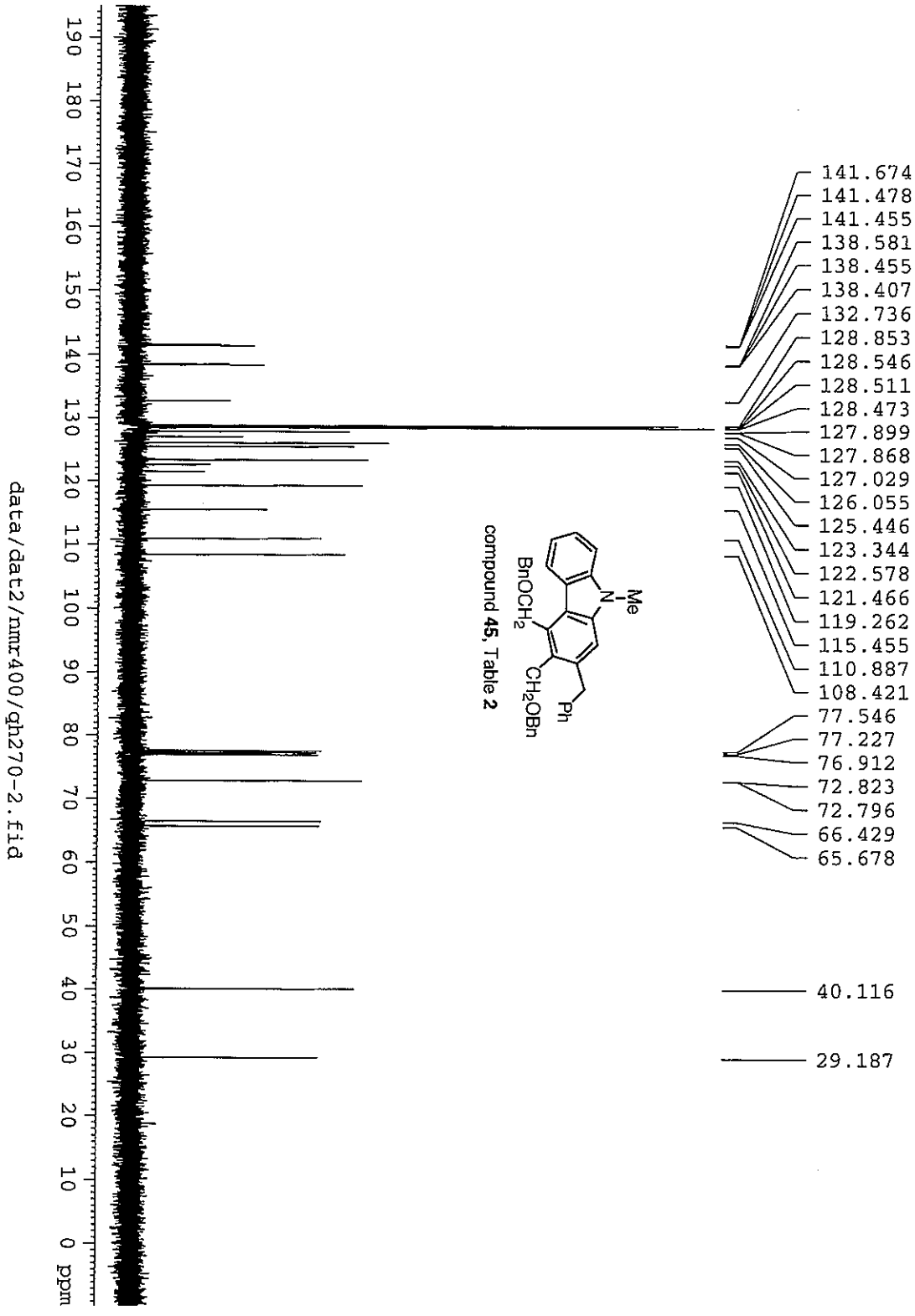
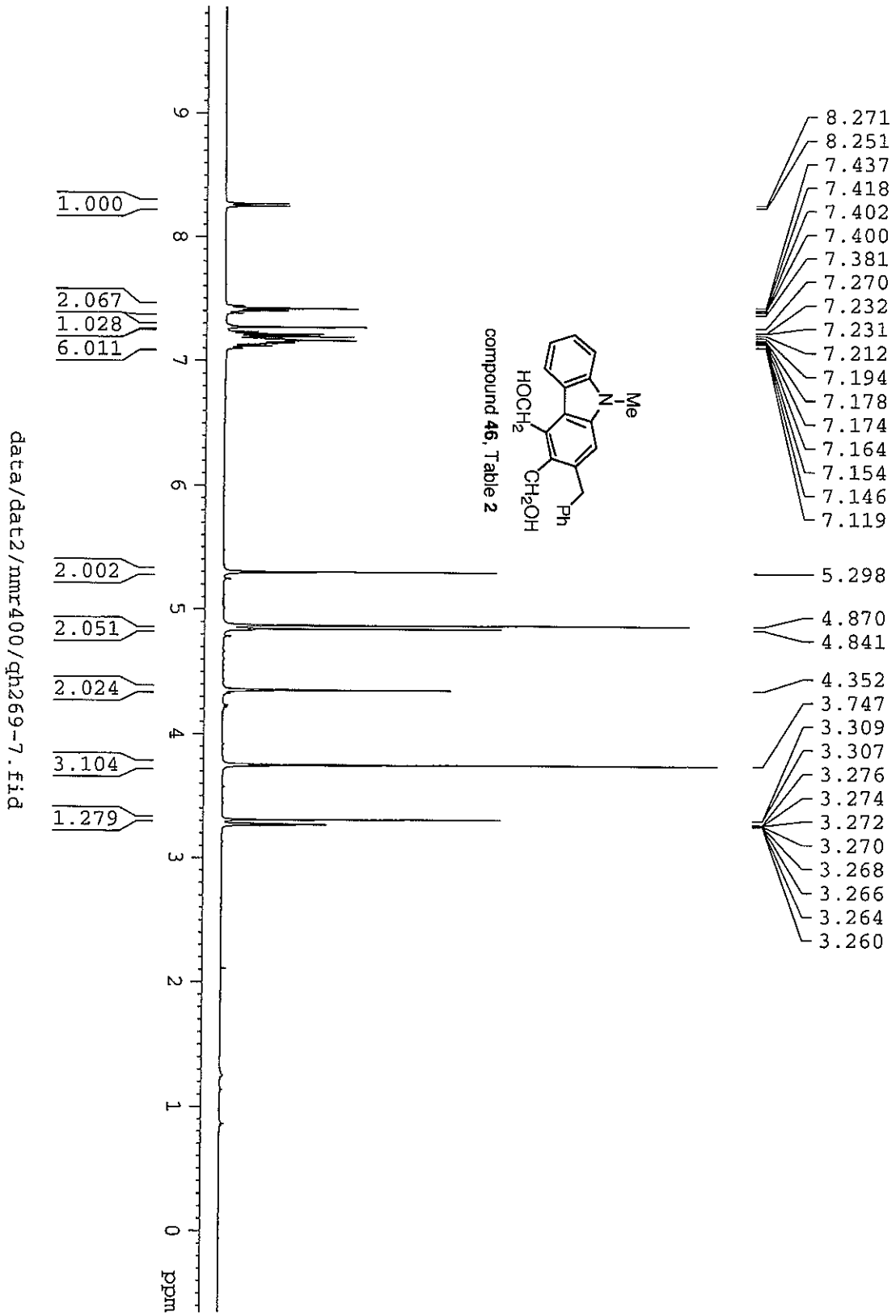
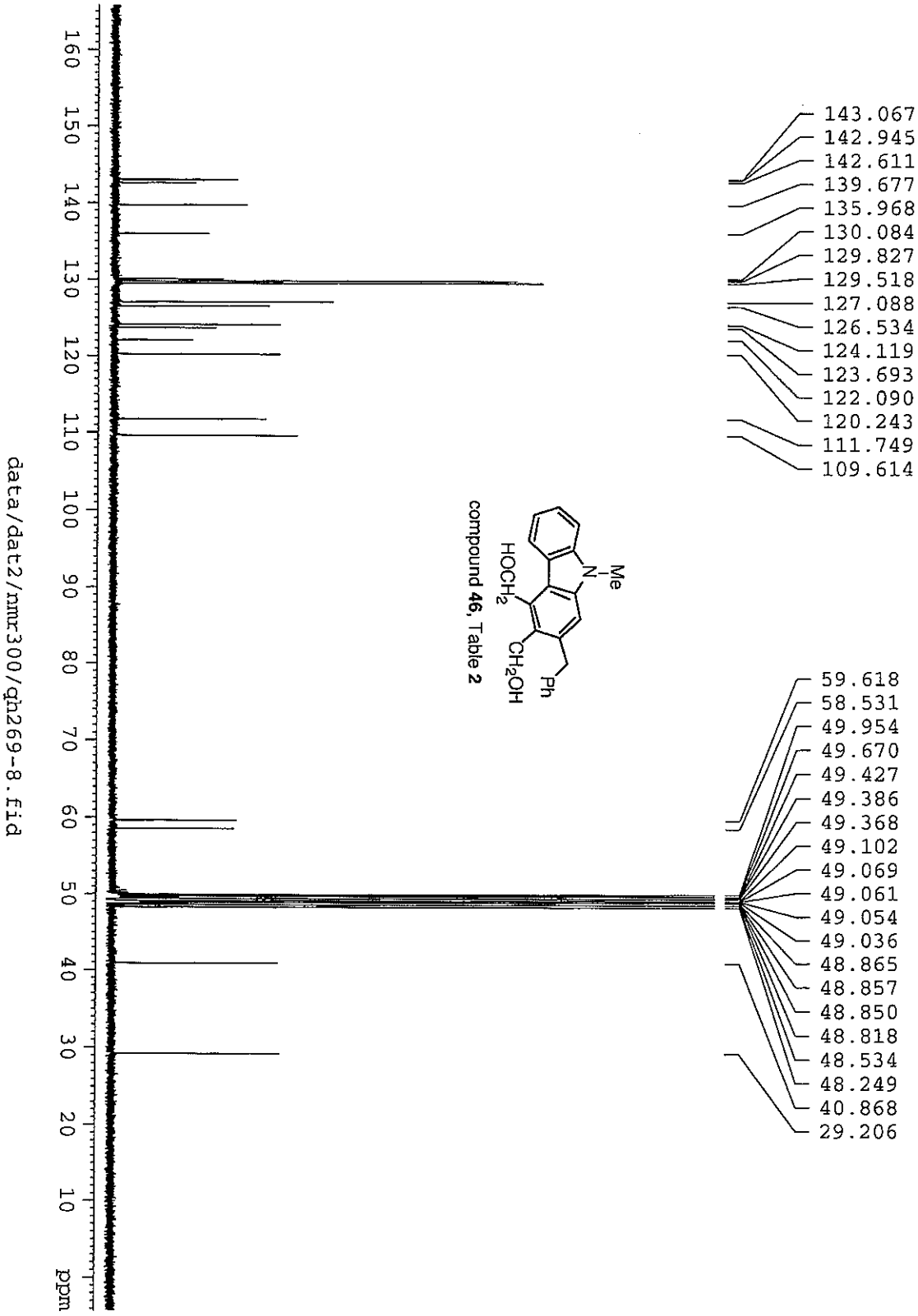
compound 44, Table 2
n-Pr
n-Pr
N
Me
Ph
1.000
1.043
1.063
2.109
4.563
1.030
2.064
3.105
2.041
2.014
2.017
2.717
3.089
3.087
8.081
8.061
7.450
7.432
7.415
7.412
7.368
7.348
7.295
7.277
7.258
7.235
7.219
7.212
7.202
7.199
7.194
7.188
7.175
7.157
7.015
4.235
3.733
3.231
3.217
3.210
3.202
3.189
2.739
2.725
2.718
2.709
2.697
1.838
1.819
1.808
1.798
1.779
1.533
1.510
1.499
1.488
1.469
1.254
1.204
1.185
1.167
1.033
1.015
ppm

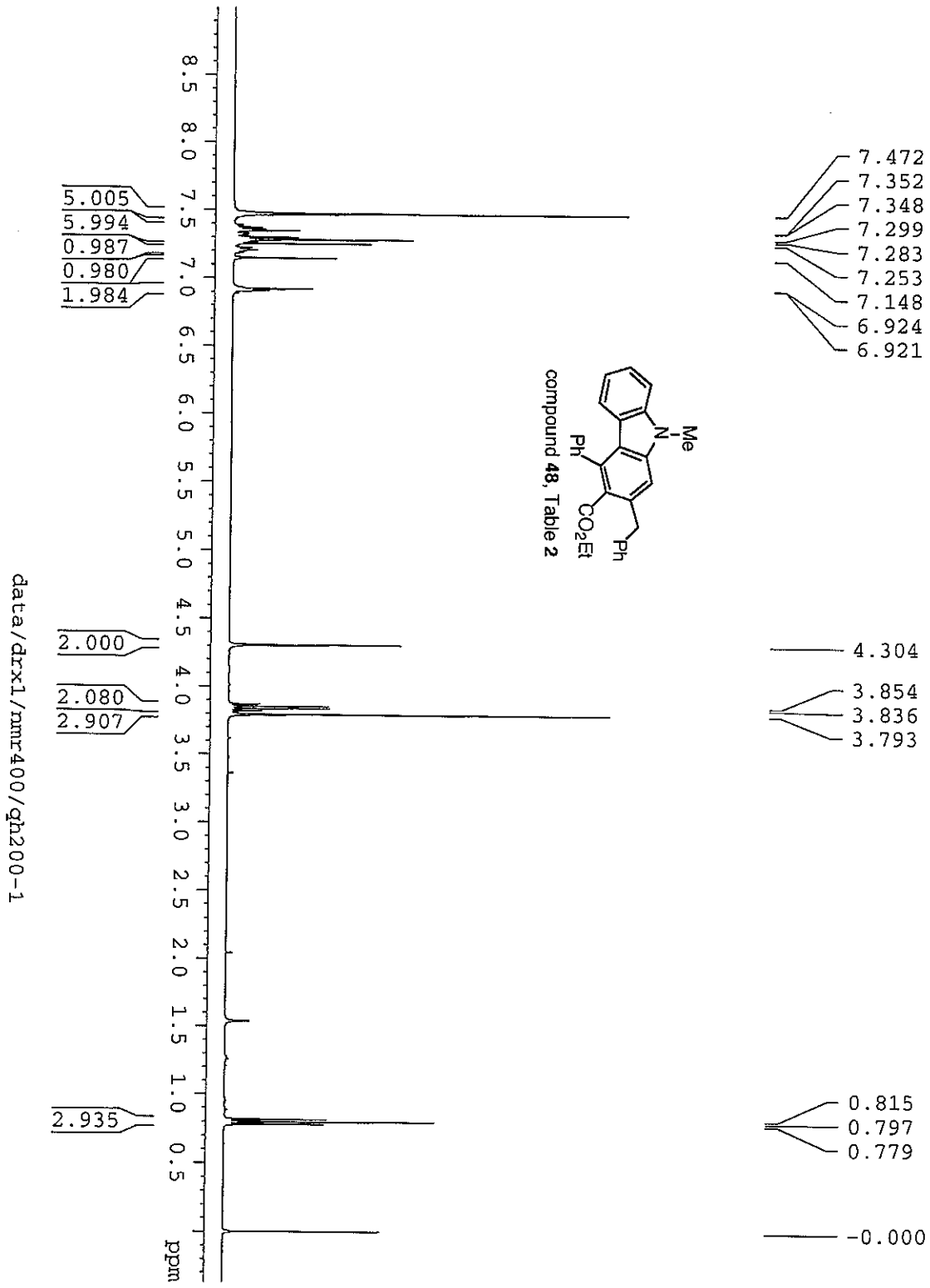

141.844
141.422
139.972
137.125
136.846
130.344
128.936
128.546
126.060
124.785
122.965
122.445
119.999
118.874
108.526
108.326
77.548
77.231
76.913
40.715
32.712
31.298
29.084
25.336
23.515
15.079
15.049
Me
N
n-Pr
n-Pr
Ph
compound 44, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh271-2.fid

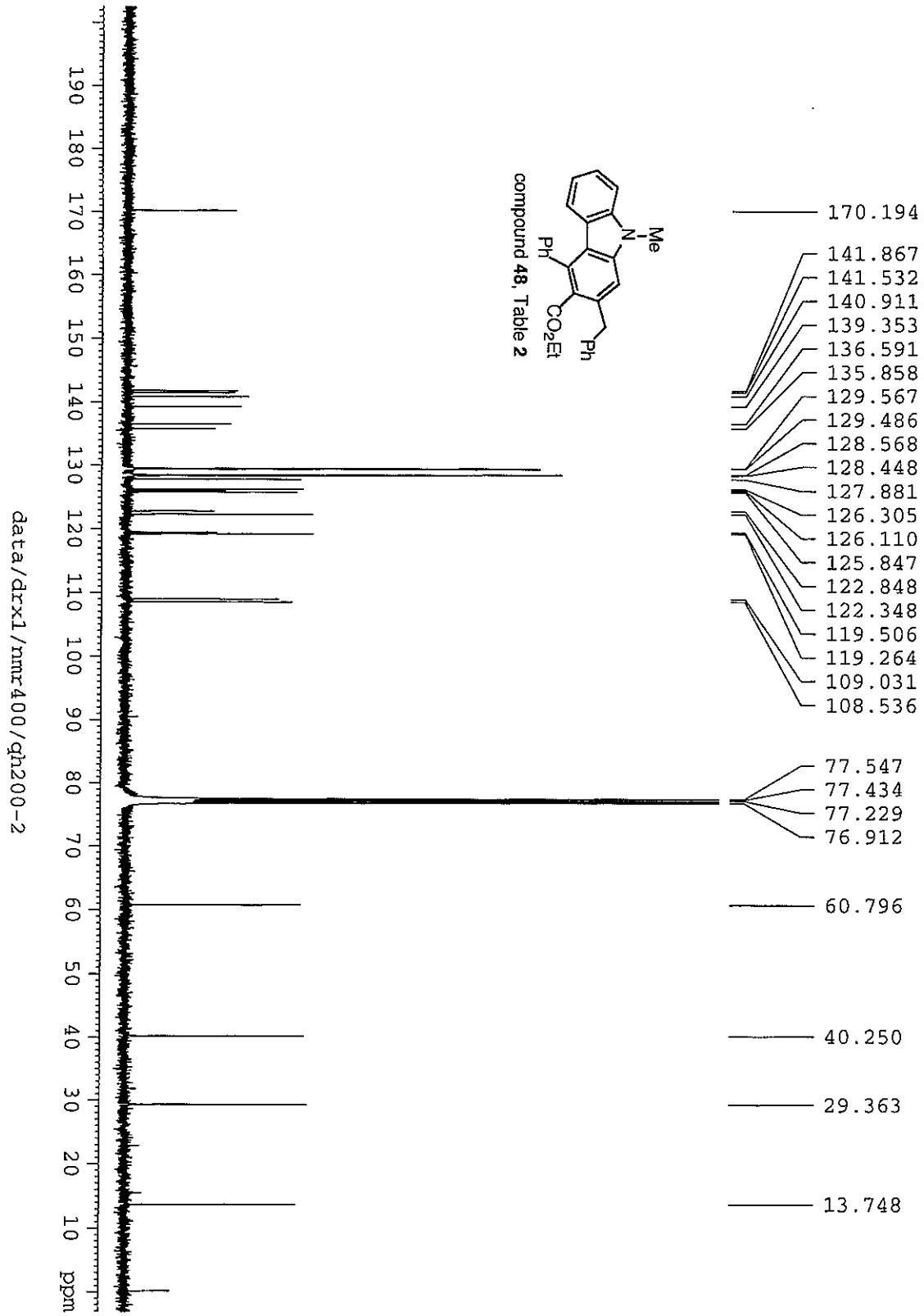

8.071
8.051
7.438
7.418
7.353
7.330
7.328
7.320
7.301
7.283
7.246
7.228
7.211
7.205
7.194
7.191
7.176
7.174
7.157
7.064
7.046
5.106
4.623
4.573
4.426
4.269
3.732
1.508
1.000
1.137
11.882
5.820
2.087
2.169
2.122
2.158
2.114
3.137
Me
N
BnOCH2
CH2OBn
Ph
compound 45, Table 2
data/dat2/nmr400/qh270-1.fid
ppm

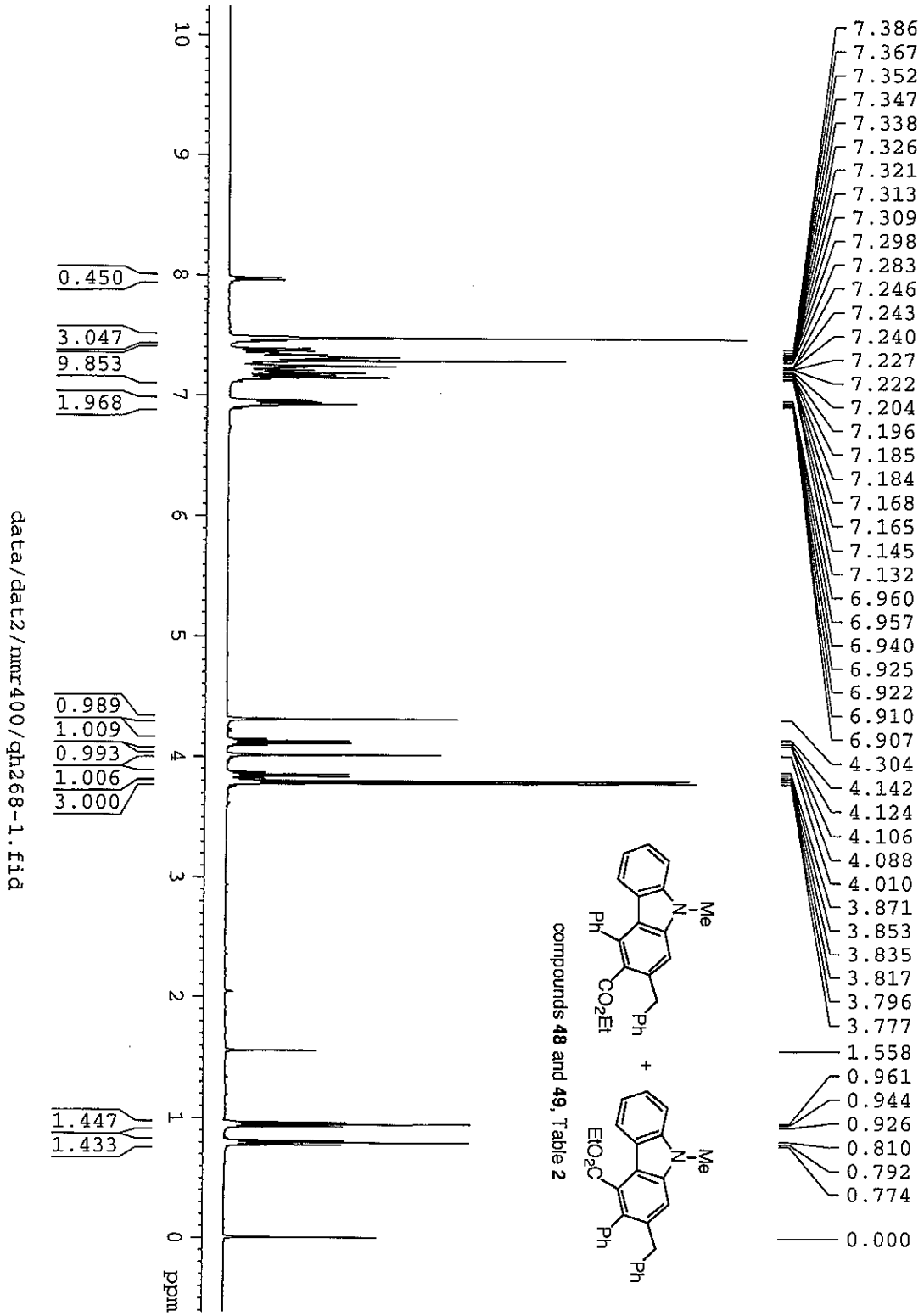

141.674
141.478
141.455
138.581
138.455
138.407
132.736
128.853
128.546
128.511
128.473
127.899
127.868
127.029
126.055
125.446
123.344
122.578
121.466
119.262
115.455
110.887
108.421
77.546
77.227
76.912
72.823
72.796
66.429
65.678
40.116
29.187
Me
N
BnOCH2
CH2OBn
Ph
compound 45, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh270-2.fid

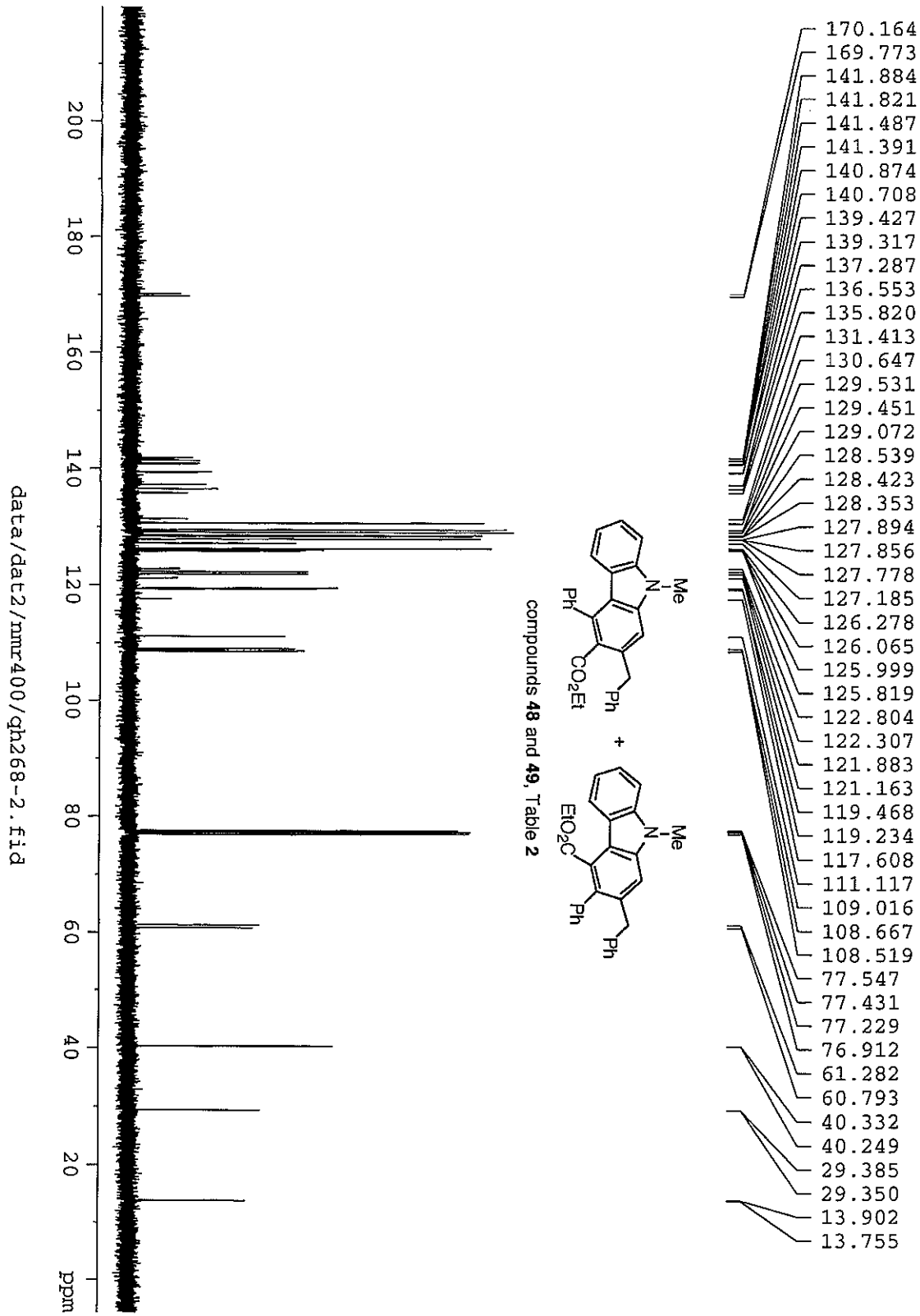

data/dat2/nmr400/qh269-7.fid
compound 46, Table 2
HOCH2
Me
N
CH2OH
Ph
1.000
2.067
1.028
6.011
2.002
2.051
2.024
3.104
1.279
8.271
8.251
7.437
7.418
7.402
7.400
7.381
7.270
7.232
7.231
7.212
7.194
7.178
7.174
7.164
7.154
7.146
7.119
5.298
4.870
4.841
4.352
3.747
3.309
3.307
3.276
3.274
3.272
3.270
3.268
3.266
3.264
3.260
ppm

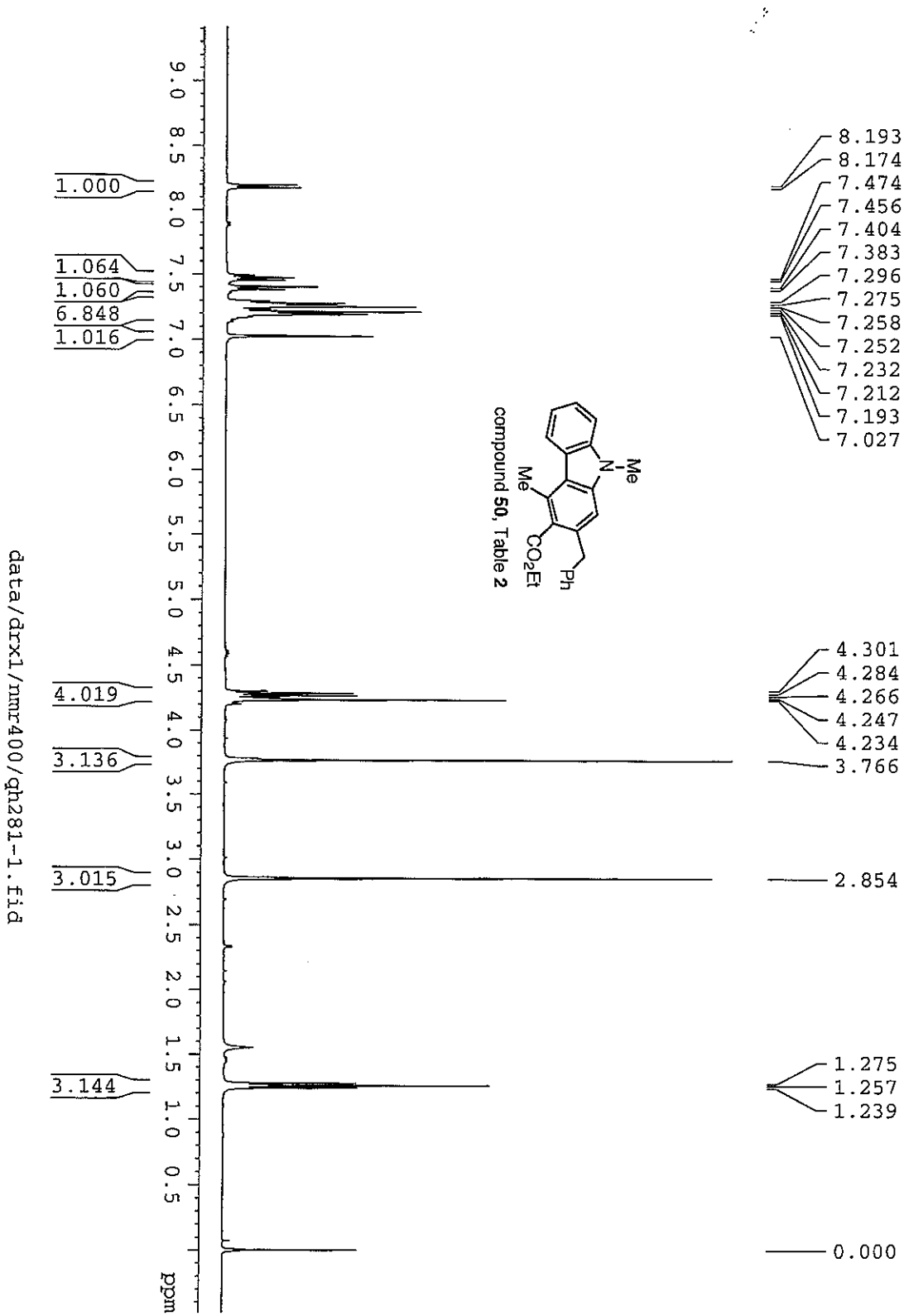

143.067
142.945
142.611
139.677
135.968
130.084
129.827
129.518
127.088
126.534
124.119
123.693
122.090
120.243
111.749
109.614
59.618
58.531
49.954
49.670
49.427
49.386
49.368
49.102
49.069
49.061
49.054
49.036
48.865
48.857
48.850
48.818
48.534
48.249
40.868
29.206
Me
N
HOCH2
CH2OH
Ph
compound 46, Table 2
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh269-8.fid

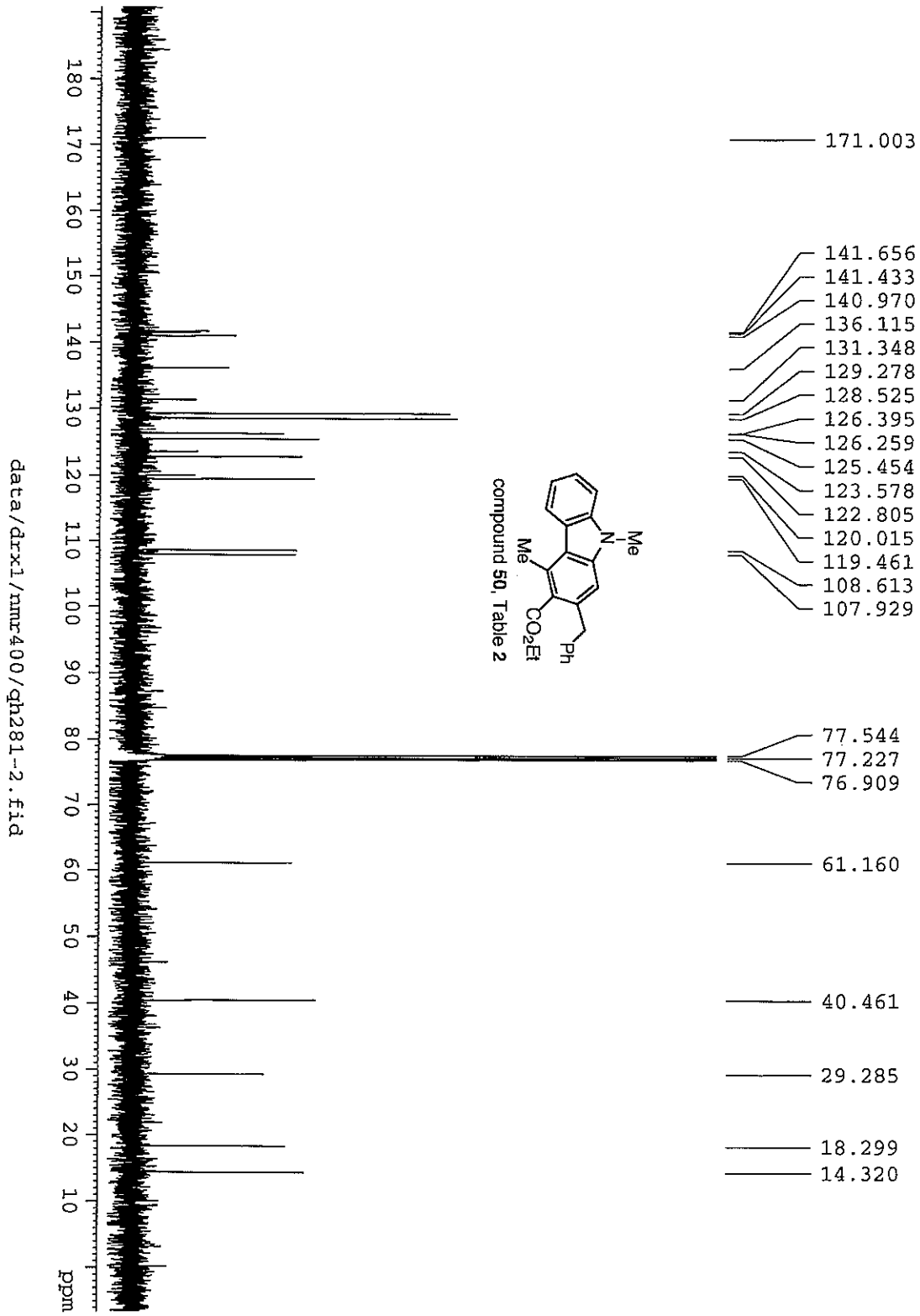

7.472
7.352
7.348
7.299
7.283
7.253
7.148
6.924
6.921
4.304
3.854
3.836
3.793
0.815
0.797
0.779
-0.000
5.005
5.994
0.987
0.980
1.984
2.000
2.080
2.907
2.935
Me
N
Ph
CO2Et
Ph
compound 48, Table 2
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/drx1/nmr400/qh200-1

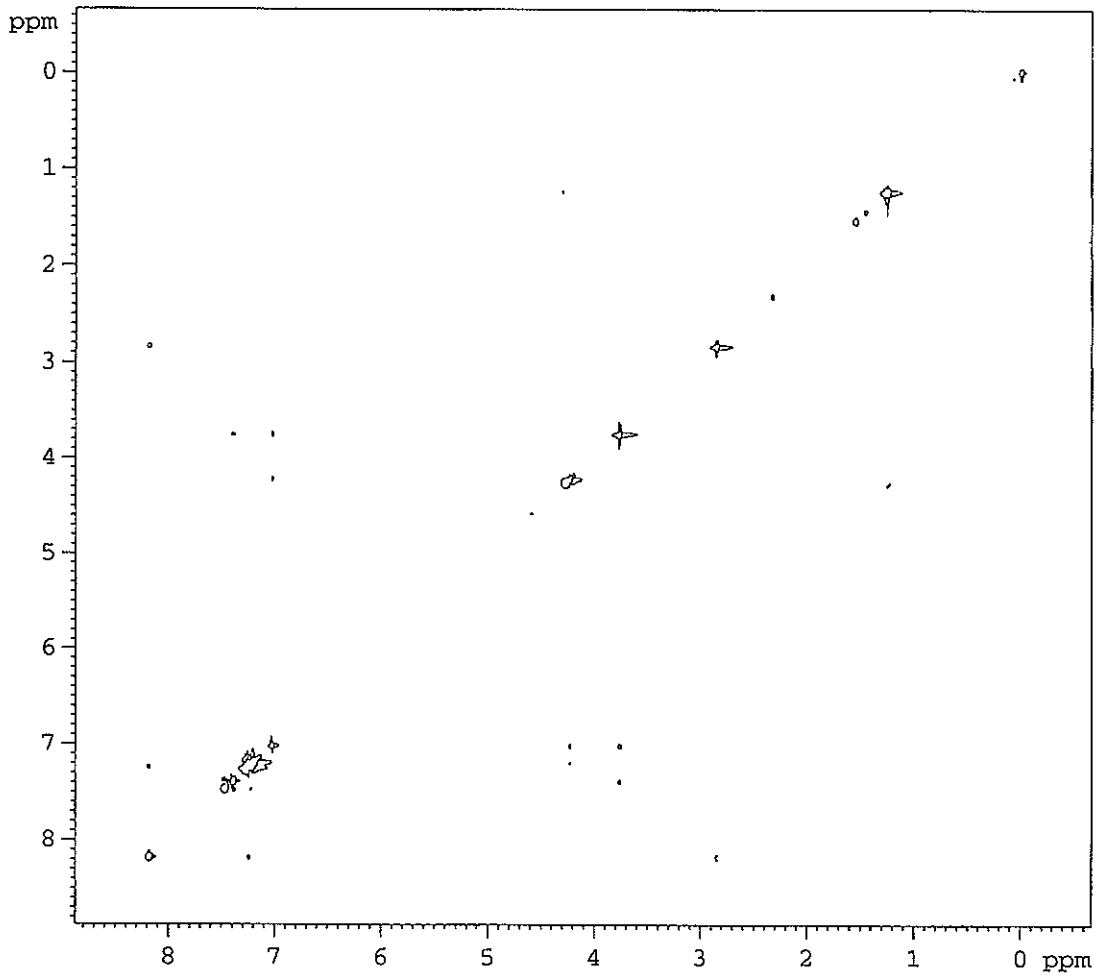

compound 48, Table 2
Me
N
Ph
CO2Et
Ph
170.194
141.867
141.532
140.911
139.353
136.591
135.858
129.567
129.486
128.568
128.448
127.881
126.305
126.110
125.847
122.848
122.348
119.506
119.264
109.031
108.536
77.547
77.434
77.229
76.912
60.796
40.250
29.363
13.748
ppm
data/drx1/nmr400/qh200-2

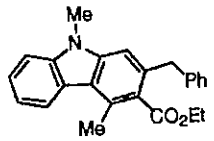

7.386
7.367
7.352
7.347
7.338
7.326
7.321
7.313
7.309
7.298
7.283
7.246
7.243
7.240
7.227
7.222
7.204
7.196
7.185
7.184
7.168
7.165
7.145
7.132
6.960
6.957
6.940
6.925
6.922
6.910
6.907
4.304
4.142
4.124
4.106
4.088
4.010
3.871
3.853
3.835
3.817
3.796
3.777
1.558
0.961
0.944
0.926
0.810
0.792
0.774
0.000
0.450
3.047
9.853
1.968
0.989
1.009
0.993
1.006
3.000
1.447
1.433
10
9
8
7
6
5
4
3
2
1
0
ppm
Me
N
Ph
CO2Et
Ph
+
Me
N
EtO2C
Ph
Ph
compounds 48 and 49, Table 2
data/dat2/nmr400/qh268-1.fid


170.164
169.773
141.884
141.821
141.487
141.391
140.874
140.708
139.427
139.317
137.287
136.553
135.820
131.413
130.647
129.531
129.451
129.072
128.539
128.423
128.353
127.894
127.856
127.778
127.185
126.278
126.065
125.999
125.819
122.804
122.307
121.883
121.163
119.468
119.234
117.608
111.117
109.016
108.667
108.519
77.547
77.431
77.229
76.912
61.282
60.793
40.332
40.249
29.385
29.350
13.902
13.755
Me
N
Ph
CO2Et
Ph
+
Me
N
EtO2C
Ph
Ph
compounds 48 and 49, Table 2
200
180
160
140
120
100
80
60
40
20
ppm
data/dat2/nmr400/qh268-2.fid


8.193
8.174
7.474
7.456
7.404
7.383
7.296
7.275
7.258
7.252
7.232
7.212
7.193
7.027
4.301
4.284
4.266
4.247
4.234
3.766
2.854
1.275
1.257
1.239
0.000
1.000
1.064
1.060
6.848
1.016
4.019
3.136
3.015
3.144
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
Me
N
Me
CO2Et
Ph
compound 50, Table 2
data/drx1/nmr400/qh281-1.fid

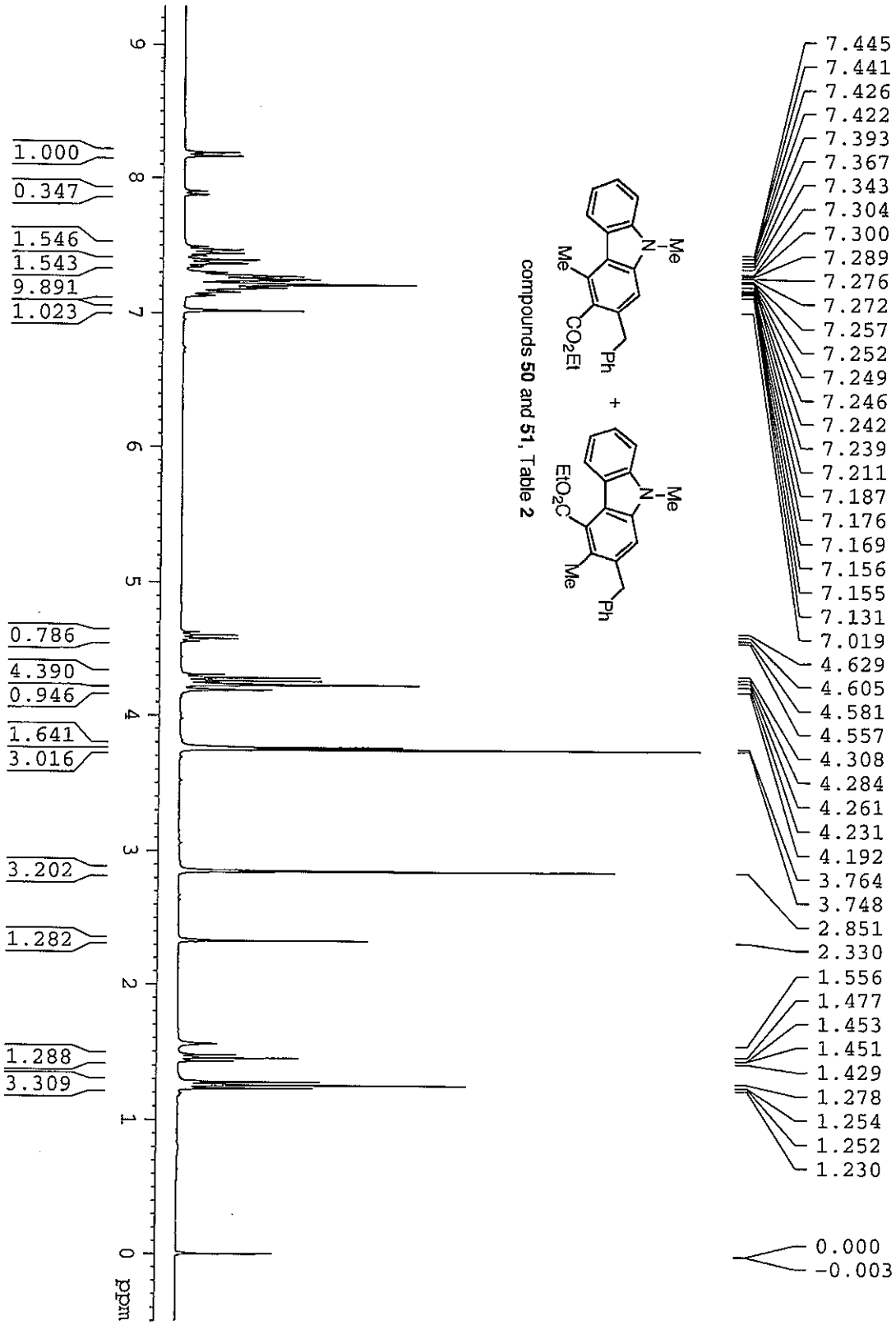

171.003
141.656
141.433
140.970
136.115
131.348
129.278
128.525
126.395
126.259
125.454
123.578
122.805
120.015
119.461
108.613
107.929
77.544
77.227
76.909
61.160
40.461
29.285
18.299
14.320
Me
N
Me
CO2Et
Ph
compound 50, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh281-2.fid

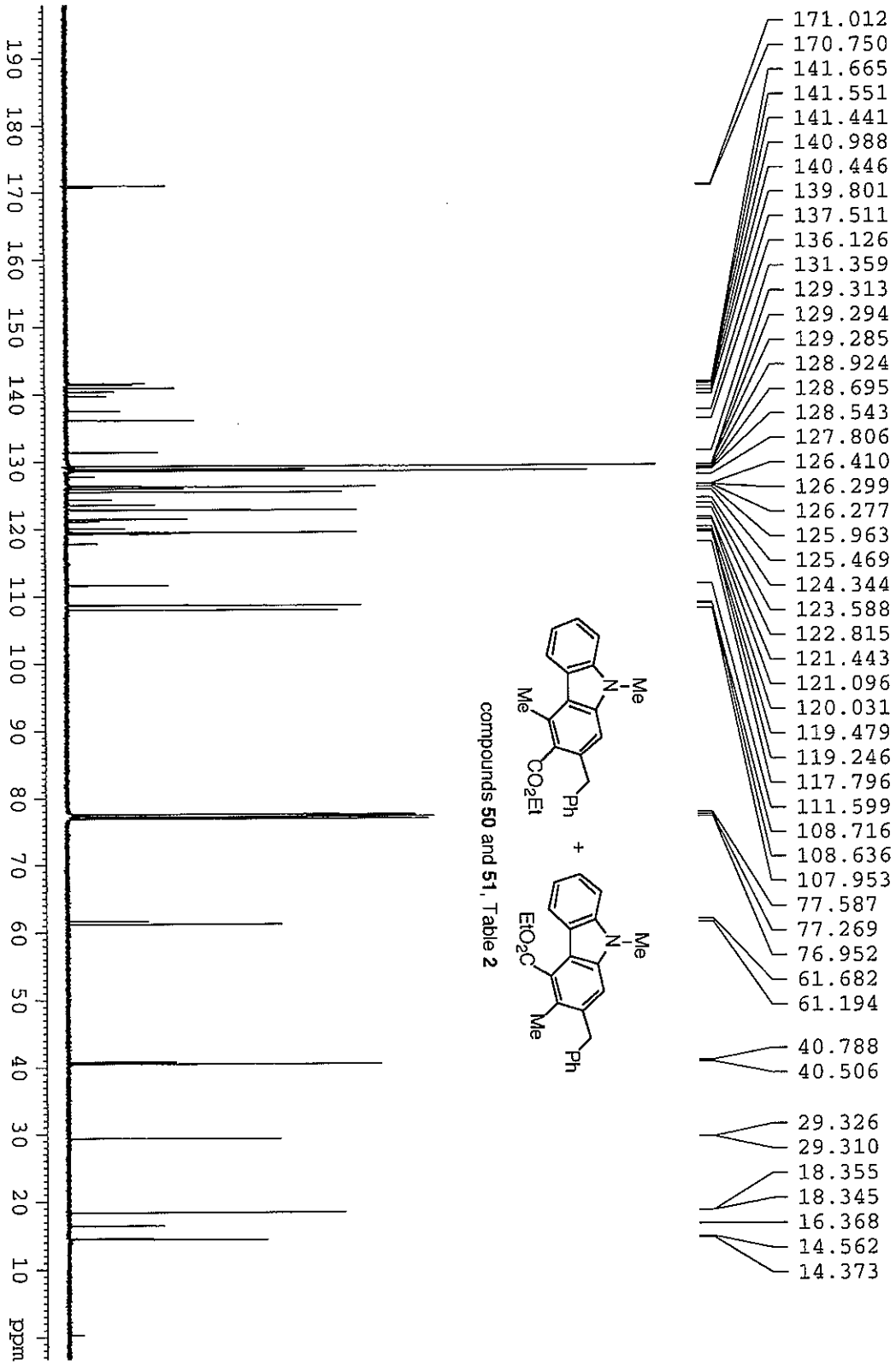


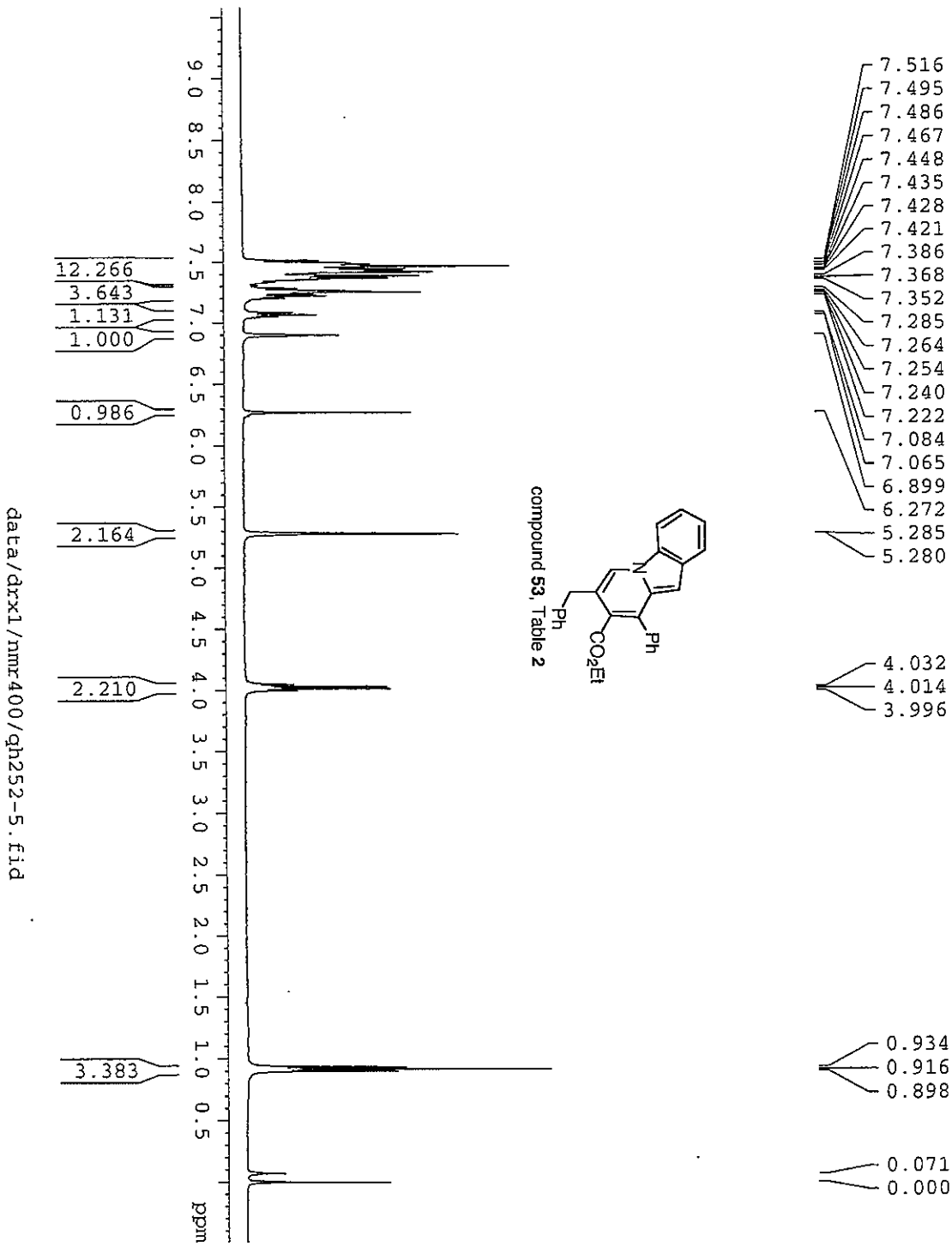


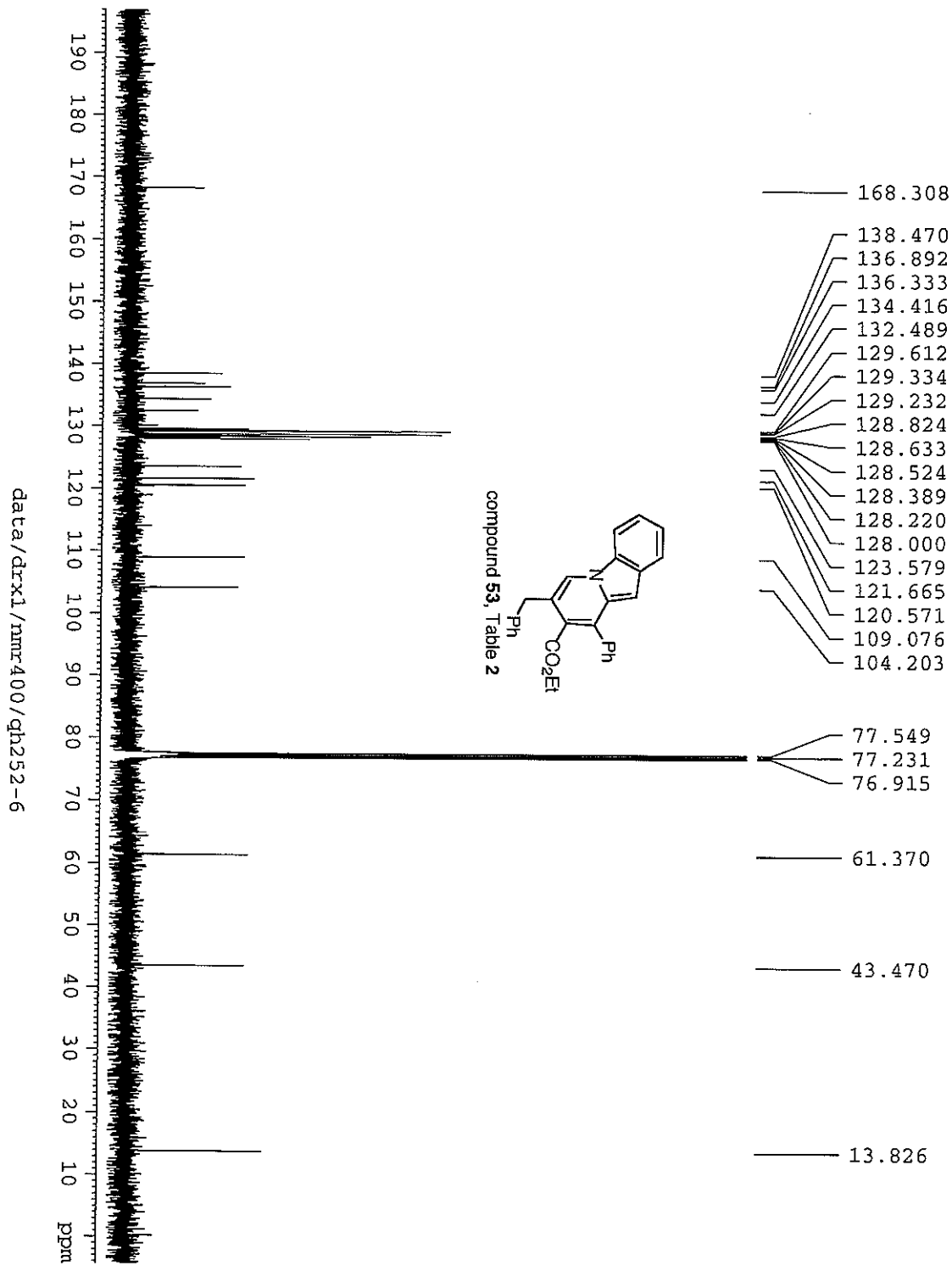
compound **50**, Table **2**

data/drx1/nmr400/qh281-5.fid

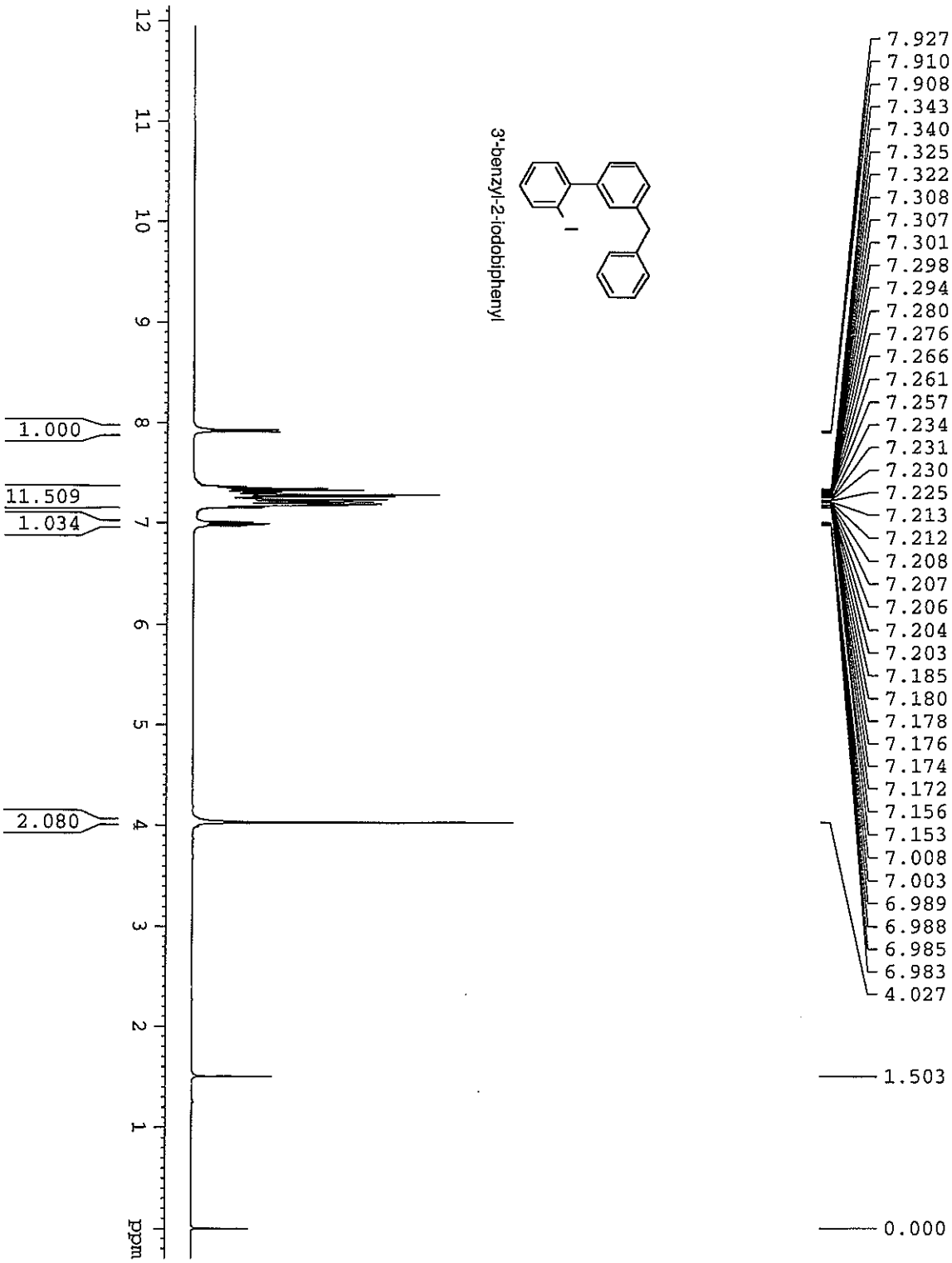

compounds 50 and 51, Table 2
Me
N
Me
CO2Et
Ph
+
EtO2C
Me
Ph
1.000
0.347
1.546
1.543
9.891
1.023
0.786
4.390
0.946
1.641
3.016
3.202
1.282
1.288
3.309
7.445
7.441
7.426
7.422
7.393
7.367
7.343
7.304
7.300
7.289
7.276
7.272
7.257
7.252
7.249
7.246
7.242
7.239
7.211
7.187
7.176
7.169
7.156
7.155
7.131
7.019
4.629
4.605
4.581
4.557
4.308
4.284
4.261
4.231
4.192
3.764
3.748
2.851
2.330
1.556
1.477
1.453
1.451
1.429
1.278
1.254
1.252
1.230
0.000
-0.003
ppm

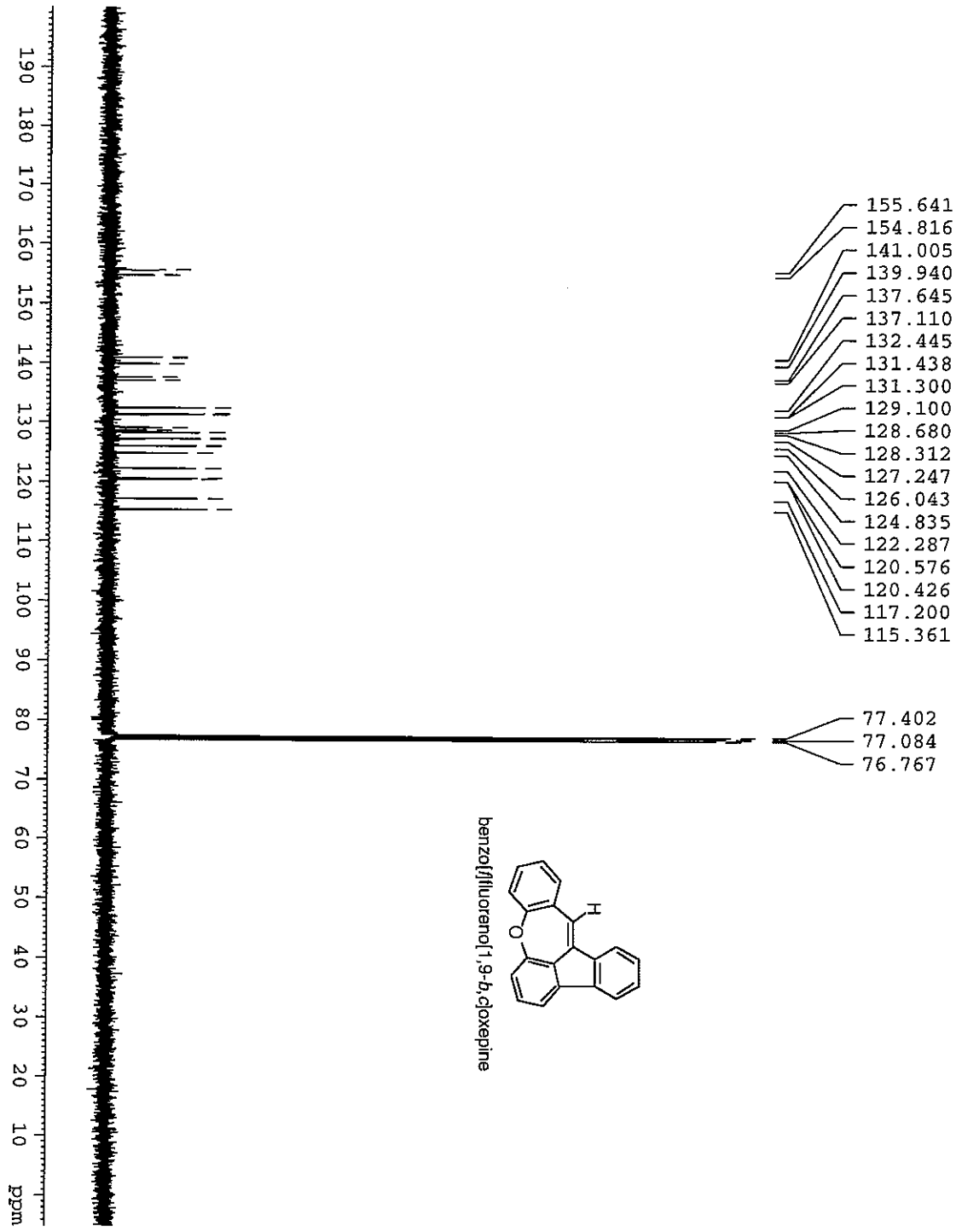

171.012
170.750
141.665
141.551
141.441
140.988
140.446
139.801
137.511
136.126
131.359
129.313
129.294
129.285
128.924
128.695
128.543
127.806
126.410
126.299
126.277
125.963
125.469
124.344
123.588
122.815
121.443
121.096
120.031
119.479
119.246
117.796
111.599
108.716
108.636
107.953
77.587
77.269
76.952
61.682
61.194
40.788
40.506
29.326
29.310
18.355
18.345
16.368
14.562
14.373
Me
N
Me
CO2Et
Ph
+
Me
N
EtO2C
Me
Ph
compounds 50 and 51, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr400/qh280-6.fid


7.516
7.495
7.486
7.467
7.448
7.435
7.428
7.421
7.386
7.368
7.352
7.285
7.264
7.254
7.240
7.222
7.084
7.065
6.899
6.272
5.285
5.280
4.032
4.014
3.996
0.934
0.916
0.898
0.071
0.000
compound 53, Table 2
Ph
CO2Et
Ph
12.266
3.643
1.131
1.000
0.986
2.164
2.210
3.383
ppm
data/drx1/nmr400/qh252-5.fid

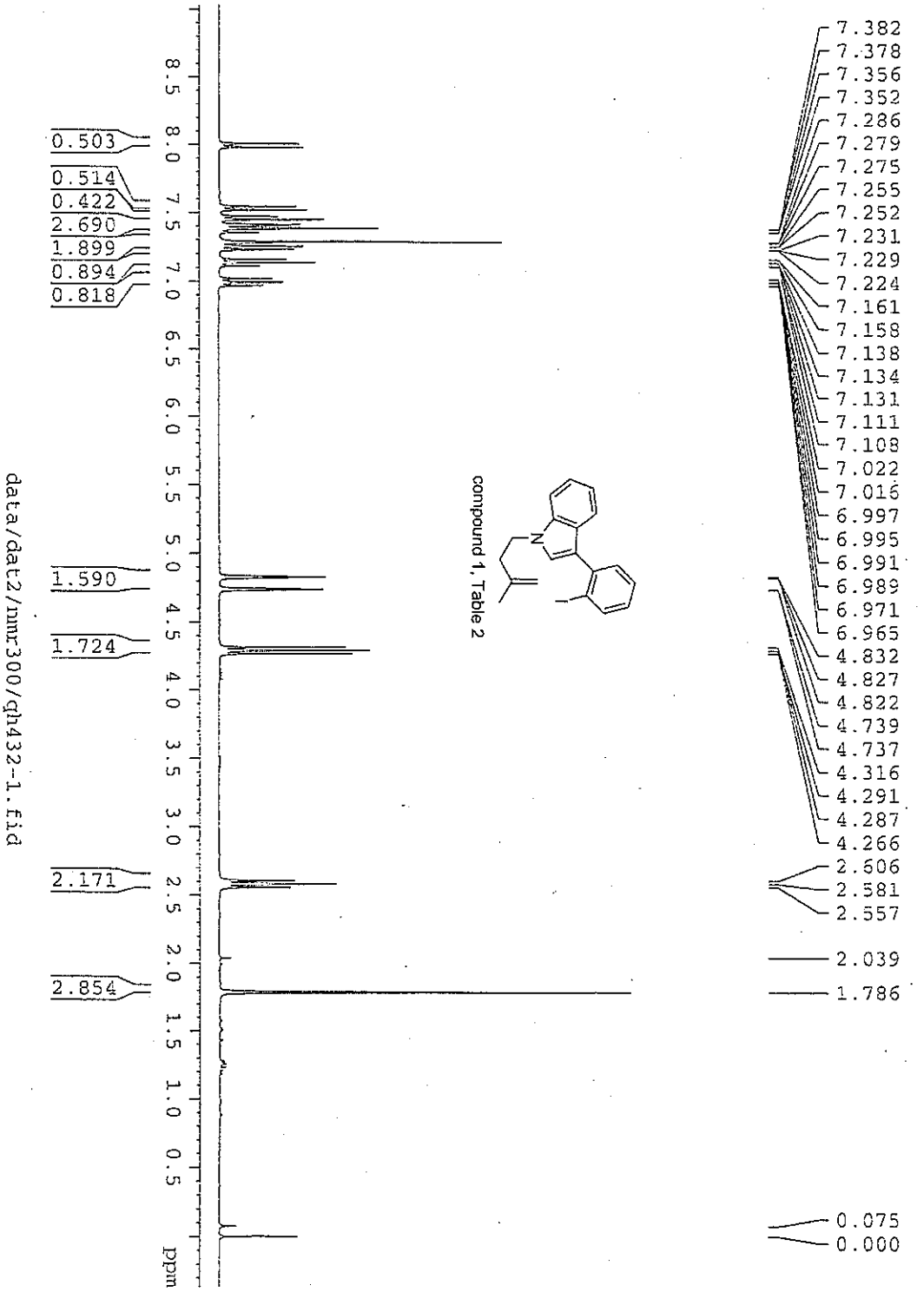

168.308
138.470
136.892
136.333
134.416
132.489
129.612
129.334
129.232
128.824
128.633
128.524
128.389
128.220
128.000
123.579
121.665
120.571
109.076
104.203
77.549
77.231
76.915
61.370
43.470
13.826
compound 53, Table 2
Ph
CO2Et
Ph
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh252-6

APPENDIX D. CHAPTER 4 ^{1}H AND ^{13}C NMR SPECTRA


3'-benzyl-2-iodobiphenyl
1.000
11.509
1.034
2.080
ppm
12
11
10
9
8
7
6
5
4
3
2
1
7.927
7.910
7.908
7.343
7.340
7.325
7.322
7.308
7.307
7.301
7.298
7.294
7.280
7.276
7.266
7.261
7.257
7.234
7.231
7.230
7.225
7.213
7.212
7.208
7.207
7.206
7.204
7.203
7.185
7.180
7.178
7.176
7.174
7.172
7.156
7.153
7.008
7.003
6.989
6.988
6.985
6.983
4.027
1.503
0.000


155.641
154.816
141.005
139.940
137.645
137.110
132.445
131.438
131.300
129.100
128.680
128.312
127.247
126.043
124.835
122.287
120.576
120.426
117.200
115.361
77.402
77.084
76.767
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
benzo[f]fluoreno[1,9-b]oxepine
O
H

APPENDIX E. CHAPTER 5 ^{1}H AND ^{13}C NMR SPECTRA


7.382
7.378
7.356
7.352
7.286
7.279
7.275
7.255
7.252
7.231
7.229
7.224
7.161
7.158
7.138
7.134
7.131
7.111
7.108
7.022
7.016
6.997
6.995
6.991
6.989
6.971
6.965
4.832
4.827
4.822
4.739
4.737
4.316
4.291
4.287
4.266
2.606
2.581
2.557
2.039
1.786
0.075
0.000
0.503
0.514
0.422
2.690
1.899
0.894
0.818
1.590
1.724
2.171
2.854
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
compound 1, Table 2
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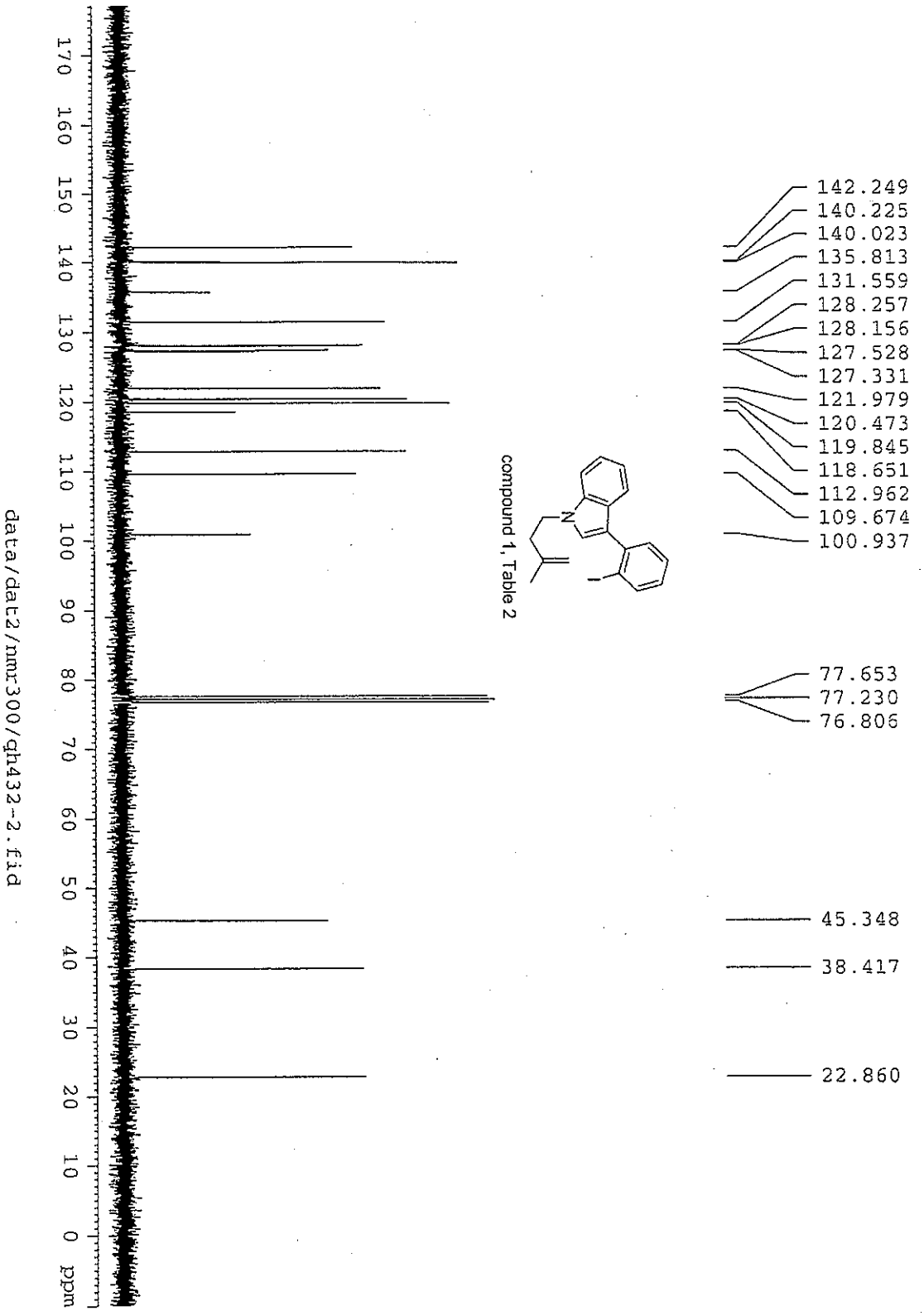
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140.225
140.023
135.813
131.559
128.257
128.156
127.528
127.331
121.979
120.473
119.845
118.651
112.962
109.674
100.937
77.653
77.230
76.806
45.348
38.417
22.860
compound 1, Table 2
data/dat2/nmr300/qh432-2.fid
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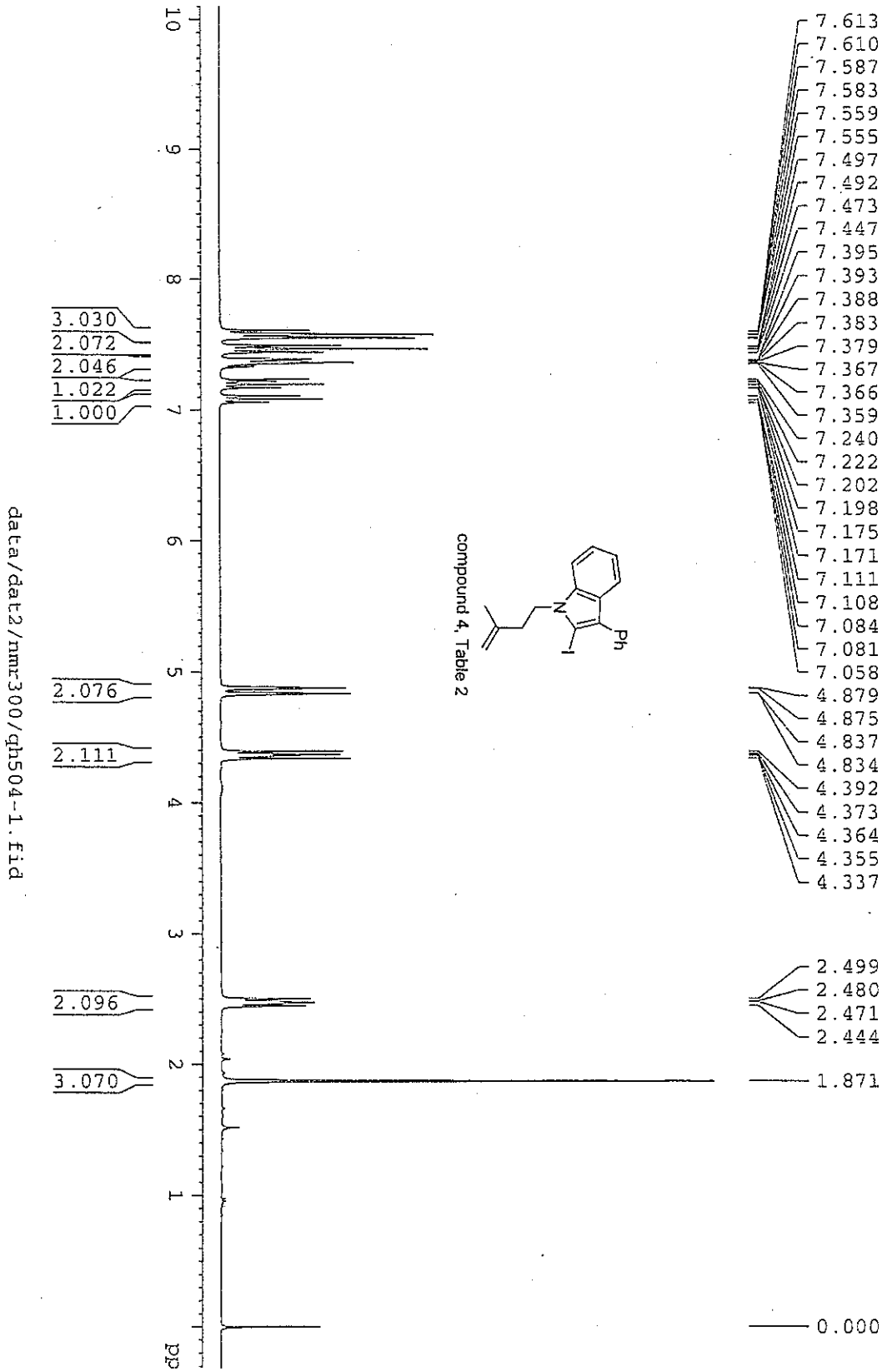
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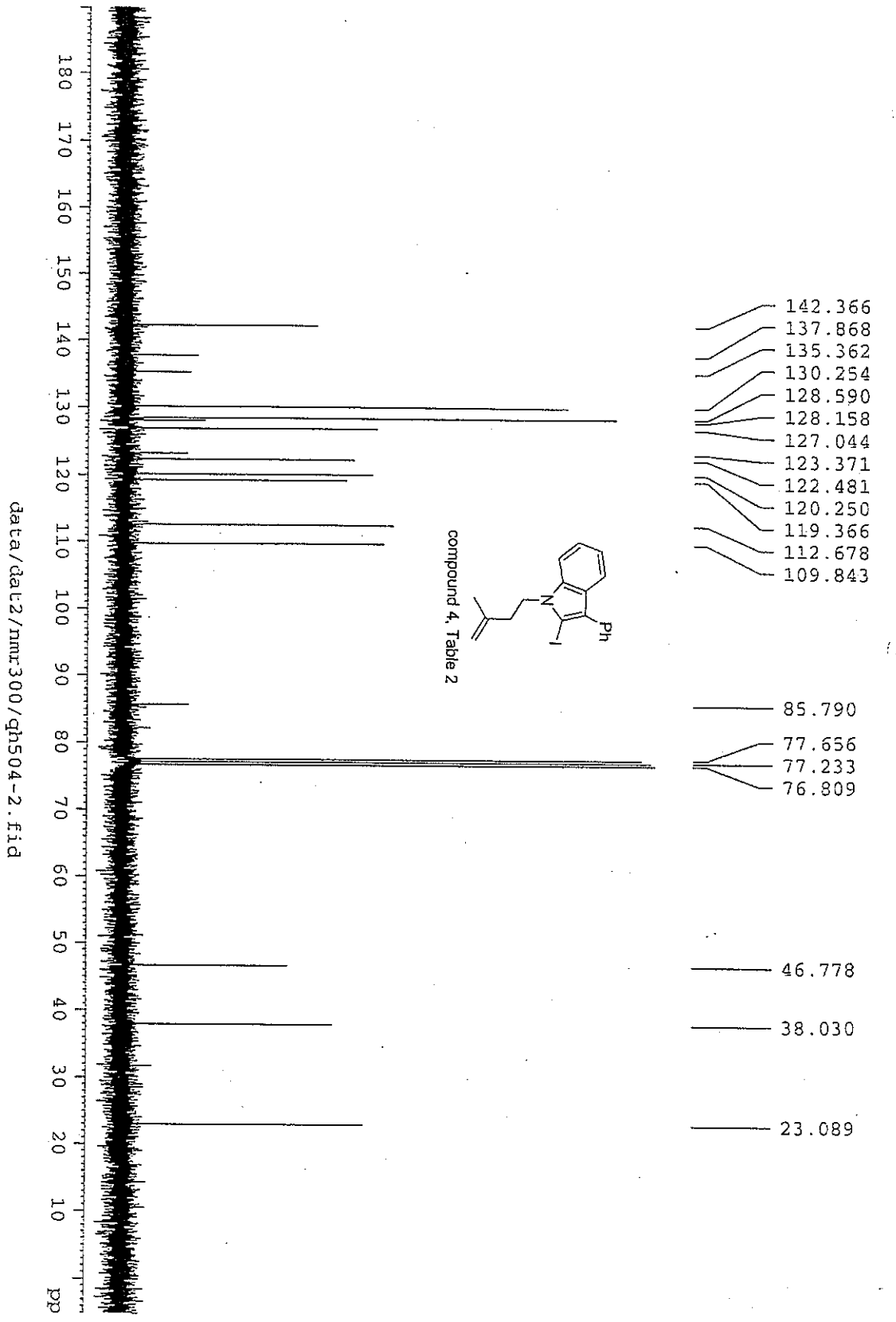
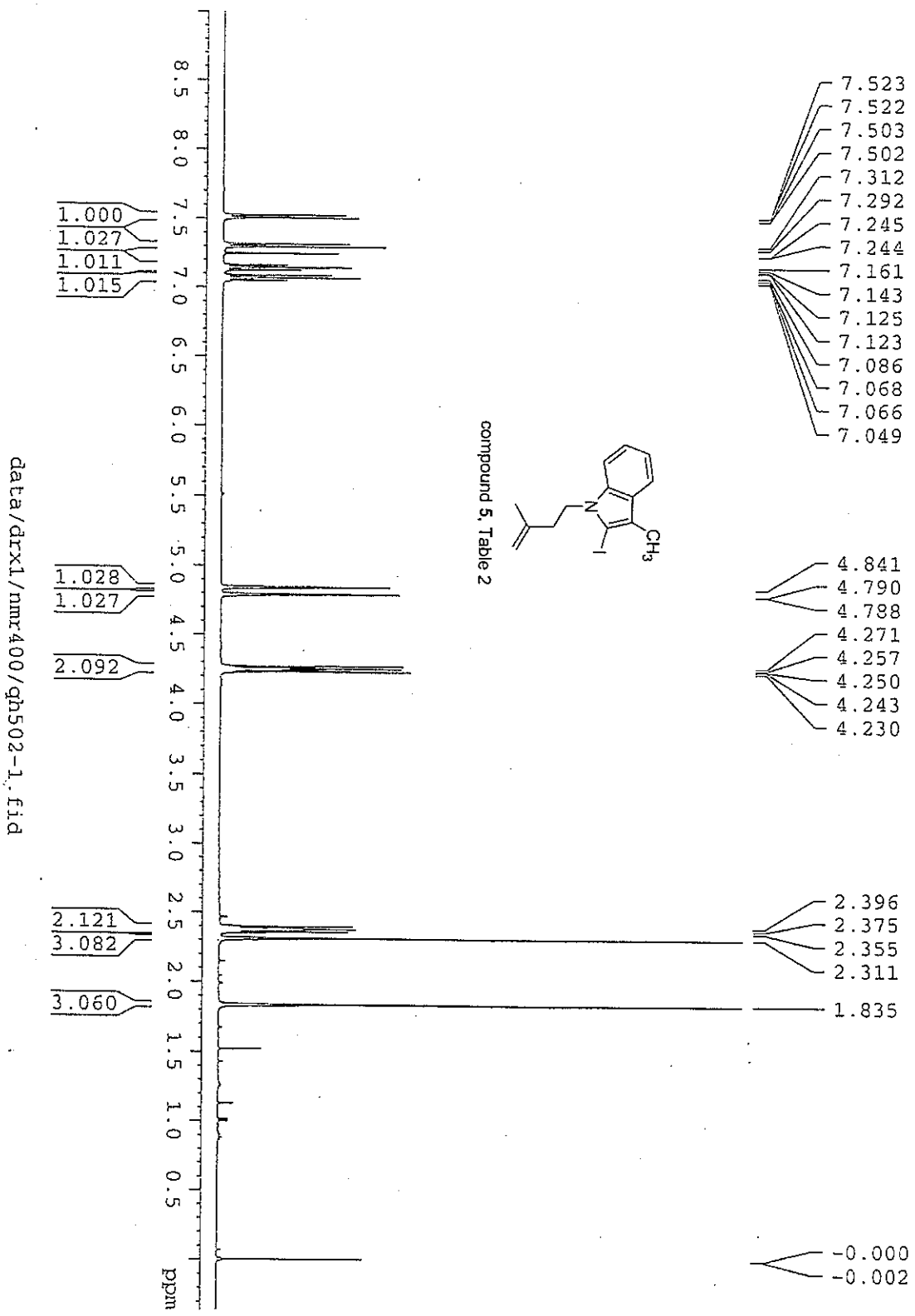
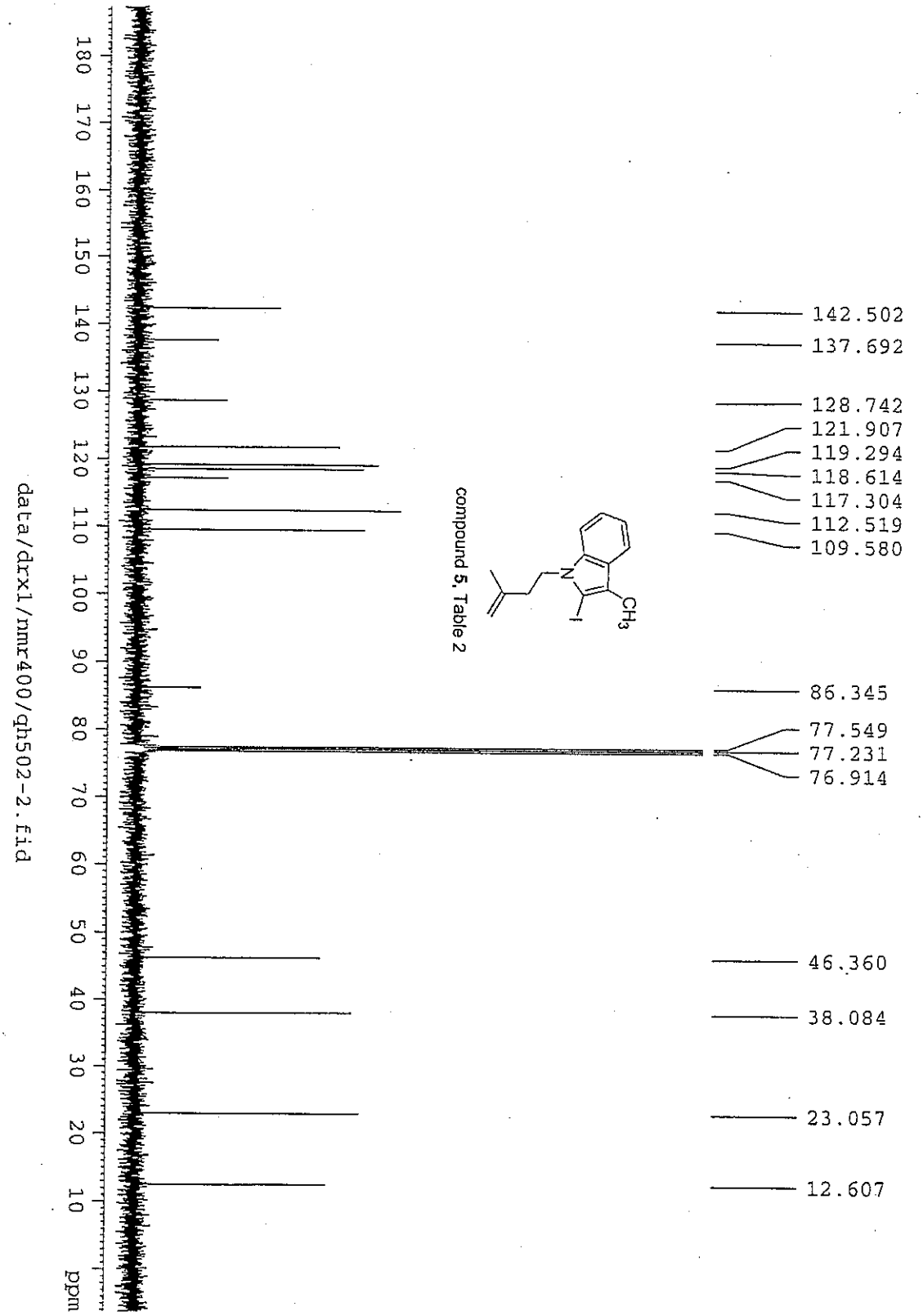
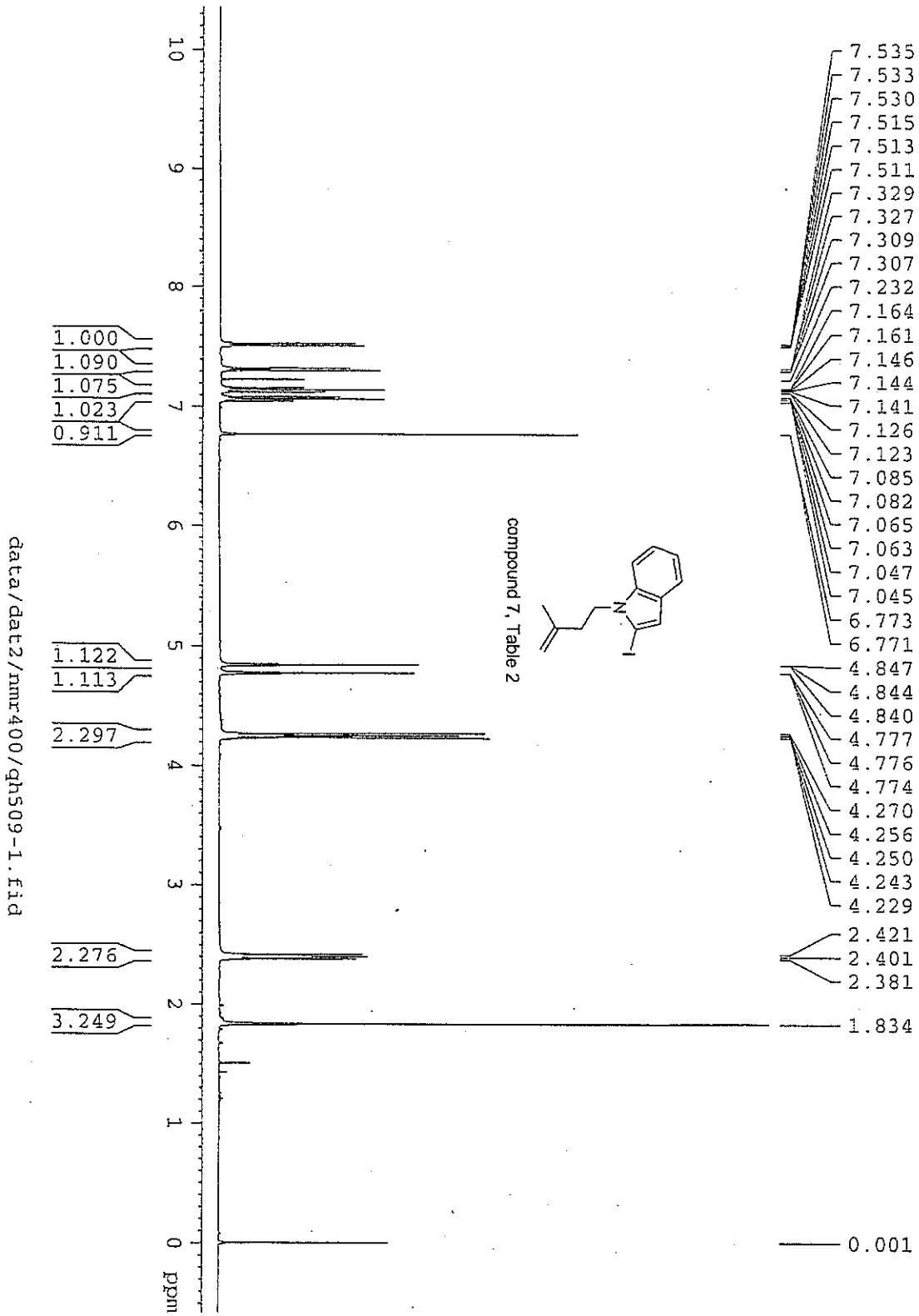
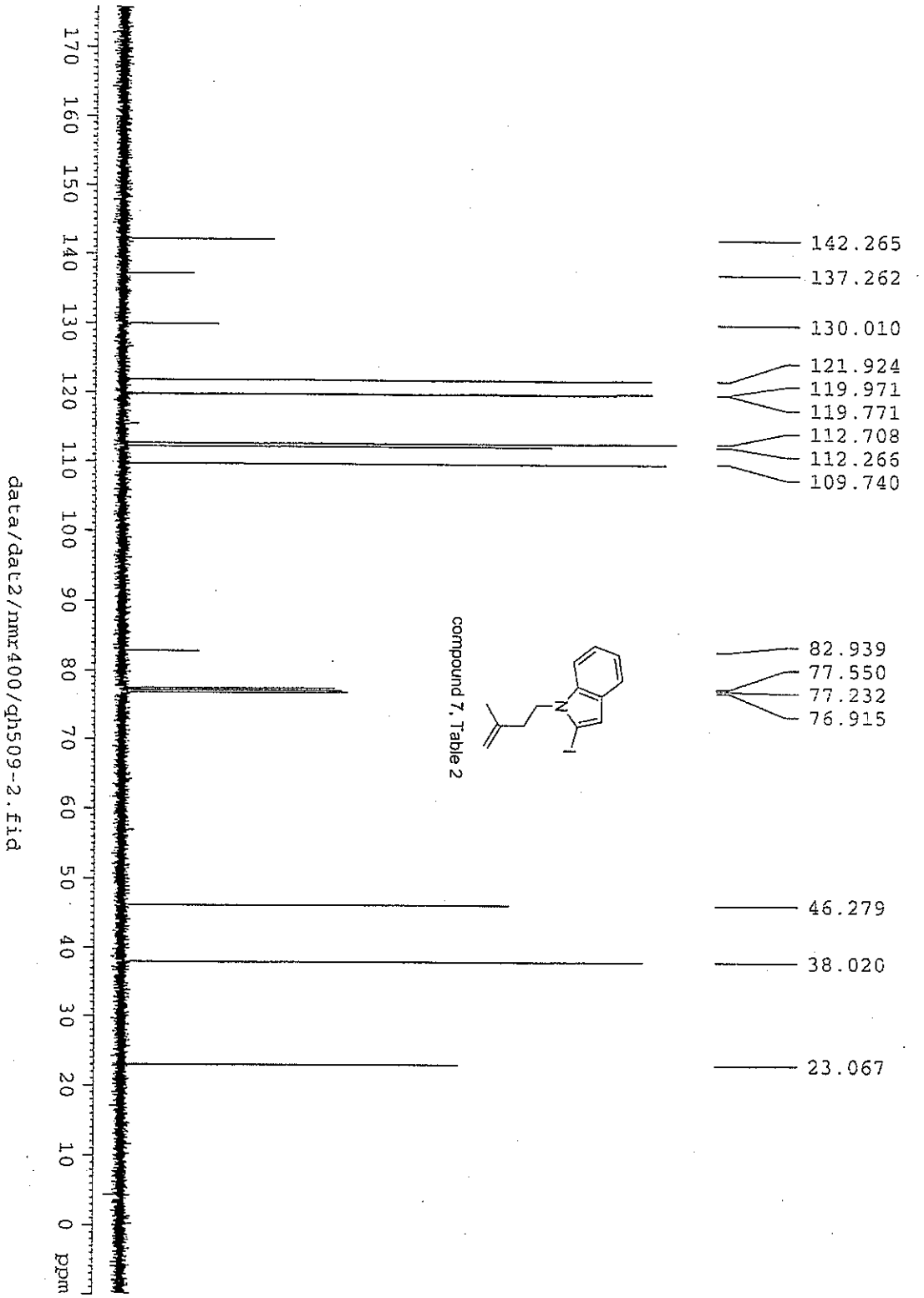
7.610
7.587
7.583
7.559
7.555
7.497
7.492
7.473
7.447
7.395
7.393
7.388
7.383
7.379
7.367
7.366
7.359
7.240
7.222
7.202
7.198
7.175
7.171
7.111
7.108
7.084
7.081
7.058
4.879
4.875
4.837
4.834
4.392
4.373
4.364
4.355
4.337
2.499
2.480
2.471
2.444
1.871
0.000
3.030
2.072
2.046
1.022
1.000
2.076
2.111
2.096
3.070
compound 4, Table 2
N
Ph
I
data/dat2/nmr300/qh504-1.fid
10
9
8
7
6
5
4
3
2
1
ppm

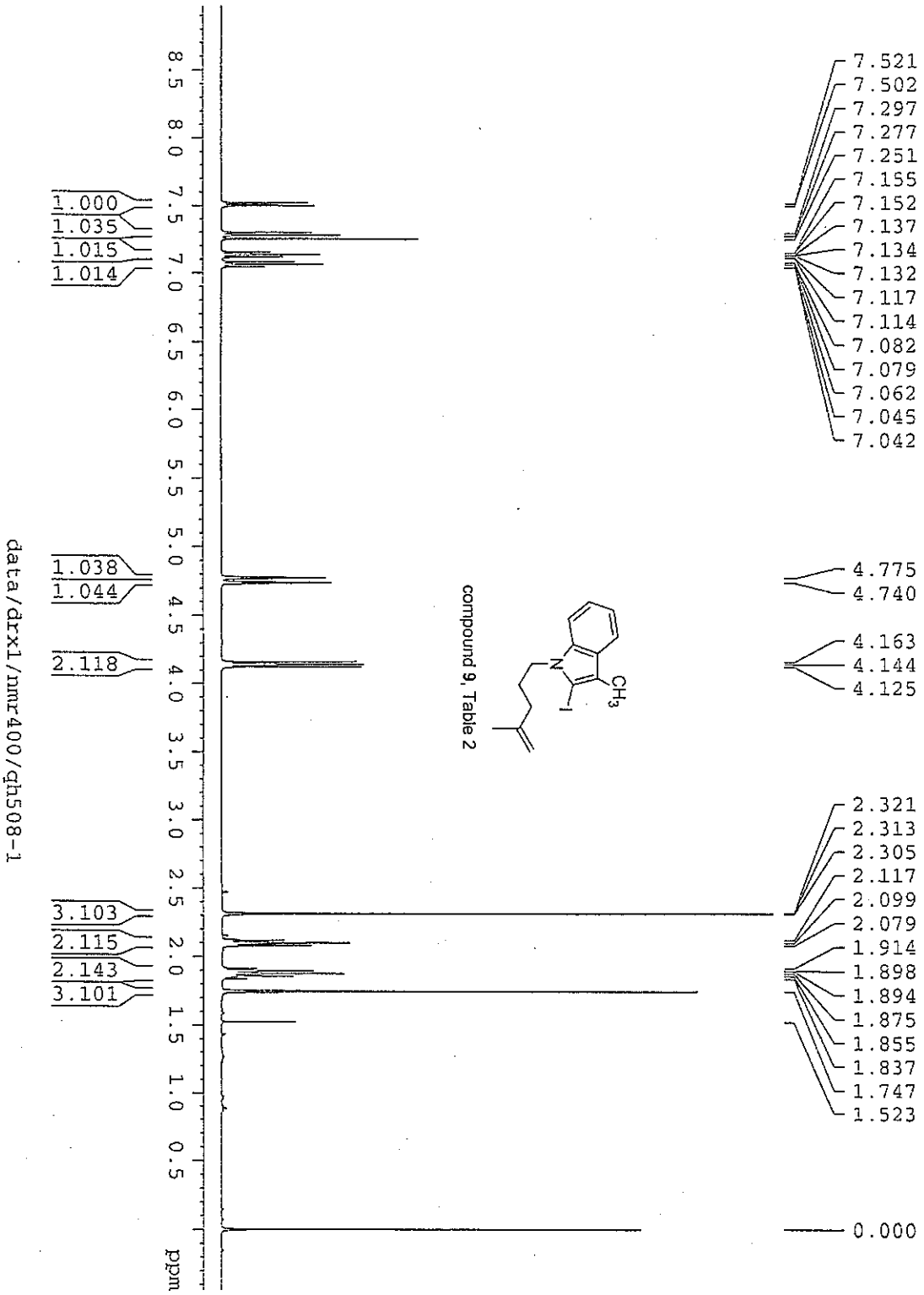

142.366
137.868
135.362
130.254
128.590
128.158
127.044
123.371
122.481
120.250
119.366
112.678
109.843
85.790
77.656
77.233
76.809
46.778
38.030
23.089
compound 4, Table 2
Ph
I
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm
data/data2/nmr300/qh504-2.fid

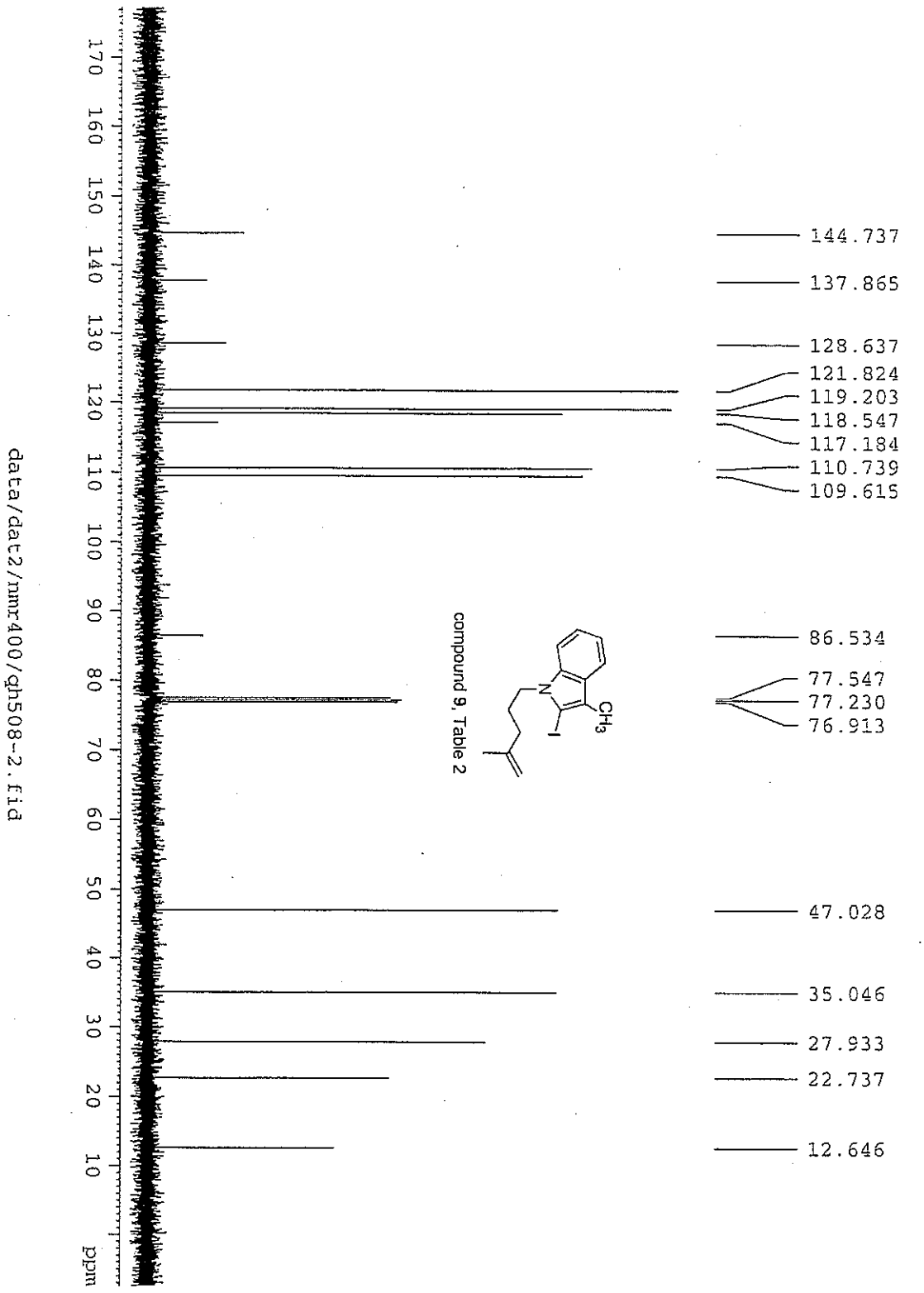

7.523
7.522
7.503
7.502
7.312
7.292
7.245
7.244
7.161
7.143
7.125
7.123
7.086
7.068
7.066
7.049
4.841
4.790
4.788
4.271
4.257
4.250
4.243
4.230
2.396
2.375
2.355
2.311
1.835
-0.000
-0.002
1.000
1.027
1.011
1.015
1.028
1.027
2.092
2.121
3.082
3.060
compound 5, Table 2
CH3
I
N
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/drx1/nmr400/qh502-1.fid


142.502
137.692
128.742
121.907
119.294
118.614
117.304
112.519
109.580
86.345
77.549
77.231
76.914
46.360
38.084
23.057
12.607
compound 5, Table 2
CH3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh502-2.fid


7.535
7.533
7.530
7.515
7.513
7.511
7.329
7.327
7.309
7.307
7.232
7.164
7.161
7.146
7.144
7.141
7.126
7.123
7.085
7.082
7.065
7.063
7.047
7.045
6.773
6.771
4.847
4.844
4.840
4.777
4.776
4.774
4.270
4.256
4.250
4.243
4.229
2.421
2.401
2.381
1.834
0.001
1.000
1.090
1.075
1.023
0.911
1.122
1.113
2.297
2.276
3.249
compound 7, Table 2
data/dat2/nmr400/qh509-1.fid
ppm


142.265
137.262
130.010
121.924
119.971
119.771
112.708
112.266
109.740
82.939
77.550
77.232
76.915
46.279
38.020
23.067
compound 7, Table 2
N
I
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh509-2.fid


7.521
7.502
7.297
7.277
7.251
7.155
7.152
7.137
7.134
7.132
7.117
7.114
7.082
7.079
7.062
7.045
7.042
4.775
4.740
4.163
4.144
4.125
2.321
2.313
2.305
2.117
2.099
2.079
1.914
1.898
1.894
1.875
1.855
1.837
1.747
1.523
0.000
1.000
1.035
1.015
1.014
1.038
1.044
2.118
3.103
2.115
2.143
3.101
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
compound 9, Table 2
CH3
N
I
data/drx1/nmr400/qh508-1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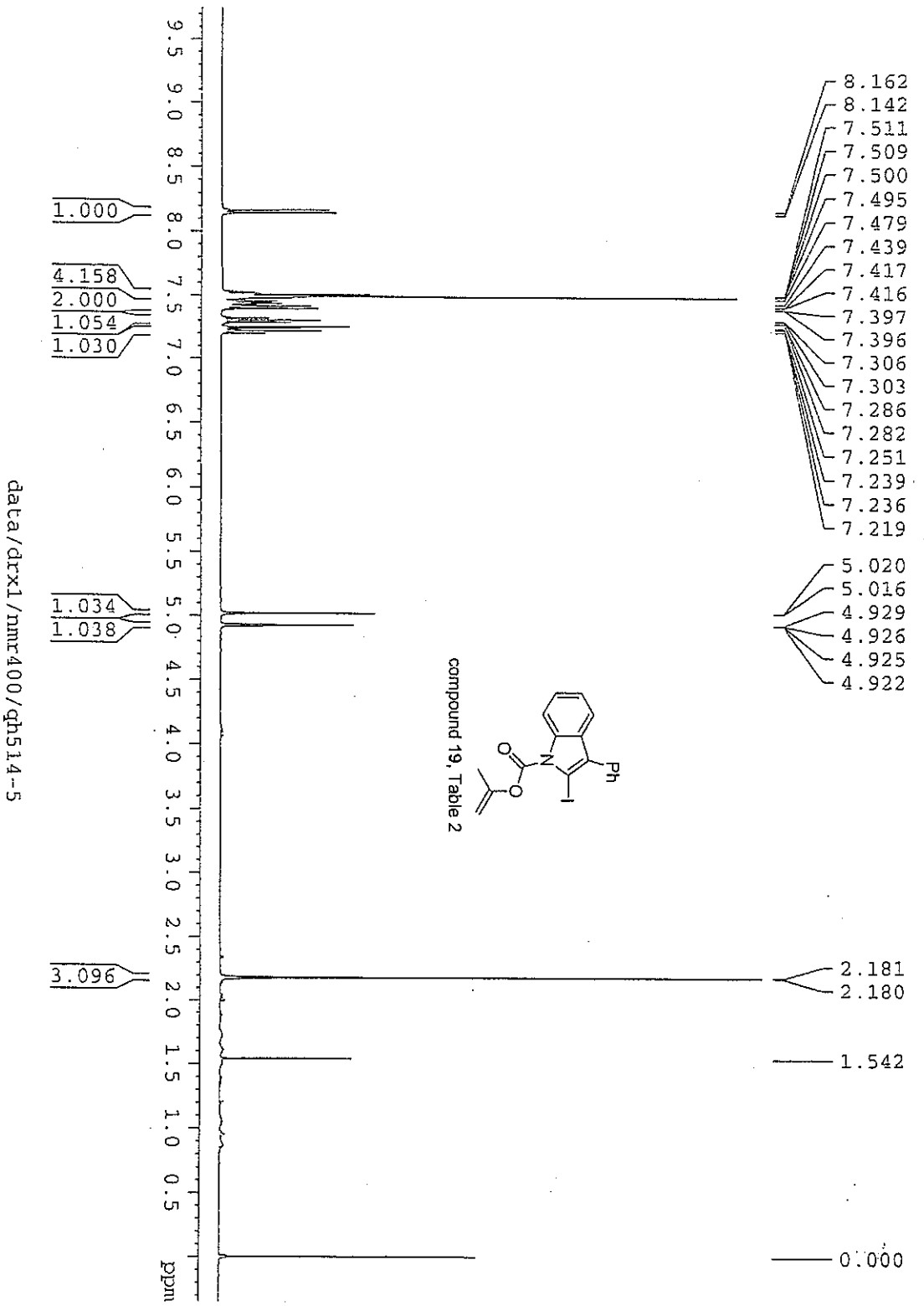
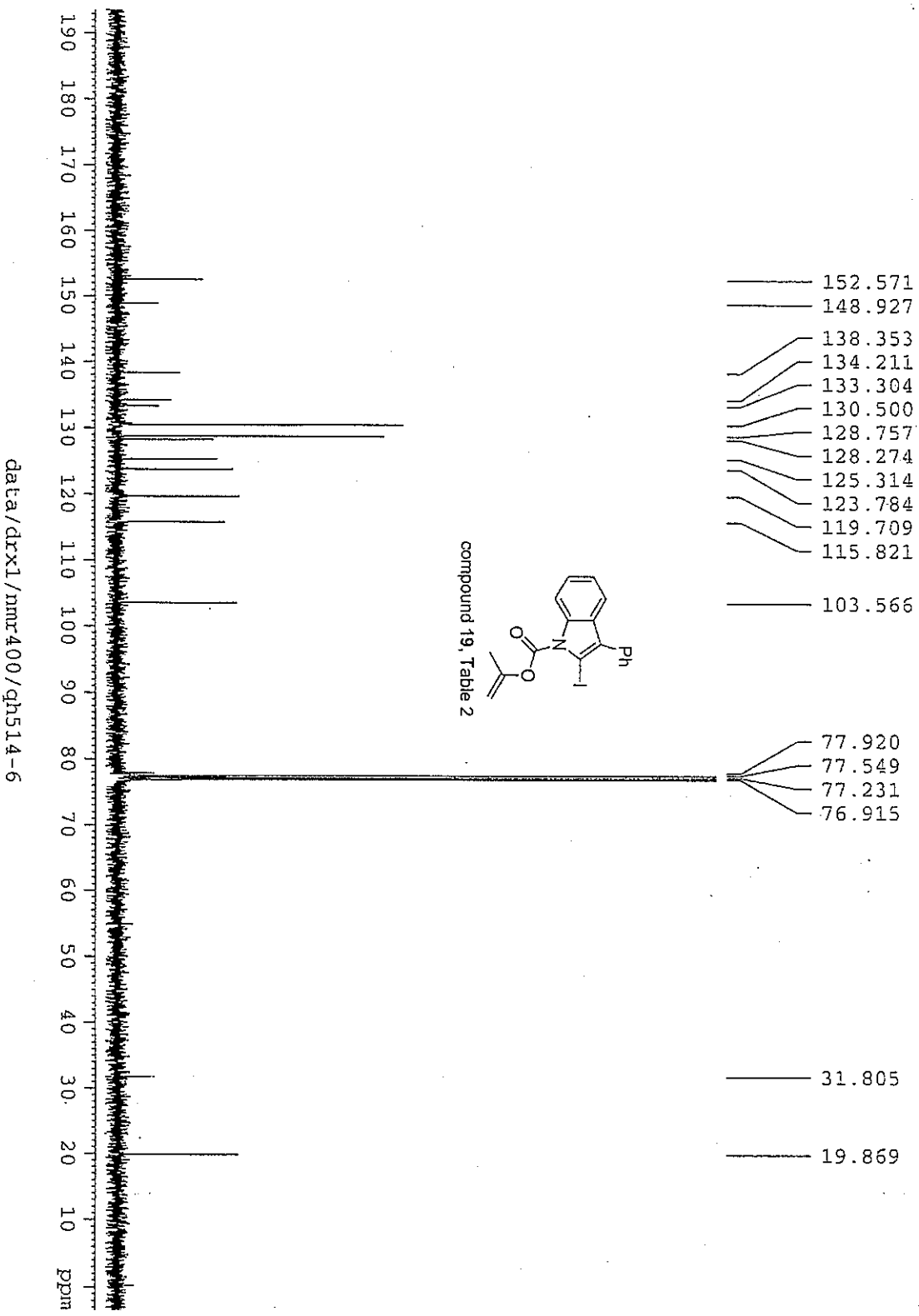
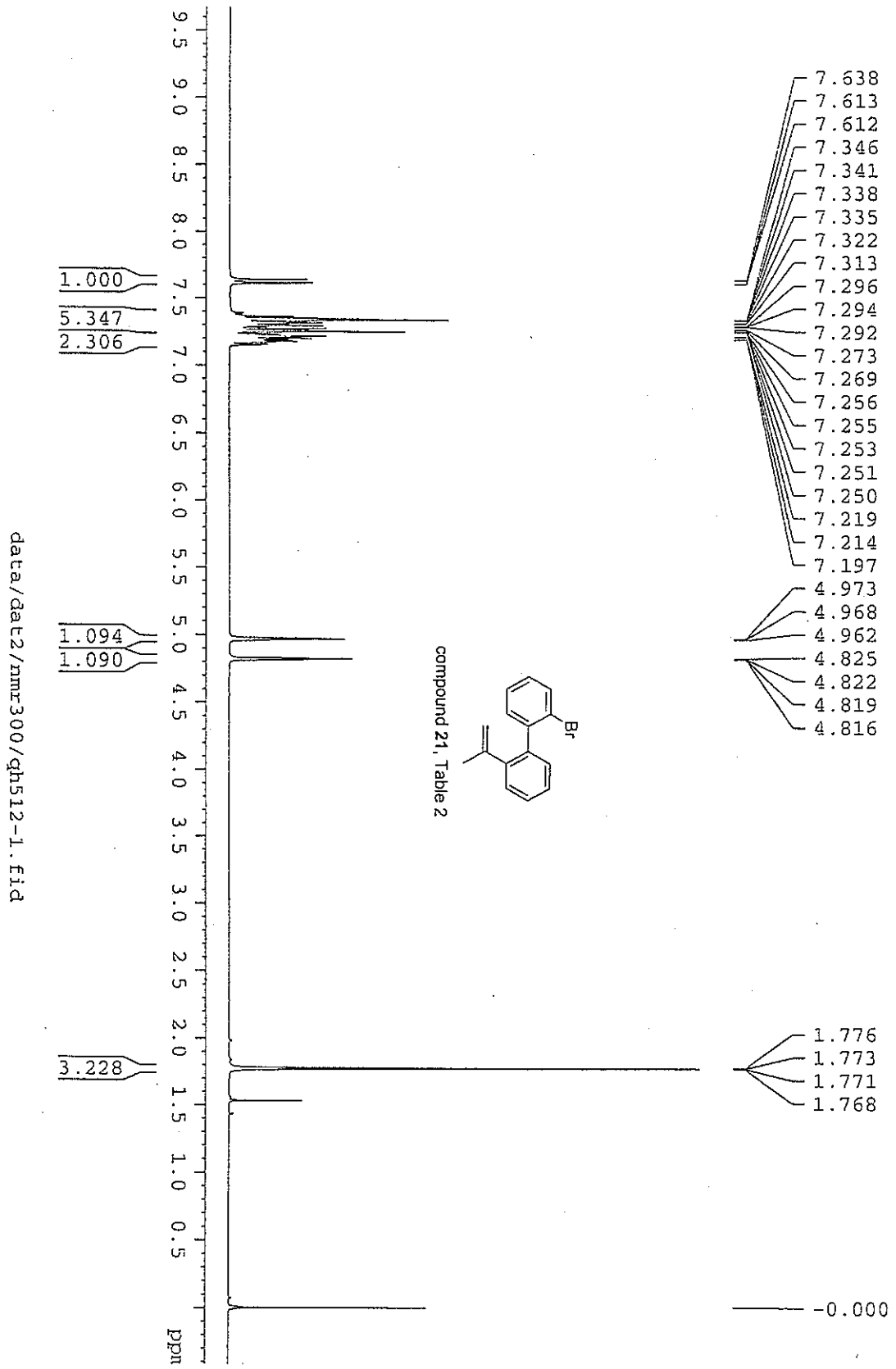
128.637
121.824
119.203
118.547
117.184
110.739
109.615
86.534
77.547
77.230
76.913
47.028
35.046
27.933
22.737
12.646
compound 9, Table 2
CH3
I
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm
data/dat2/nmr400/qh508-2.fid


8.162
8.142
7.511
7.509
7.500
7.495
7.479
7.439
7.417
7.416
7.397
7.396
7.306
7.303
7.286
7.282
7.251
7.239
7.236
7.219
5.020
5.016
4.929
4.926
4.925
4.922
2.181
2.180
1.542
0.000
1.000
4.158
2.000
1.054
1.030
1.034
1.038
3.096
ppm
compound 19, Table 2
Ph
I
data/drx1/nmr400/qh514-5


152.571
148.927
138.353
134.211
133.304
130.500
128.757
128.274
125.314
123.784
119.709
115.821
103.566
77.920
77.549
77.231
76.915
31.805
19.869
compound 19, Table 2
Ph
I
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh514-6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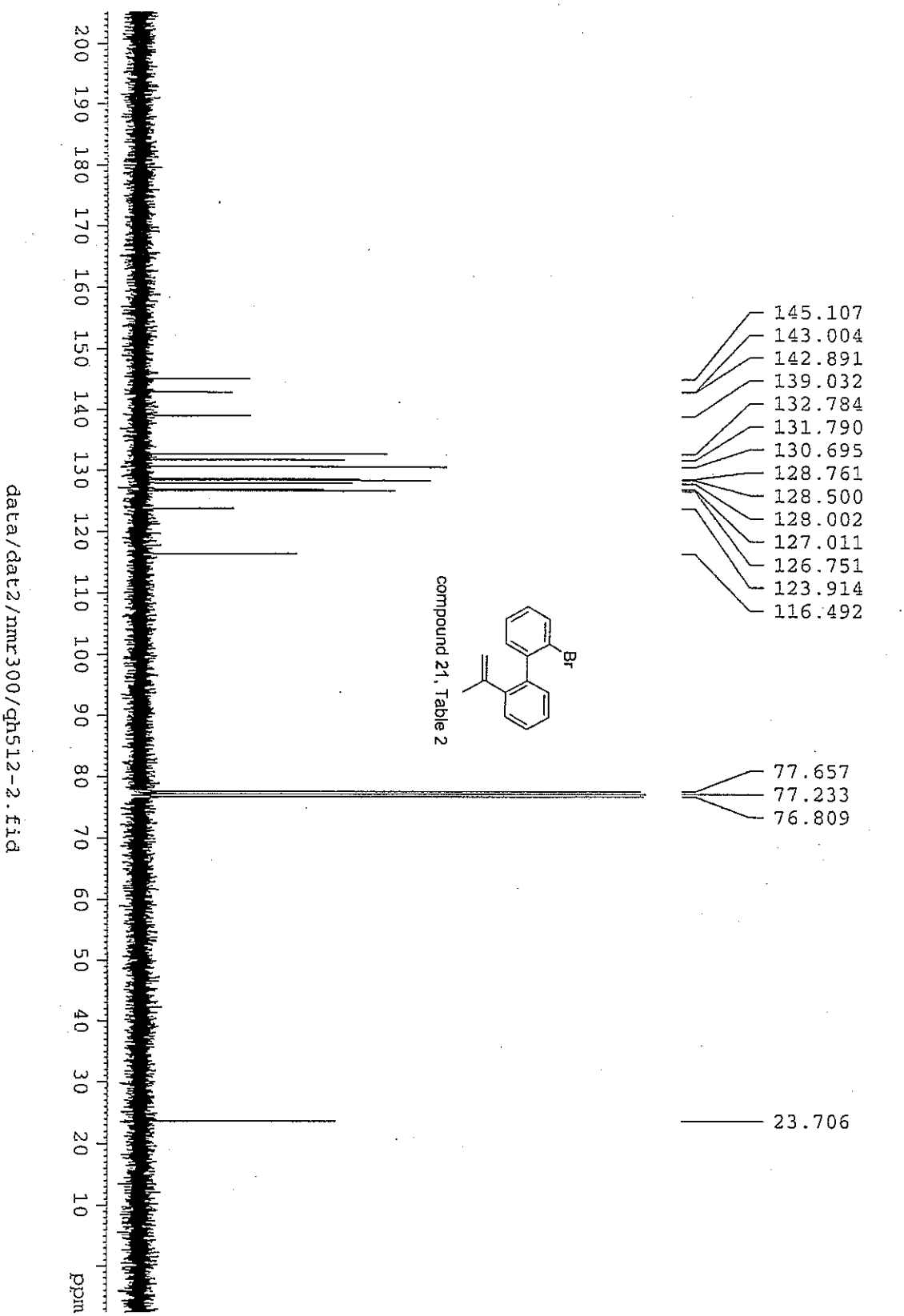
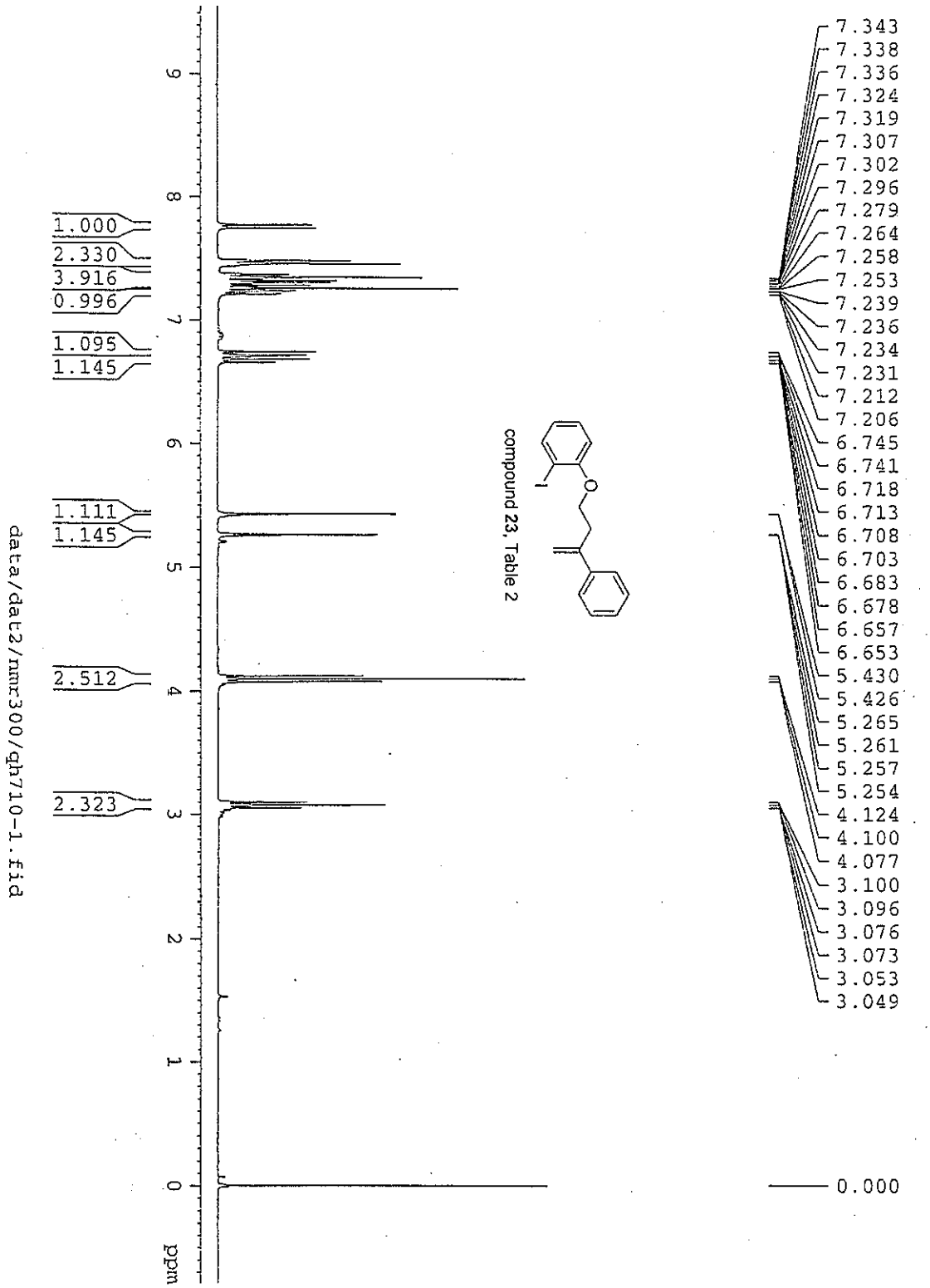
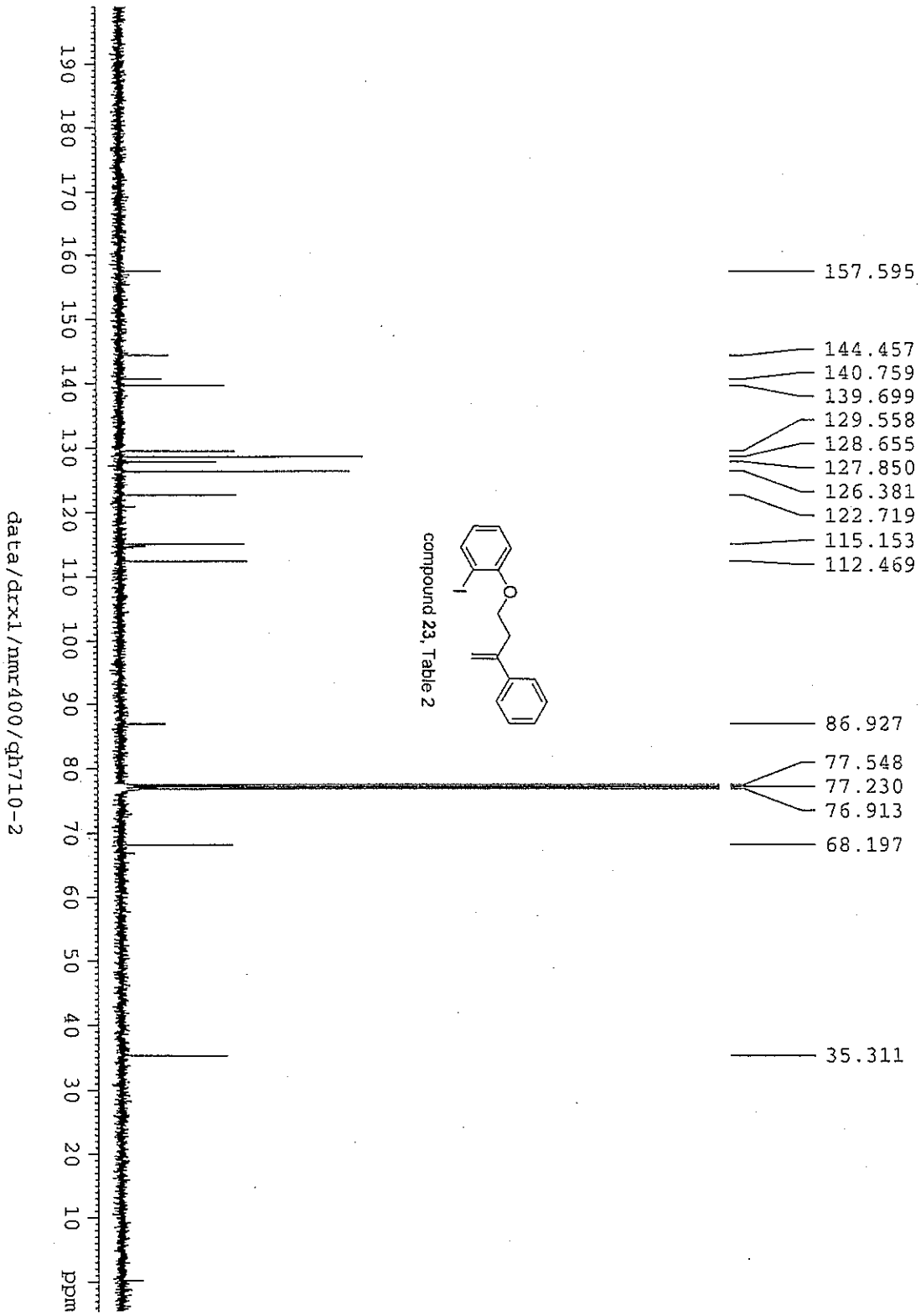
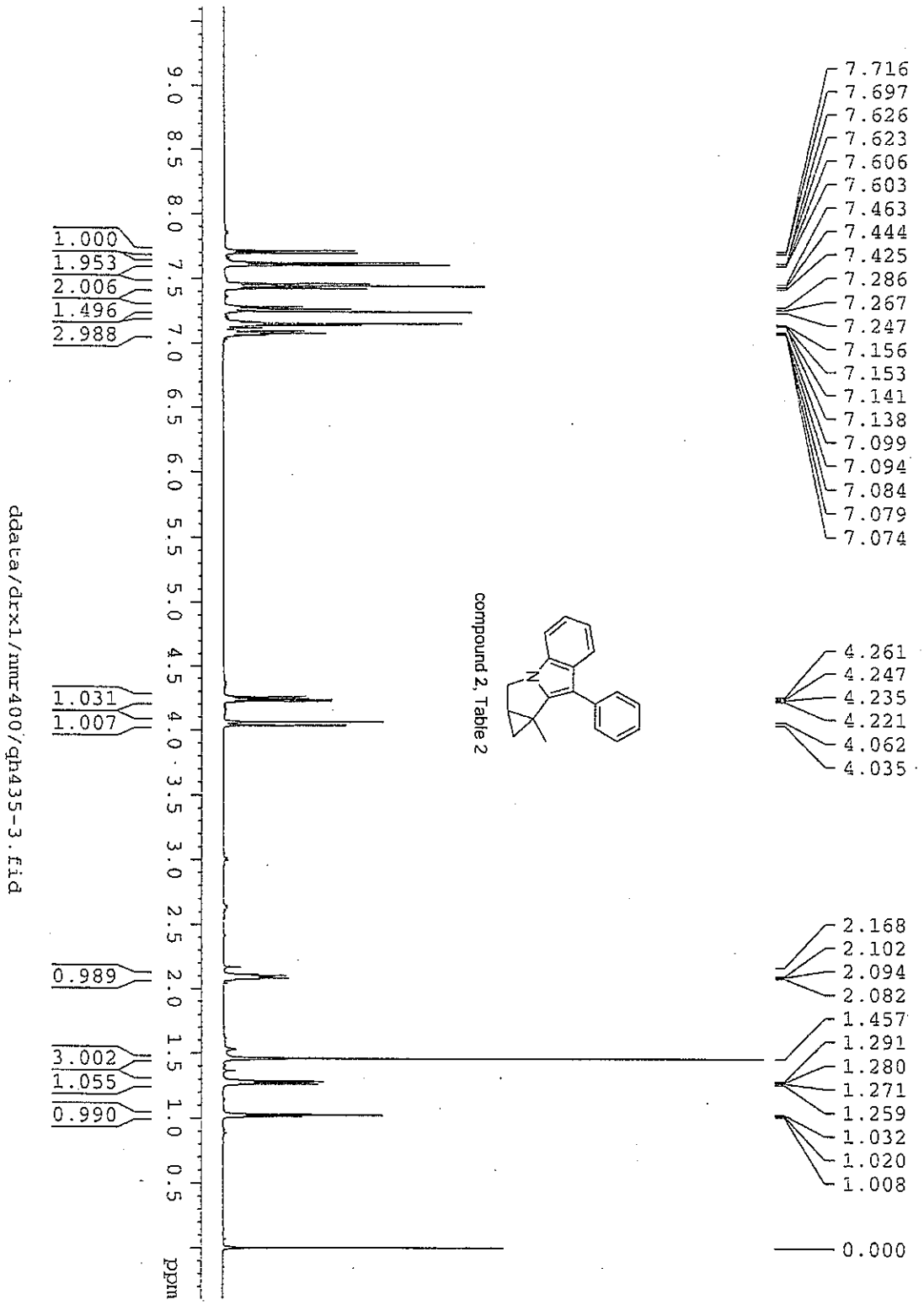
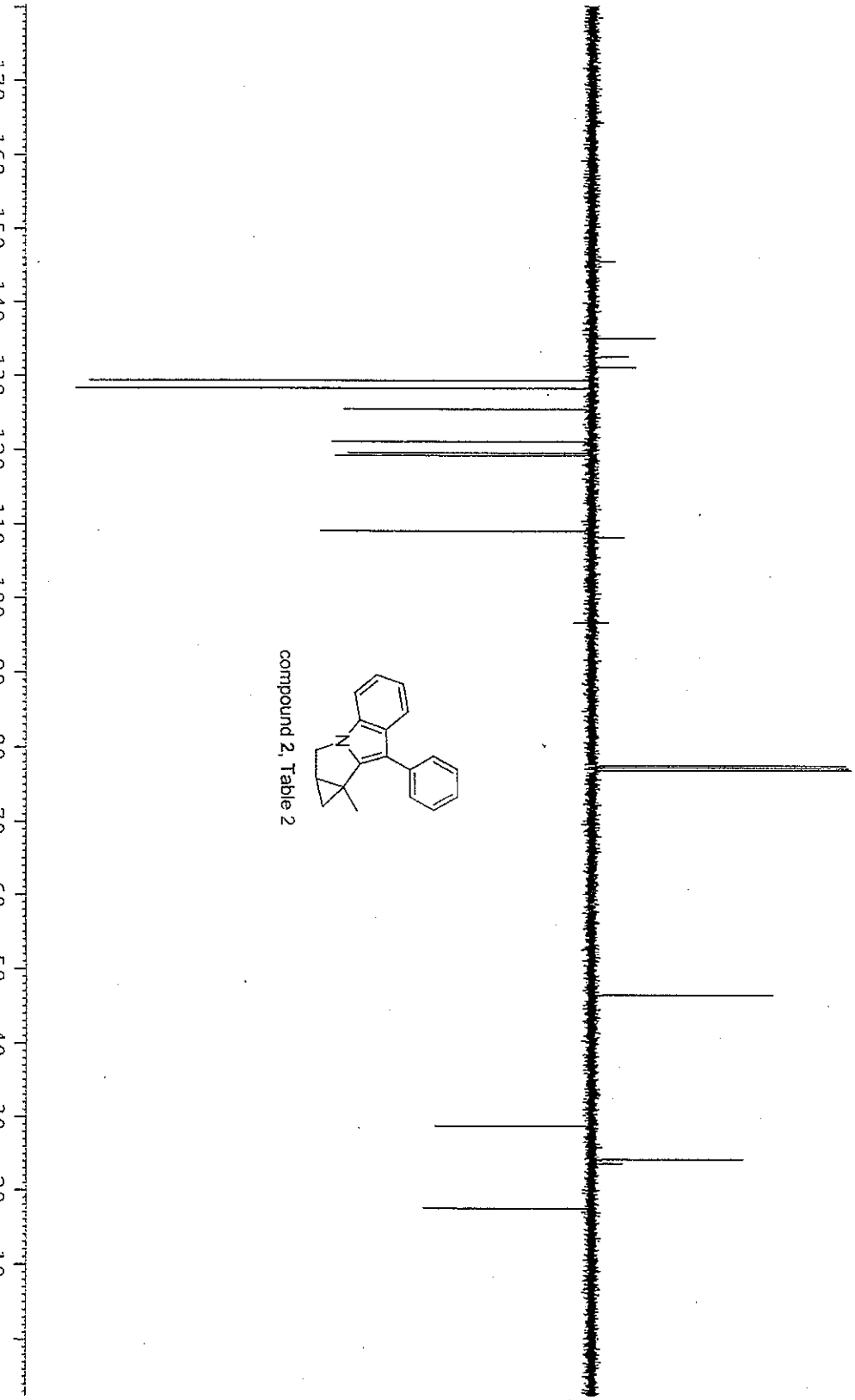
7.612
7.346
7.341
7.338
7.335
7.322
7.313
7.296
7.294
7.292
7.273
7.269
7.256
7.255
7.253
7.251
7.250
7.219
7.214
7.197
4.973
4.968
4.962
4.825
4.822
4.819
4.816
1.776
1.773
1.771
1.768
-0.000
1.000
5.347
2.306
1.094
1.090
3.228
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
Br
compound 21, Table 2
data/dat2/nmr300/qh512-1.fid

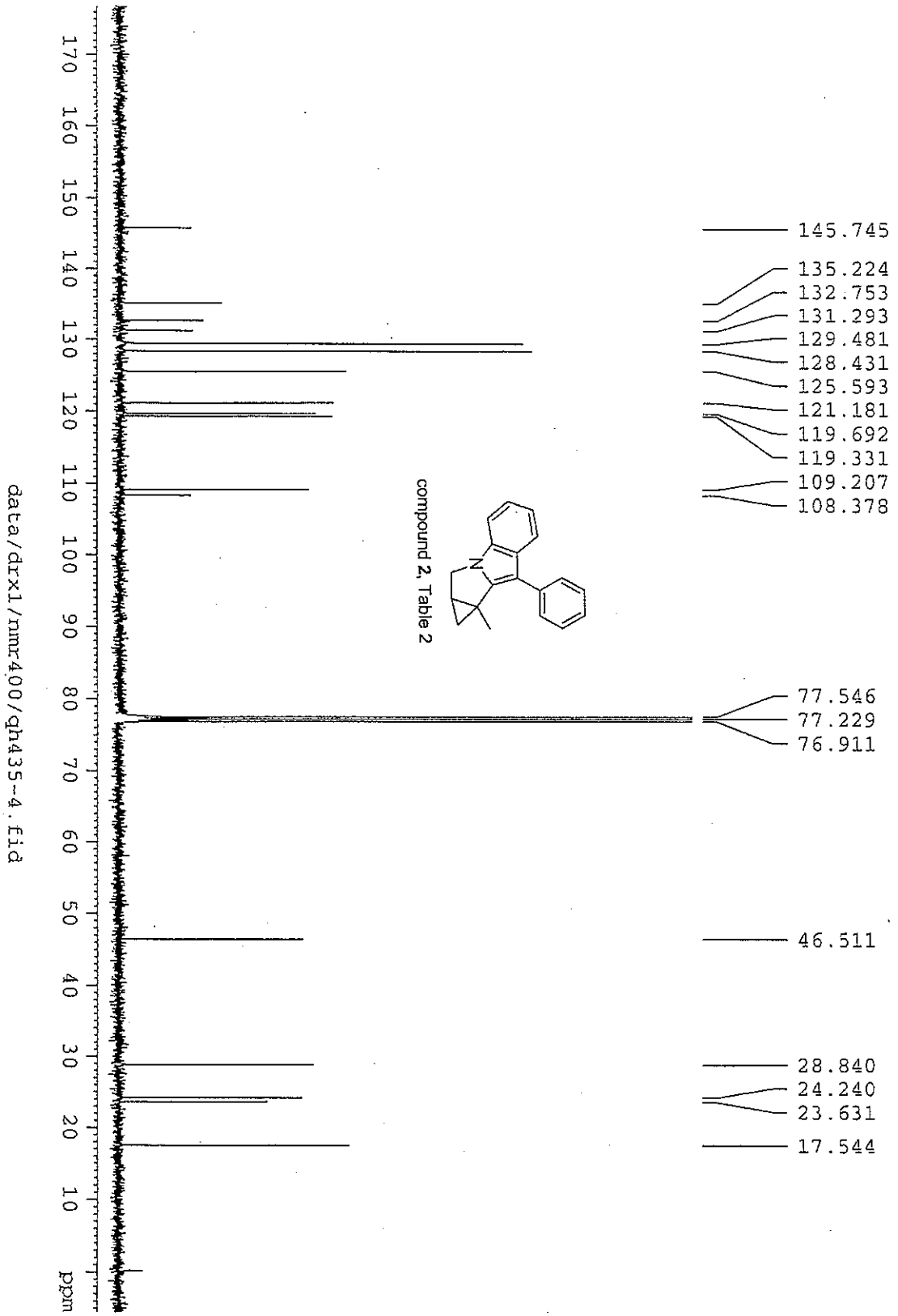

145.107
143.004
142.891
139.032
132.784
131.790
130.695
128.761
128.500
128.002
127.011
126.751
123.914
116.492
77.657
77.233
76.809
23.706
Br
compound 21, Table 2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh512-2.fid


7.343
7.338
7.336
7.324
7.319
7.307
7.302
7.296
7.279
7.264
7.258
7.253
7.239
7.236
7.234
7.231
7.212
7.206
6.745
6.741
6.718
6.713
6.708
6.703
6.683
6.678
6.657
6.653
5.430
5.426
5.265
5.261
5.257
5.254
4.124
4.100
4.077
3.100
3.096
3.076
3.073
3.053
3.049
0.000
compound 23, Table 2
1.000
2.330
3.916
0.996
1.095
1.145
1.111
1.145
2.512
2.323
ppm
data/dat2/nmr300/qh710-1.fid


157.595
144.457
140.759
139.699
129.558
128.655
127.850
126.381
122.719
115.153
112.469
86.927
77.548
77.230
76.913
68.197
35.311
compound 23, Table 2
data/drx1/nmr400/qh710-2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.716
7.697
7.626
7.623
7.606
7.603
7.463
7.444
7.425
7.286
7.267
7.247
7.156
7.153
7.141
7.138
7.099
7.094
7.084
7.079
7.074
4.261
4.247
4.235
4.221
4.062
4.035
2.168
2.102
2.094
2.082
1.457
1.291
1.280
1.271
1.259
1.032
1.020
1.008
0.000
1.000
1.953
2.006
1.496
2.988
1.031
1.007
0.989
3.002
1.055
0.990
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
compound 2, Table 2
N
ddata/drx1/nmr400/qh435-3.fid


170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
compound 2, Table 2
data/dat2/nmr400/qh435-10.fid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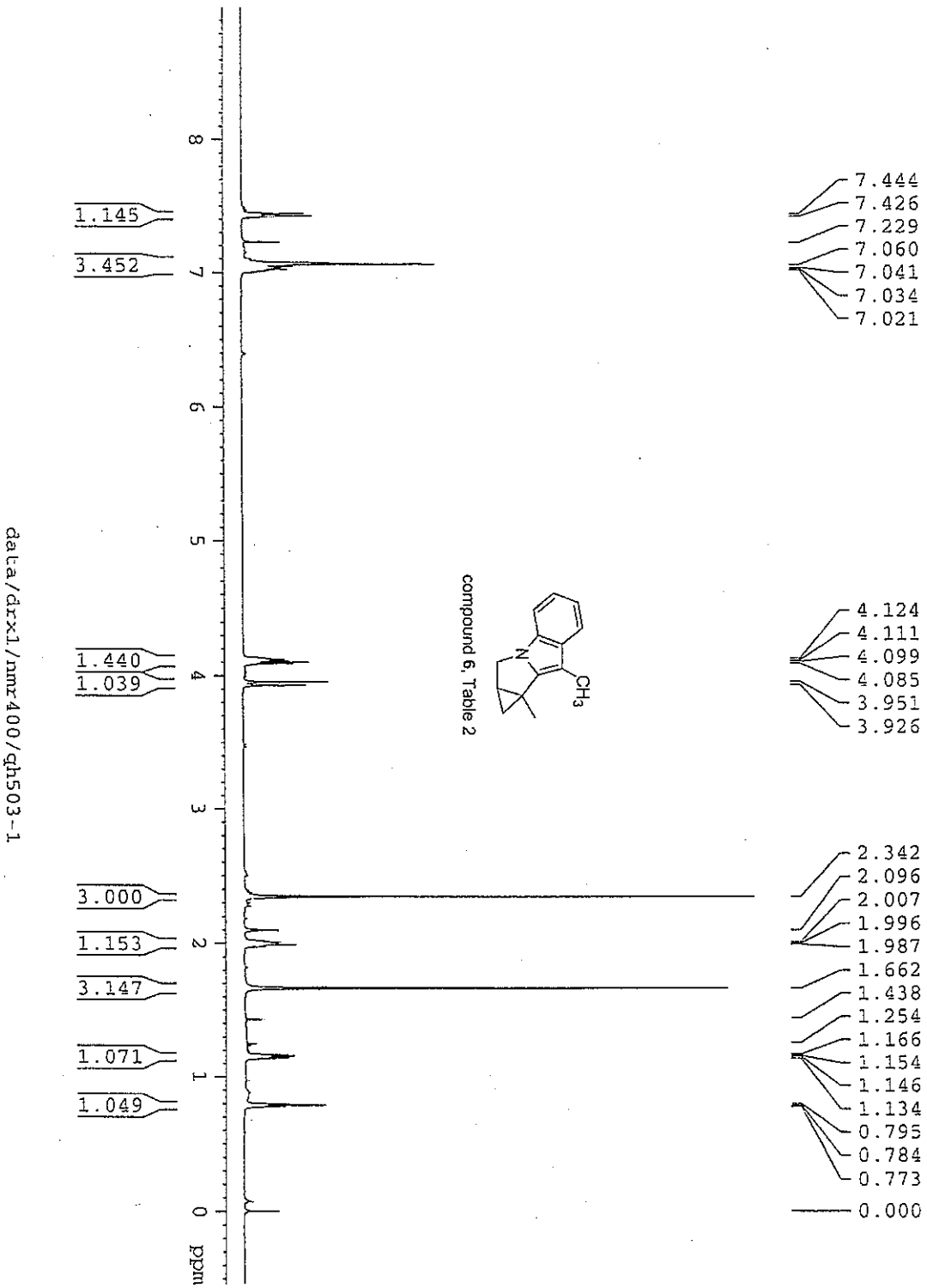
135.224
132.753
131.293
129.481
128.431
125.593
121.181
119.692
119.331
109.207
108.378
77.546
77.229
76.911
46.511
28.840
24.240
23.631
17.544
compound 2, Table 2
ppm
data/drx1/nmr400/qh435-4.fid


data/drx1/nmr400/qh503-1
compound 6, Table 2
CH3
N
ppm
0
1
2
3
4
5
6
7
8
1.145
3.452
1.440
1.039
3.000
1.153
3.147
1.071
1.049
7.444
7.426
7.229
7.060
7.041
7.034
7.021
4.124
4.111
4.099
4.085
3.951
3.926
2.342
2.096
2.007
1.996
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1.146
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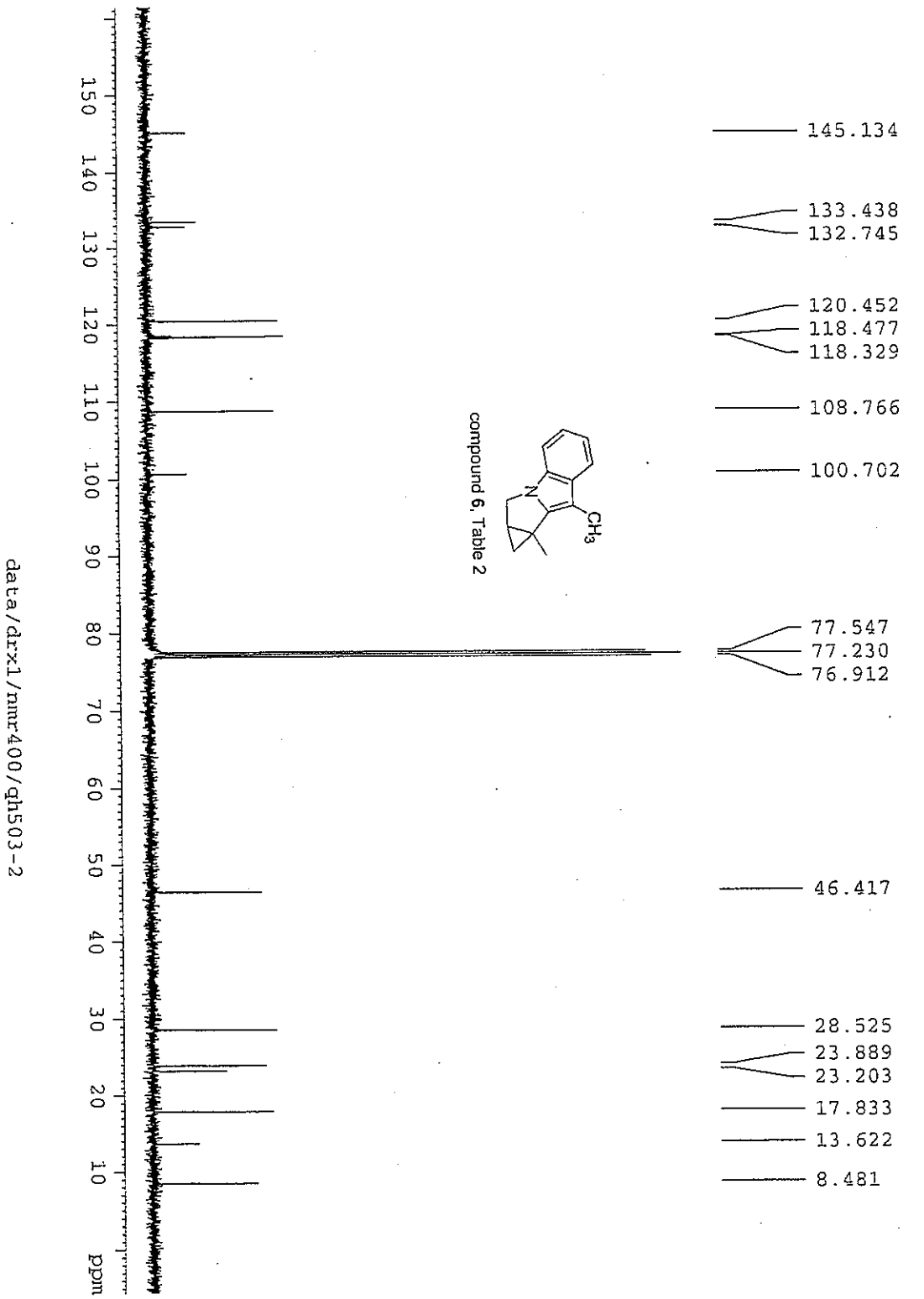
0.795
0.784
0.773
0.000


145.134
133.438
132.745
120.452
118.477
118.329
108.766
100.702
77.547
77.230
76.912
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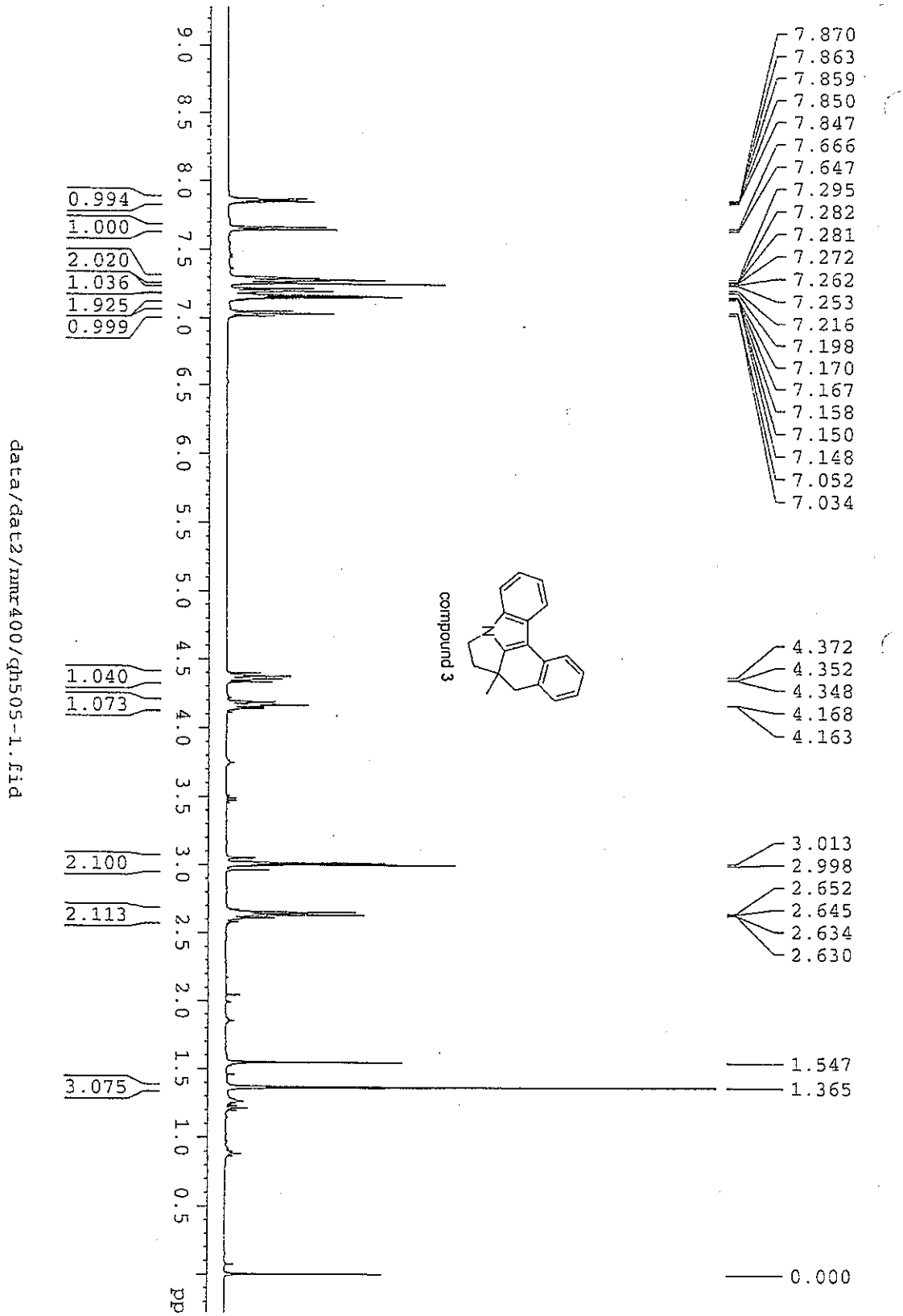
28.525
23.889
23.203
17.833
13.622
8.481
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
compound 6, Table 2
CH3
N
data/drx1/nmr400/qh503-2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compound 3
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7.863
7.859
7.850
7.847
7.666
7.647
7.295
7.282
7.281
7.272
7.262
7.253
7.216
7.198
7.170
7.167
7.158
7.150
7.148
7.052
7.034
4.372
4.352
4.348
4.168
4.163
3.013
2.998
2.652
2.645
2.634
2.630
1.547
1.365
0.000
0.994
1.000
2.020
1.036
1.925
0.999
1.040
1.073
2.100
2.113
3.075
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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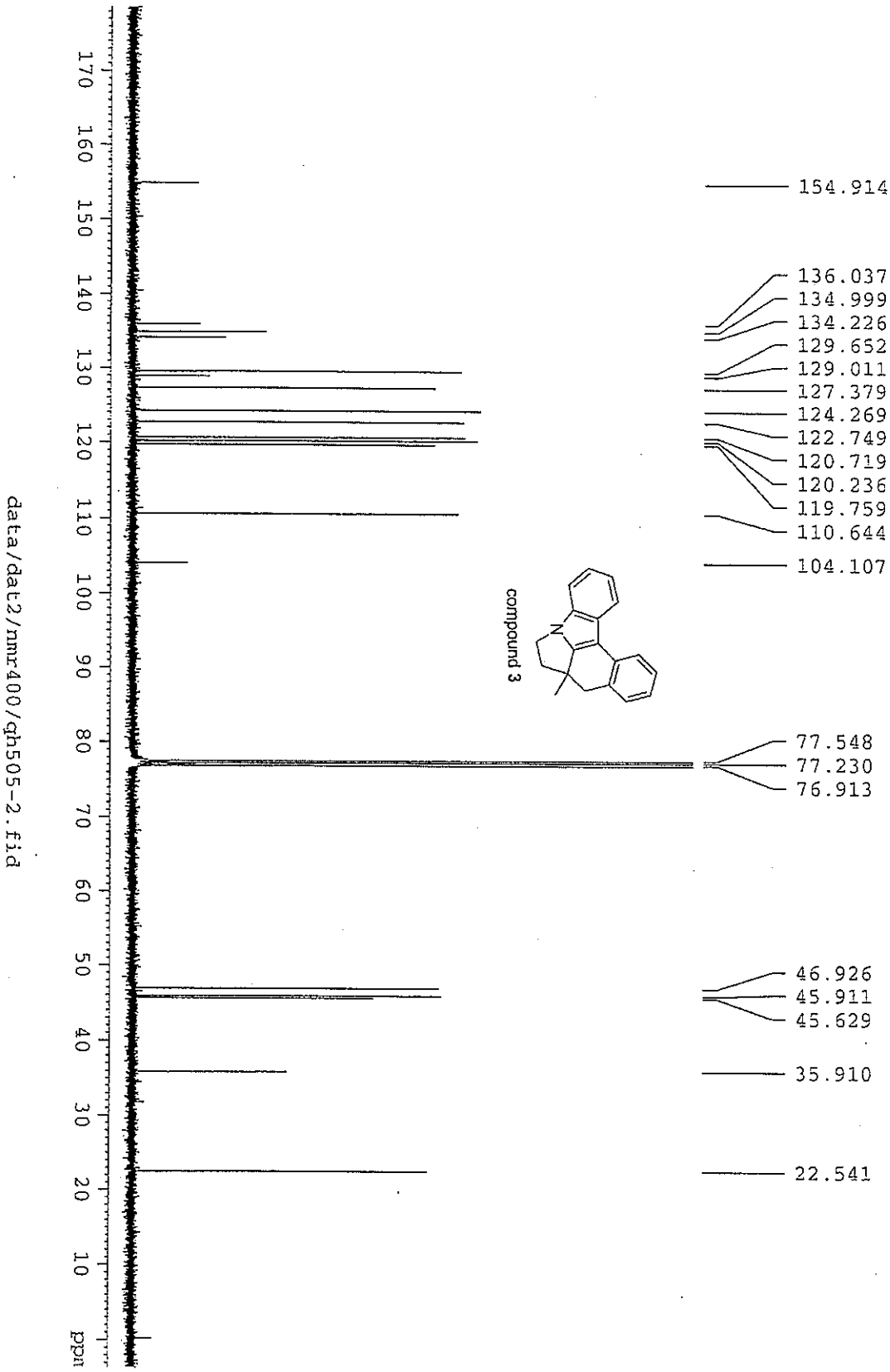
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110.644
104.107
77.548
77.230
76.913
46.926
45.911
45.629
35.910
22.541
compound 3
ppm
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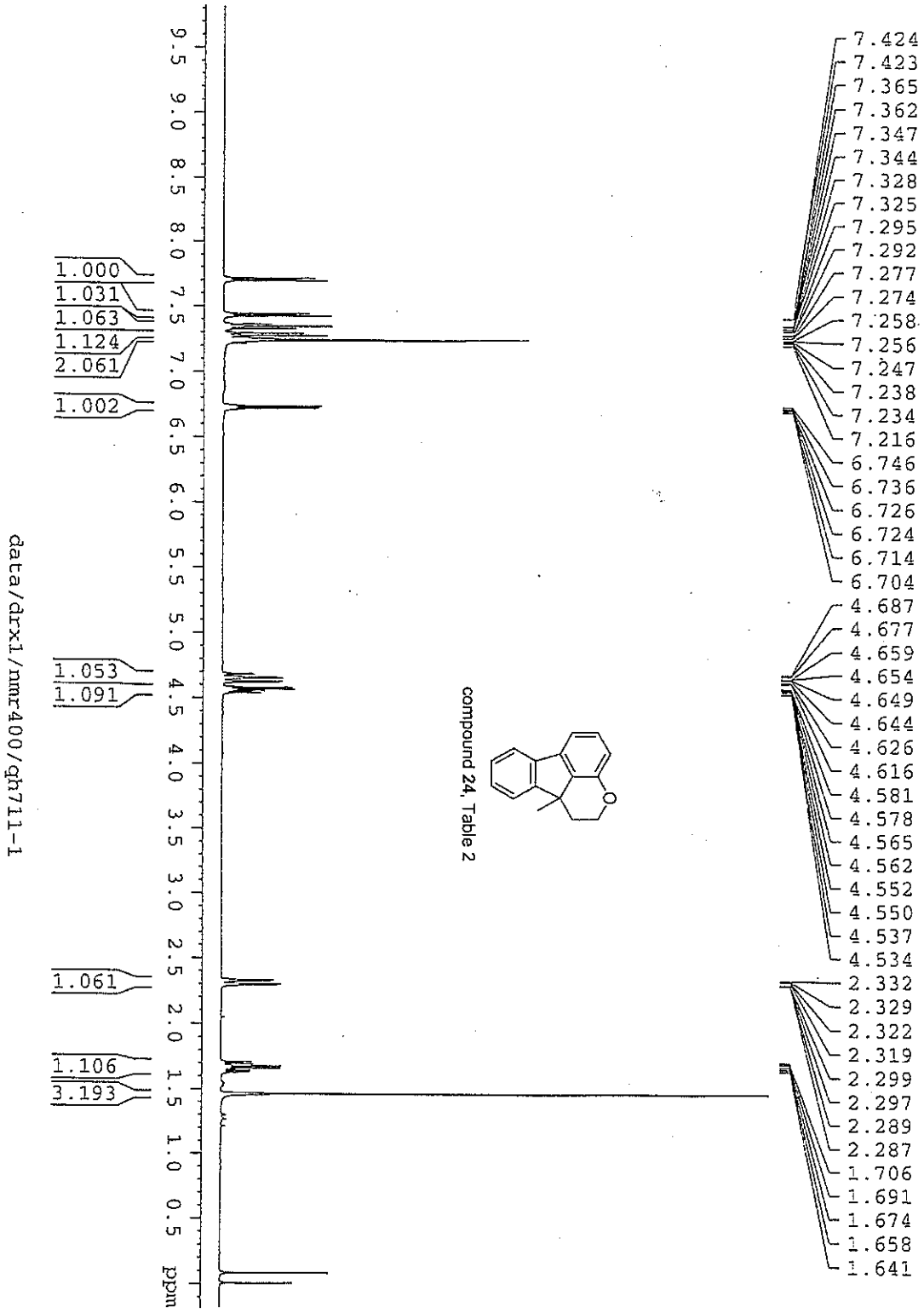
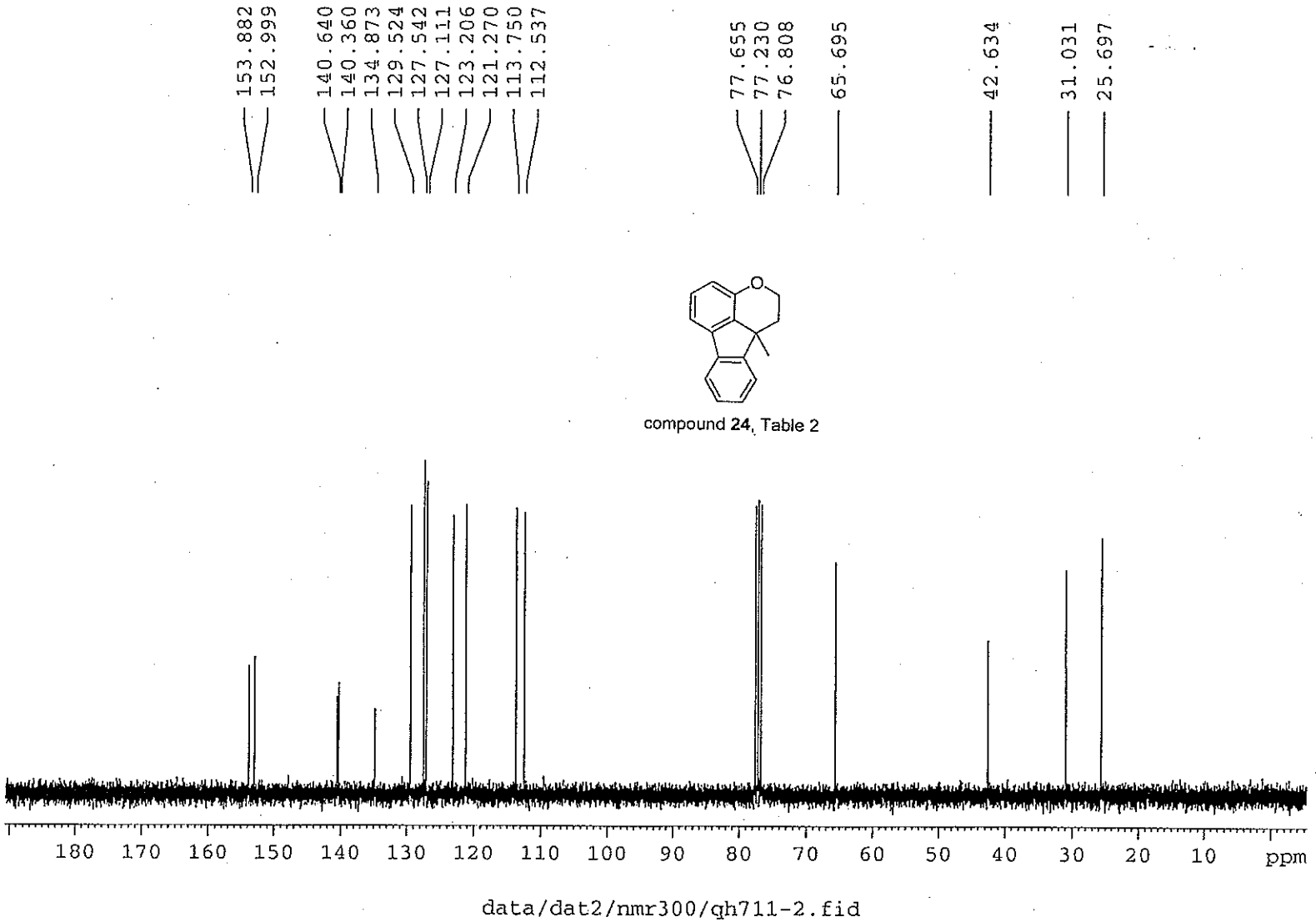
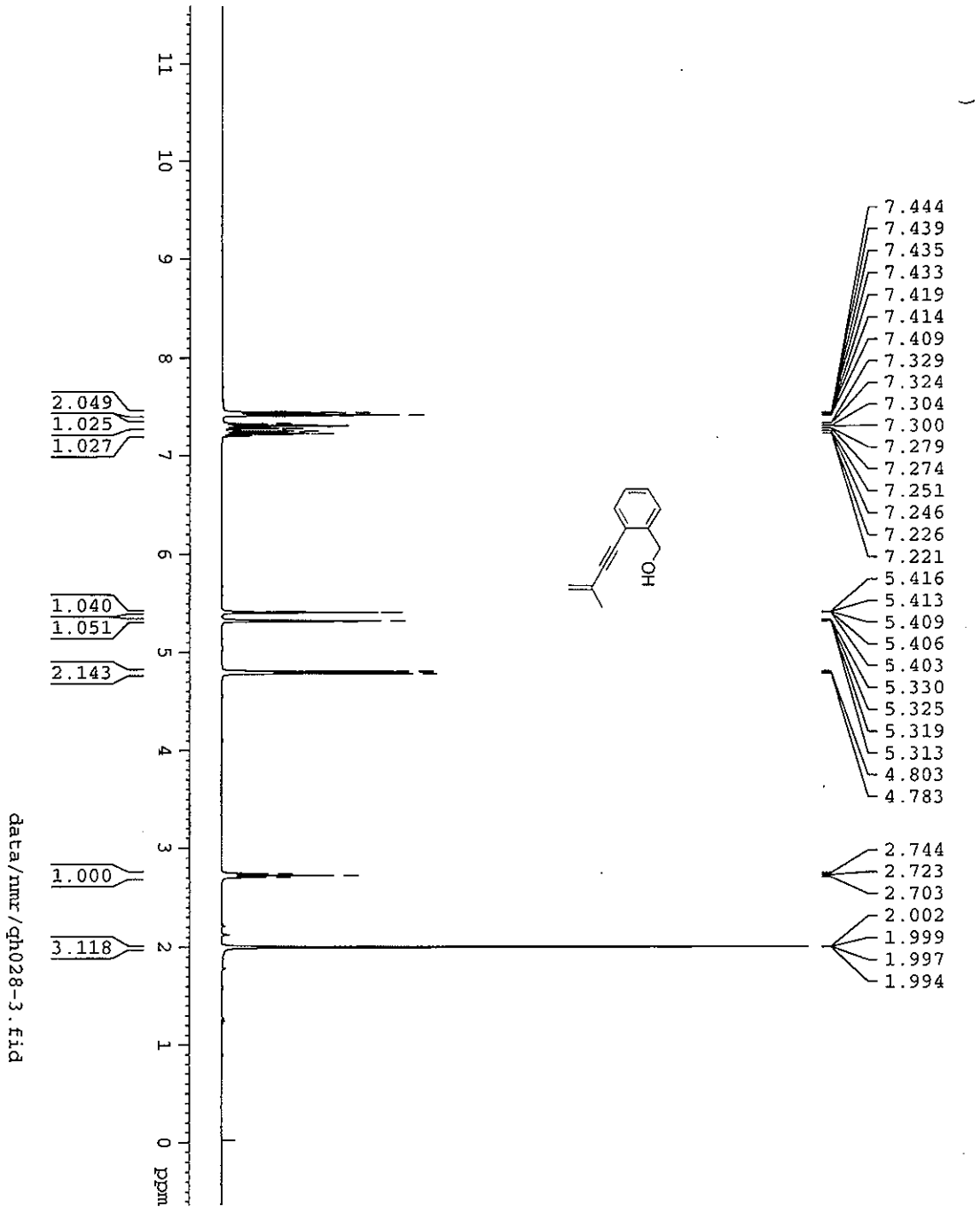

7.424
7.423
7.365
7.362
7.347
7.344
7.328
7.325
7.295
7.292
7.277
7.274
7.258
7.256
7.247
7.238
7.234
7.216
6.746
6.736
6.726
6.724
6.714
6.704
4.687
4.677
4.659
4.654
4.649
4.644
4.626
4.616
4.581
4.578
4.565
4.562
4.552
4.550
4.537
4.534
2.332
2.329
2.322
2.319
2.299
2.297
2.289
2.287
1.706
1.691
1.674
1.658
1.641
1.000
1.031
1.063
1.124
2.061
1.002
1.053
1.091
1.061
1.106
3.193
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
compound 24, Table 2
data/drx1/nmr400/qh711-1



compound **24**, Table 2

APPENDIX A. CHAPTER 1 ^{1}H AND ^{13}C NMR SPECTRA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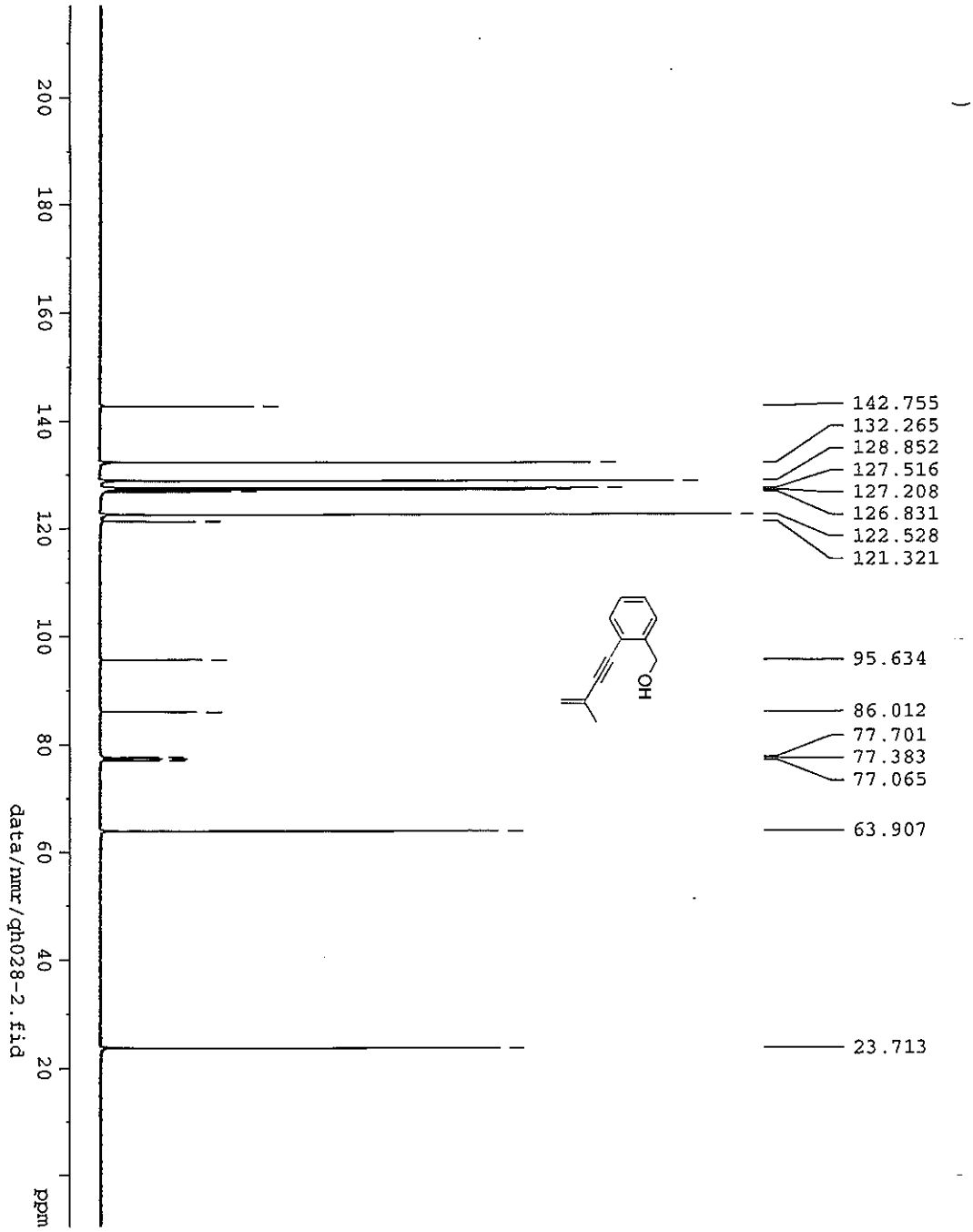
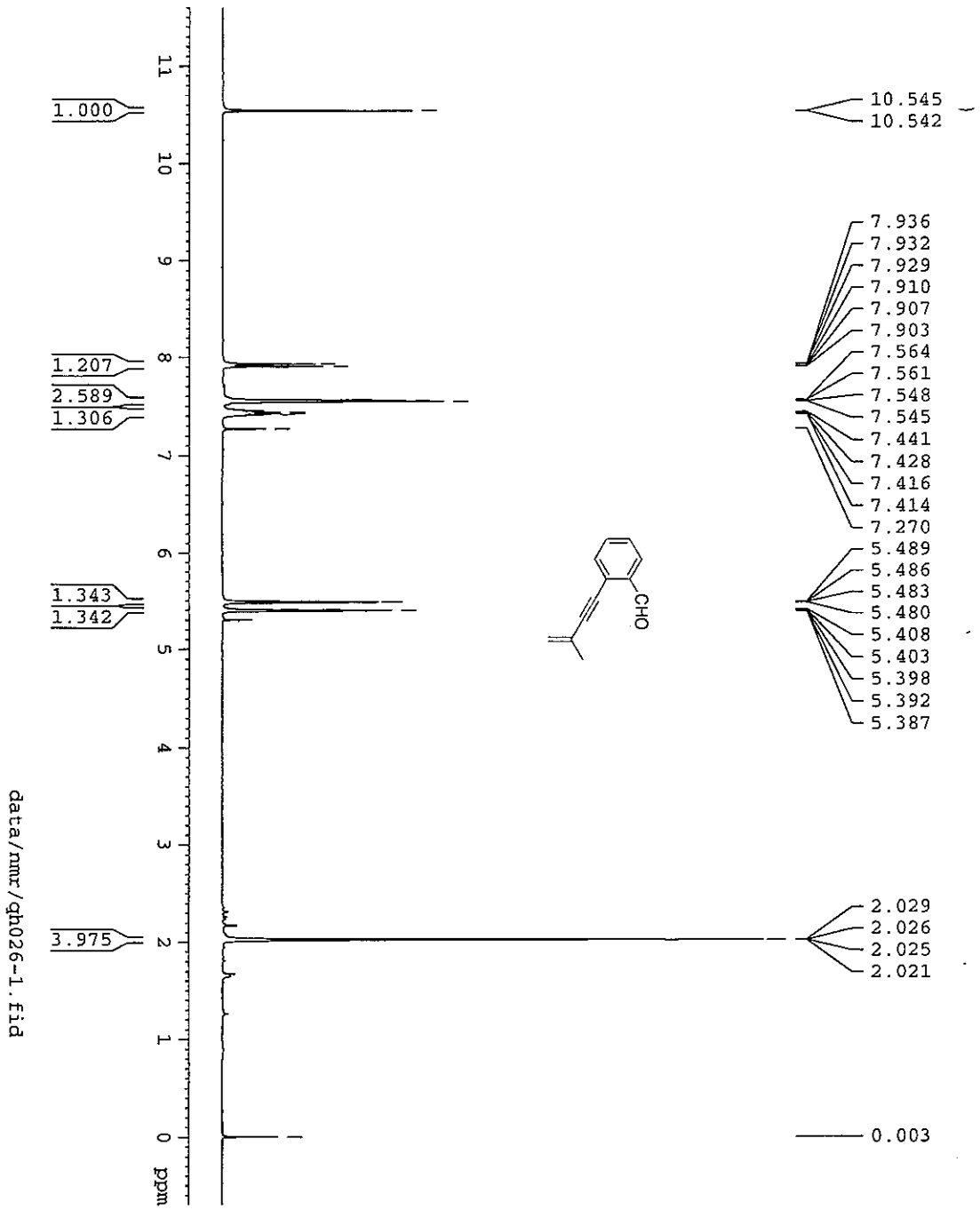
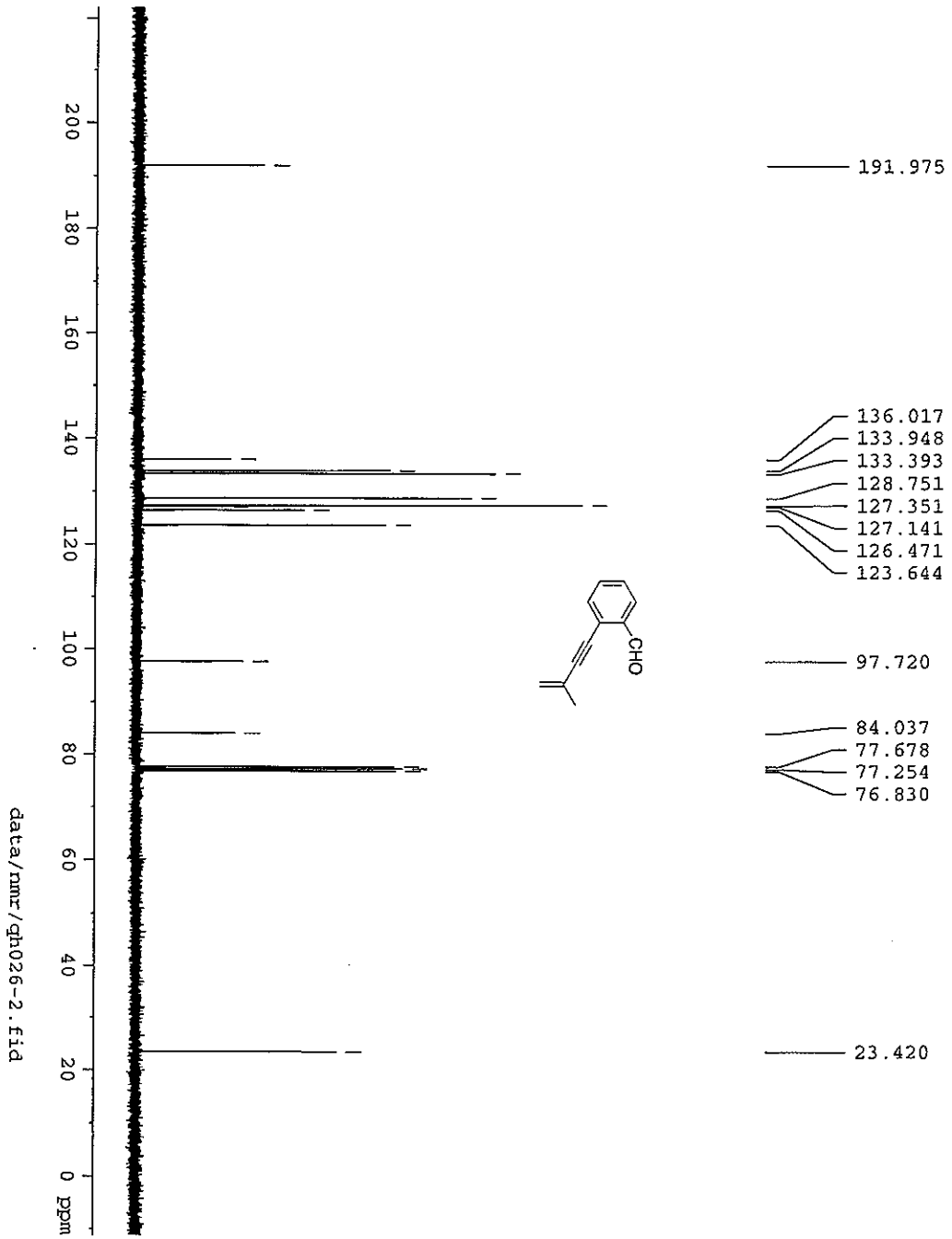
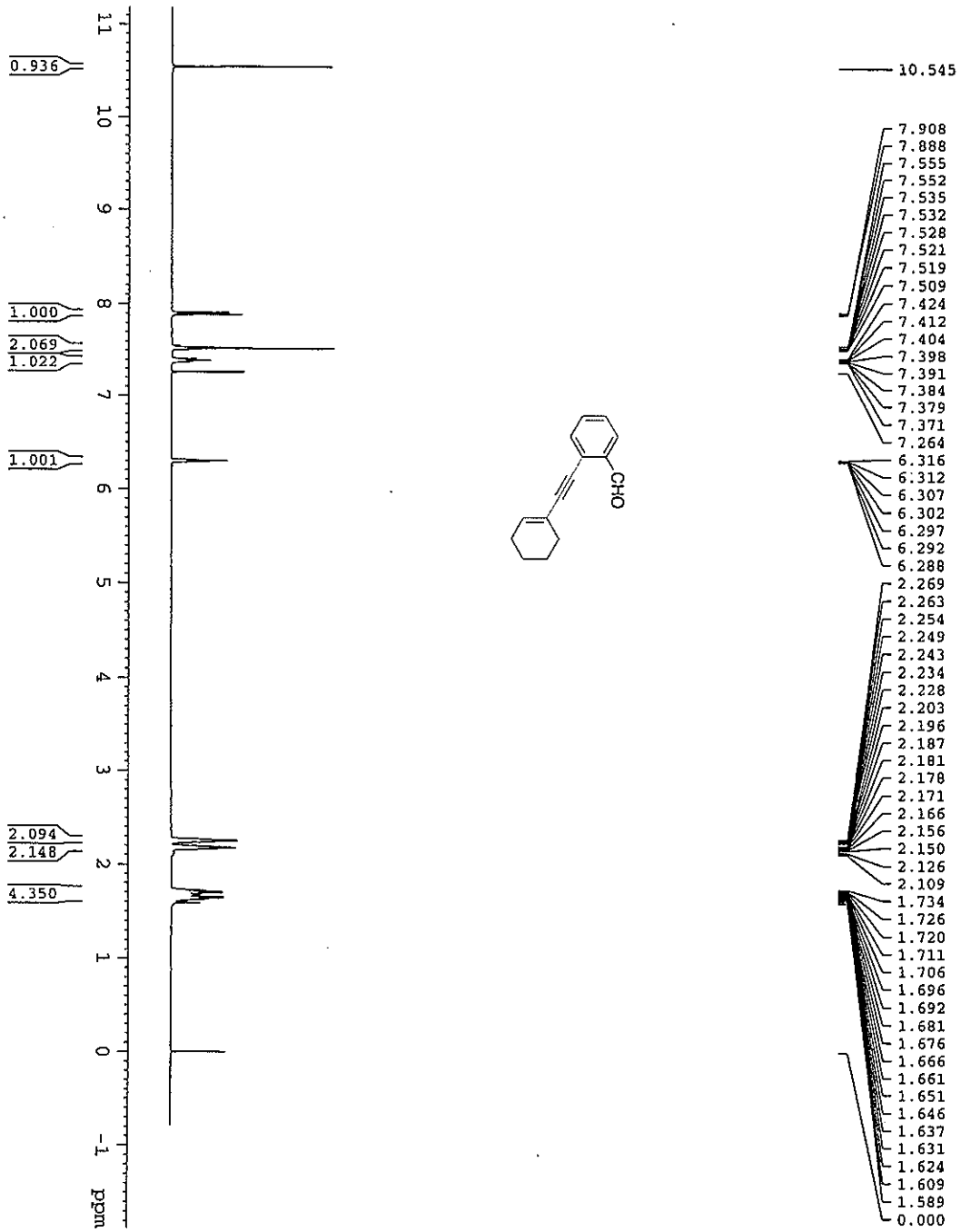
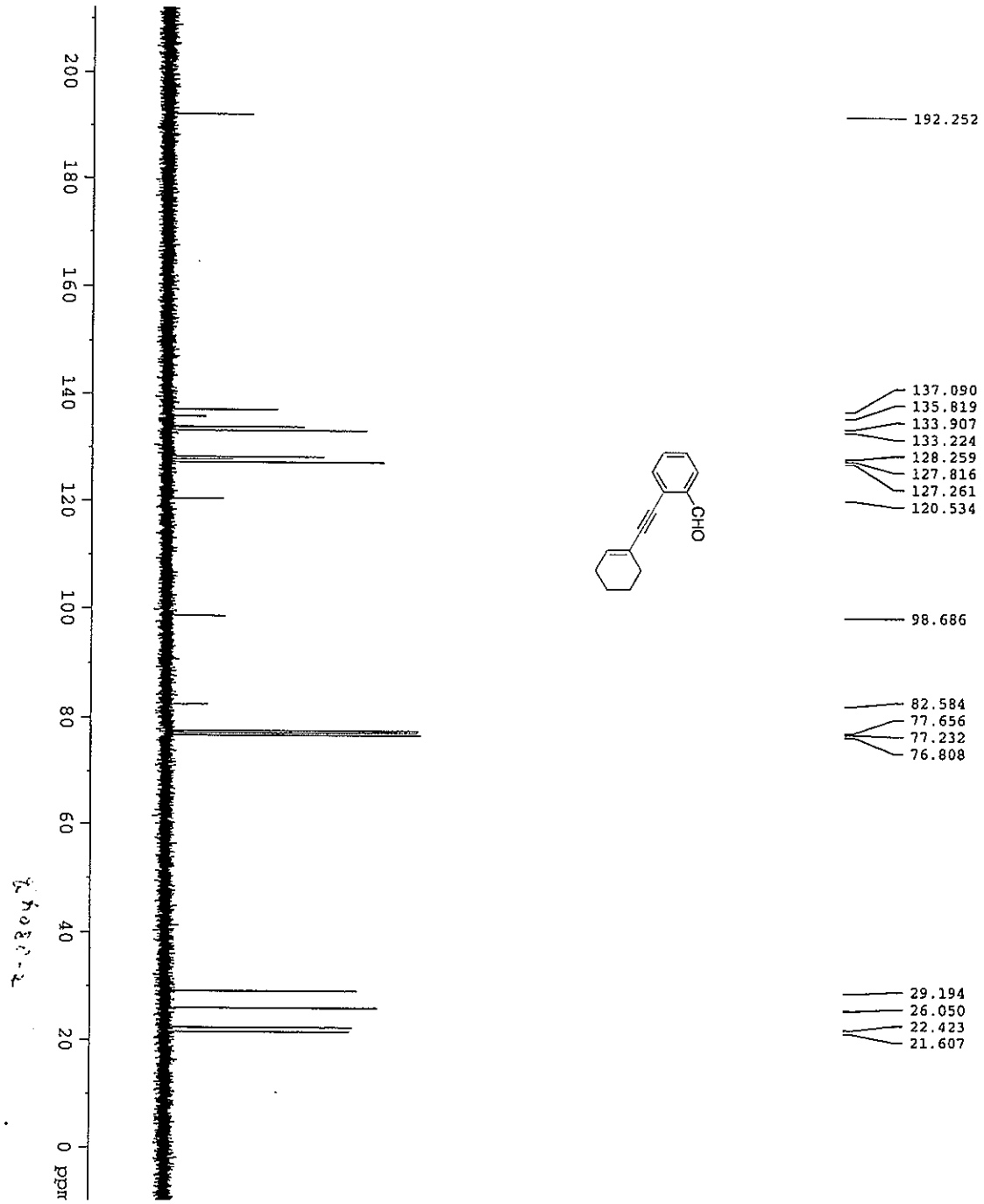
7.439
7.435
7.433
7.419
7.414
7.409
7.329
7.324
7.304
7.300
7.279
7.274
7.251
7.246
7.226
7.221
5.416
5.413
5.409
5.406
5.403
5.330
5.325
5.319
5.313
4.803
4.783
2.744
2.723
2.703
2.002
1.999
1.997
1.994
OH
2.049
1.025
1.027
1.040
1.051
2.143
1.000
3.118
ppm
data/nmr/qh028-3.fid

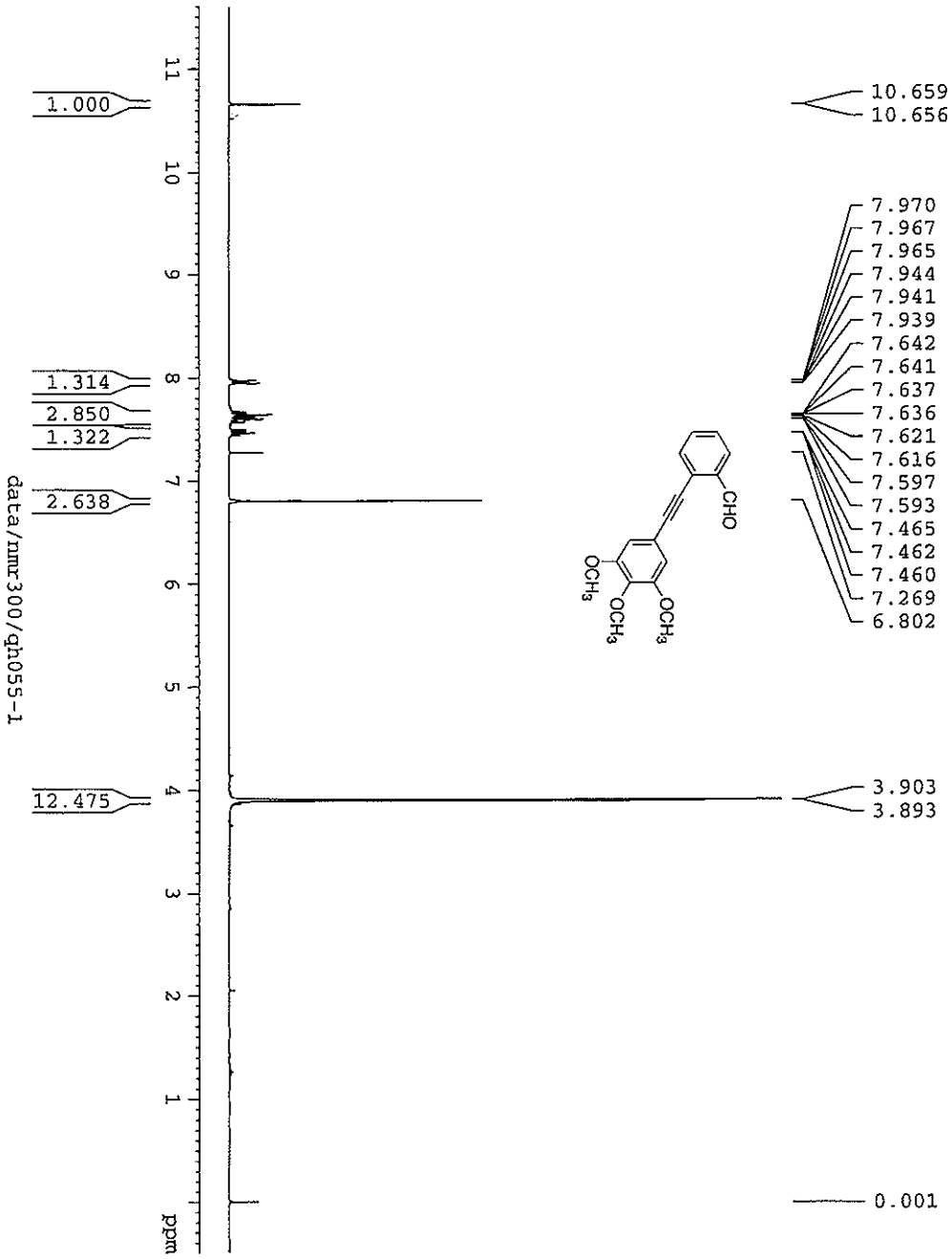

142.755
132.265
128.852
127.516
127.208
126.831
122.528
121.321
95.634
86.012
77.701
77.383
77.065
63.907
23.713
OH
200
180
160
140
120
100
80
60
40
20
ppm
data/nmr/qh028-2.fid

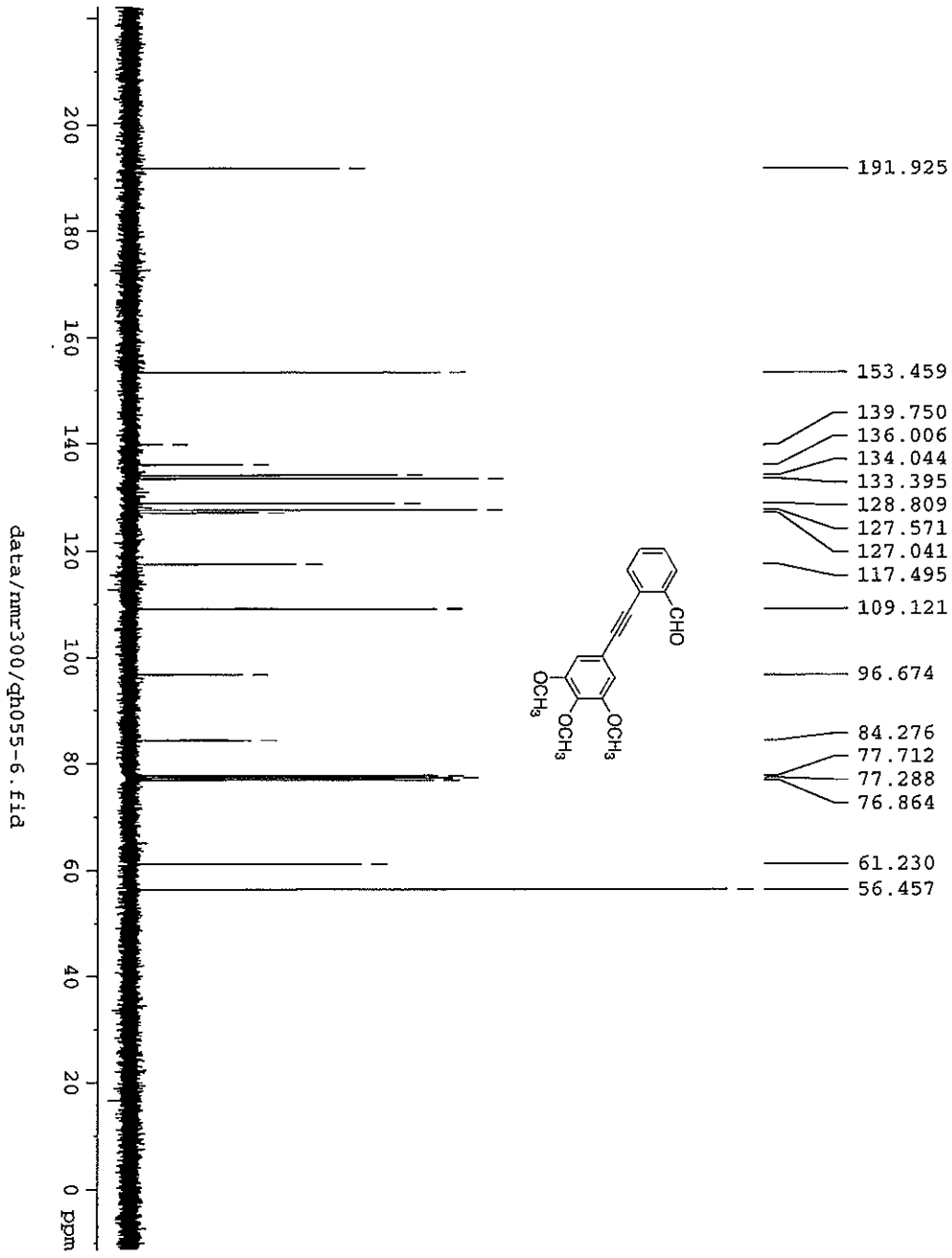

1.000
1.207
2.589
1.306
1.343
1.342
3.975
10.545
10.542
7.936
7.932
7.929
7.910
7.907
7.903
7.564
7.561
7.548
7.545
7.441
7.428
7.416
7.414
7.270
5.489
5.486
5.483
5.480
5.408
5.403
5.398
5.392
5.387
2.029
2.026
2.025
2.021
0.003
CHO
ppm
data/nmr/qh026-1.fid

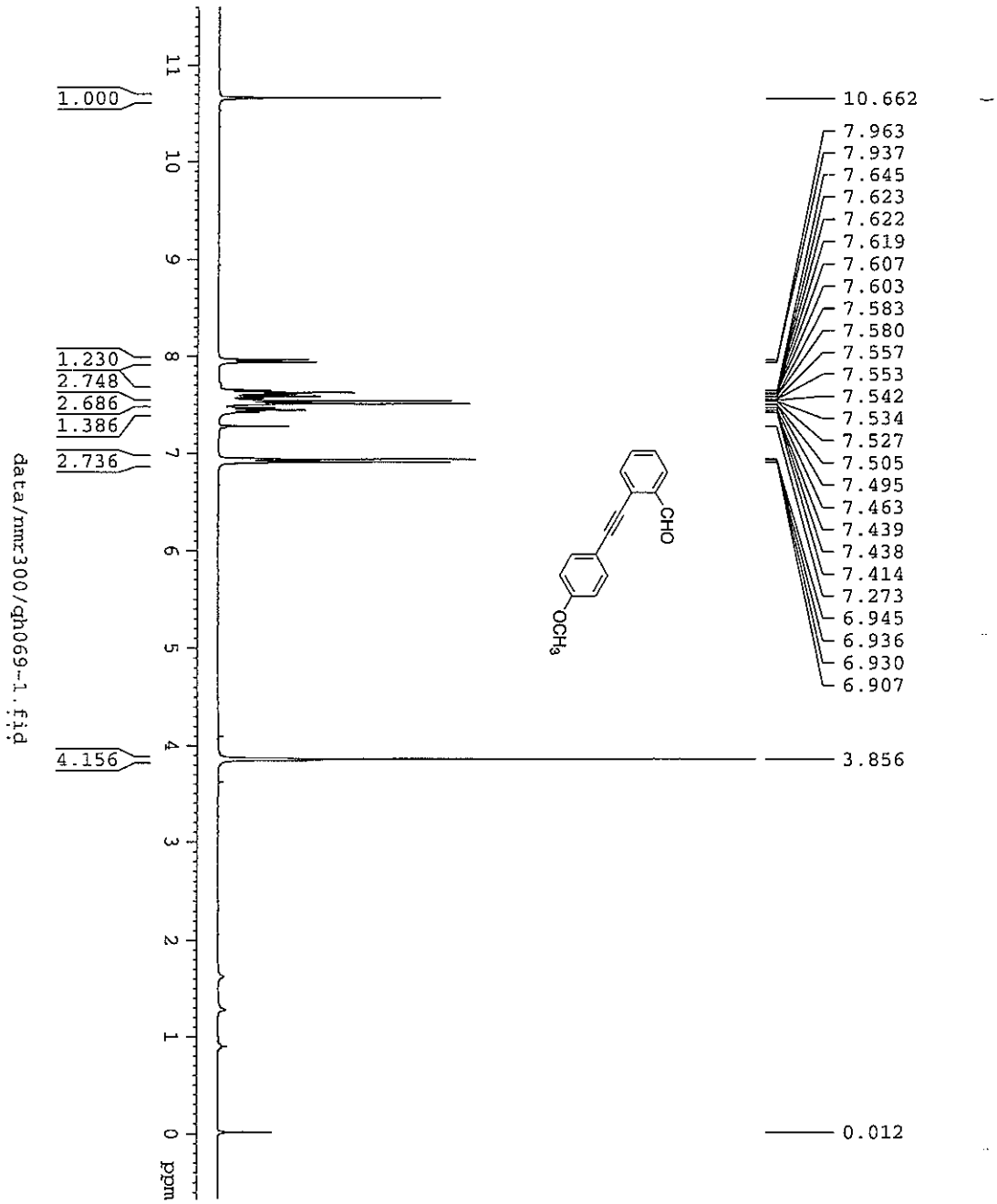

191.975
136.017
133.948
133.393
128.751
127.351
127.141
126.471
123.644
97.720
84.037
77.678
77.254
76.830
23.420
CHO
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh026-2.fid

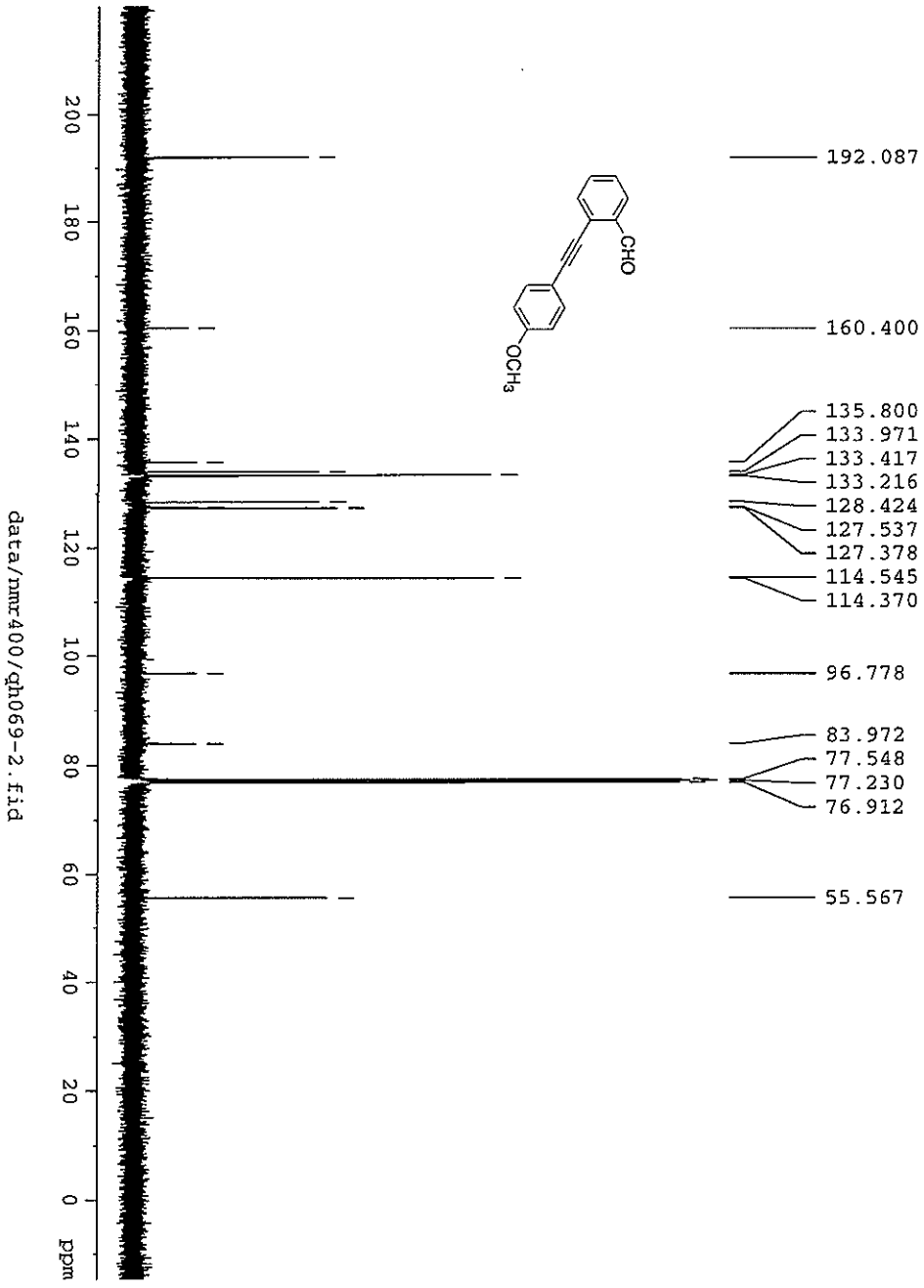

0.936
1.000
2.069
1.022
1.001
2.094
2.148
4.350
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm
CHO
10.545
7.908
7.888
7.555
7.552
7.535
7.532
7.528
7.521
7.519
7.509
7.424
7.412
7.404
7.398
7.391
7.384
7.379
7.371
7.264
6.316
6.312
6.307
6.302
6.297
6.292
6.288
2.269
2.263
2.254
2.249
2.243
2.234
2.228
2.203
2.196
2.187
2.181
2.178
2.171
2.166
2.156
2.150
2.126
2.109
1.734
1.726
1.720
1.711
1.706
1.696
1.692
1.681
1.676
1.666
1.661
1.651
1.646
1.637
1.631
1.624
1.609
1.589
0.000

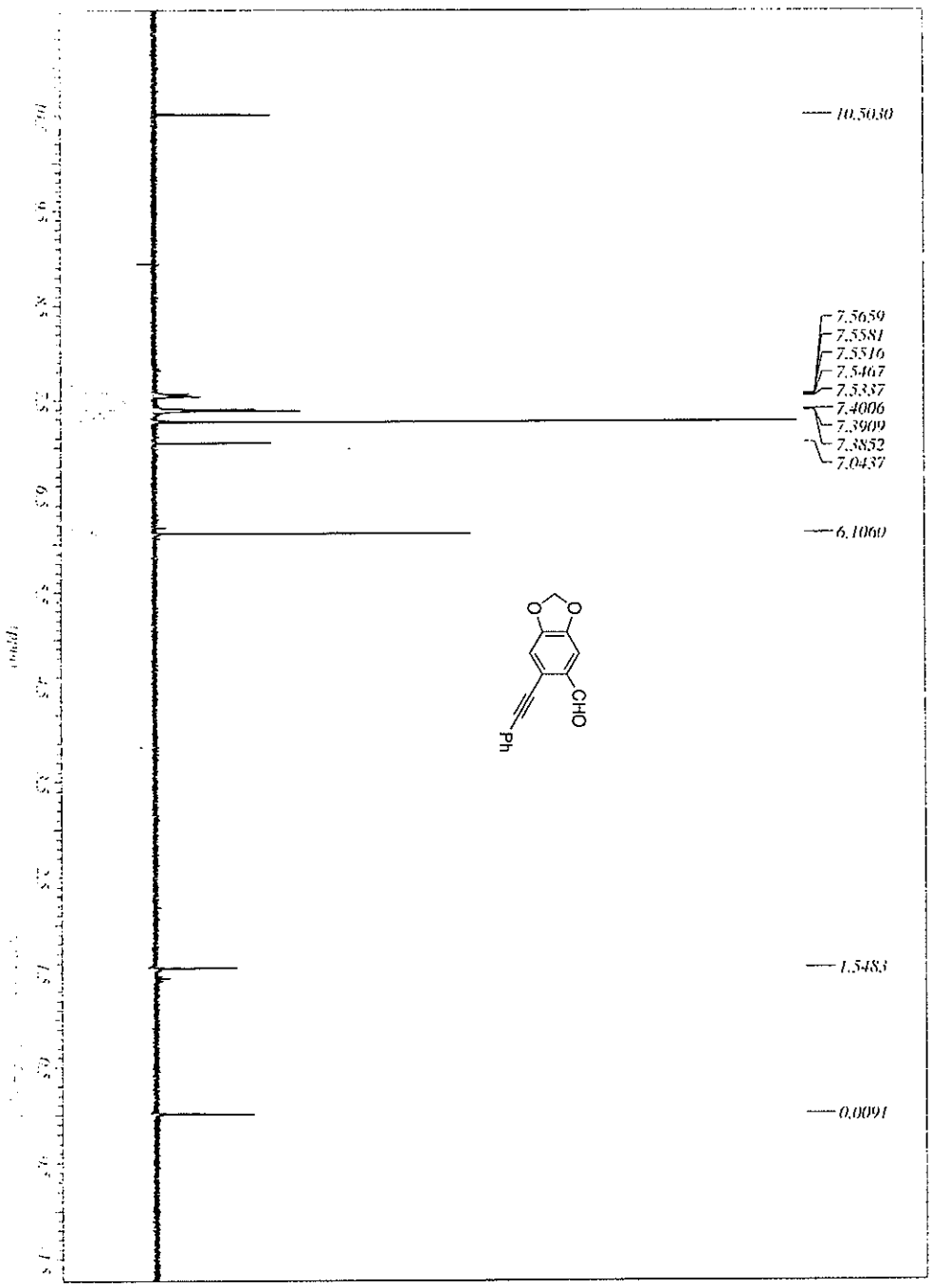

192.252
137.090
135.819
133.907
133.224
128.259
127.816
127.261
120.534
98.686
82.584
77.656
77.232
76.808
29.194
26.050
22.423
21.607
CHO
200
180
160
140
120
100
80
60
40
20
0 ppm


10.659
10.656
7.970
7.967
7.965
7.944
7.941
7.939
7.642
7.641
7.637
7.636
7.621
7.616
7.597
7.593
7.465
7.462
7.460
7.269
6.802
3.903
3.893
0.001
1.000
1.314
2.850
1.322
2.638
12.475
CHO
OCH3
OCH3
OCH3
data/nmr300/qh055-1
ppm


191.925
153.459
139.750
136.006
134.044
133.395
128.809
127.571
127.041
117.495
109.121
96.674
84.276
77.712
77.288
76.864
61.230
56.457
CHO
OCH3
OCH3
OCH3
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr300/qh055-6.fid


10.662
7.963
7.937
7.645
7.623
7.622
7.619
7.607
7.603
7.583
7.580
7.557
7.553
7.542
7.534
7.527
7.505
7.495
7.463
7.439
7.438
7.414
7.273
6.945
6.936
6.930
6.907
3.856
0.012
1.000
1.230
2.748
2.686
1.386
2.736
4.156
CHO
OCH3
ppm
data/nmr300/qh069-1.fid


192.087
160.400
135.800
133.971
133.417
133.216
128.424
127.537
127.378
114.545
114.370
96.778
83.972
77.548
77.230
76.912
55.567
CHO
OCH3
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh069-2.fid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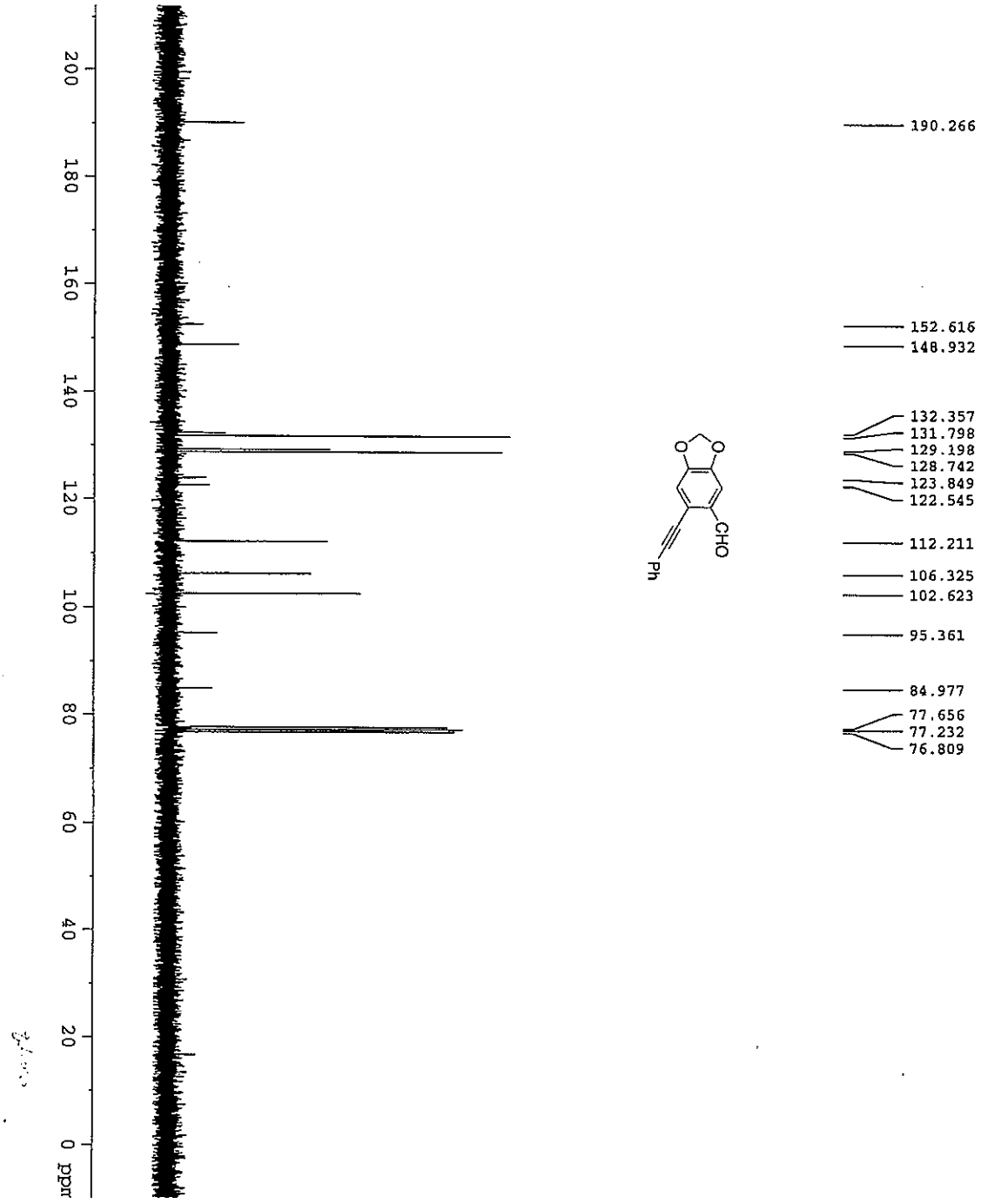
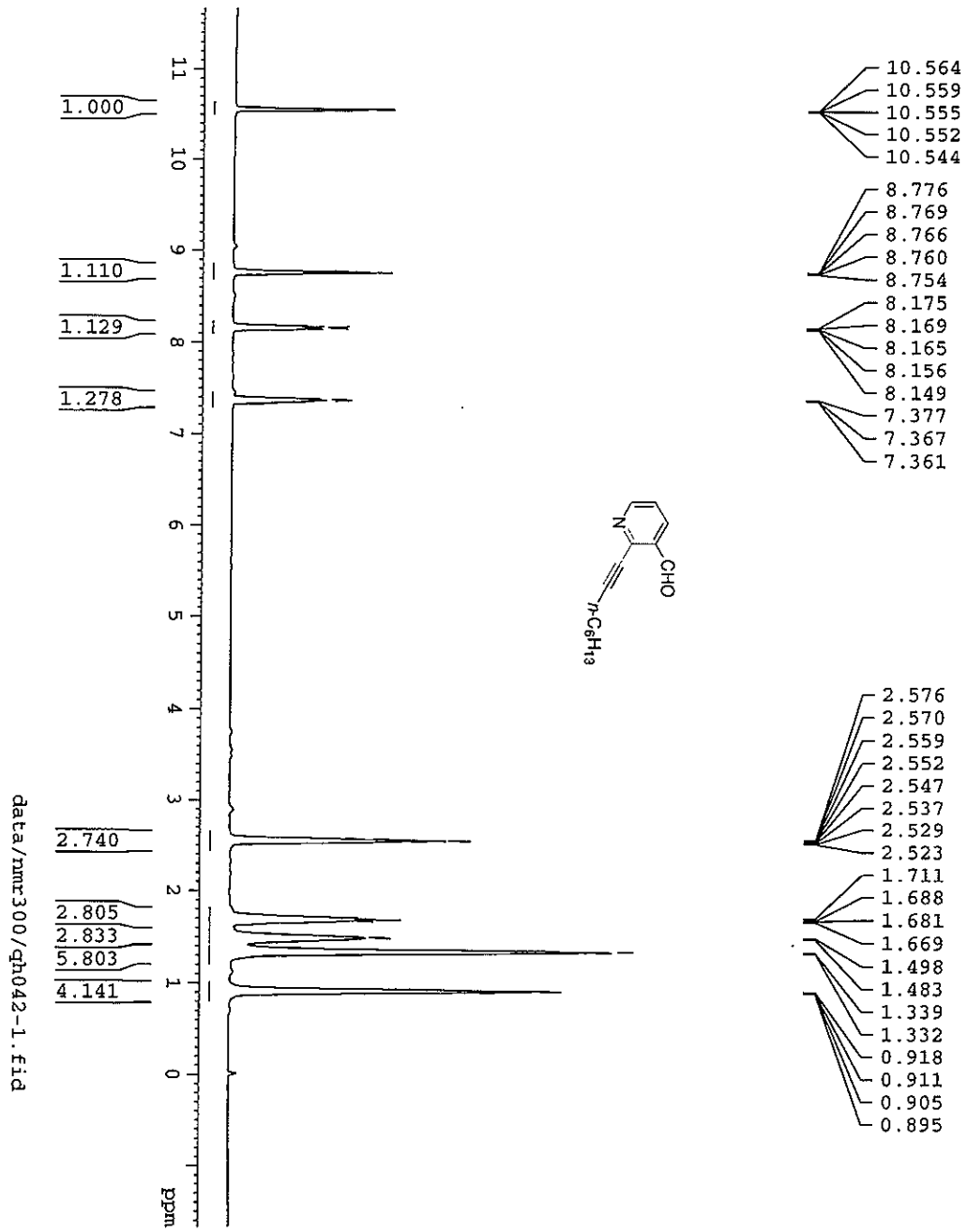
7.5659
7.5581
7.5516
7.5467
7.5387
7.4006
7.3909
7.3852
7.0437
6.1060
1.5483
0.0091
CHO
Ph


200
180
160
140
120
100
80
60
40
20
0 ppm
O
O
CHO
Ph
190.266
152.616
148.932
132.357
131.798
129.198
128.742
123.849
122.545
112.211
106.325
102.623
95.361
84.977
77.656
77.232
76.809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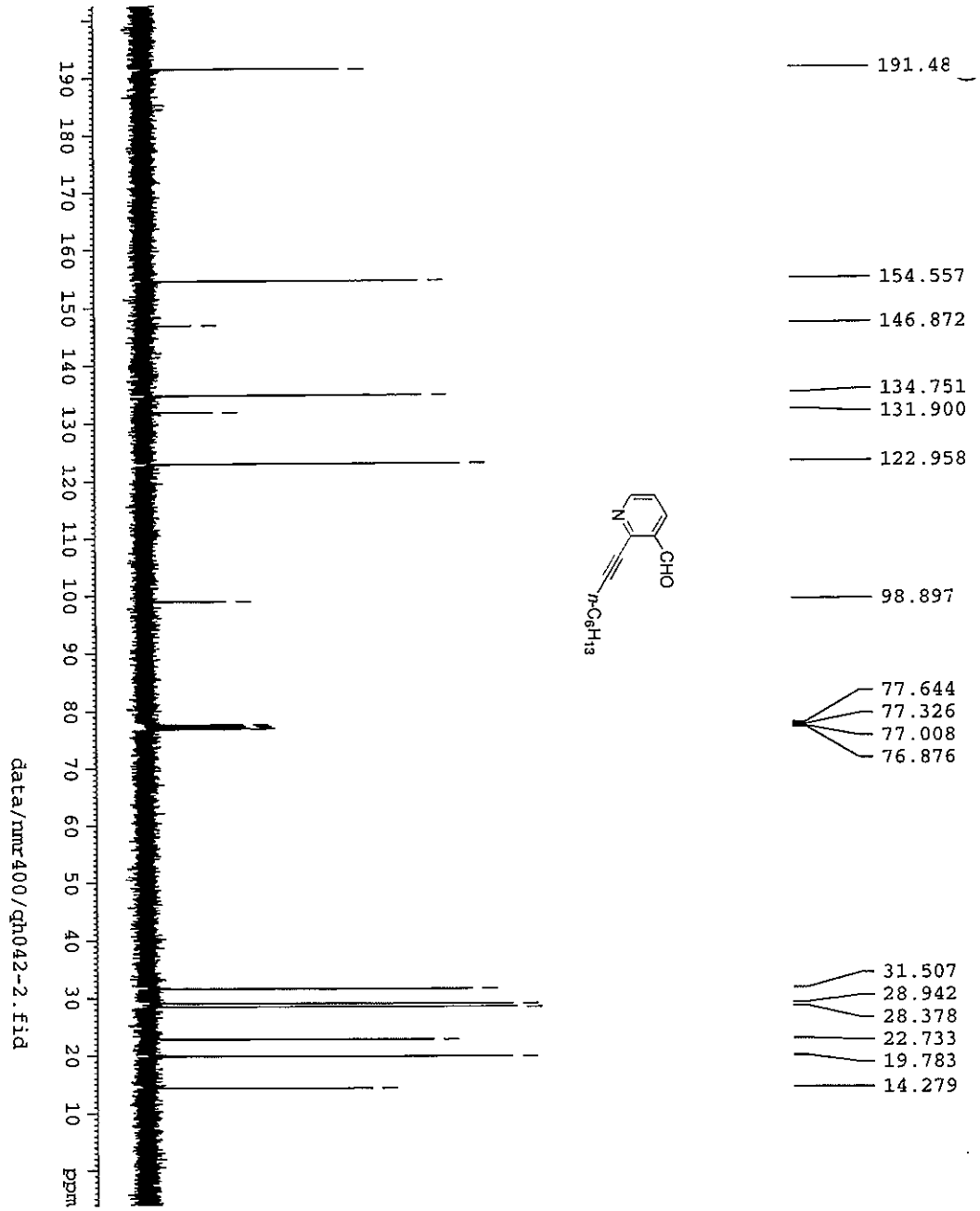
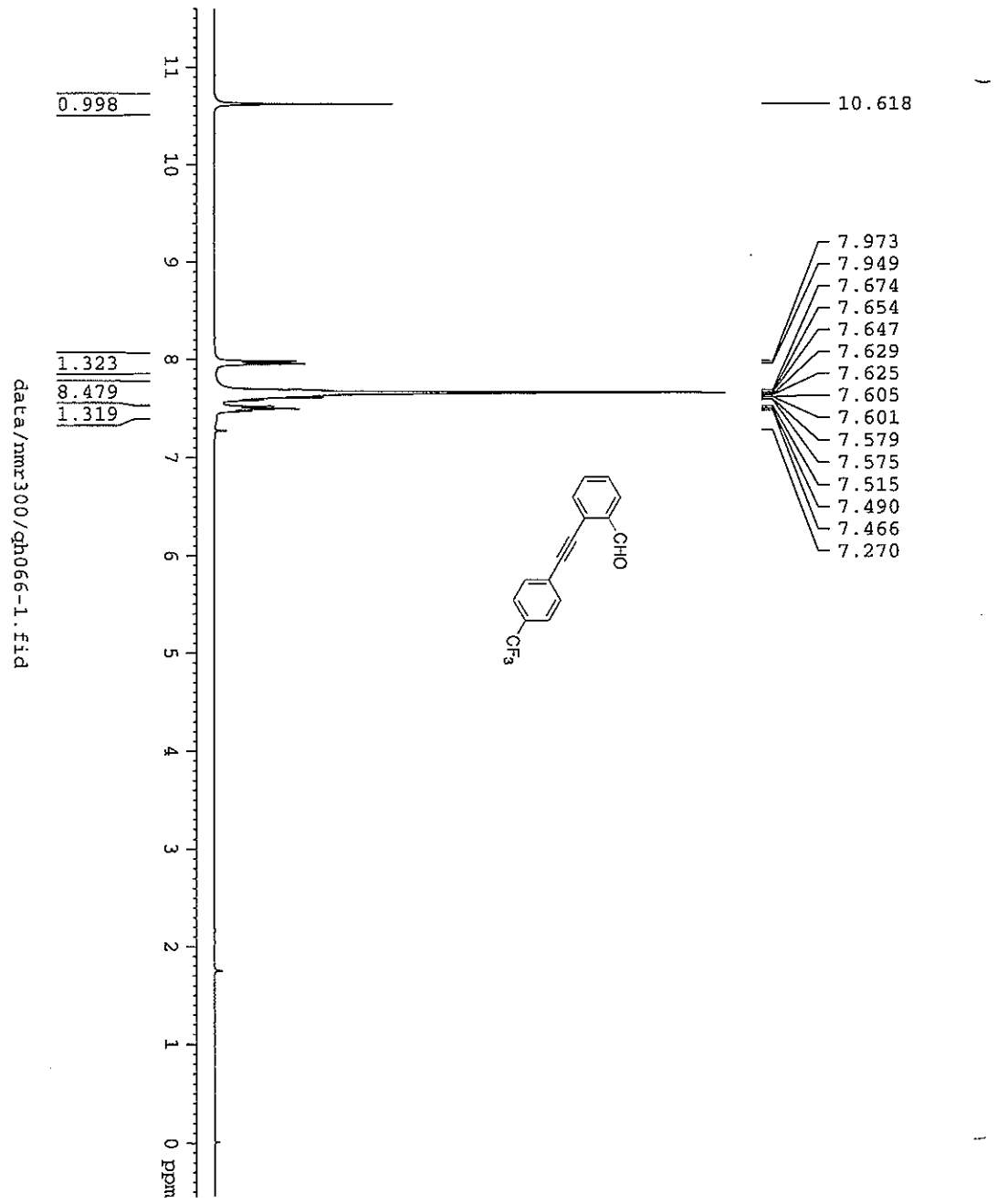
10.559
10.555
10.552
10.544
8.776
8.769
8.766
8.760
8.754
8.175
8.169
8.165
8.156
8.149
7.377
7.367
7.361
2.576
2.570
2.559
2.552
2.547
2.537
2.529
2.523
1.711
1.688
1.681
1.669
1.498
1.483
1.339
1.332
0.918
0.911
0.905
0.895
1.000
1.110
1.129
1.278
2.740
2.805
2.833
5.803
4.141
ppm
data/nmr300/qh042-1.fid
N
CHO
n-C6H13


191.48
154.557
146.872
134.751
131.900
122.958
98.897
77.644
77.326
77.008
76.876
31.507
28.942
28.378
22.733
19.783
14.279
N
CHO
n-C6H13
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/nmr400/qh042-2.fid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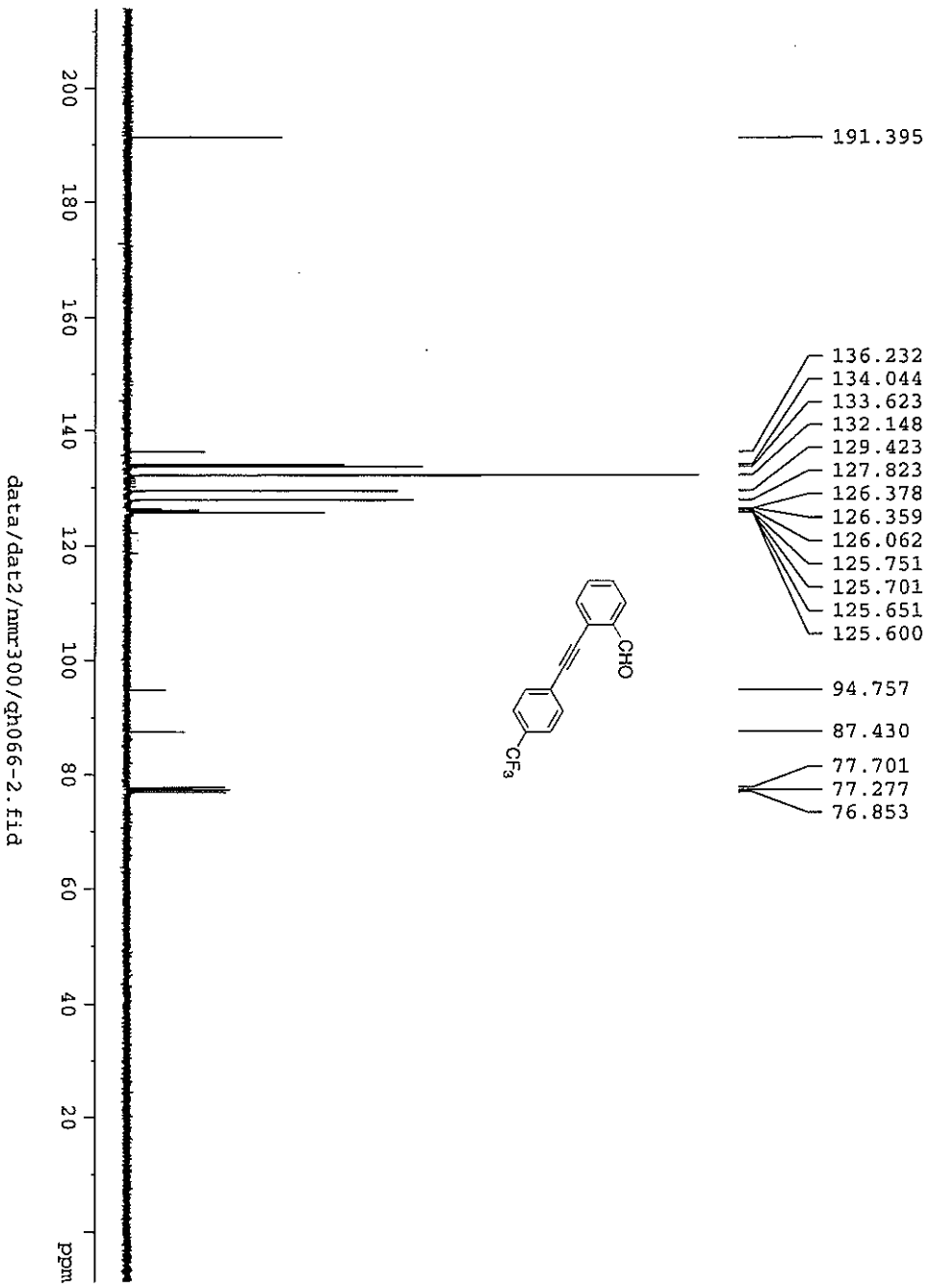
7.973
7.949
7.674
7.654
7.647
7.629
7.625
7.605
7.601
7.579
7.575
7.515
7.490
7.466
7.270
0.998
1.323
8.479
1.319
CHO
CF3
11
10
9
8
7
6
5
4
3
2
1
0 ppm
data/nmr300/qh066-1.fid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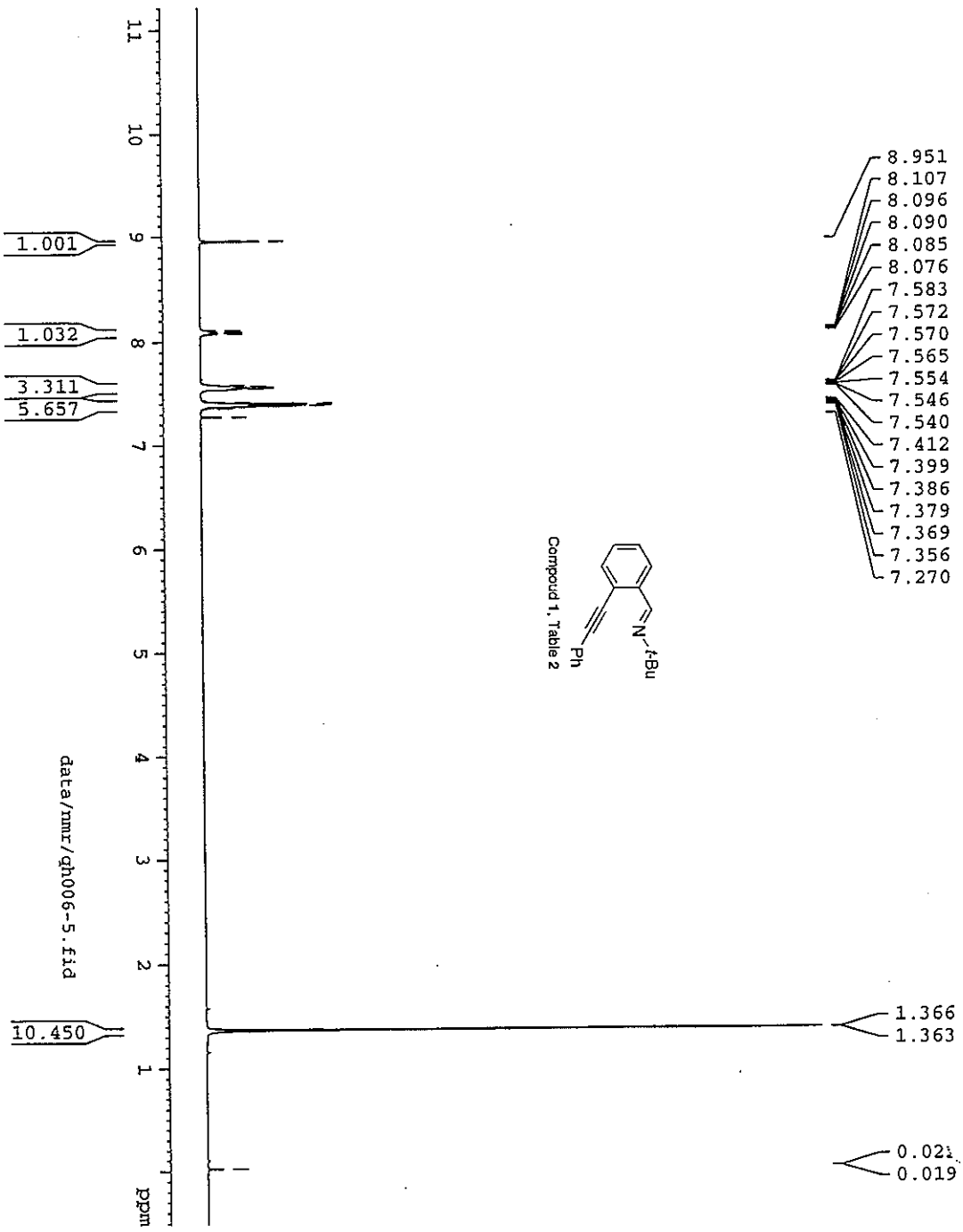
136.232
134.044
133.623
132.148
129.423
127.823
126.378
126.359
126.062
125.751
125.701
125.651
125.600
94.757
87.430
77.701
77.277
76.853
CHO
CF3
200
180
160
140
120
100
80
60
40
20
ppm
data/dat2/nmr300/qh066-2.fid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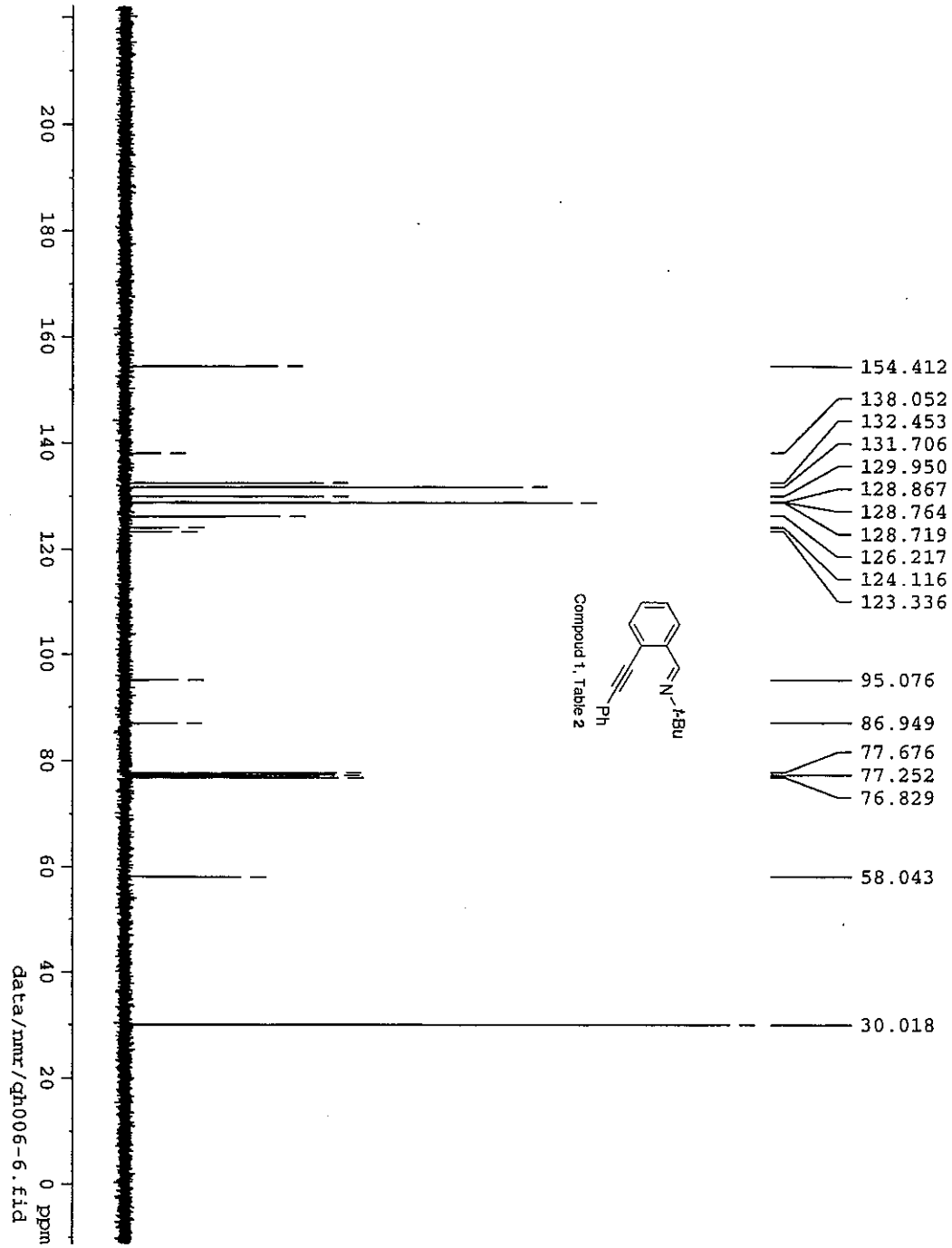
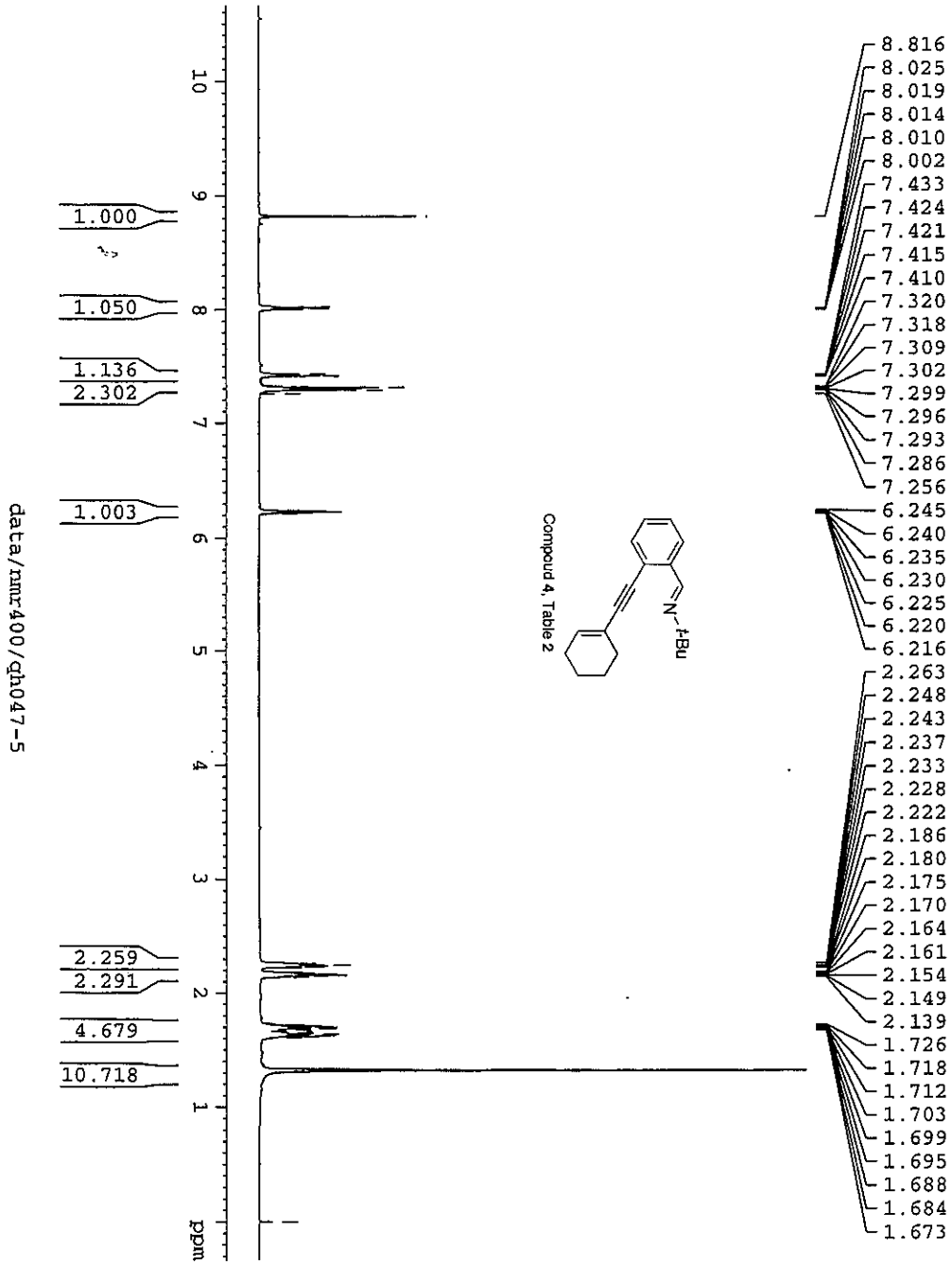
8.096
8.090
8.085
8.076
7.583
7.572
7.570
7.565
7.554
7.546
7.540
7.412
7.399
7.386
7.379
7.369
7.356
7.270
1.366
1.363
0.021
0.019
1.001
1.032
3.311
5.657
10.450
Compoud 1, Table 2
Ph
N
t-Bu
data/nmr/qh006-5.fid
ppm


154.412
138.052
132.453
131.706
129.950
128.867
128.764
128.719
126.217
124.116
123.336
95.076
86.949
77.676
77.252
76.829
58.043
30.018
Compound 1, Table 2
Ph
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh006-6.fid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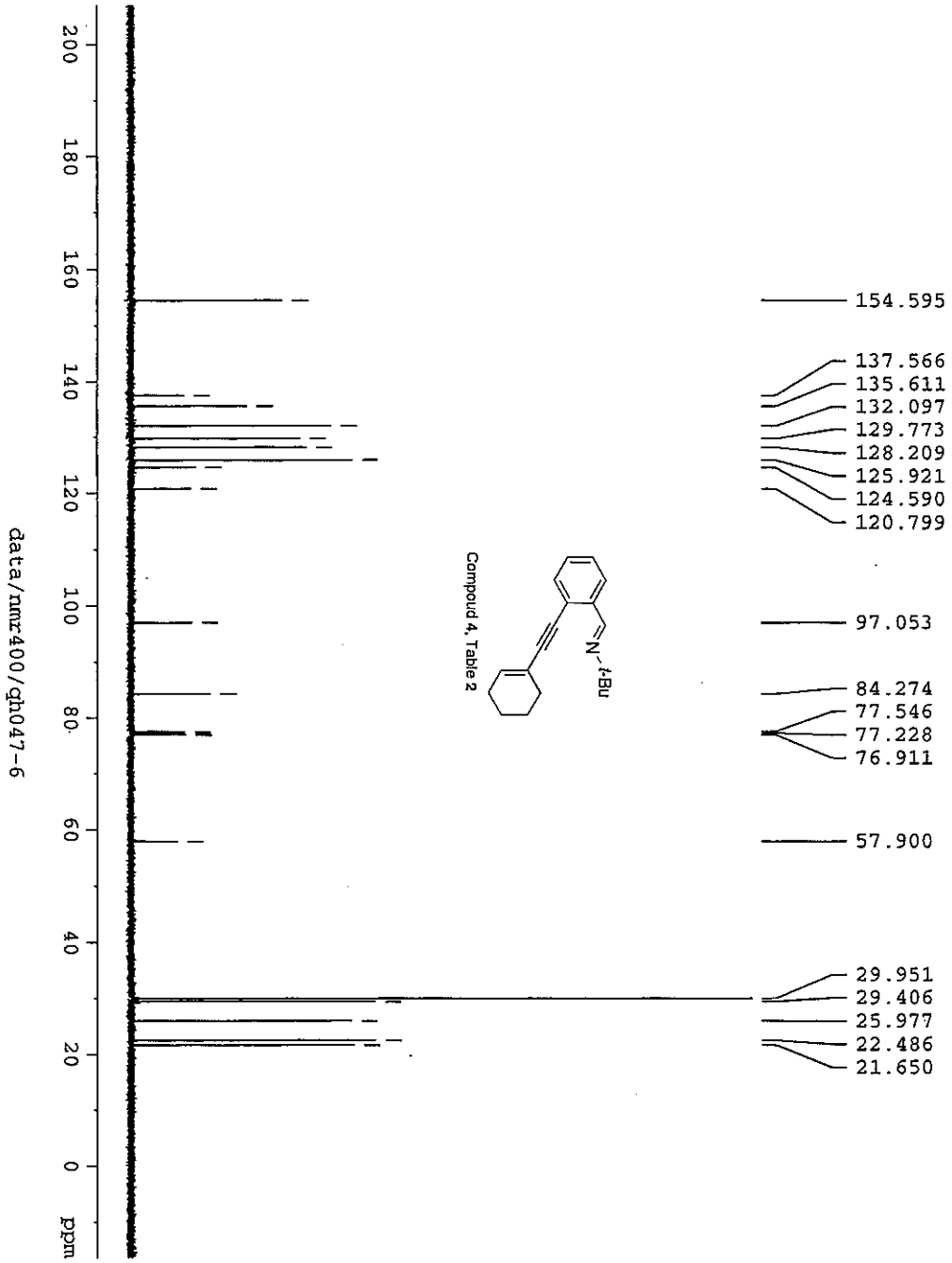
1.000
1.050
1.136
2.302
1.003
2.259
2.291
4.679
10.718
ppm
Compoud 4, Table 2
N
t-Bu
8.816
8.025
8.019
8.014
8.010
8.002
7.433
7.424
7.421
7.415
7.410
7.320
7.318
7.309
7.302
7.299
7.296
7.293
7.286
7.256
6.245
6.240
6.235
6.230
6.225
6.220
6.216
2.263
2.248
2.243
2.237
2.233
2.228
2.222
2.186
2.180
2.175
2.170
2.164
2.161
2.154
2.149
2.139
1.726
1.718
1.712
1.703
1.699
1.695
1.688
1.684
1.673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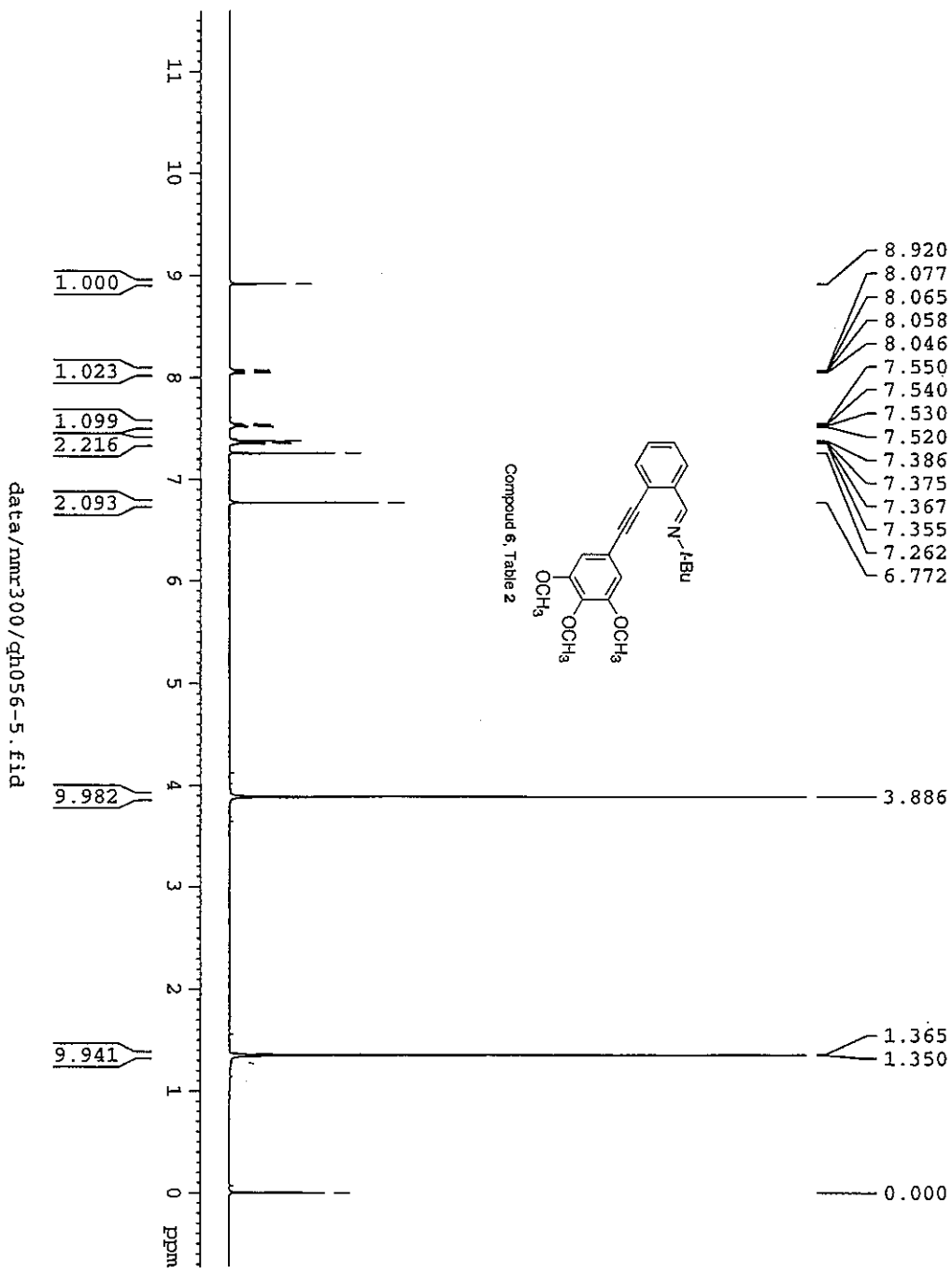
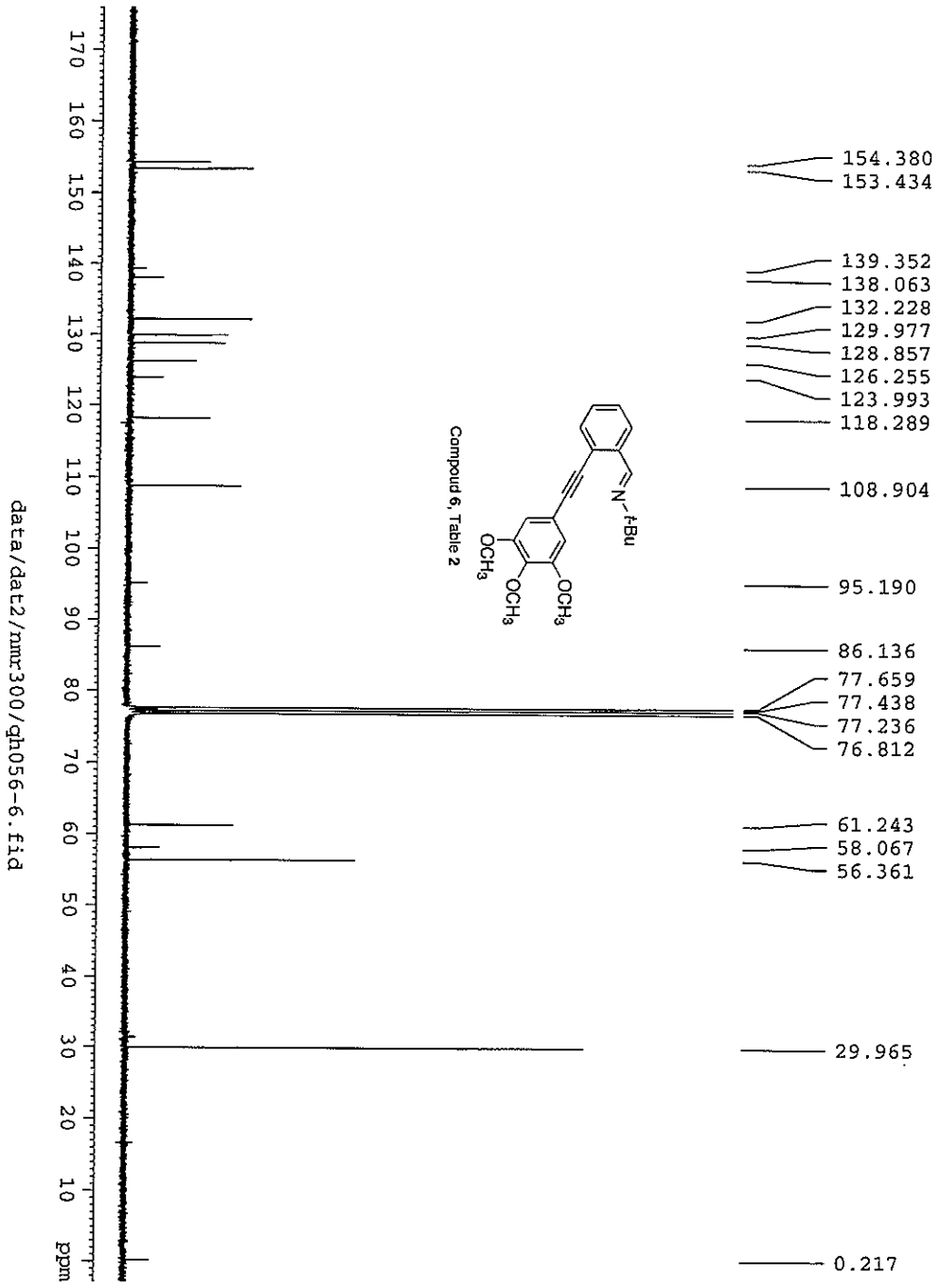
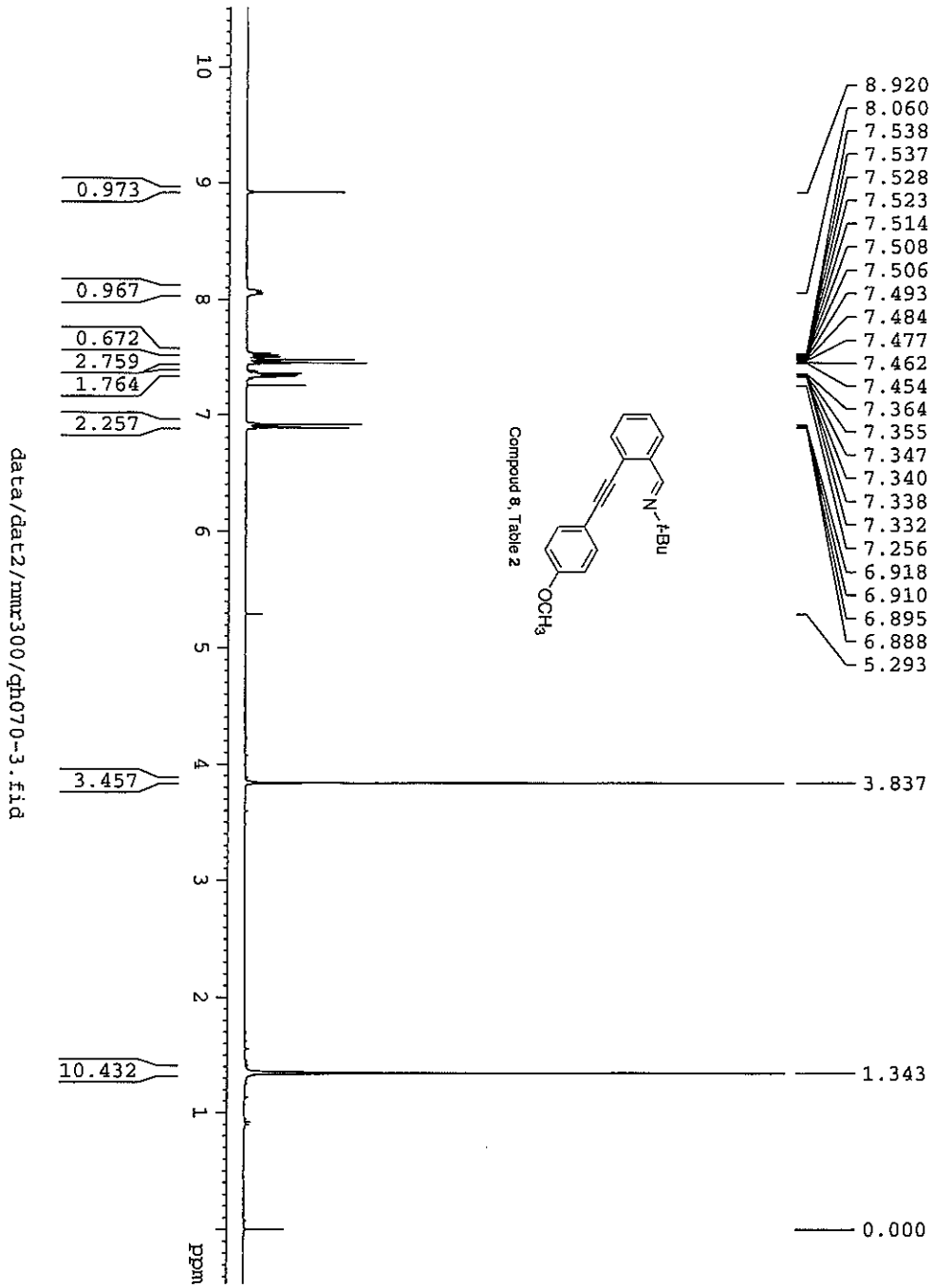
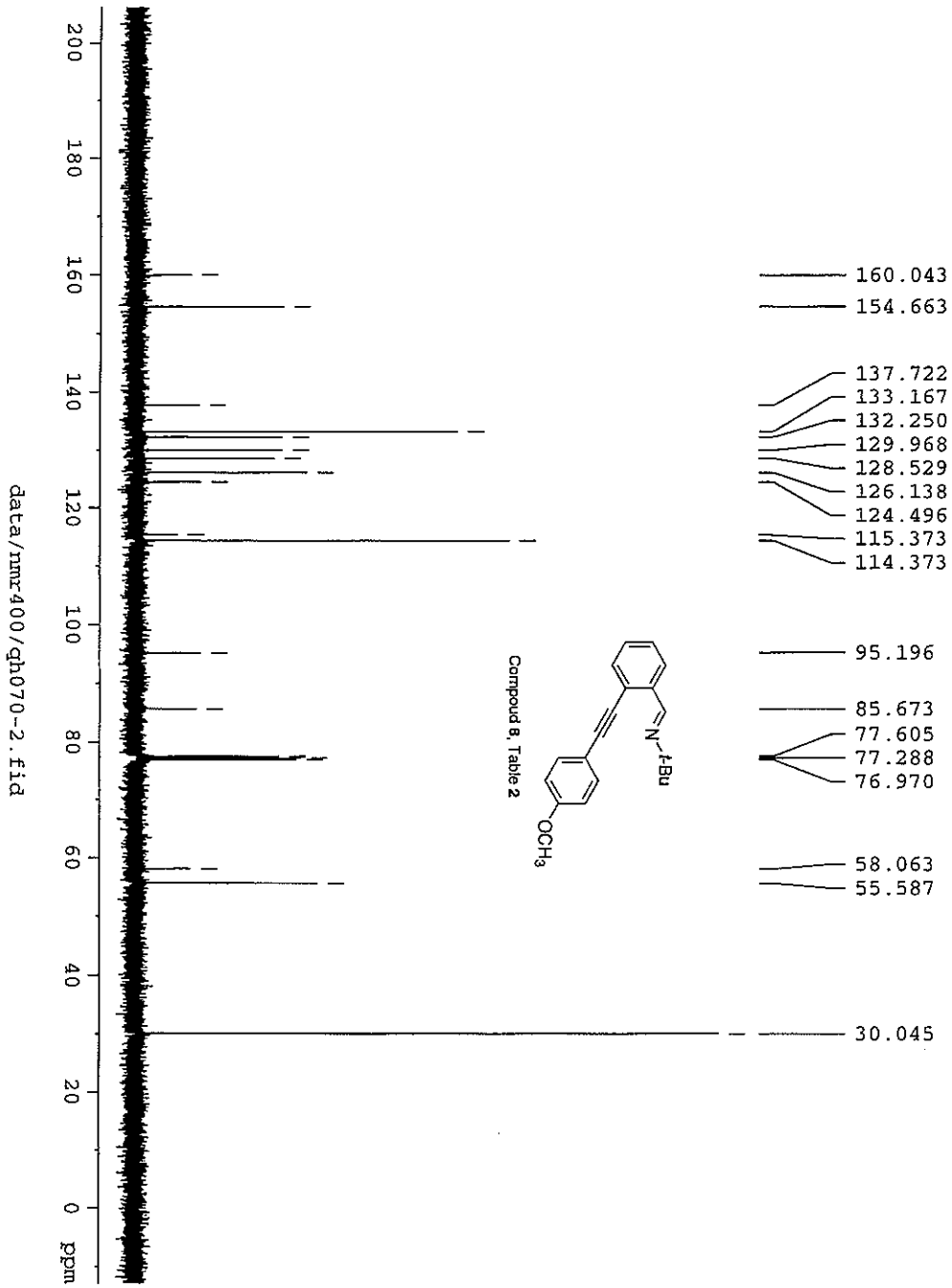
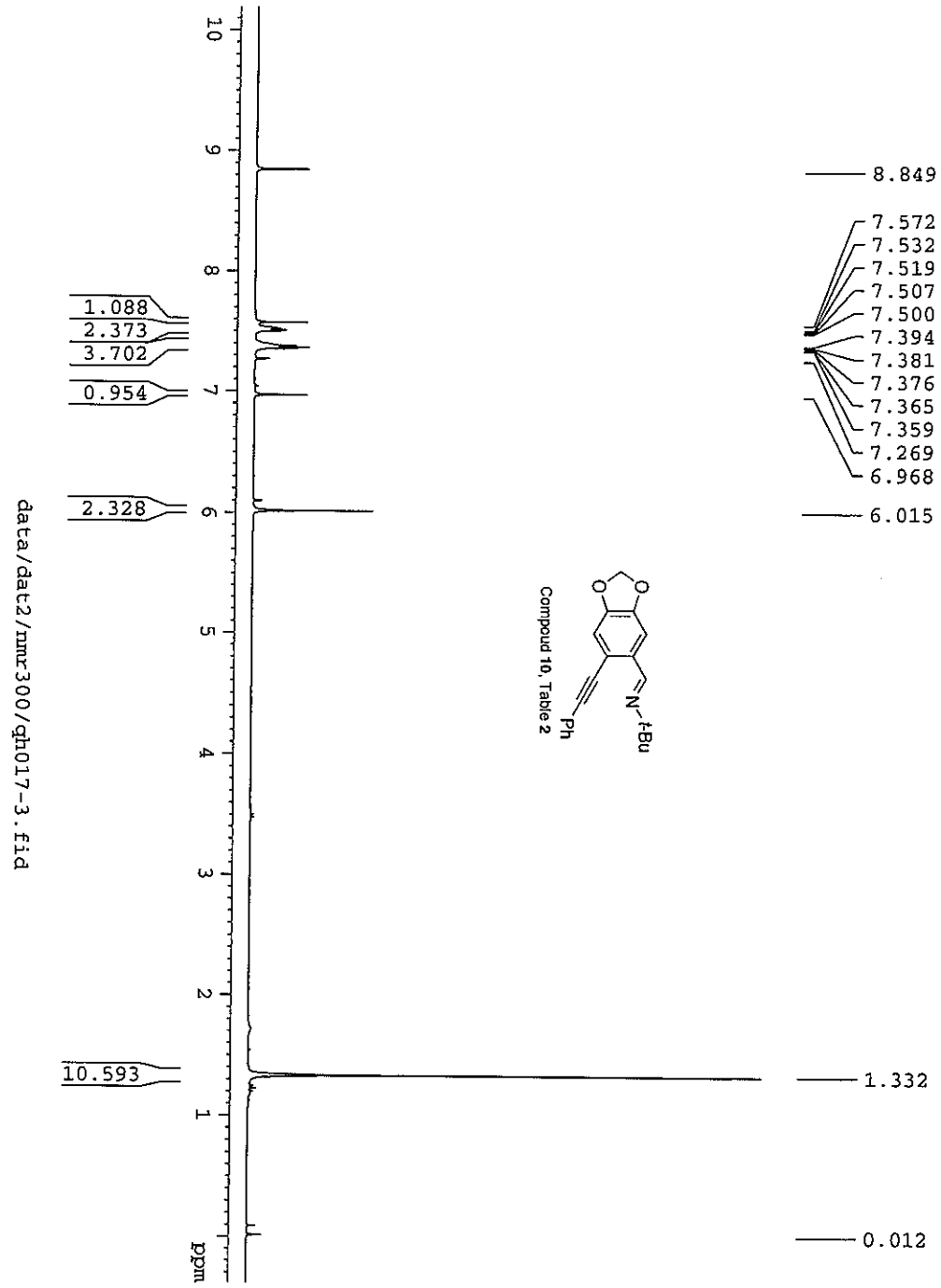
137.566
135.611
132.097
129.773
128.209
125.921
124.590
120.799
97.053
84.274
77.546
77.228
76.911
57.900
29.951
29.406
25.977
22.486
21.650
Compound 4, Table 2
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh047-6

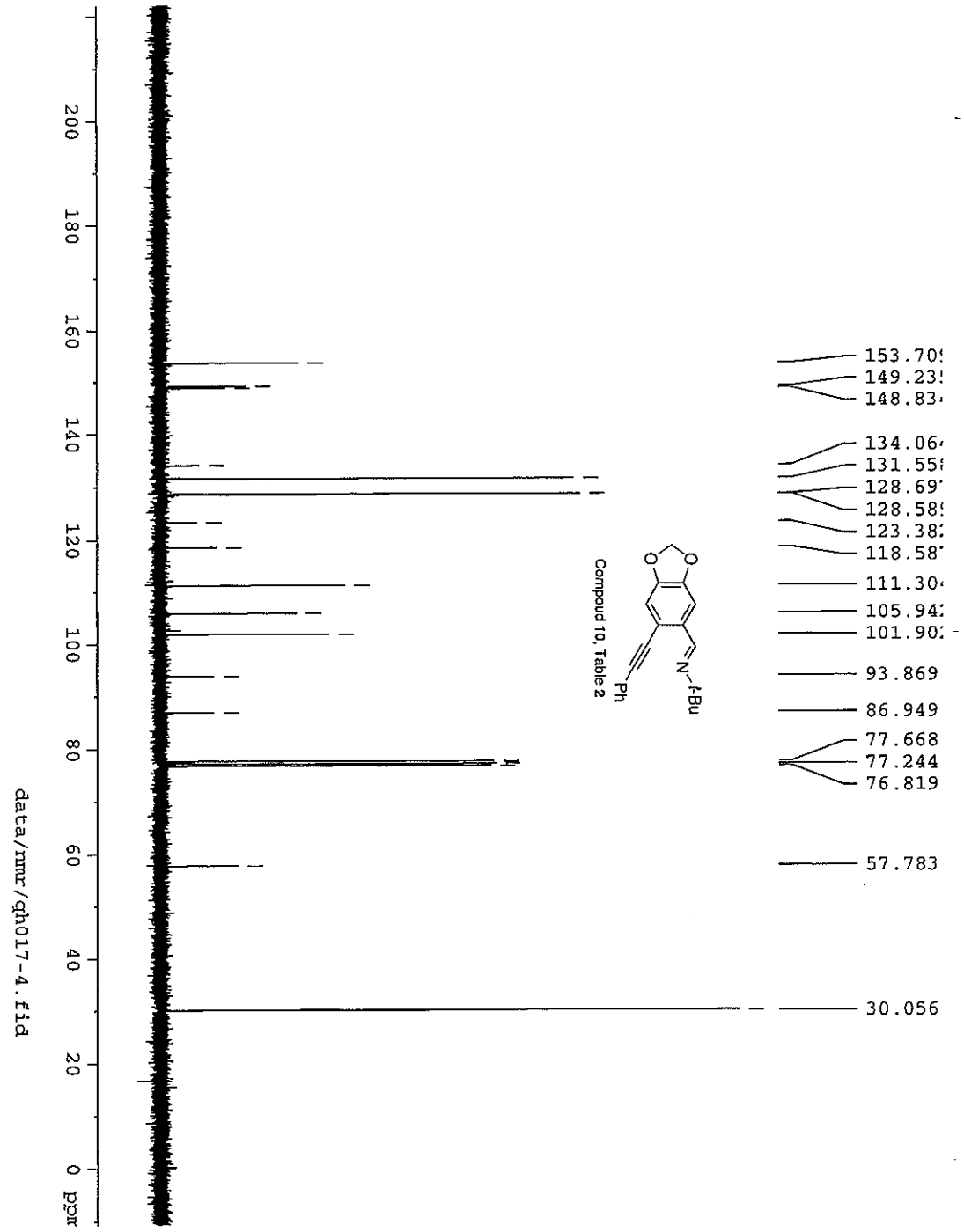

data/nmr300/qh056-5.fid
1.000
1.023
1.099
2.216
2.093
9.982
9.941
ppm
Compoud 6, Table 2
8.920
8.077
8.065
8.058
8.046
7.550
7.540
7.530
7.520
7.386
7.375
7.367
7.355
7.262
6.772
3.886
1.365
1.350
0.000

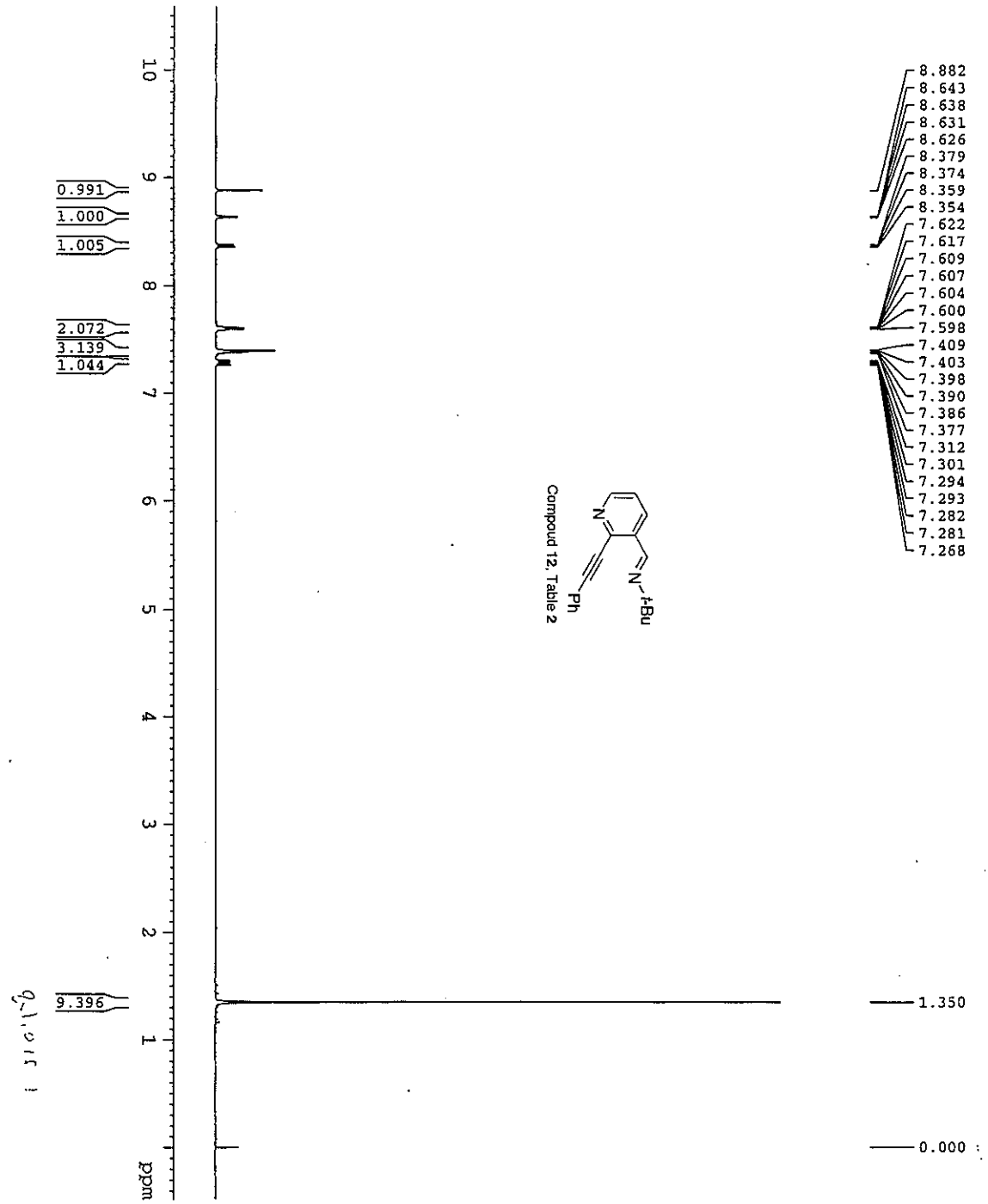

154.380
153.434
139.352
138.063
132.228
129.977
128.857
126.255
123.993
118.289
108.904
95.190
86.136
77.659
77.438
77.236
76.812
61.243
58.067
56.361
29.965
0.217
Compound 6, Table 2
N
t-Bu
OCH3
OCH3
OCH3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh056-6.fid

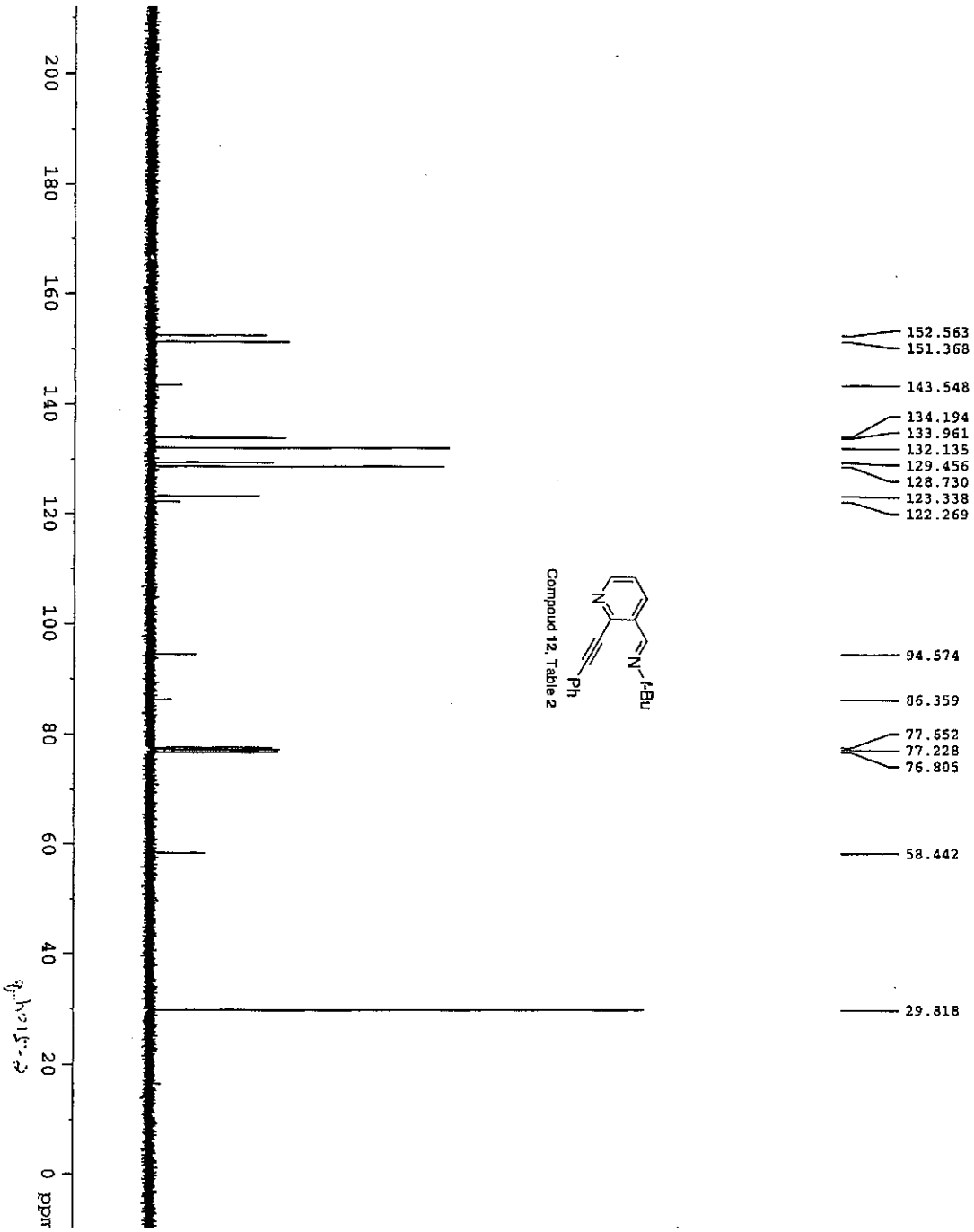

data/dat2/nmr300/qh070-3.fid
Compoud 8, Table 2
N-t-Bu
OCH3
8.920
8.060
7.538
7.537
7.528
7.523
7.514
7.508
7.506
7.493
7.484
7.477
7.462
7.454
7.364
7.355
7.347
7.340
7.338
7.332
7.256
6.918
6.910
6.895
6.888
5.293
3.837
1.343
0.000
0.973
0.967
0.672
2.759
1.764
2.257
3.457
10.432
ppm

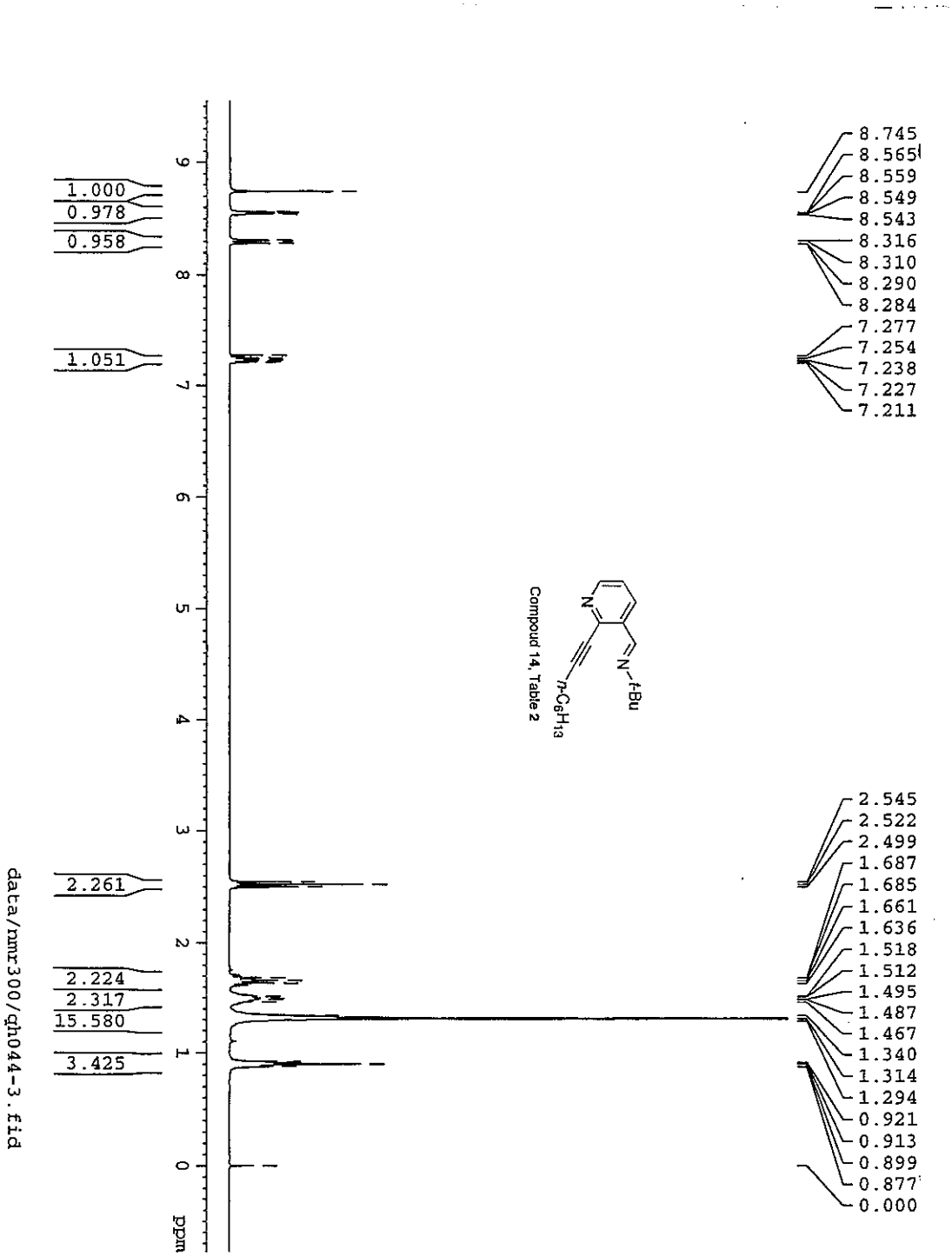

160.043
154.663
137.722
133.167
132.250
129.968
128.529
126.138
124.496
115.373
114.373
95.196
85.673
77.605
77.288
76.970
58.063
55.587
30.045
Compoud 8, Table 2
N
t-Bu
OCH3
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh070-2.fid

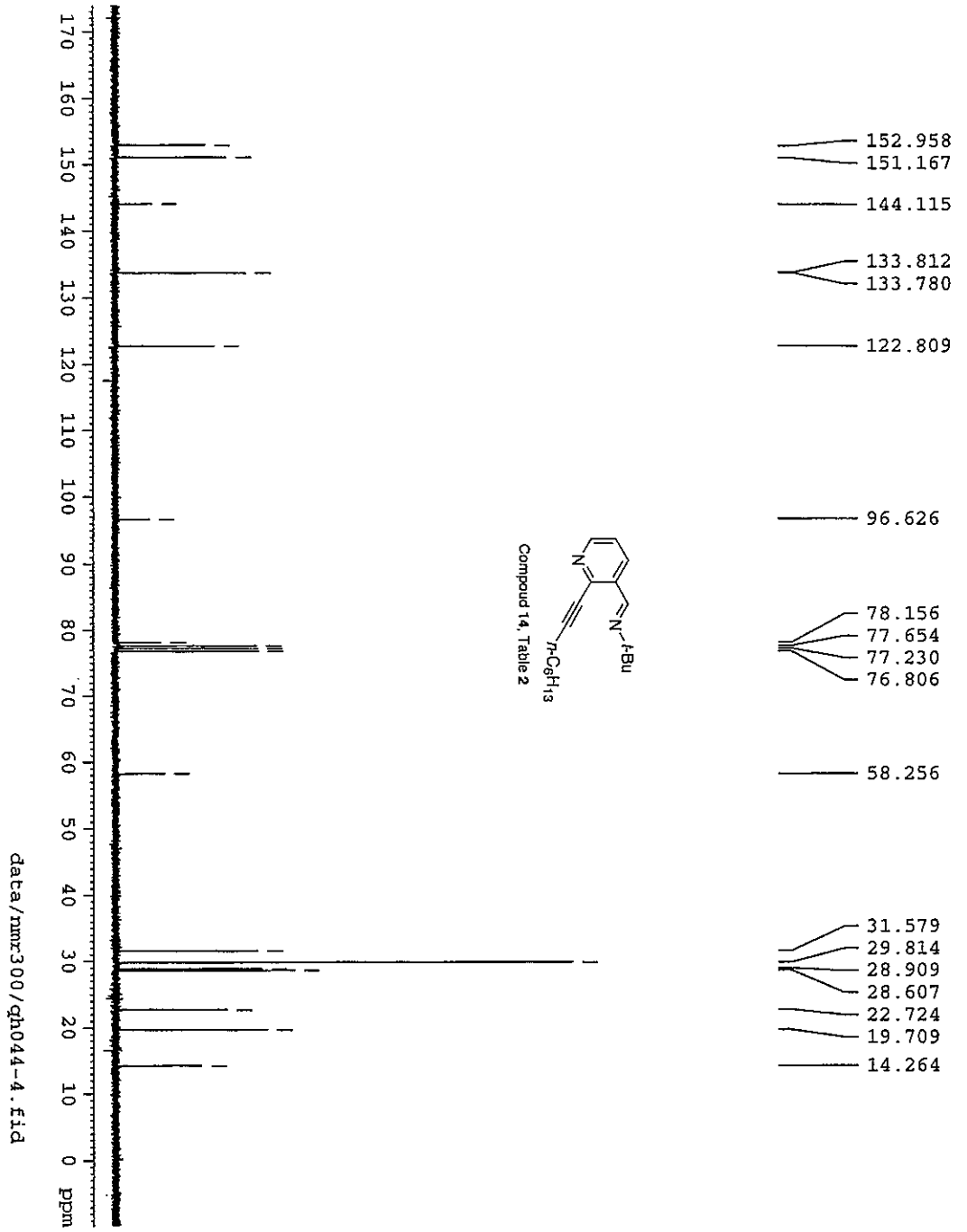

8.849
7.572
7.532
7.519
7.507
7.500
7.394
7.381
7.376
7.365
7.359
7.269
6.968
6.015
1.332
0.012
1.088
2.373
3.702
0.954
2.328
10.593
Compoud 10, Table 2
Ph
N
t-Bu
ppm
data/dat2/nmr300/qh017-3.fid

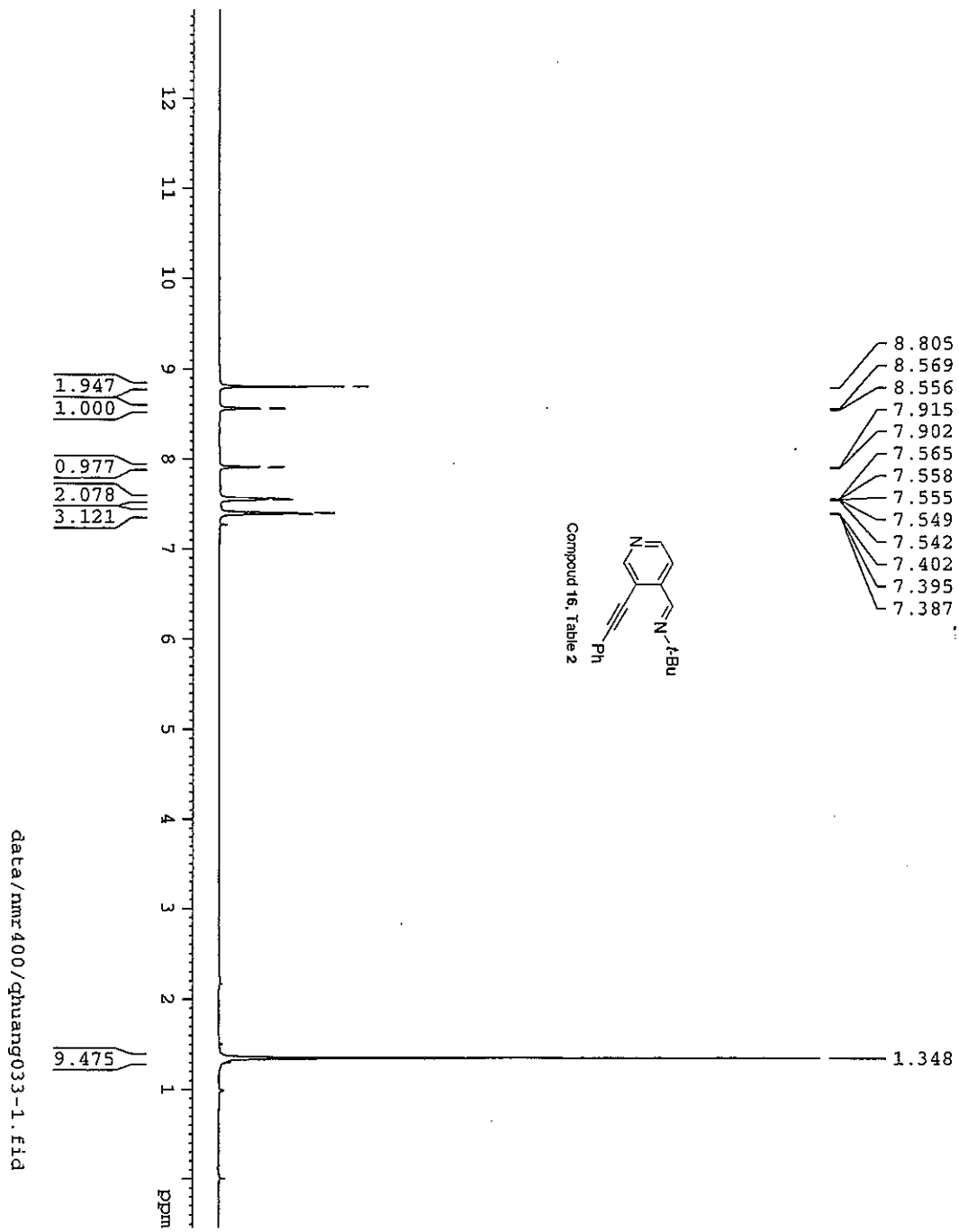

153.70
149.23
148.83
134.06
131.55
128.69
128.58
123.38
118.58
111.30
105.94
101.90
93.869
86.949
77.668
77.244
76.819
57.783
30.056
Compoud 10, Table 2
Ph
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh017-4.fid

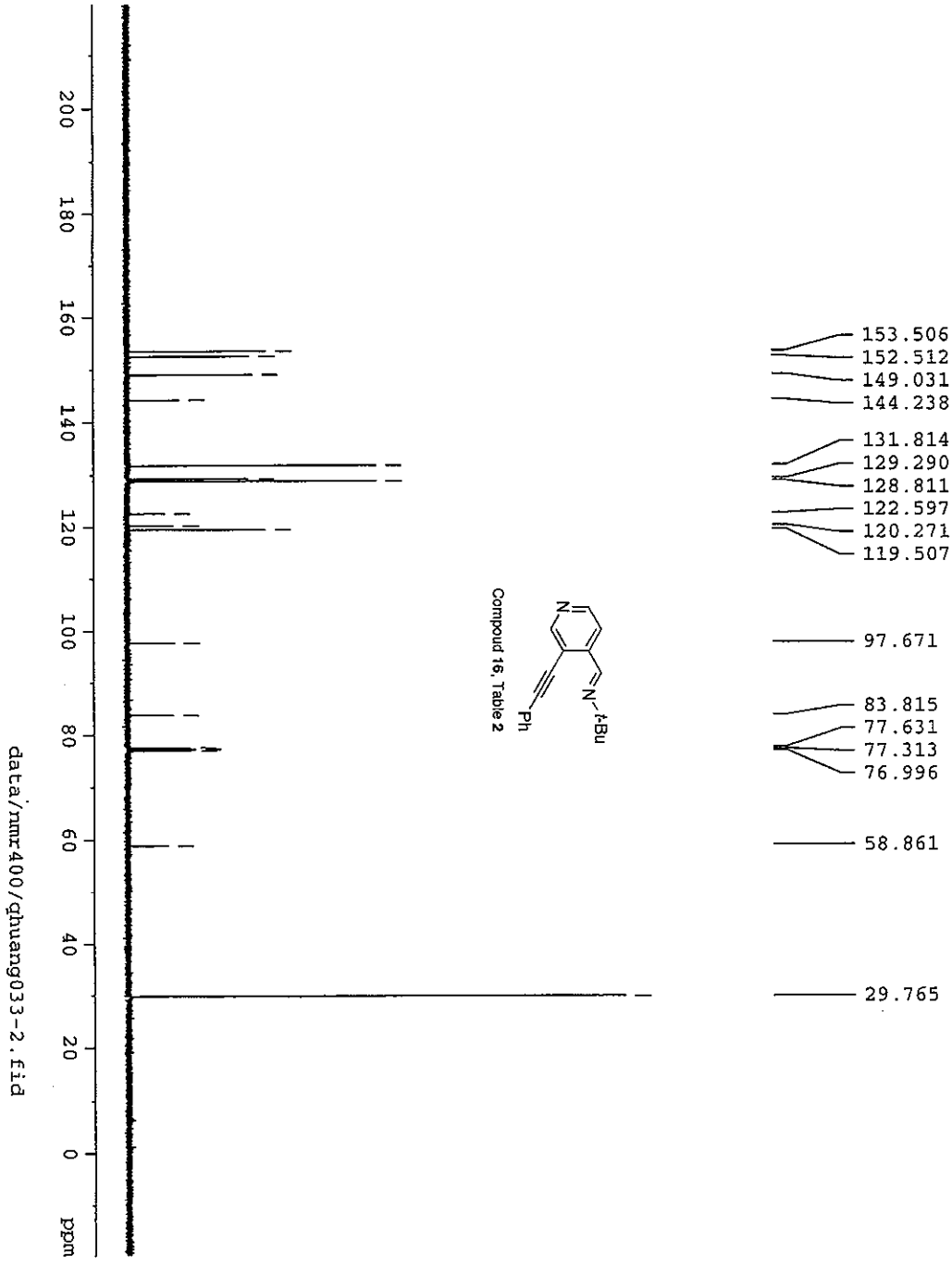

8.882
8.643
8.638
8.631
8.626
8.379
8.374
8.359
8.354
7.622
7.617
7.609
7.607
7.604
7.600
7.598
7.409
7.403
7.398
7.390
7.386
7.377
7.312
7.301
7.294
7.293
7.282
7.281
7.268
0.991
1.000
1.005
2.072
3.139
1.044
9.396
1.350
0.000
Compound 12, Table 2
Ph
N
N
t-Bu
ppm

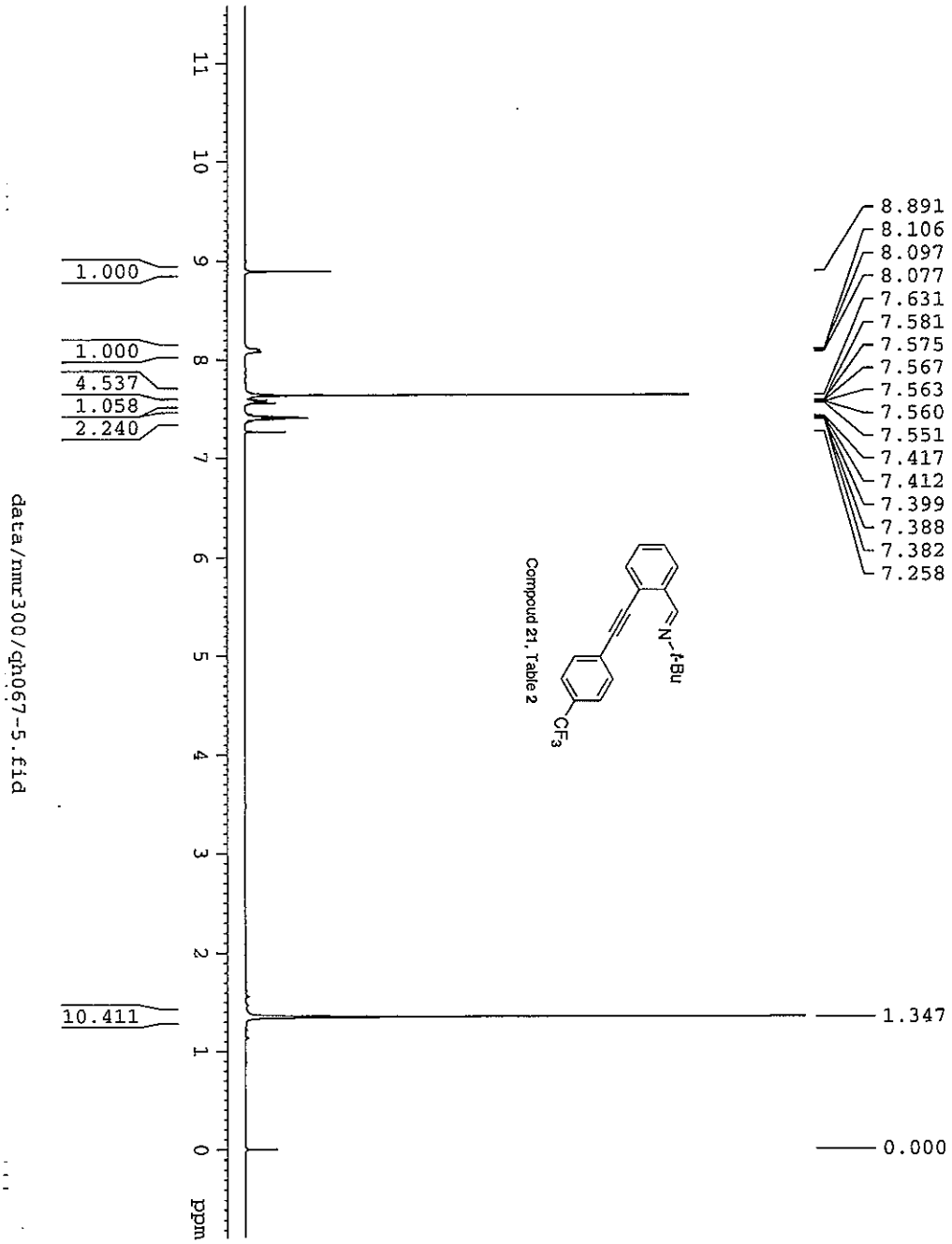

152.563
151.368
143.548
134.194
133.961
132.135
129.456
128.730
123.338
122.269
94.574
86.359
77.652
77.228
76.805
58.442
29.818
Compound 12, Table 2
Ph
N
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0 ppm

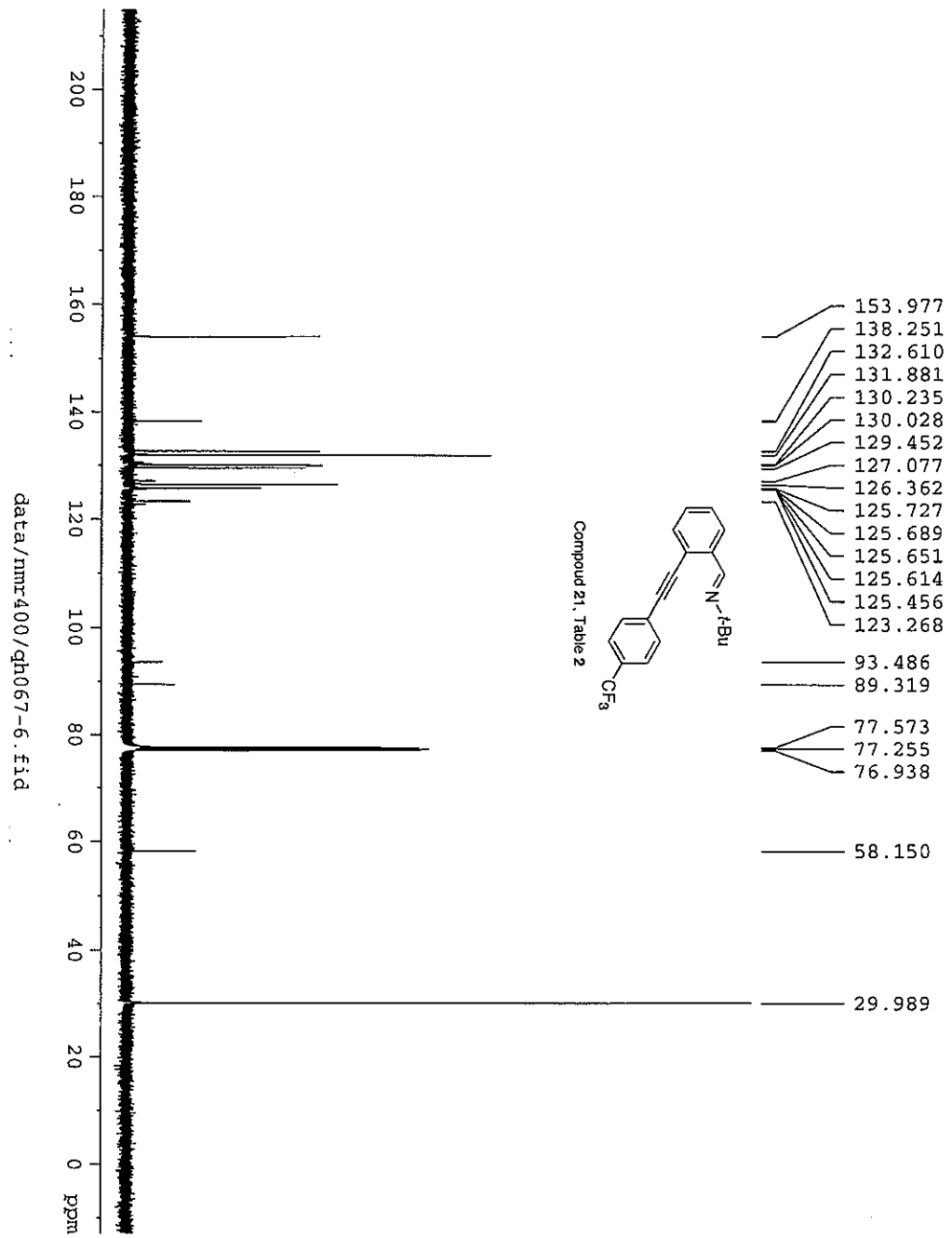

8.745
8.565
8.559
8.549
8.543
8.316
8.310
8.290
8.284
7.277
7.254
7.238
7.227
7.211
2.545
2.522
2.499
1.687
1.685
1.661
1.636
1.518
1.512
1.495
1.487
1.467
1.340
1.314
1.294
0.921
0.913
0.899
0.877
0.000
1.000
0.978
0.958
1.051
2.261
2.224
2.317
15.580
3.425
ppm
Compound 14, Table 2
n-C6H13
t-Bu
data/nmr300/qh044-3.fid

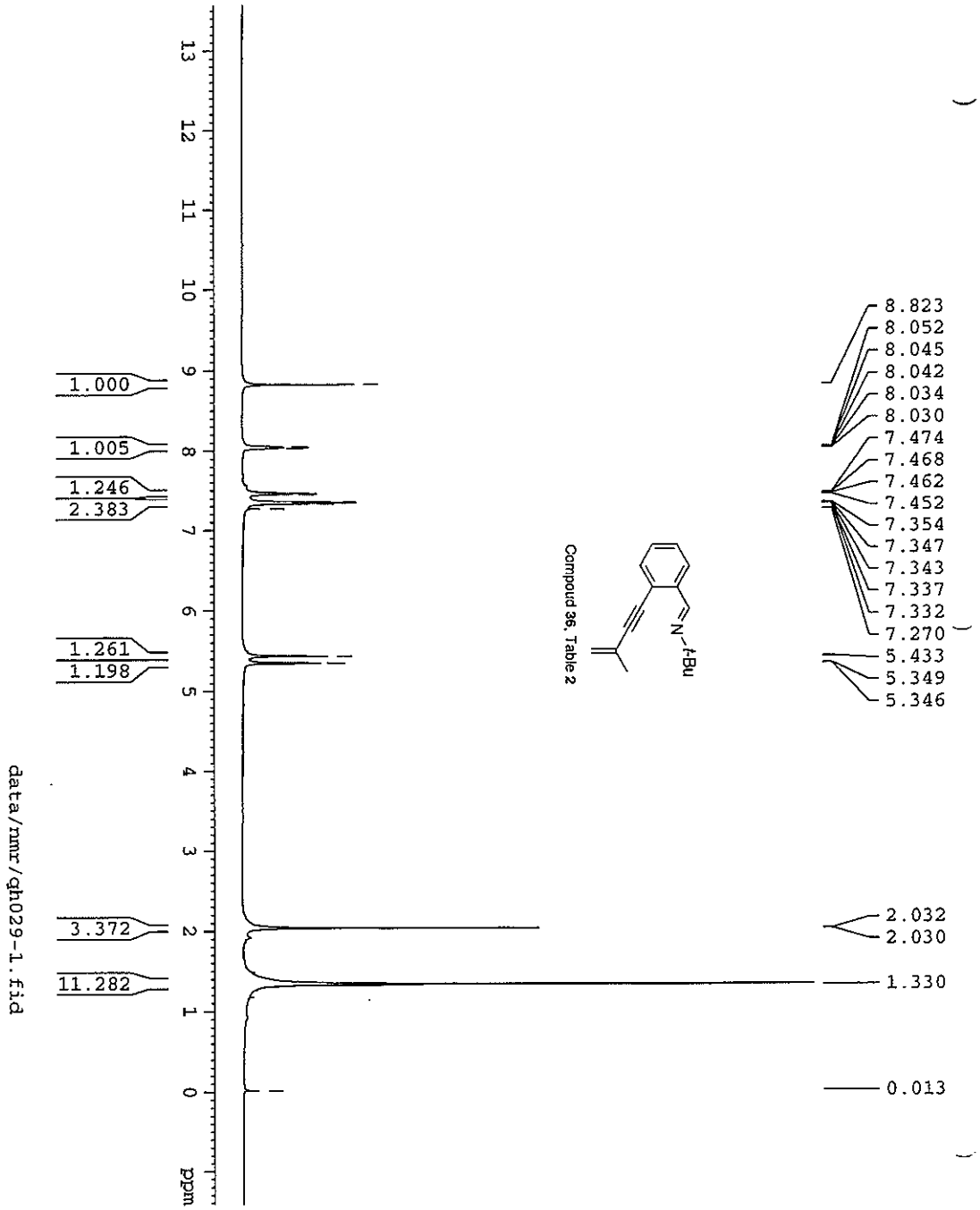

152.958
151.167
144.115
133.812
133.780
122.809
96.626
78.156
77.654
77.230
76.806
58.256
31.579
29.814
28.909
28.607
22.724
19.709
14.264
Compoud 14, Table 2
n-C6H13
t-Bu
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/nmr300/qh044-4.fid

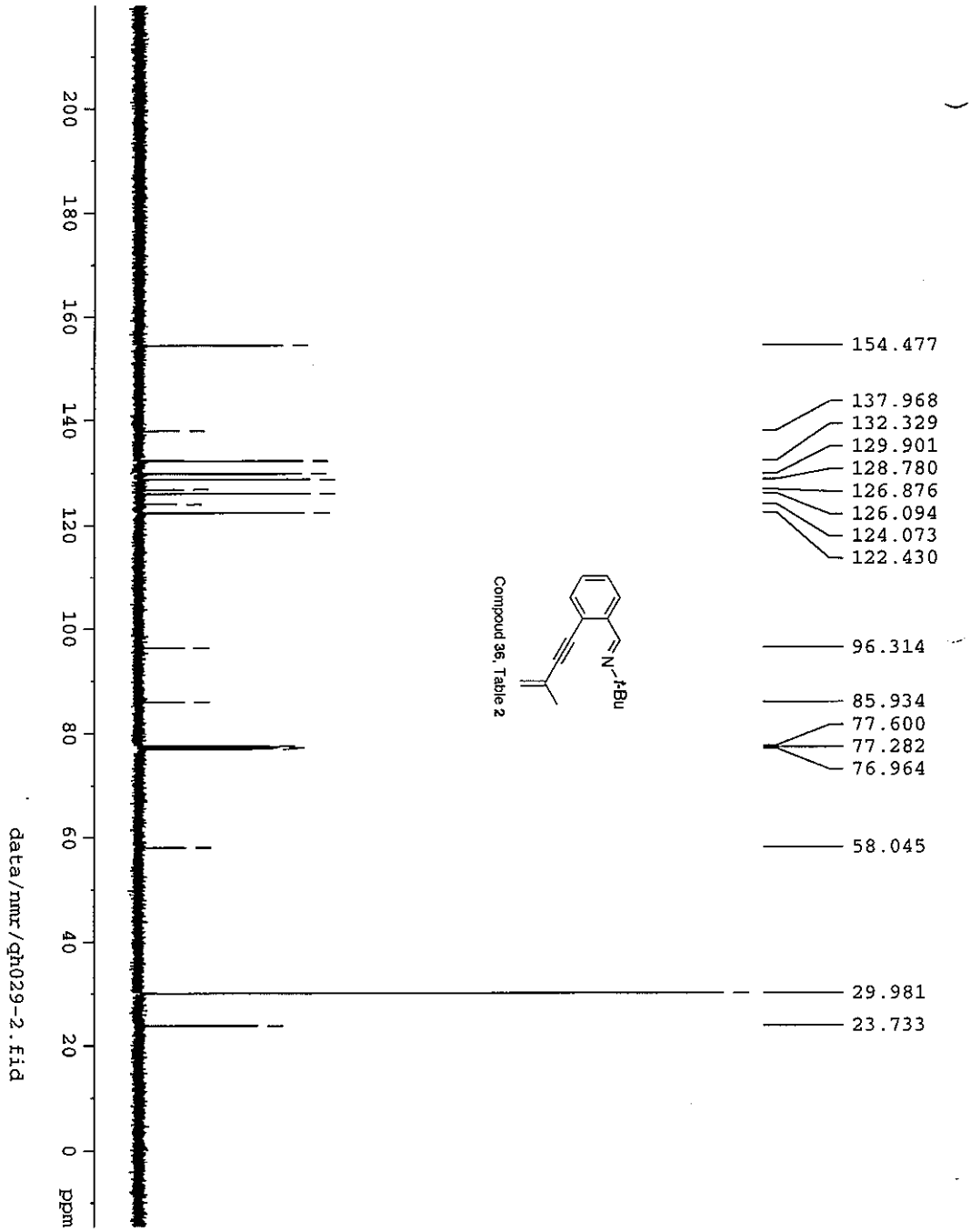

8.805
8.569
8.556
7.915
7.902
7.565
7.558
7.555
7.549
7.542
7.402
7.395
7.387
1.348
1.947
1.000
0.977
2.078
3.121
9.475
Ph
N
N
t-Bu
Compoud 16, Table 2
ppm
data/nmr400/qhuang033-1.fid

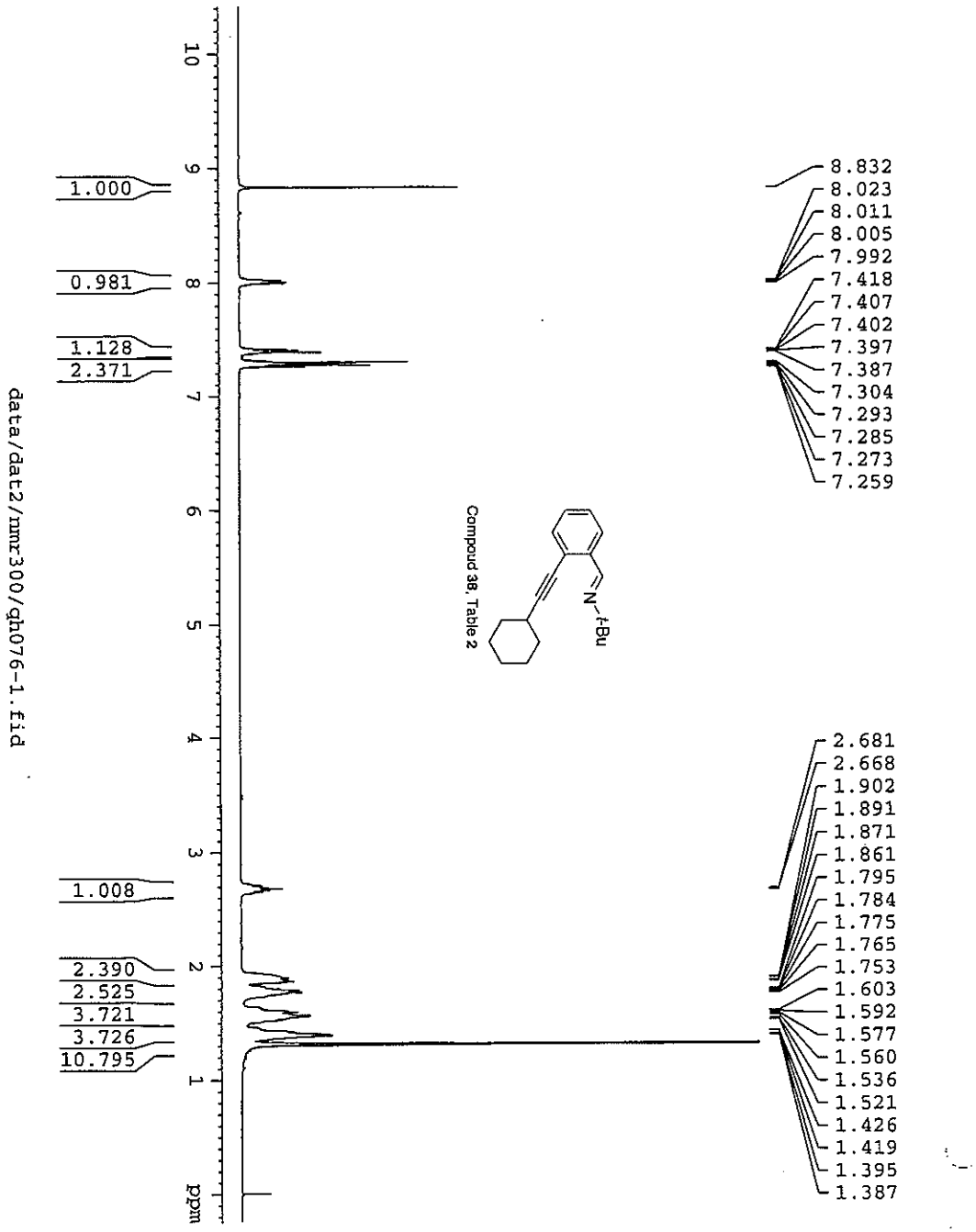

153.506
152.512
149.031
144.238
131.814
129.290
128.811
122.597
120.271
119.507
97.671
83.815
77.631
77.313
76.996
58.861
29.765
Compound 16, Table 2
Ph
N
N
tBu
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qhuang033-2.fid

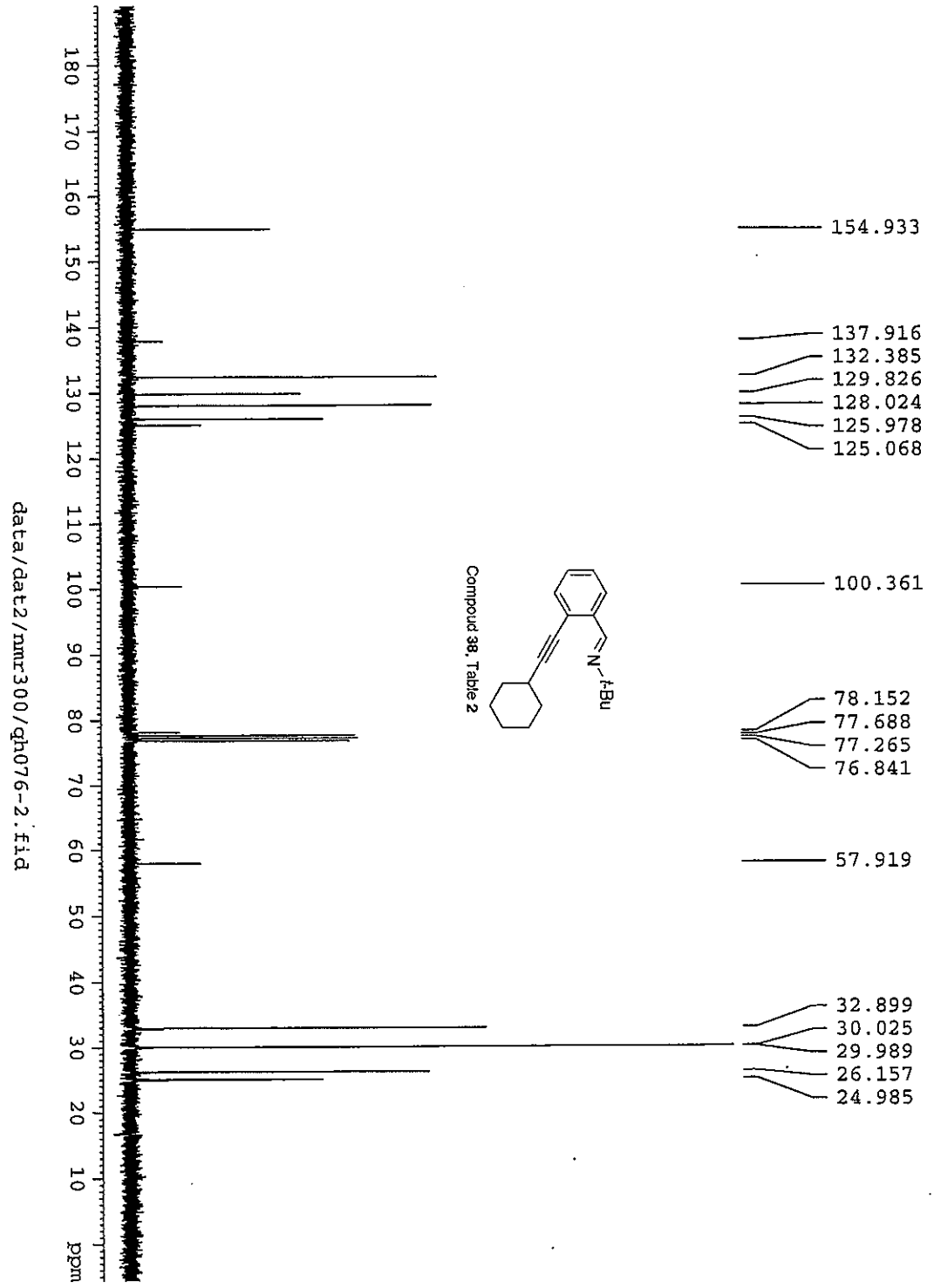

8.891
8.106
8.097
8.077
7.631
7.581
7.575
7.567
7.563
7.560
7.551
7.417
7.412
7.399
7.388
7.382
7.258
1.000
1.000
4.537
1.058
2.240
10.411
1.347
0.000
ppm
Compound 21, Table 2
N-t-Bu
CF3
data/nmr300/qh067-5.fid

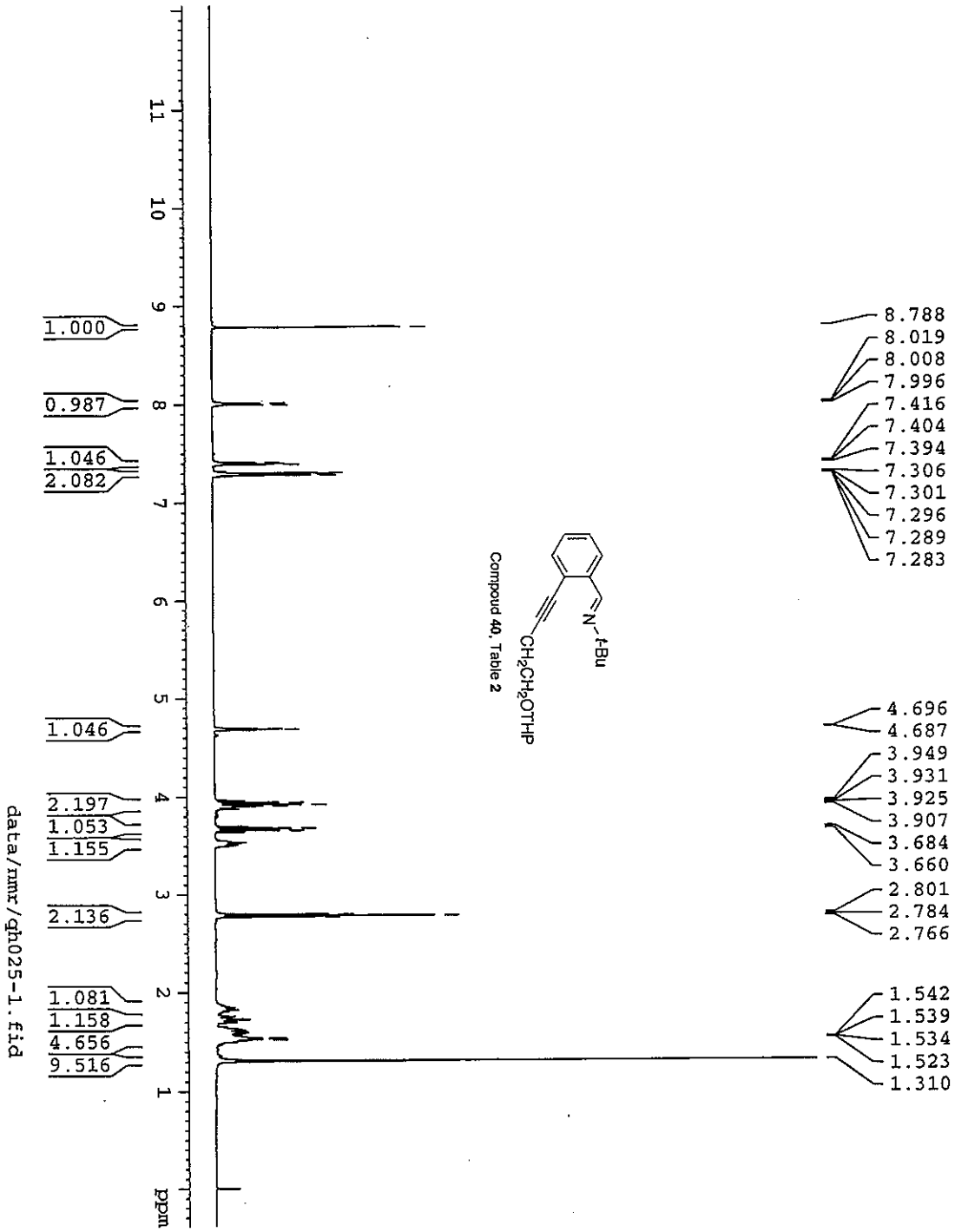

153.977
138.251
132.610
131.881
130.235
130.028
129.452
127.077
126.362
125.727
125.689
125.651
125.614
125.456
123.268
93.486
89.319
77.573
77.255
76.938
58.150
29.989
Compoud 21, Table 2
N-t-Bu
CF3
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh067-6.fid

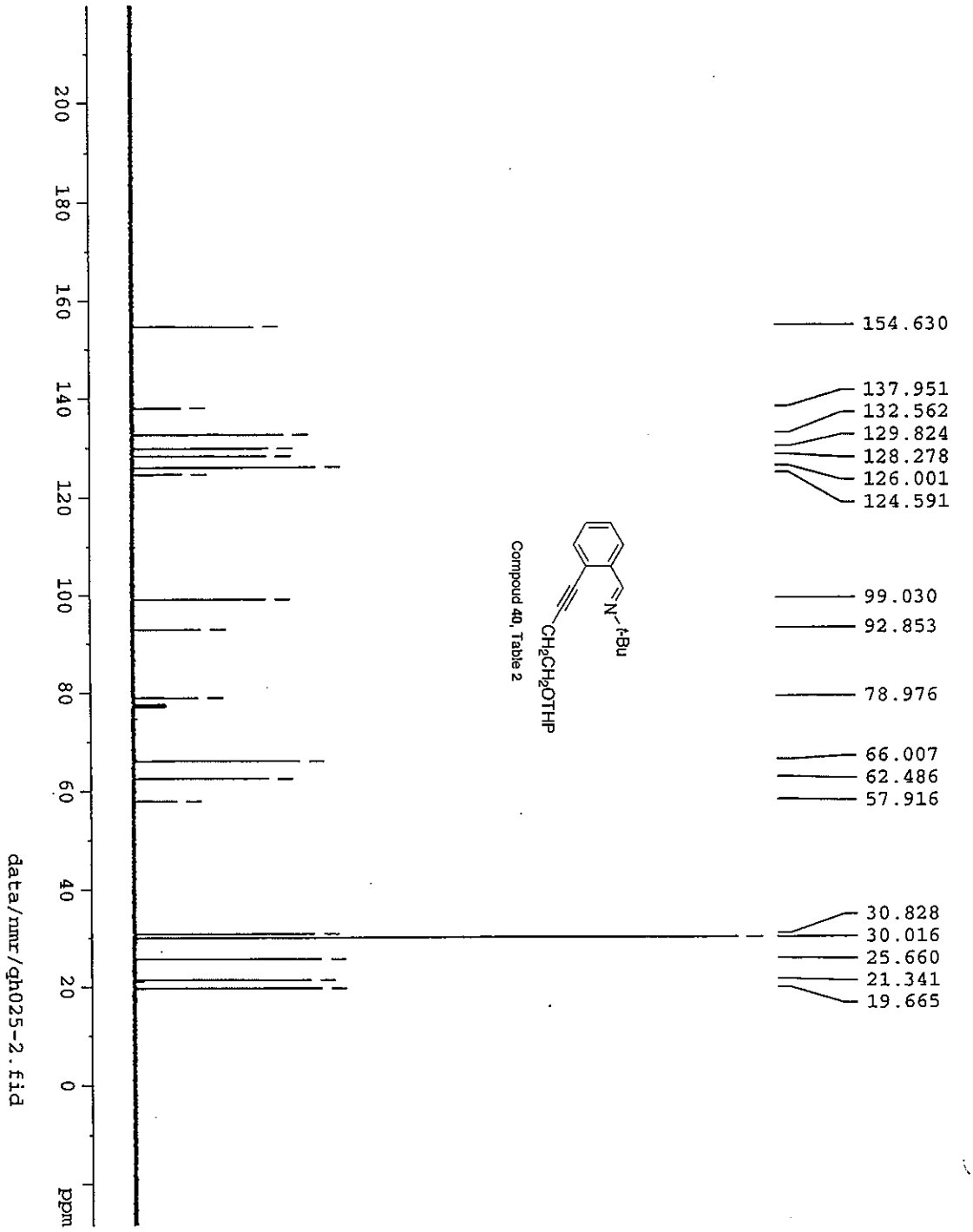

8.823
8.052
8.045
8.042
8.034
8.030
7.474
7.468
7.462
7.452
7.354
7.347
7.343
7.337
7.332
7.270
5.433
5.349
5.346
2.032
2.030
1.330
0.013
1.000
1.005
1.246
2.383
1.261
1.198
3.372
11.282
ppm
Compoud 36, Table 2
t-Bu
data/nmr/qh029-1.fid

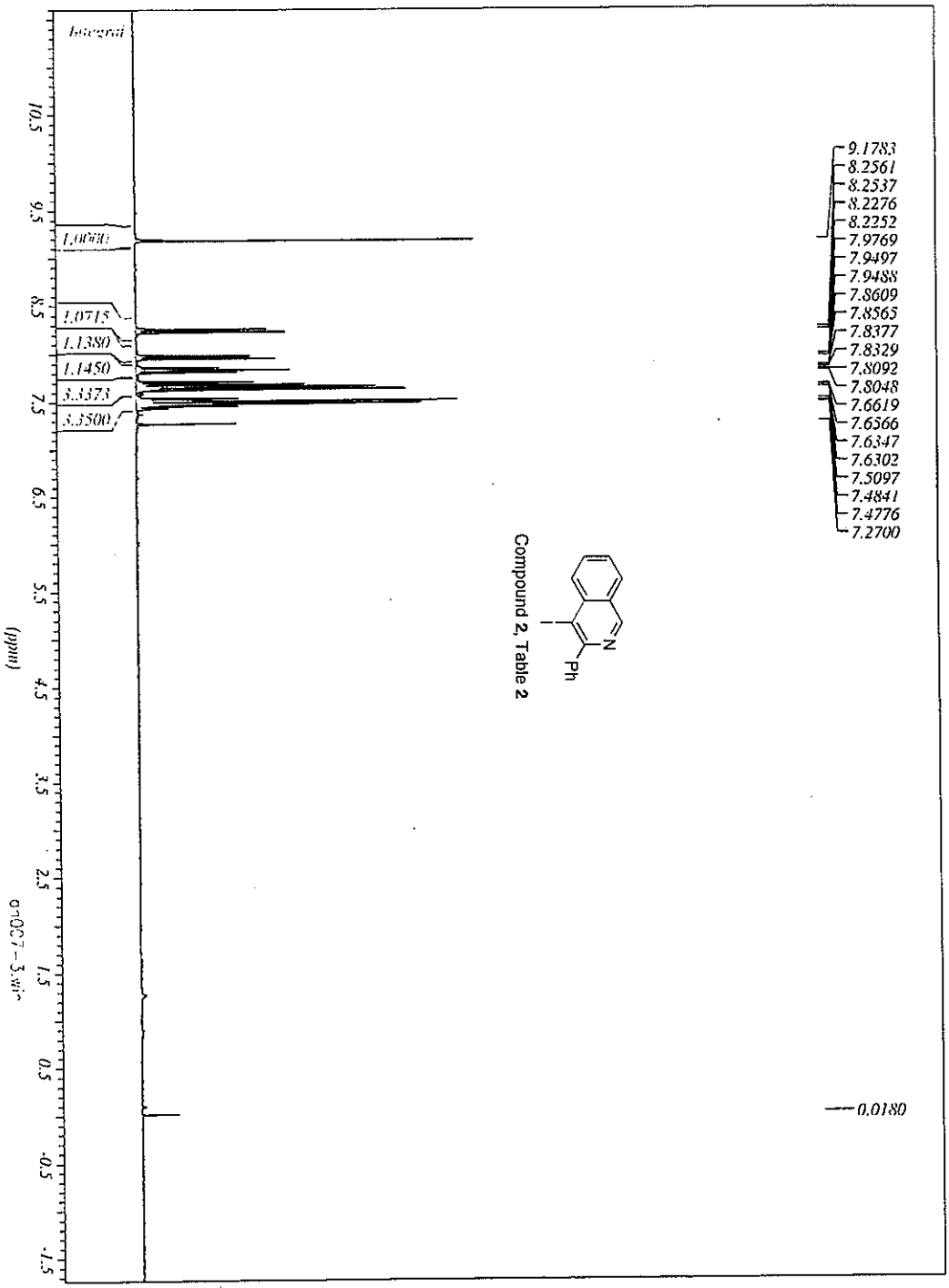

154.477
137.968
132.329
129.901
128.780
126.876
126.094
124.073
122.430
96.314
85.934
77.600
77.282
76.964
58.045
29.981
23.733
Compound 36, Table 2
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr/qh029-2.fid

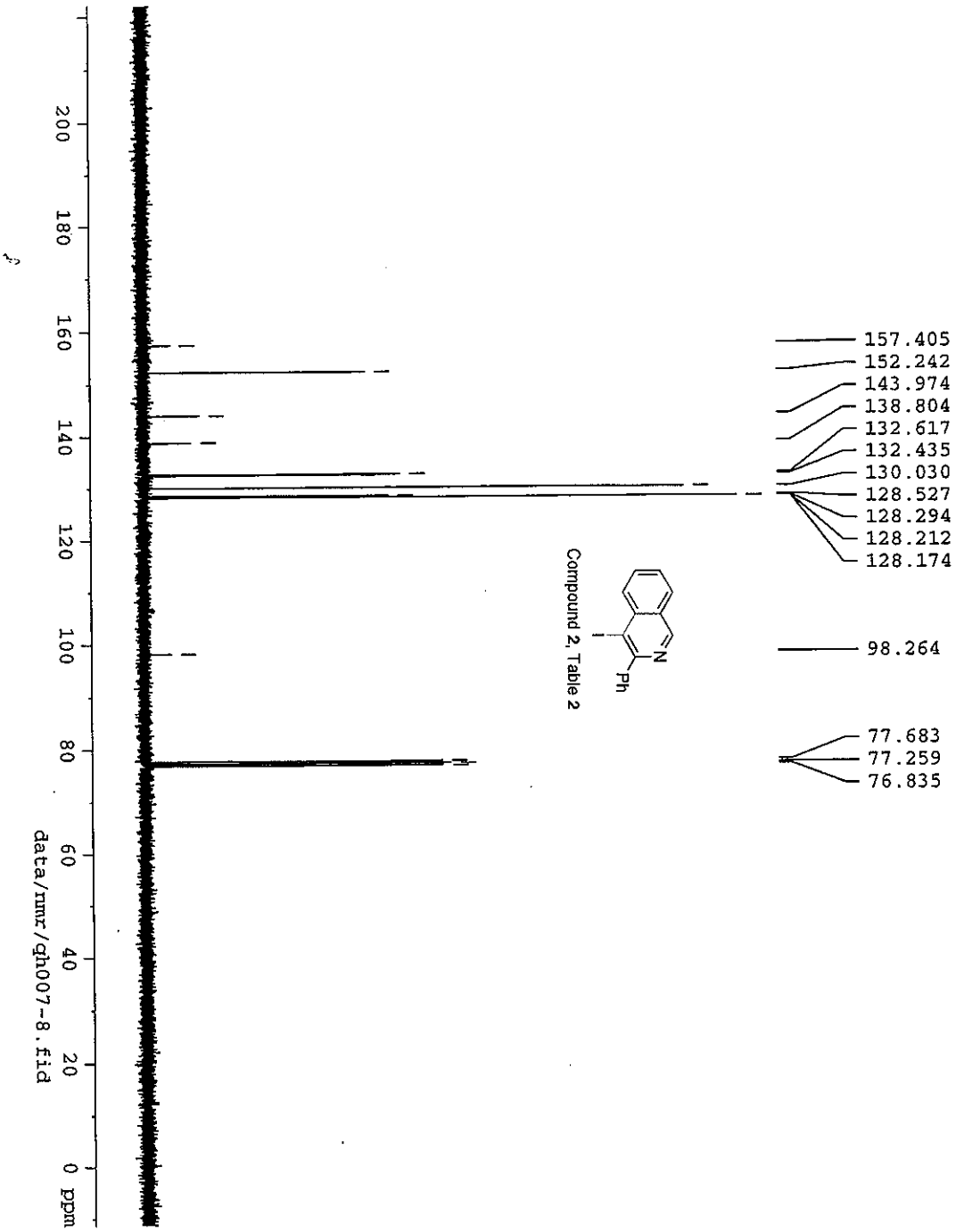

data/dat2/nmr300/qh076-1.fid
1.000
0.981
1.128
2.371
1.008
2.390
2.525
3.721
3.726
10.795
ppm
Compound 38, Table 2
8.832
8.023
8.011
8.005
7.992
7.418
7.407
7.402
7.397
7.387
7.304
7.293
7.285
7.273
7.259
2.681
2.668
1.902
1.891
1.871
1.861
1.795
1.784
1.775
1.765
1.753
1.603
1.592
1.577
1.560
1.536
1.521
1.426
1.419
1.395
1.387

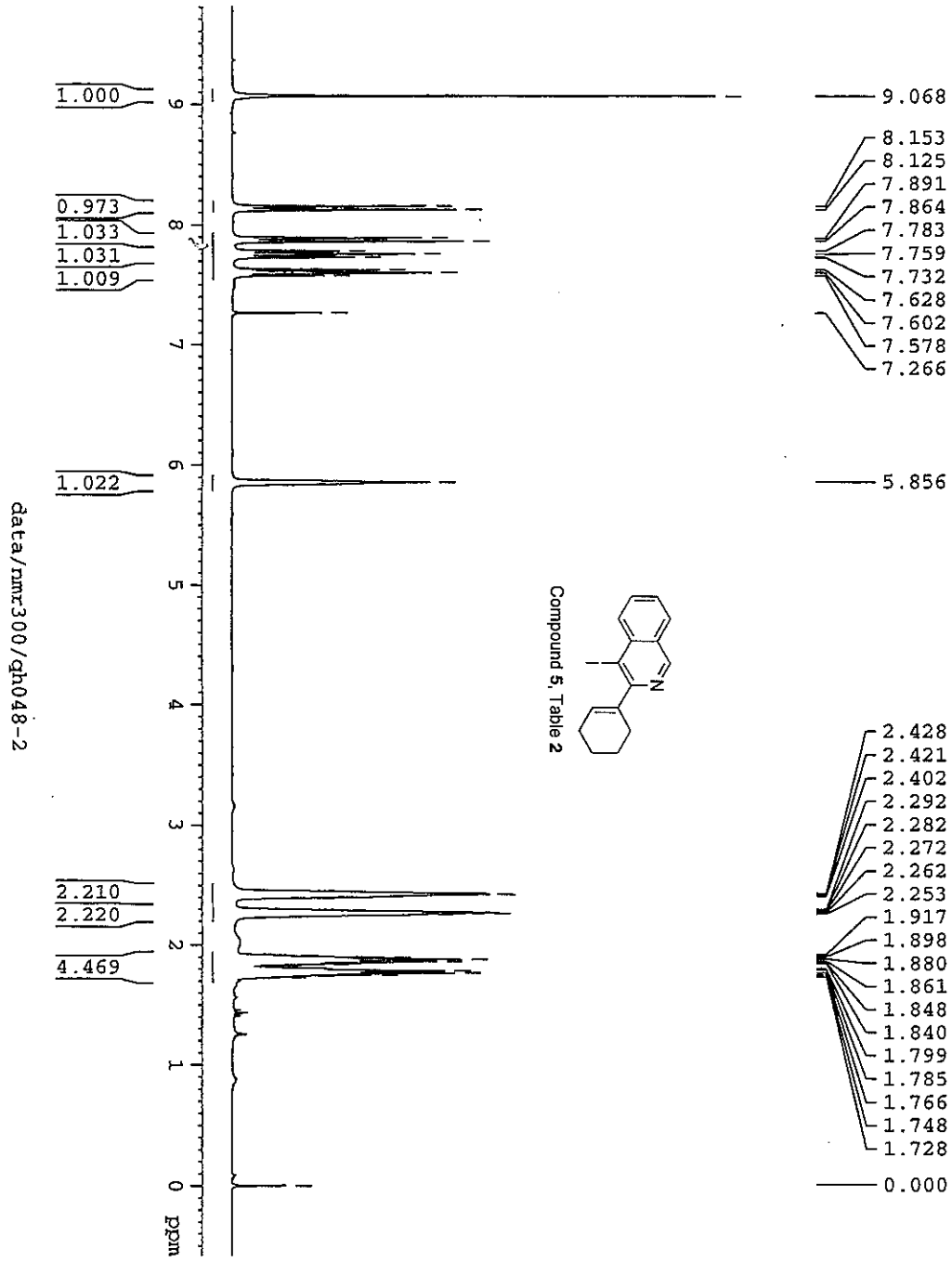

154.933
137.916
132.385
129.826
128.024
125.978
125.068
100.361
78.152
77.688
77.265
76.841
57.919
32.899
30.025
29.989
26.157
24.985
Compound 38, Table 2
N
t-Bu
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh076-2.fid

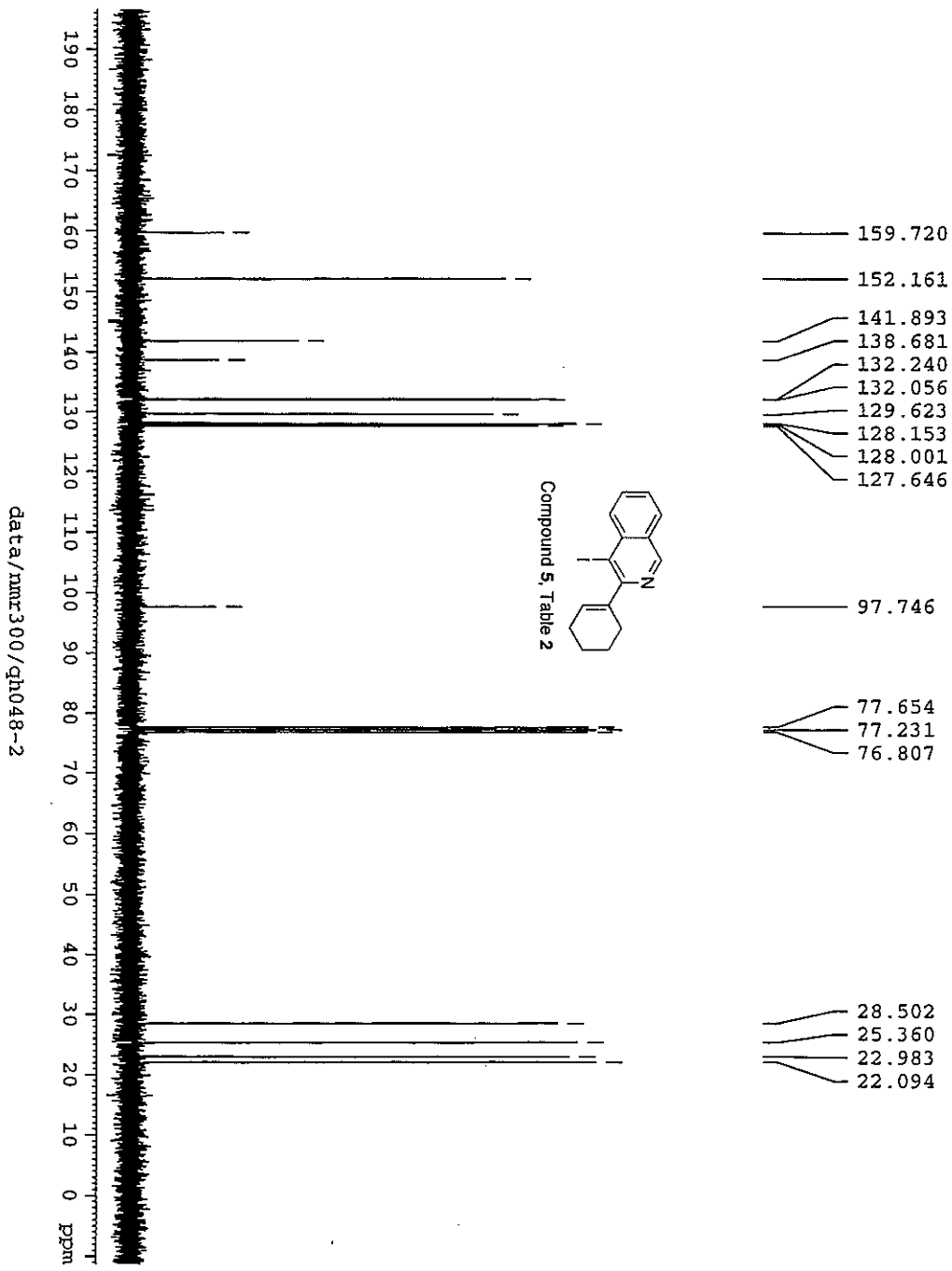

8.788
8.019
8.008
7.996
7.416
7.404
7.394
7.306
7.301
7.296
7.289
7.283
4.696
4.687
3.949
3.931
3.925
3.907
3.684
3.660
2.801
2.784
2.766
1.542
1.539
1.534
1.523
1.310
1.000
0.987
1.046
2.082
1.046
2.197
1.053
1.155
2.136
1.081
1.158
4.656
9.516
ppm
Compoud 40, Table 2
t-Bu
CH2CH2OTHP
data/nmr/qh025-1.fid

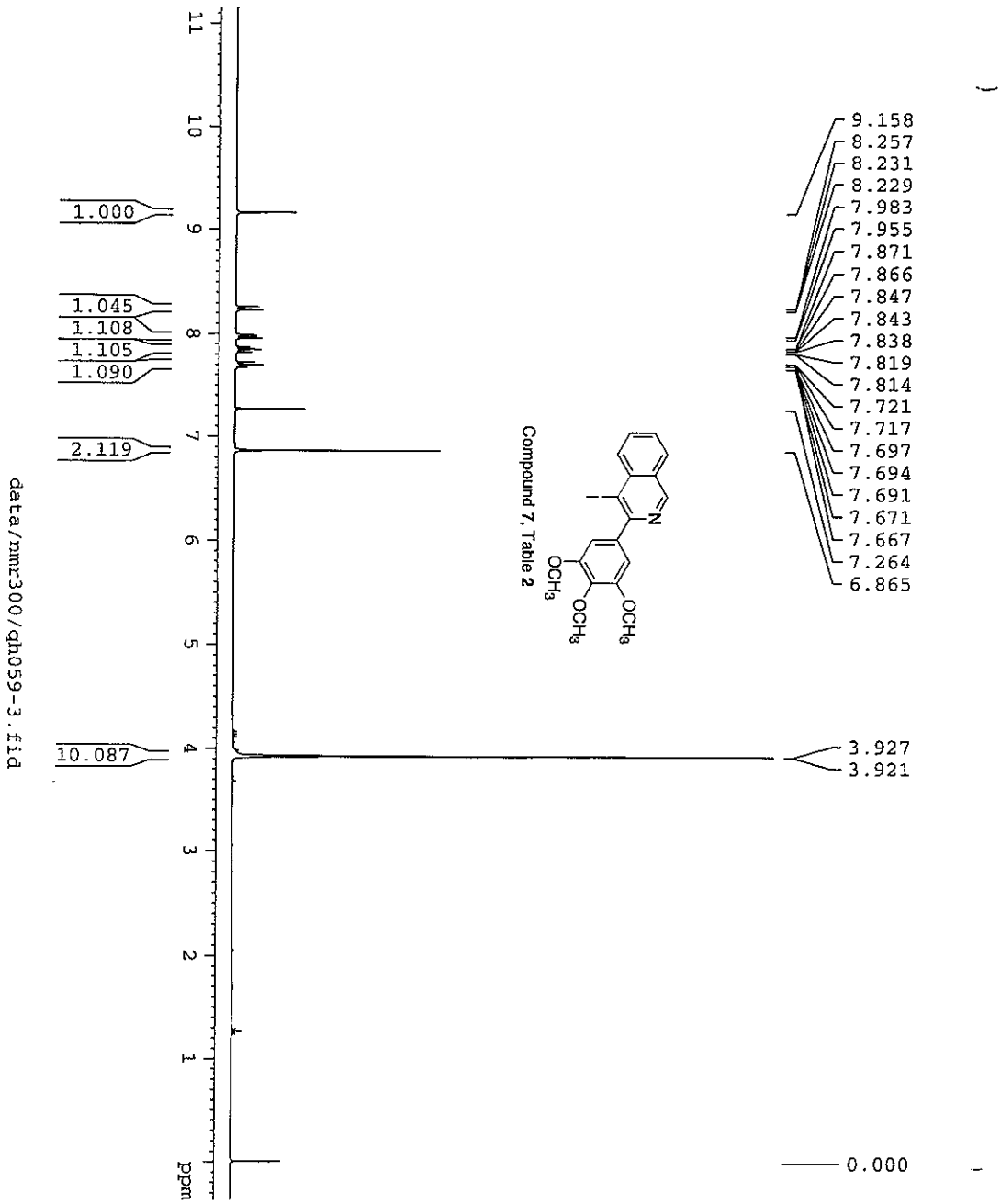

154.630
137.951
132.562
129.824
128.278
126.001
124.591
99.030
92.853
78.976
66.007
62.486
57.916
30.828
30.016
25.660
21.341
19.665
Compoud 40, Table 2
CH2CH2OTHP
N
t-Bu
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr/gh025-2.fid

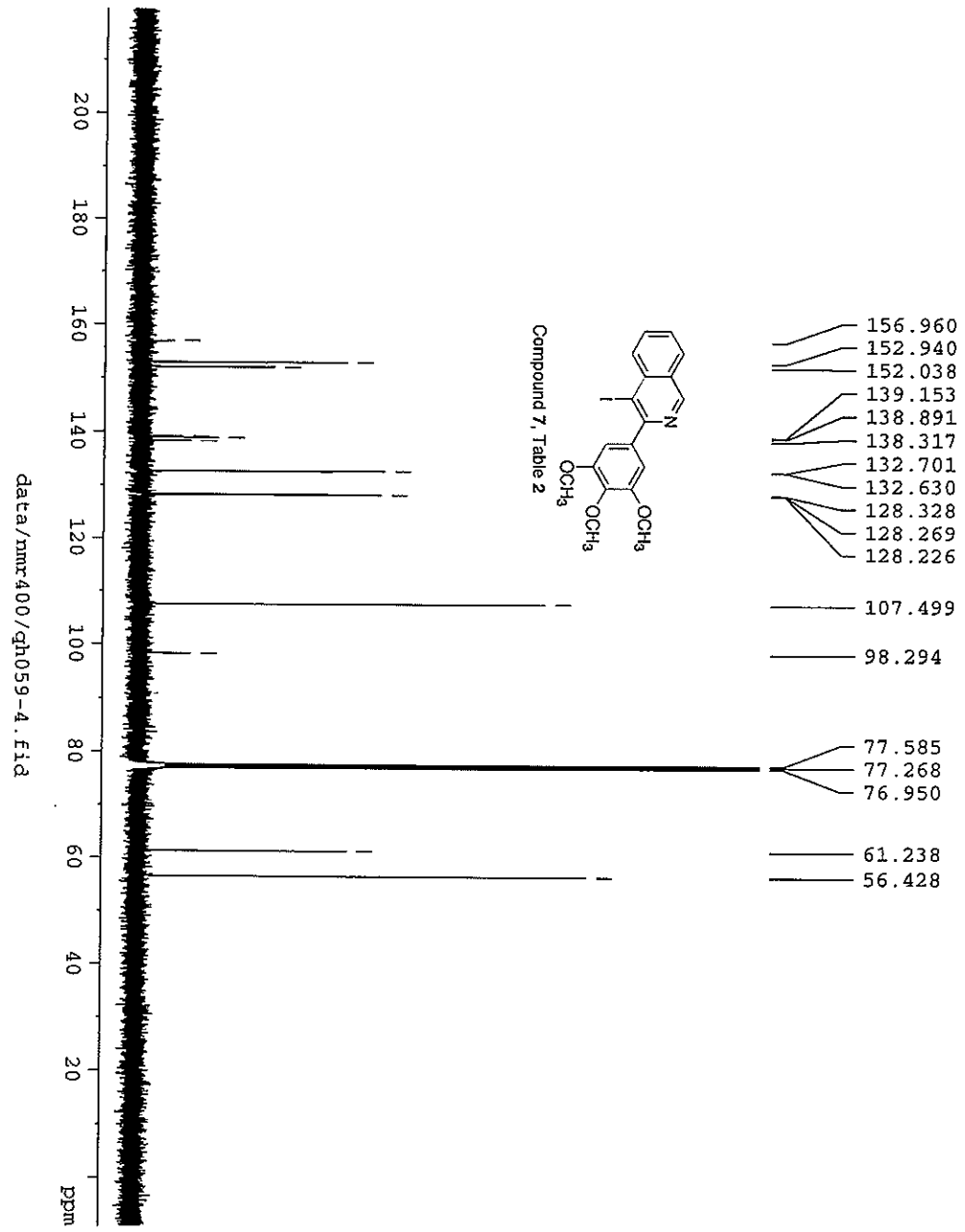

Integral
1.0000
1.0715
1.1380
1.1450
3.3373
3.3500
9.1783
8.2561
8.2537
8.2276
8.2252
7.9769
7.9497
7.9488
7.8609
7.8565
7.8377
7.8329
7.8092
7.8048
7.6619
7.6566
7.6347
7.6302
7.5097
7.4841
7.4776
7.2700
0.0180
Compound 2, Table 2
N
Ph
(ppm)

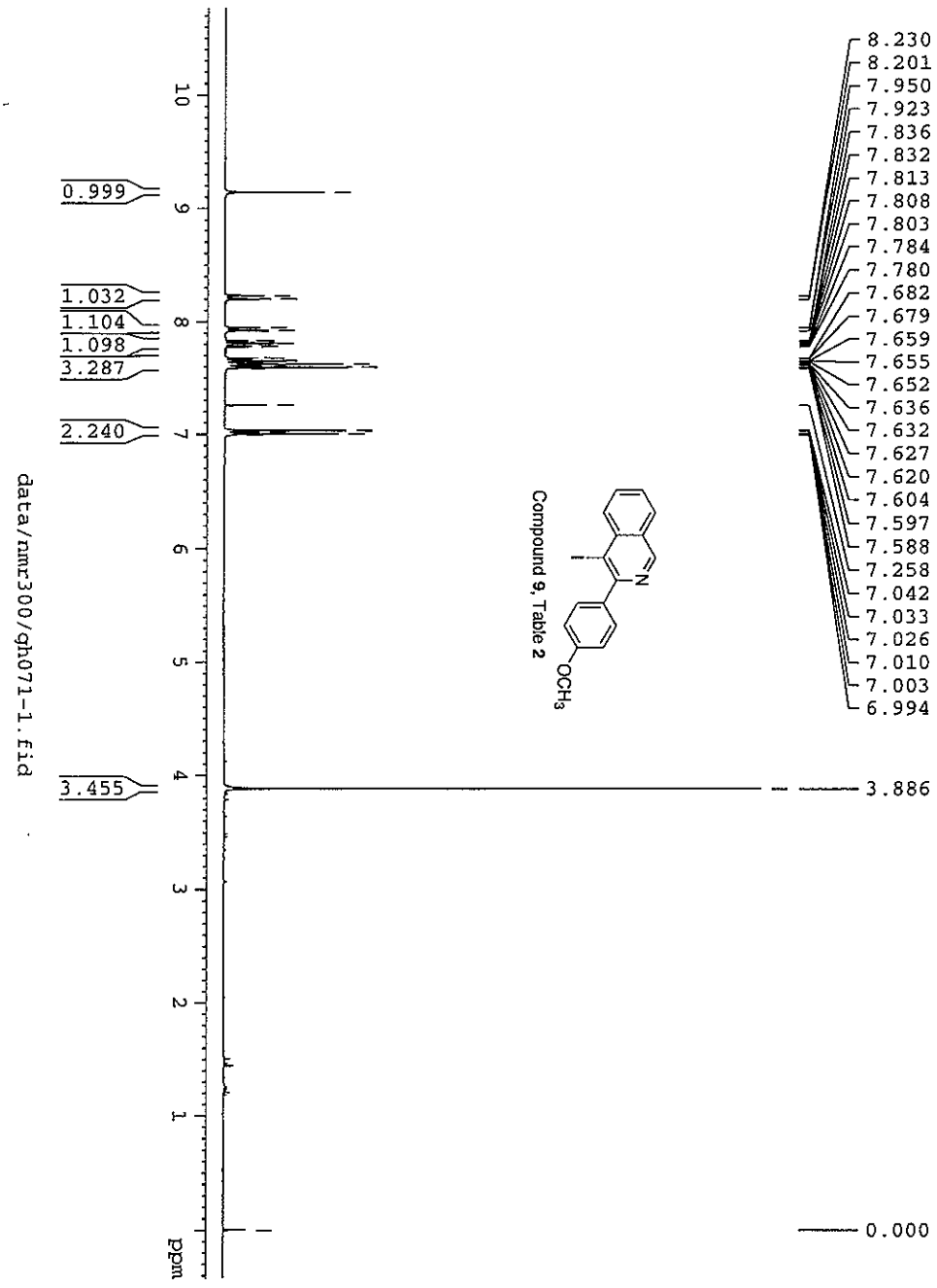

157.405
152.242
143.974
138.804
132.617
132.435
130.030
128.527
128.294
128.212
128.174
98.264
77.683
77.259
76.835
Compound 2, Table 2
N
Ph
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh007-8.fid

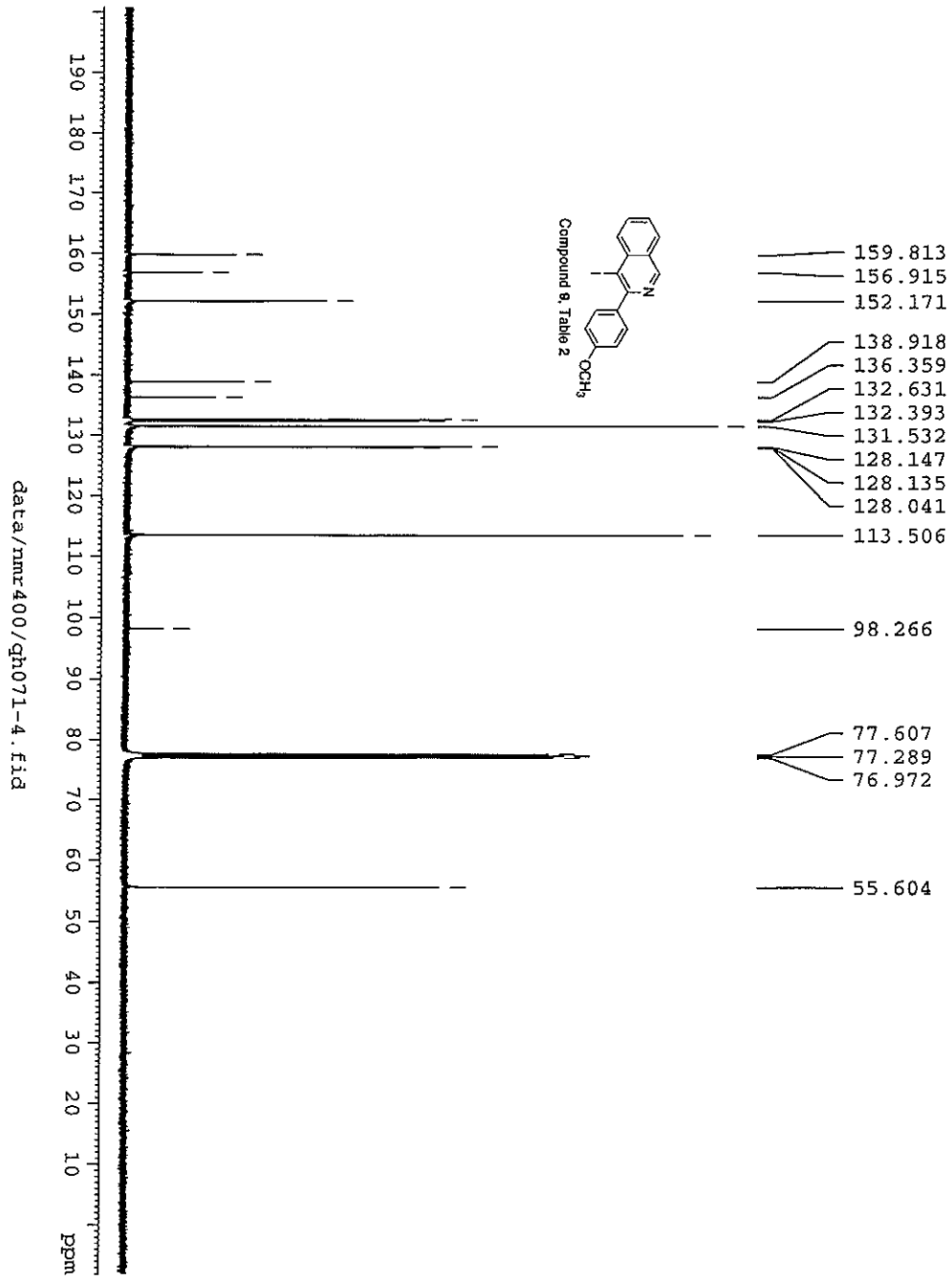

1.000
0.973
1.033
1.031
1.009
1.022
2.210
2.220
4.469
9.068
8.153
8.125
7.891
7.864
7.783
7.759
7.732
7.628
7.602
7.578
7.266
5.856
2.428
2.421
2.402
2.292
2.282
2.272
2.262
2.253
1.917
1.898
1.880
1.861
1.848
1.840
1.799
1.785
1.766
1.748
1.728
0.000
ppm
data/nmr300/qh048-2
Compound 5, Table 2

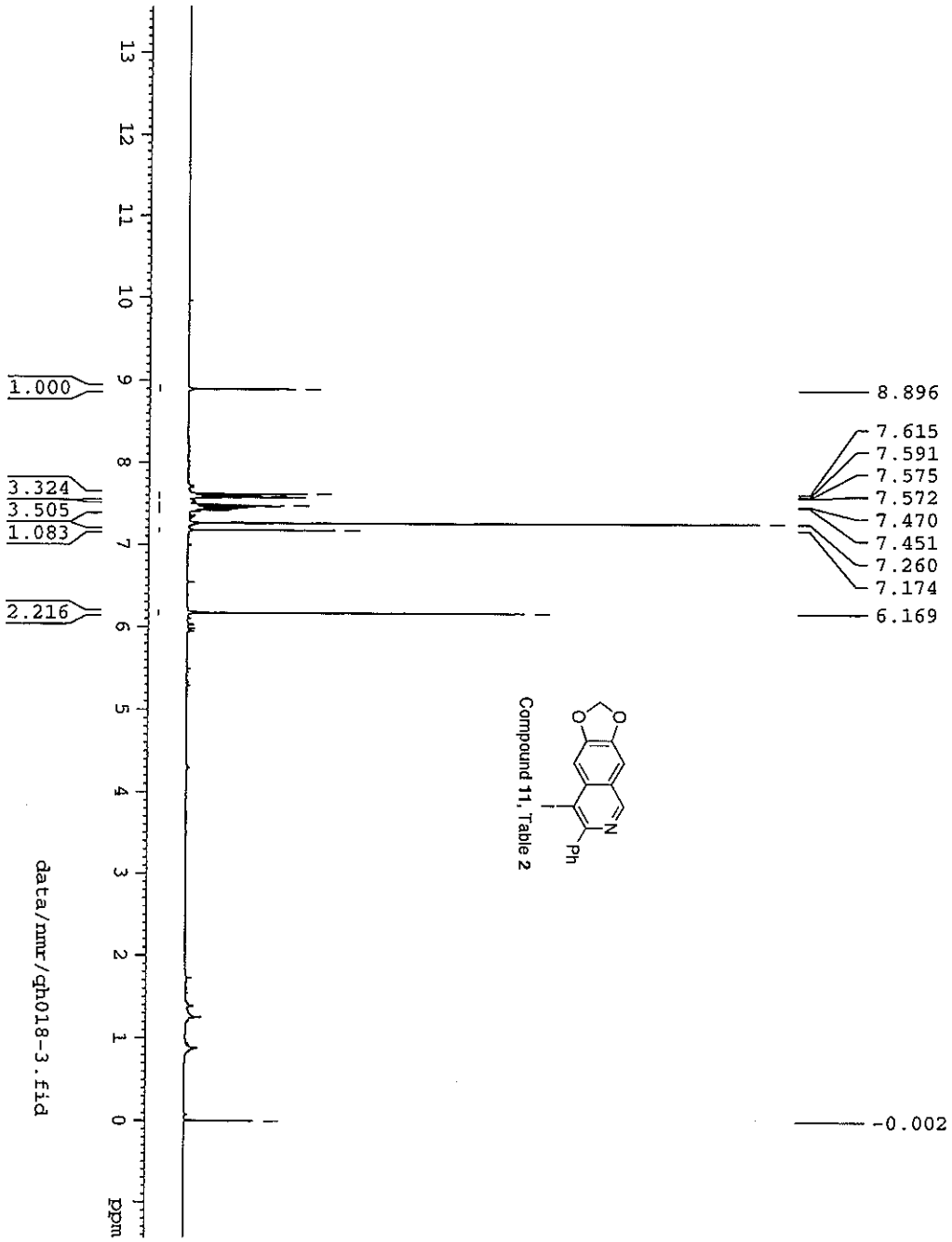

159.720
152.161
141.893
138.681
132.240
132.056
129.623
128.153
128.001
127.646
97.746
77.654
77.231
76.807
28.502
25.360
22.983
22.094
Compound 5, Table 2
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/nmr300/qh048-2

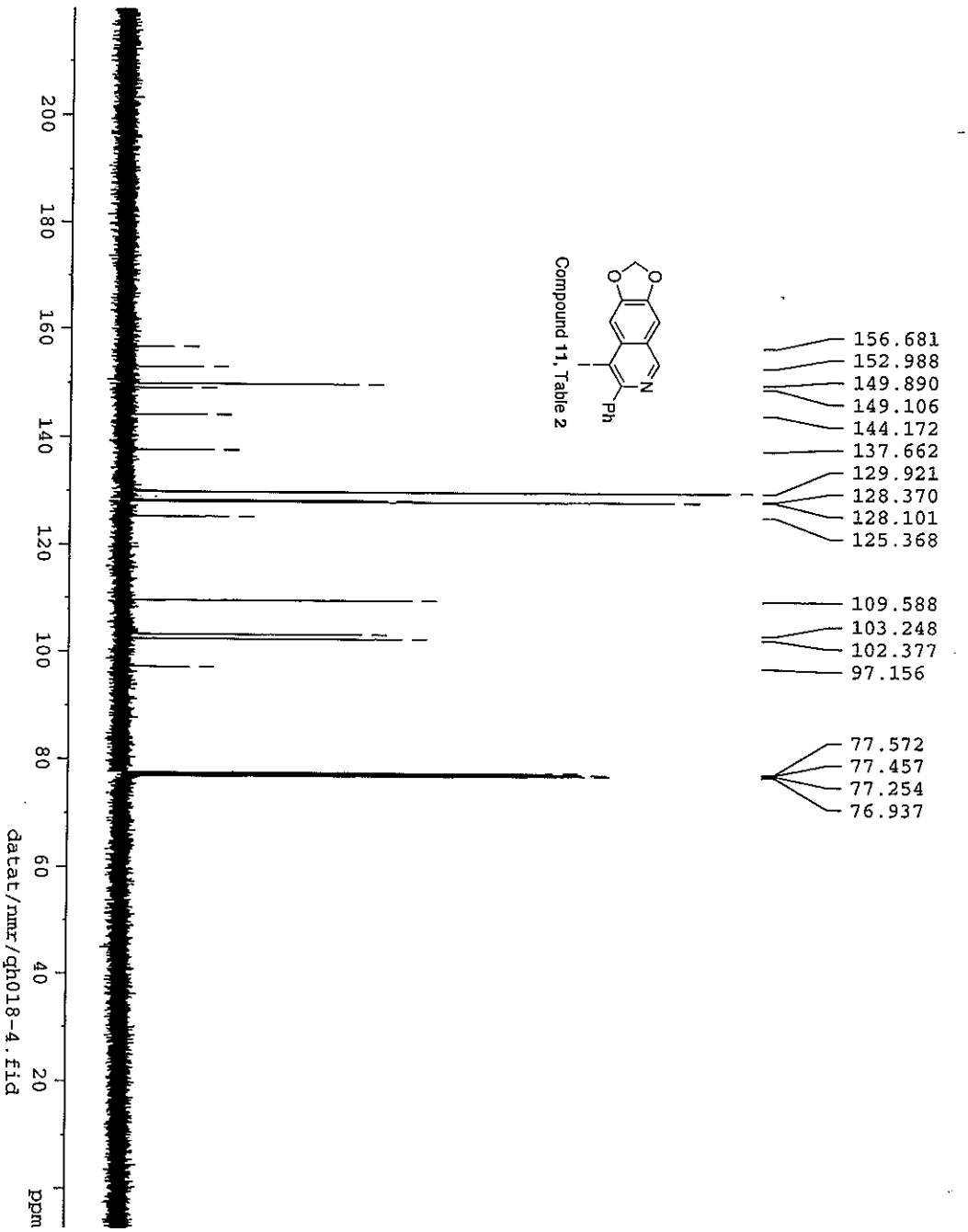

9.158
8.257
8.231
8.229
7.983
7.955
7.871
7.866
7.847
7.843
7.838
7.819
7.814
7.721
7.717
7.697
7.694
7.691
7.671
7.667
7.264
6.865
3.927
3.921
0.000
1.000
1.045
1.108
1.105
1.090
2.119
10.087
Compound 7, Table 2
OCH3
OCH3
OCH3
N
ppm
data/nmr300/qh059-3.fid

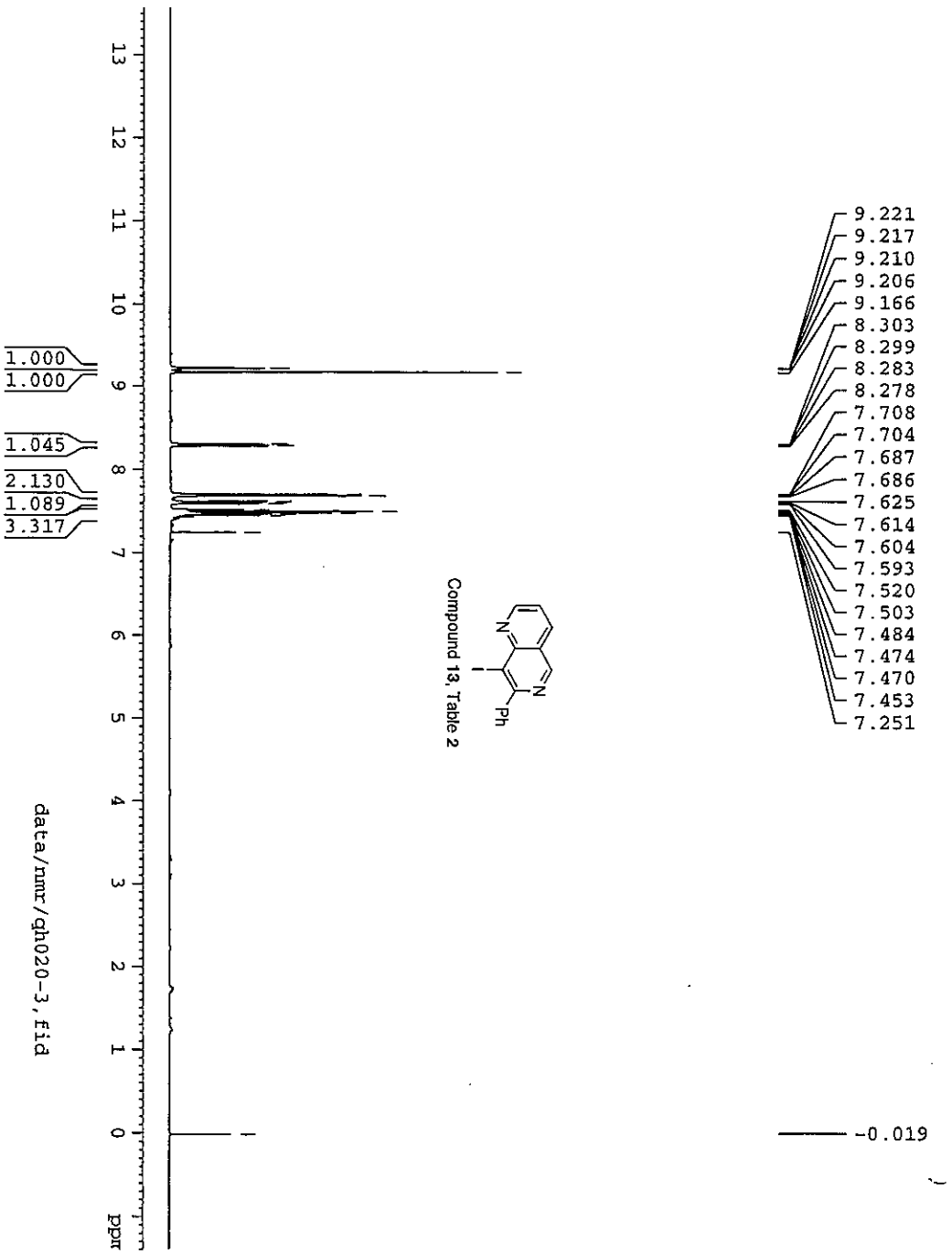

156.960
152.940
152.038
139.153
138.891
138.317
132.701
132.630
128.328
128.269
128.226
107.499
98.294
77.585
77.268
76.950
61.238
56.428
Compound 7, Table 2
OCH3
OCH3
OCH3
N
200
180
160
140
120
100
80
60
40
20
ppm
data/nmr400/qh059-4.fid

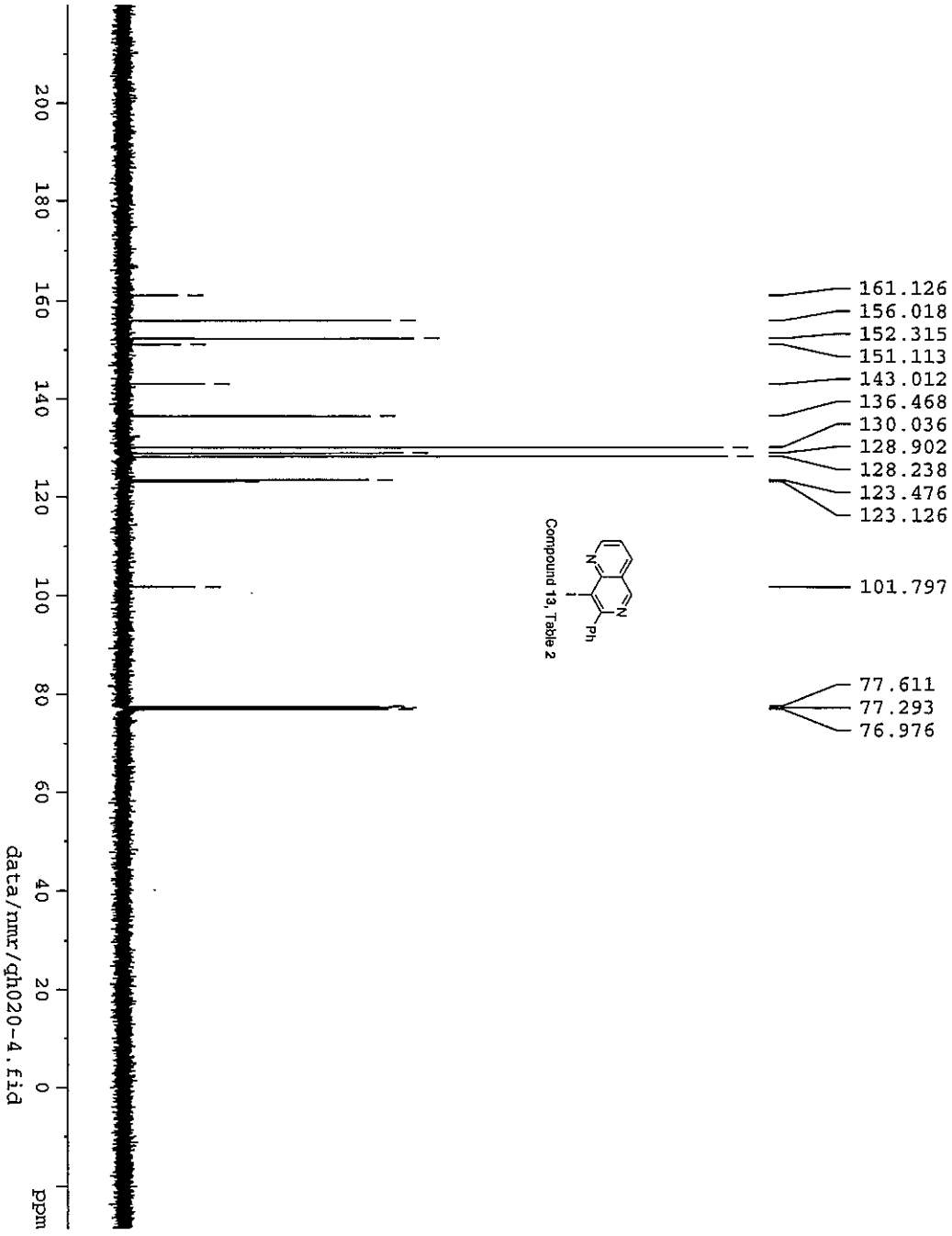

8.230
8.201
7.950
7.923
7.836
7.832
7.813
7.808
7.803
7.784
7.780
7.682
7.679
7.659
7.655
7.652
7.636
7.632
7.627
7.620
7.604
7.597
7.588
7.258
7.042
7.033
7.026
7.010
7.003
6.994
3.886
0.000
0.999
1.032
1.104
1.098
3.287
2.240
3.455
Compound 9, Table 2
OCH3
N
data/nmr300/qh071-1.fid
ppm

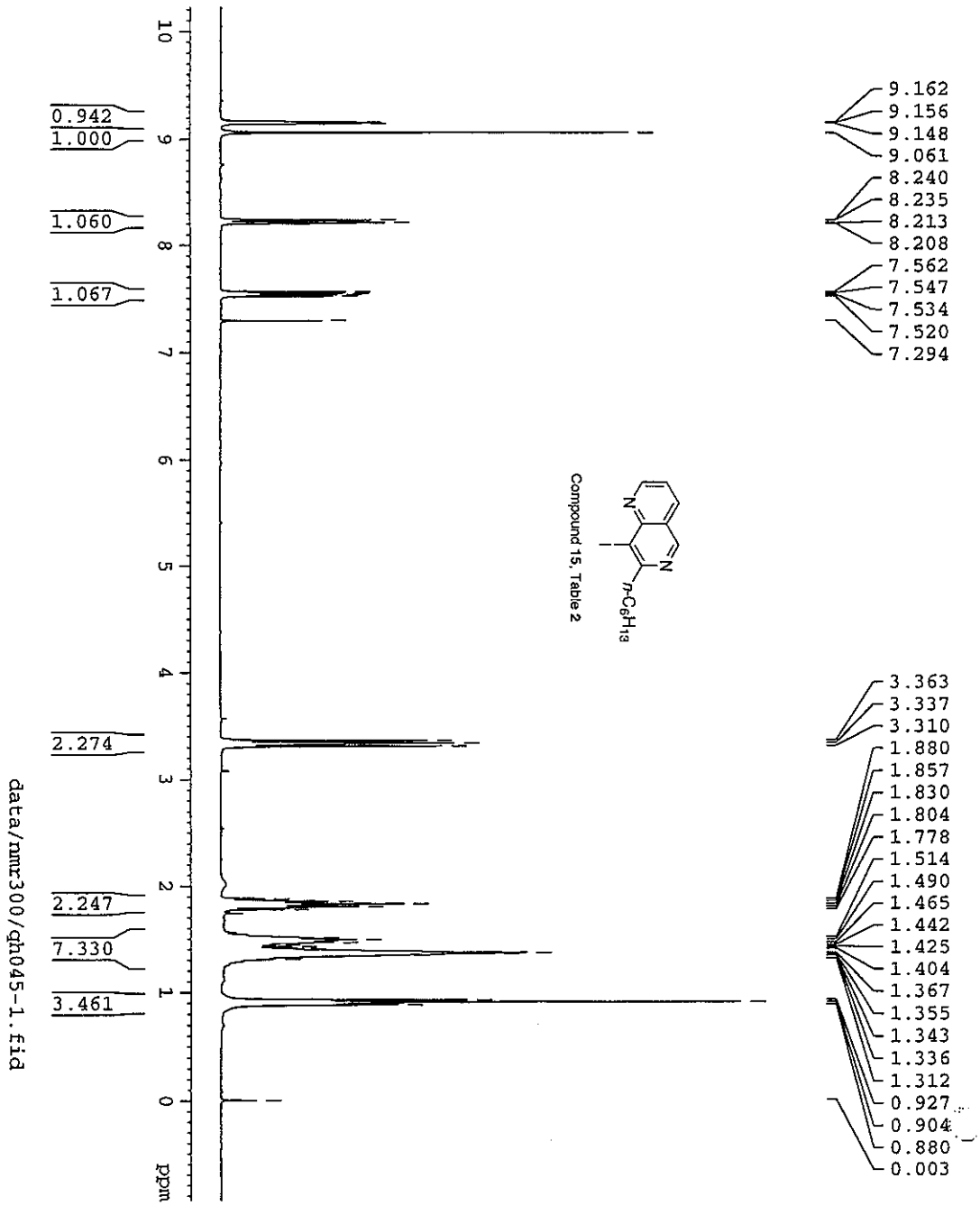

159.813
156.915
152.171
138.918
136.359
132.631
132.393
131.532
128.147
128.135
128.041
113.506
98.266
77.607
77.289
76.972
55.604
Compound 9, Table 2
OCH3
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/nmr400/qh071-4.fid

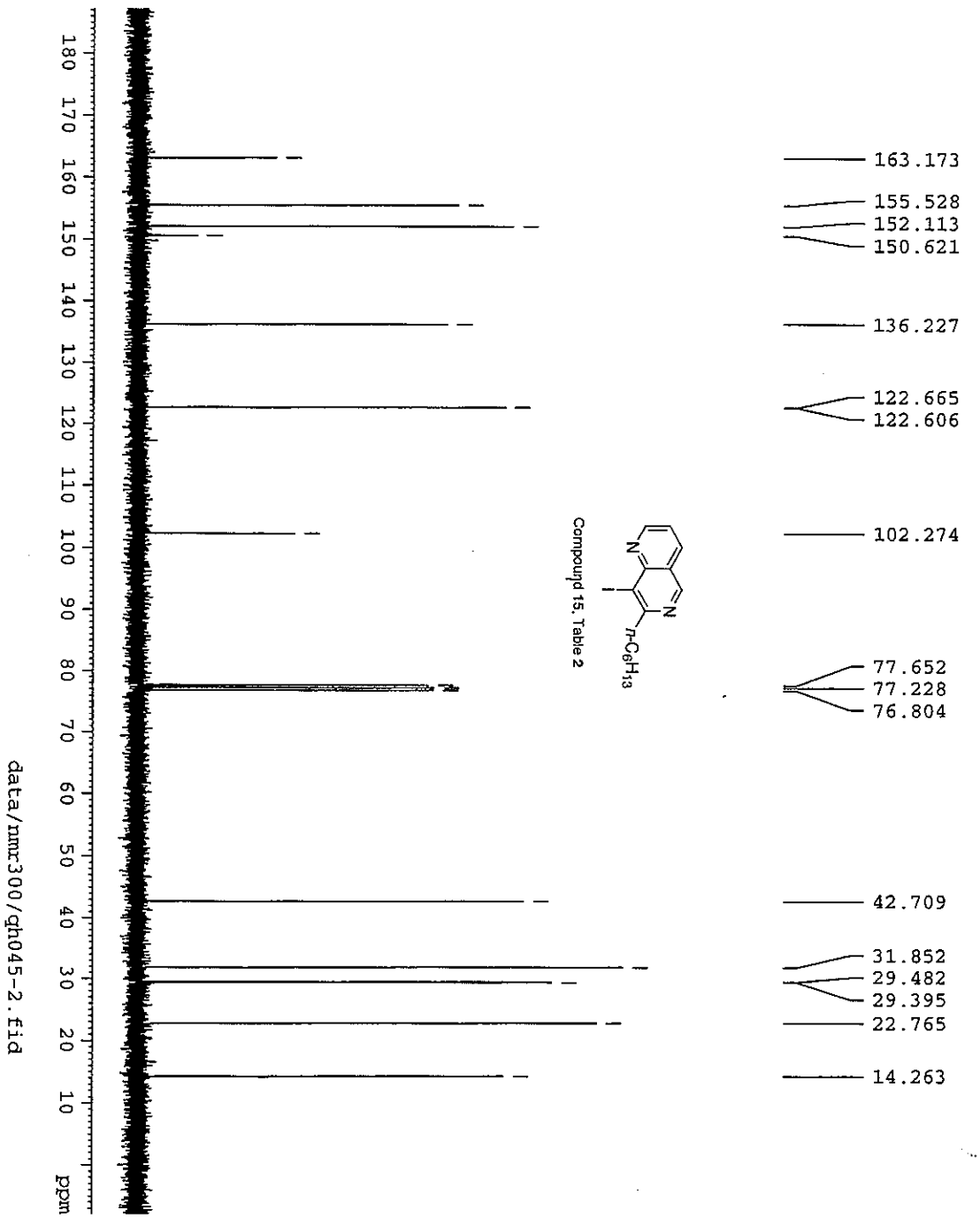

8.896
7.615
7.591
7.575
7.572
7.470
7.451
7.260
7.174
6.169
-0.002
1.000
3.324
3.505
1.083
2.216
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
data/nmr/qh018-3.fid
Compound 11, Table 2
O
O
N
Ph

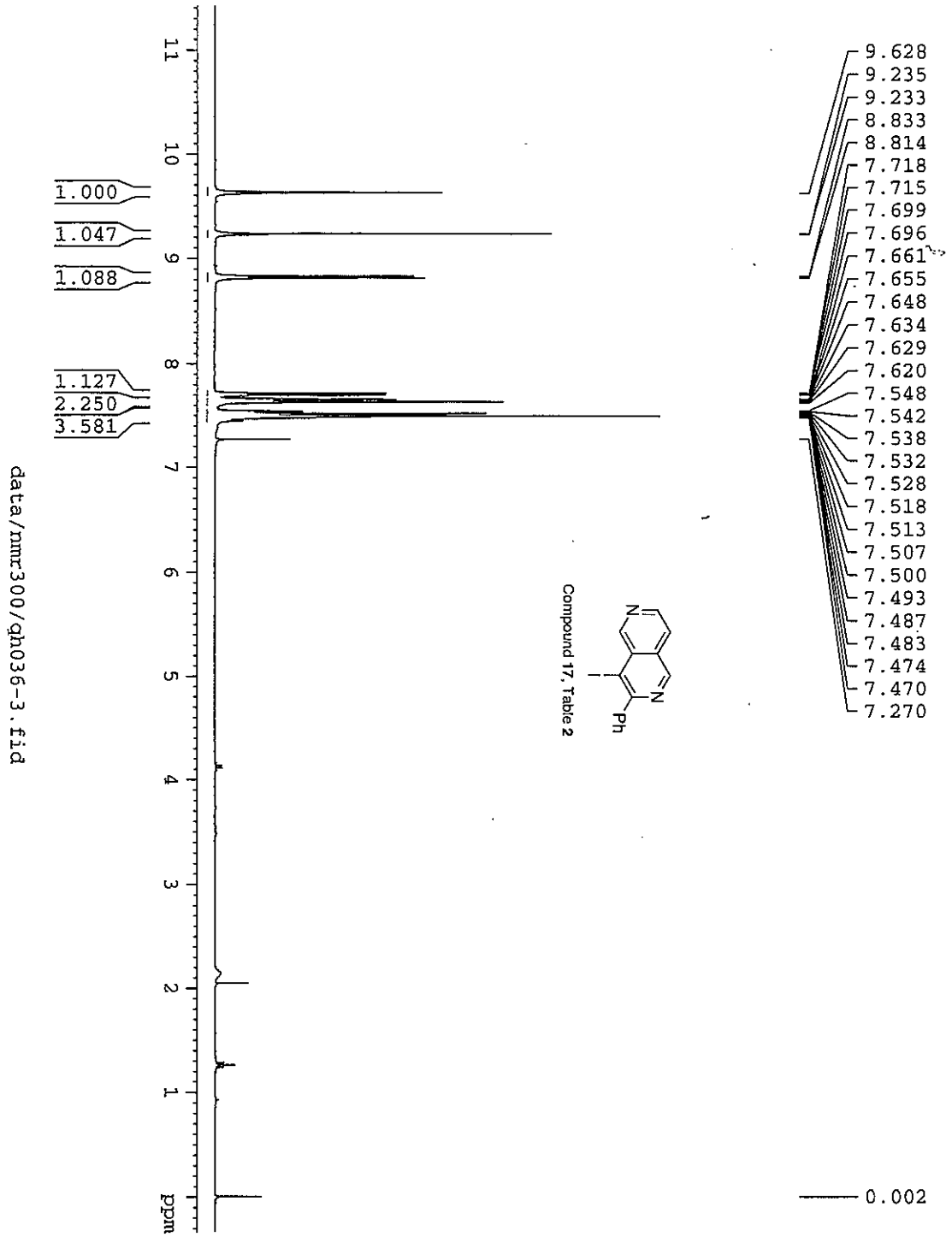

Compound 11, Table 2
Ph
156.681
152.988
149.890
149.106
144.172
137.662
129.921
128.370
128.101
125.368
109.588
103.248
102.377
97.156
77.572
77.457
77.254
76.937
200
180
160
140
120
100
80
60
40
20
ppm
datat/nmr/qh018-4.fid

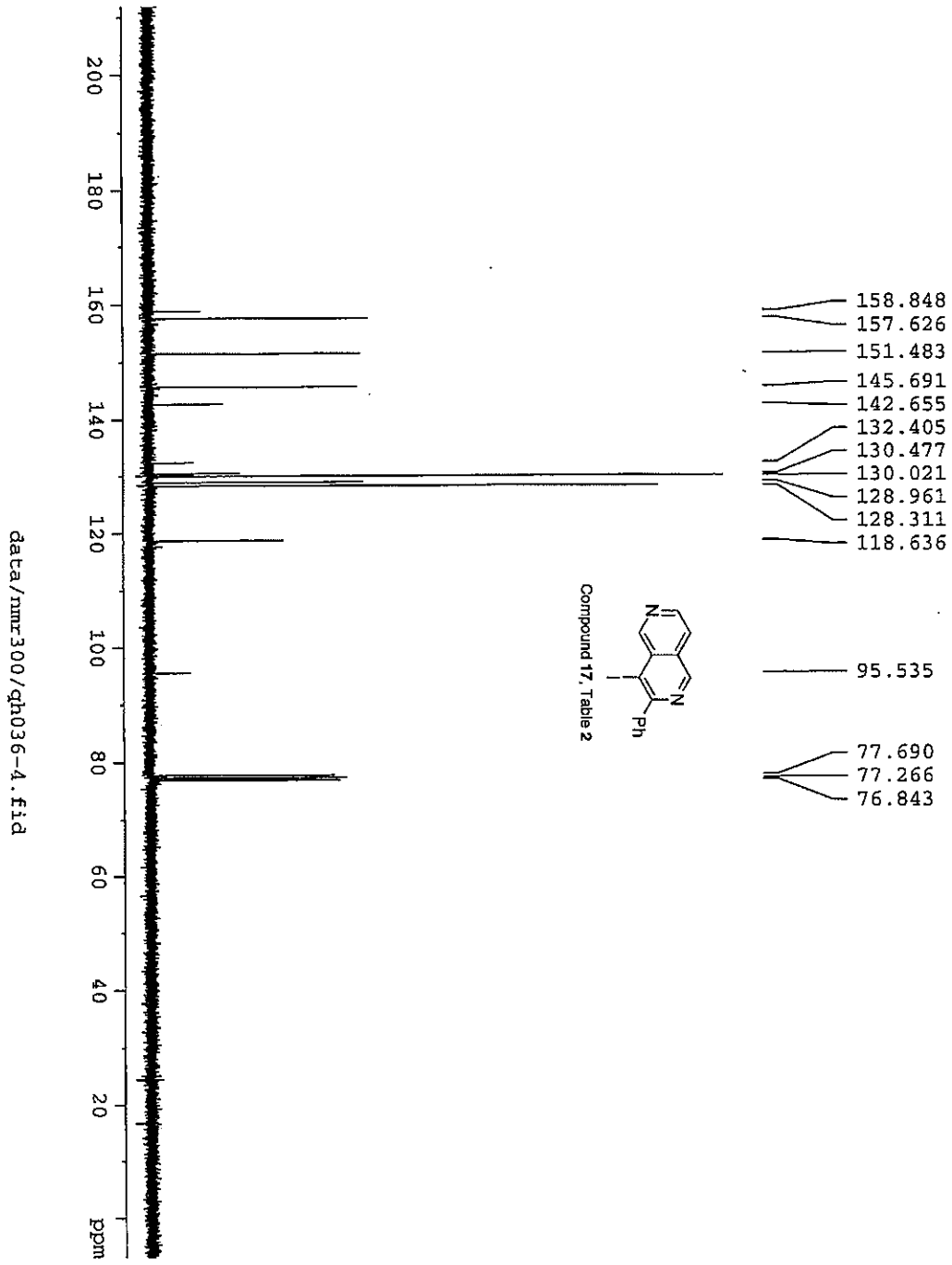

9.221
9.217
9.210
9.206
9.166
8.303
8.299
8.283
8.278
7.708
7.704
7.687
7.686
7.625
7.614
7.604
7.593
7.520
7.503
7.484
7.474
7.470
7.453
7.251
-0.019
1.000
1.000
1.045
2.130
1.089
3.317
Compound 13, Table 2
Ph
N
N
data/nmr/qh020-3,fid
ppm

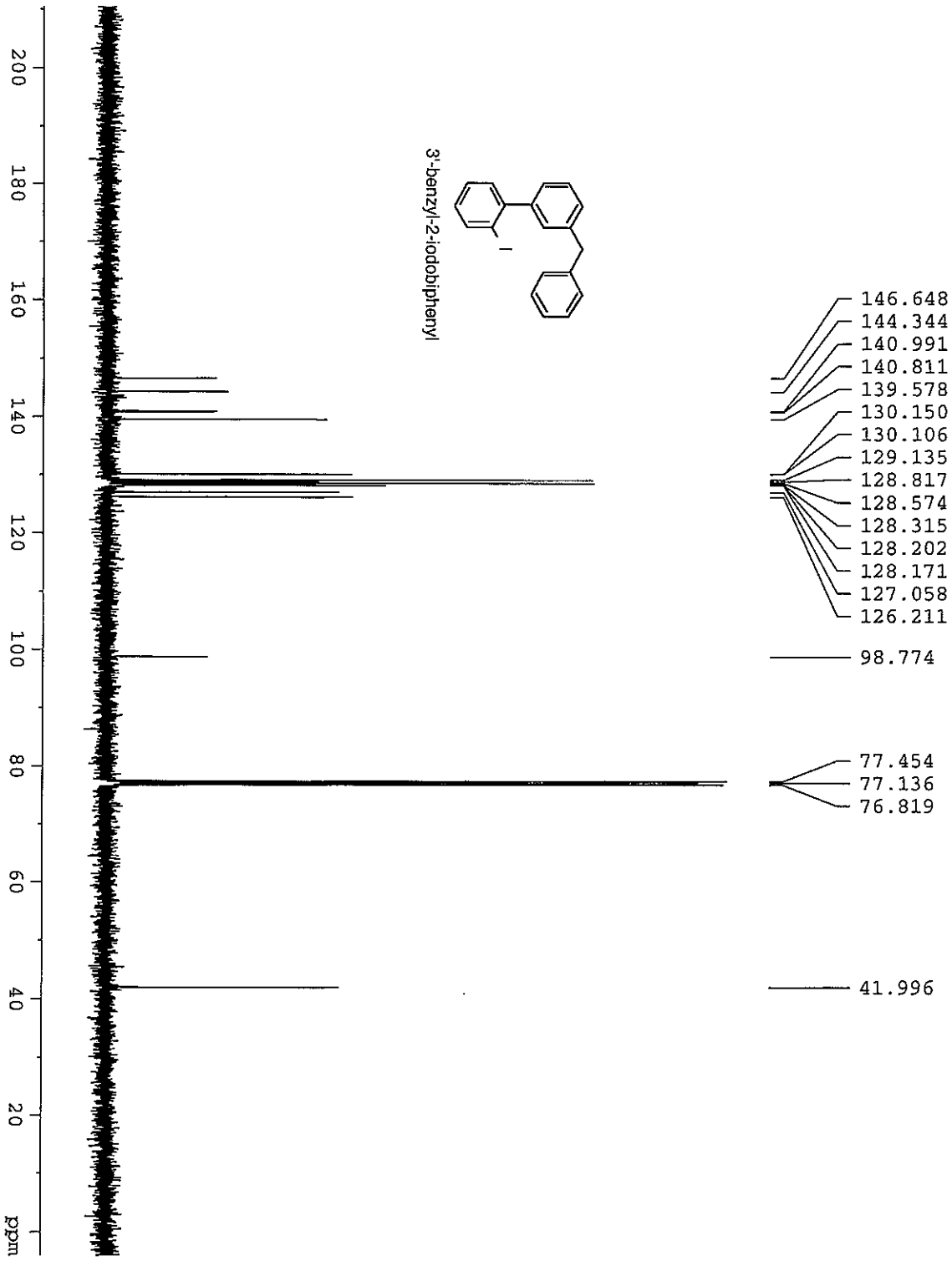

161.126
156.018
152.315
151.113
143.012
136.468
130.036
128.902
128.238
123.476
123.126
101.797
77.611
77.293
76.976
Compound 13, Table 2
Ph
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr/qh020-4.fid

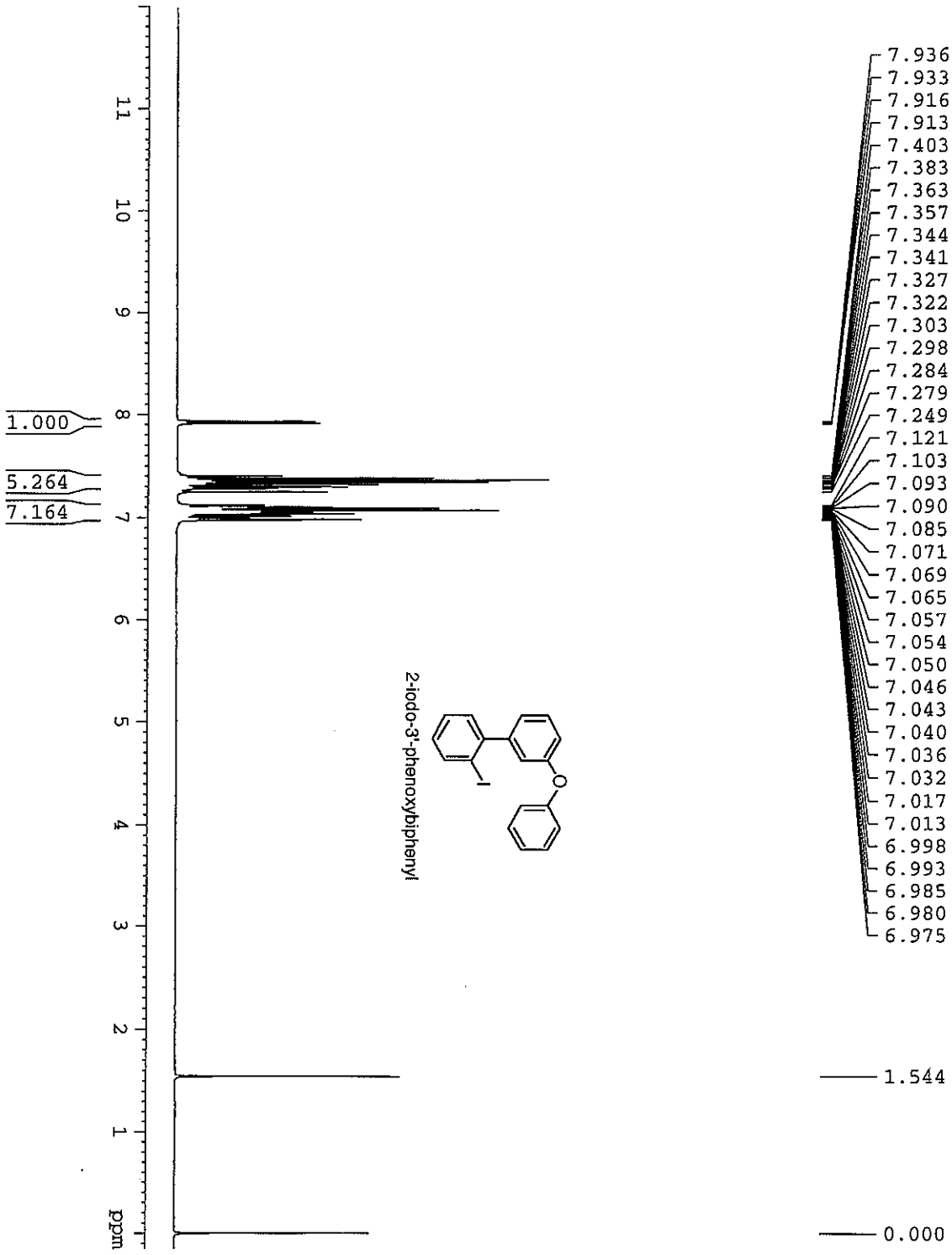

0.942
1.000
1.060
1.067
2.274
2.247
7.330
3.461
ppm
data/nmr300/qh045-1.fid
Compound 15, Table 2
n-C6H13
9.162
9.156
9.148
9.061
8.240
8.235
8.213
8.208
7.562
7.547
7.534
7.520
7.294
3.363
3.337
3.310
1.880
1.857
1.830
1.804
1.778
1.514
1.490
1.465
1.442
1.425
1.404
1.367
1.355
1.343
1.336
1.312
0.927
0.904
0.880
0.003

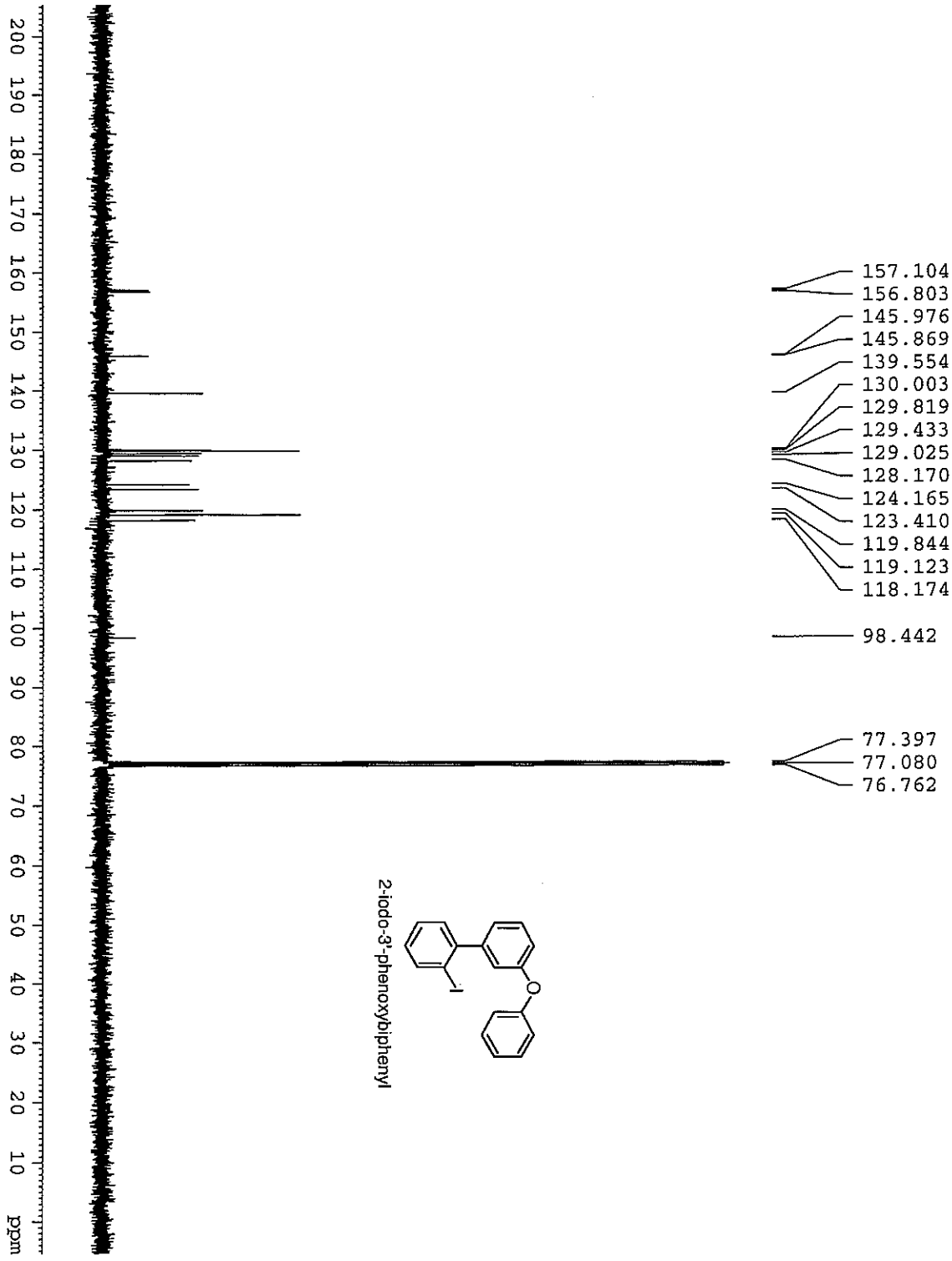

163.173
155.528
152.113
150.621
136.227
122.665
122.606
102.274
77.652
77.228
76.804
42.709
31.852
29.482
29.395
22.765
14.263
Compound 15, Table 2
n-C6H13
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/nmr300/qh045-2.fid

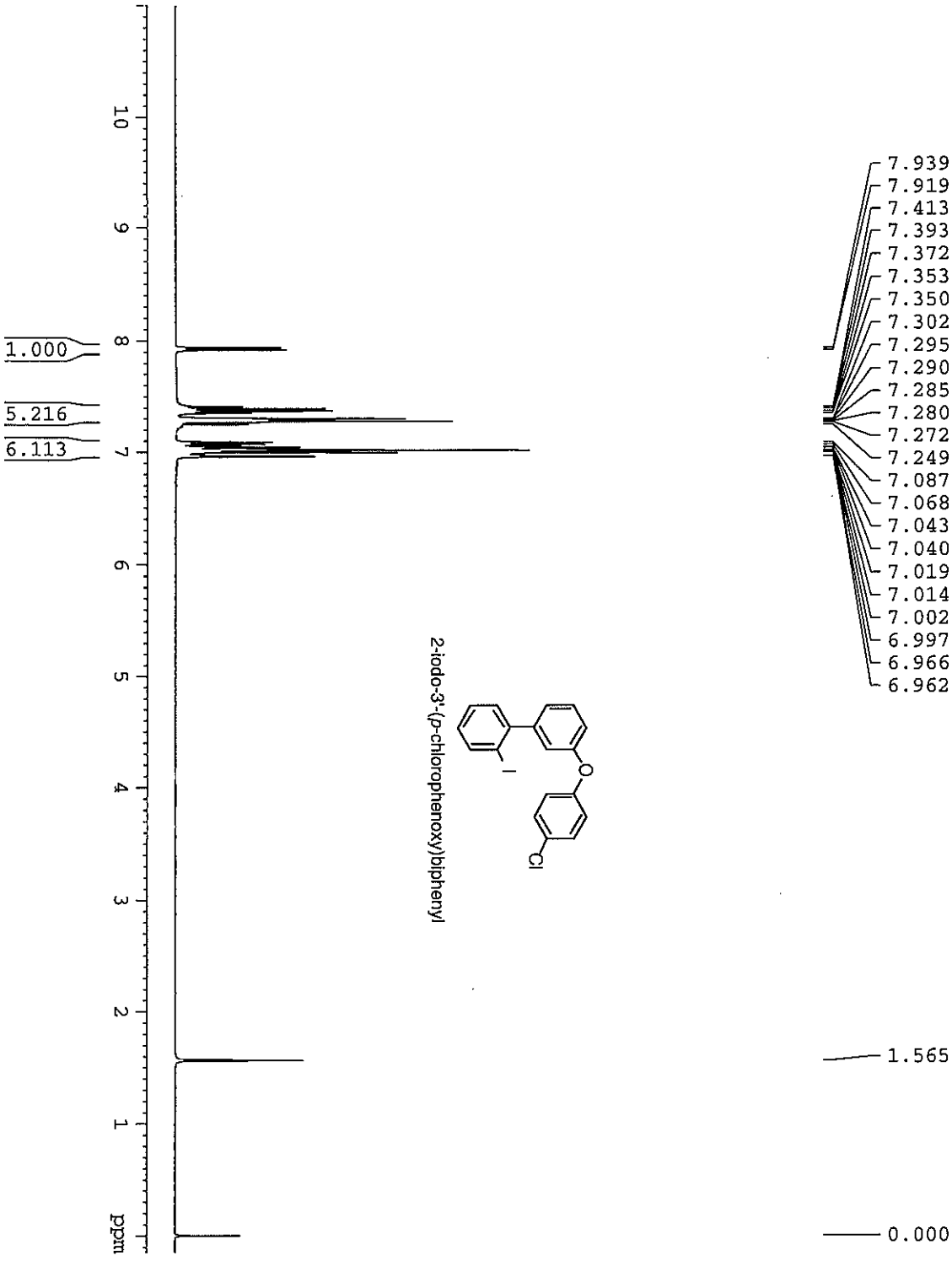

9.628
9.235
9.233
8.833
8.814
7.718
7.715
7.699
7.696
7.661
7.655
7.648
7.634
7.629
7.620
7.548
7.542
7.538
7.532
7.528
7.518
7.513
7.507
7.500
7.493
7.487
7.483
7.474
7.470
7.270
0.002
1.000
1.047
1.088
1.127
2.250
3.581
ppm
Compound 17, Table 2
data/nmr300/qh036-3.fid

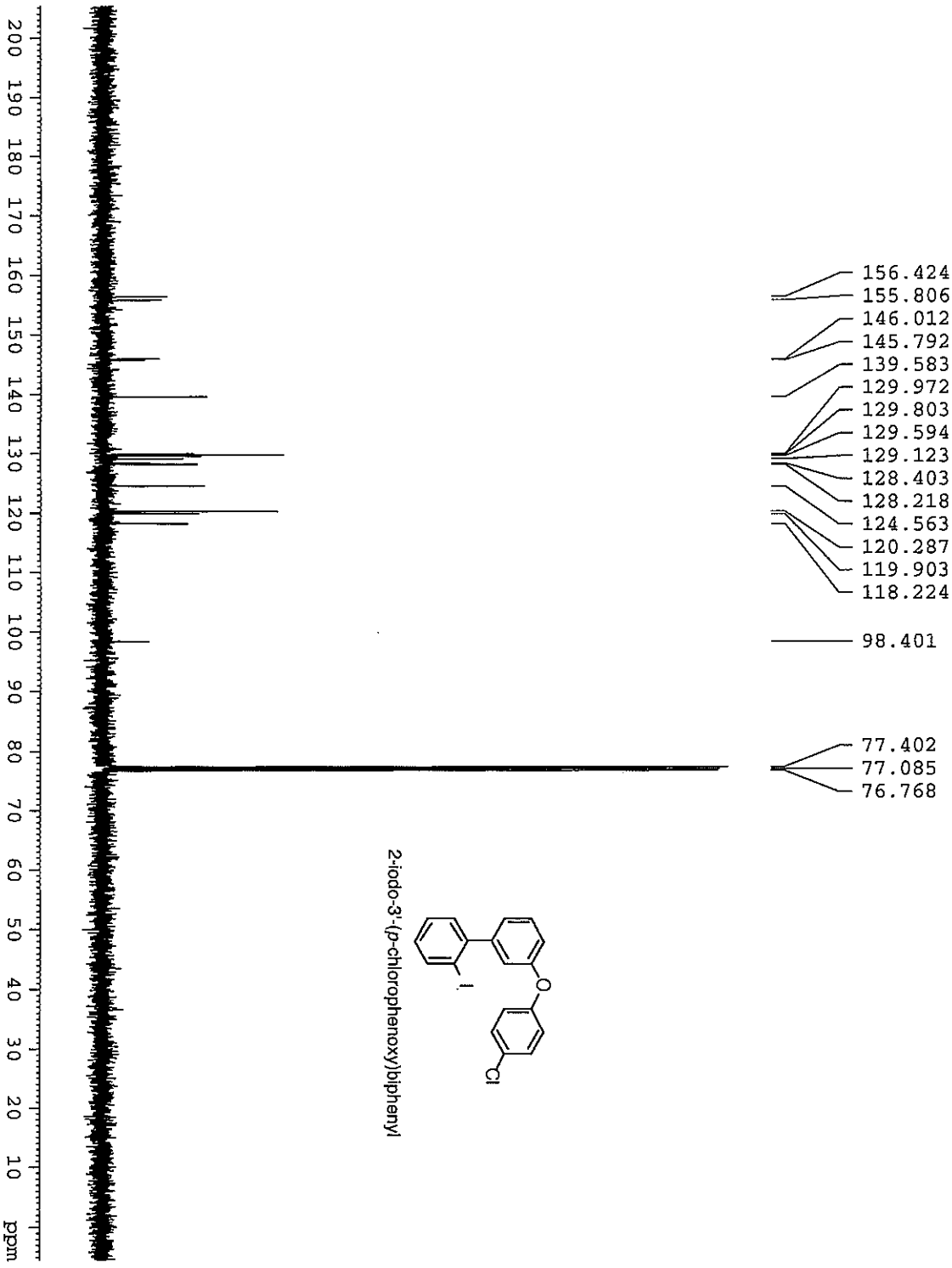

158.848
157.626
151.483
145.691
142.655
132.405
130.477
130.021
128.961
128.311
118.636
95.535
77.690
77.266
76.843
Compound 17, Table 2
N
N
Ph
200
180
160
140
120
100
80
60
40
20
ppm
data/nmr300/qh036-4.fid

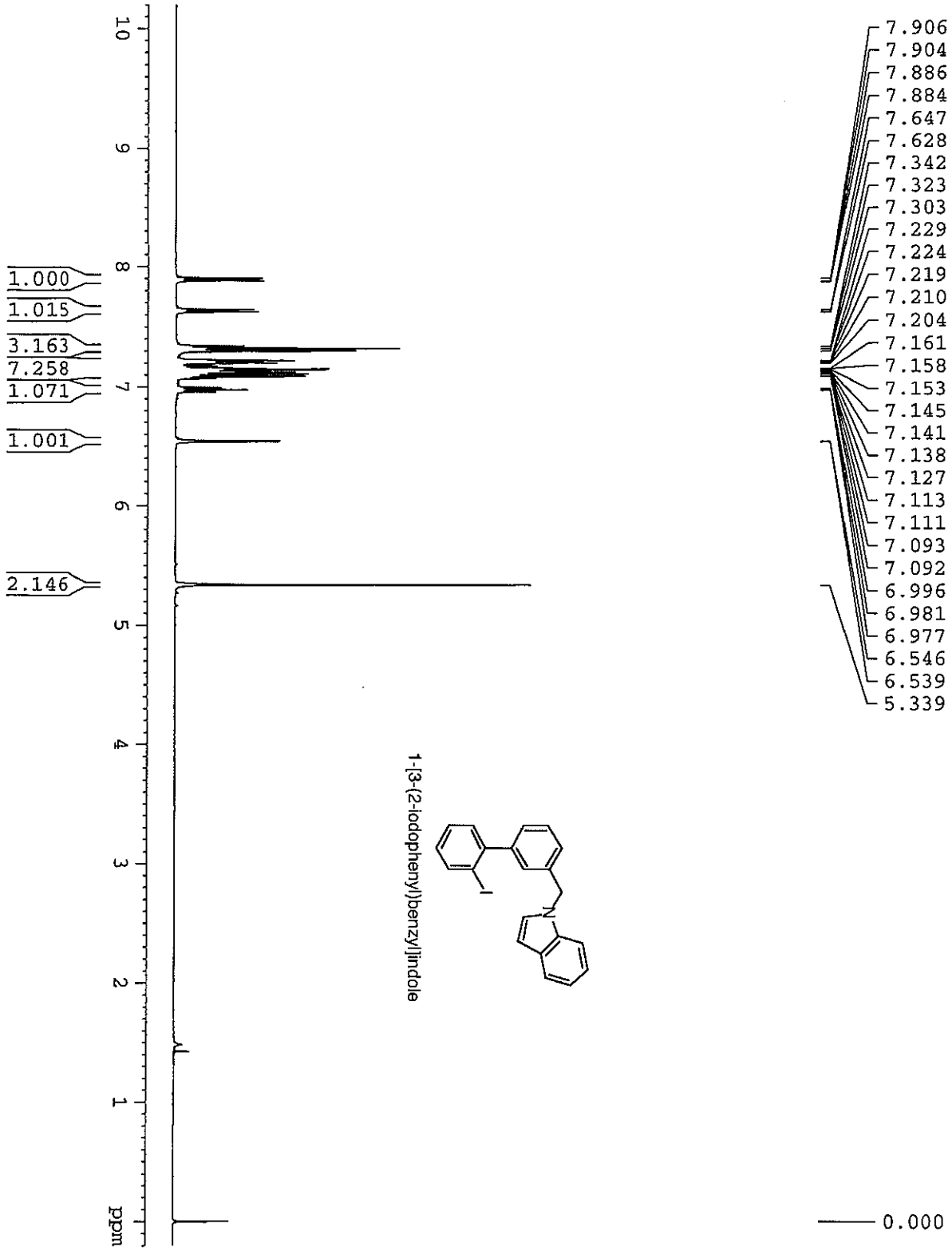

3'-benzyl-2-iodobiphenyl
I
146.648
144.344
140.991
140.811
139.578
130.150
130.106
129.135
128.817
128.574
128.315
128.202
128.171
127.058
126.211
98.774
77.454
77.136
76.819
41.996
200
180
160
140
120
100
80
60
40
20
ppm

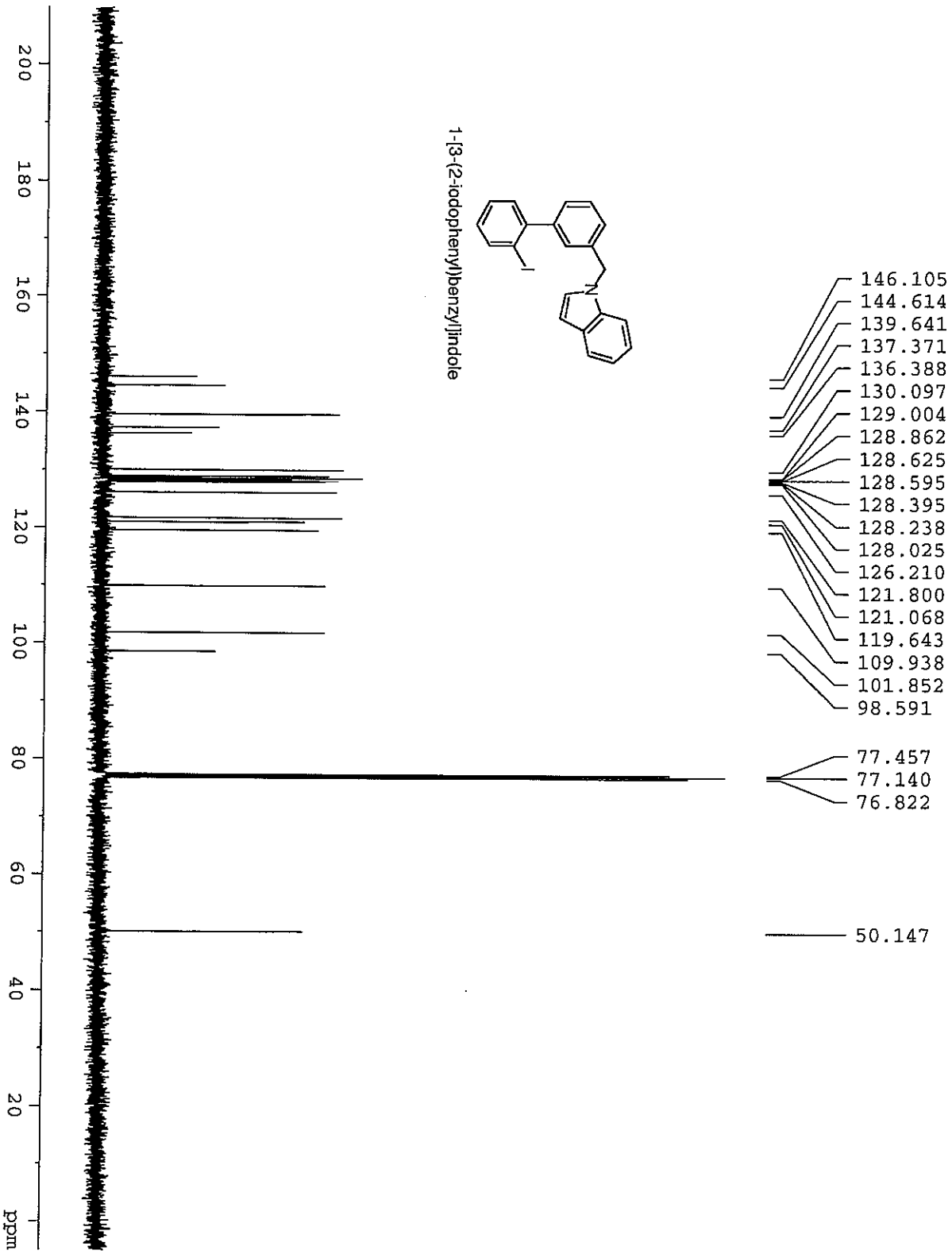

7.936
7.933
7.916
7.913
7.403
7.383
7.363
7.357
7.344
7.341
7.327
7.322
7.303
7.298
7.284
7.279
7.249
7.121
7.103
7.093
7.090
7.085
7.071
7.069
7.065
7.057
7.054
7.050
7.046
7.043
7.040
7.036
7.032
7.017
7.013
6.998
6.993
6.985
6.980
6.975
1.544
0.000
1.000
5.264
7.164
2-iodo-3'-phenoxybiphenyl
I
O
ppm

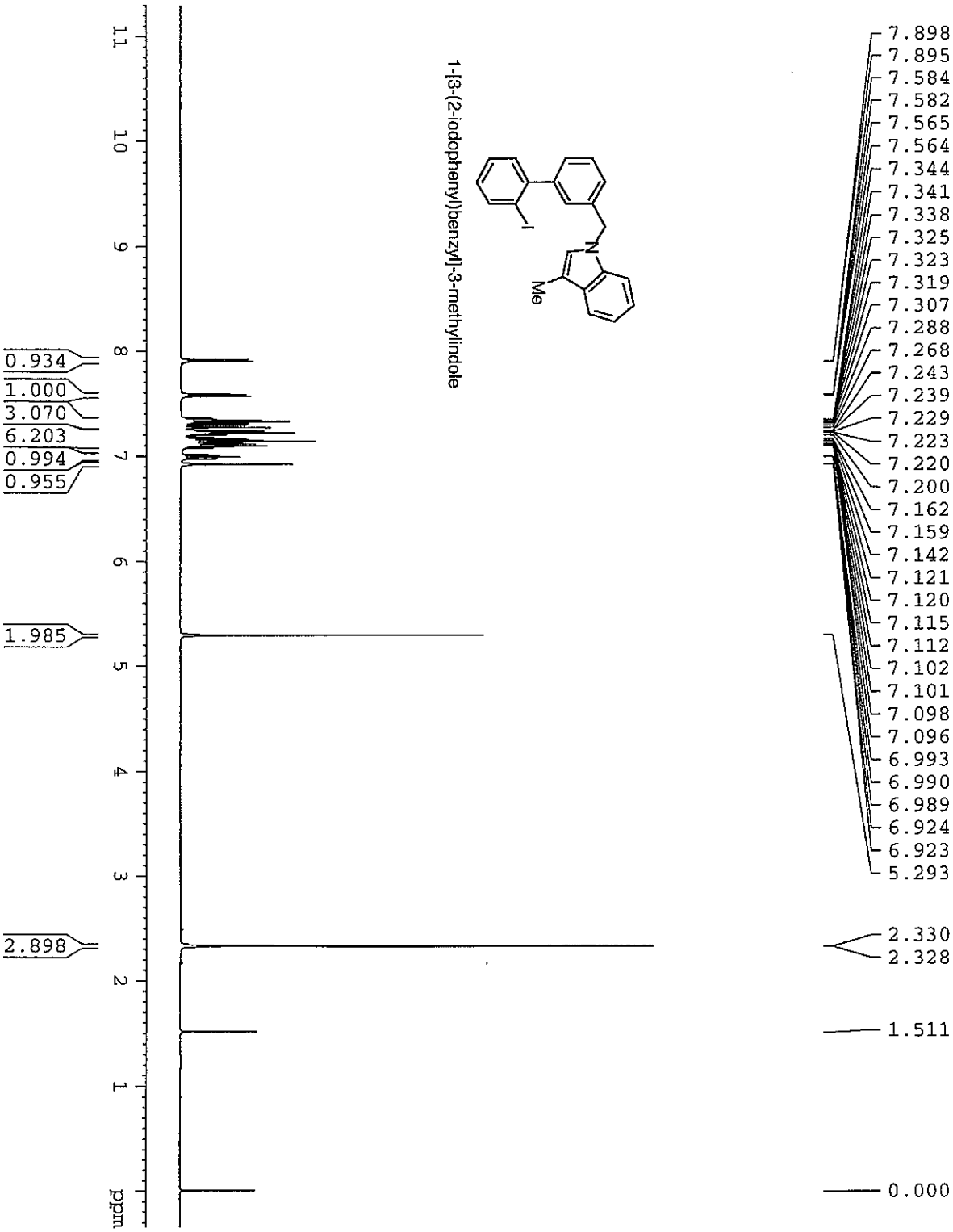

157.104
156.803
145.976
145.869
139.554
130.003
129.819
129.433
129.025
128.170
124.165
123.410
119.844
119.123
118.174
98.442
77.397
77.080
76.762
2-iodo-3'-phenoxybiphenyl
I
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

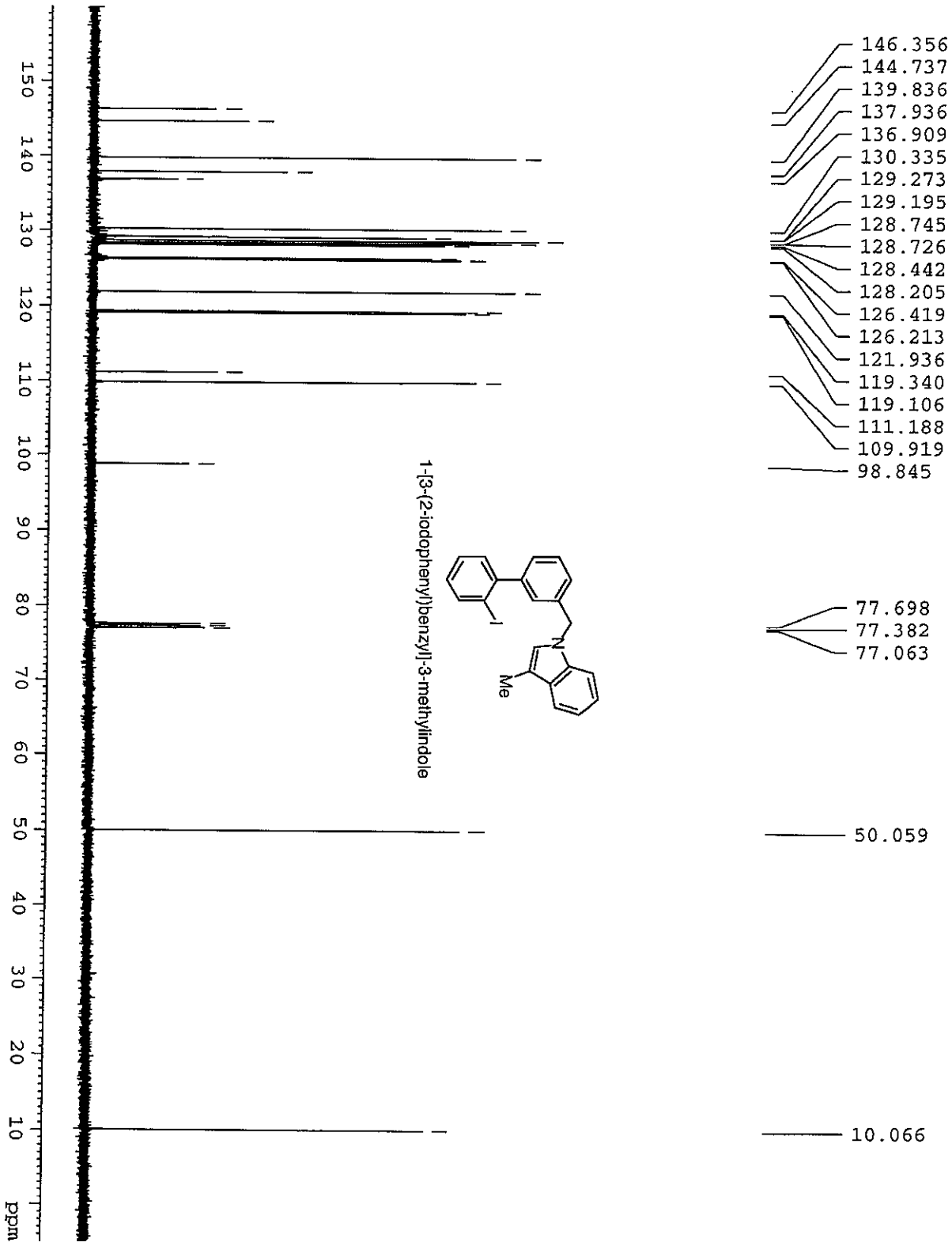

1.000
5.216
6.113
10
9
8
7
6
5
4
3
2
1
ppm
7.939
7.919
7.413
7.393
7.372
7.353
7.350
7.302
7.295
7.290
7.285
7.280
7.272
7.249
7.087
7.068
7.043
7.040
7.019
7.014
7.002
6.997
6.966
6.962
1.565
0.000
2-iodo-3'-(p-chlorophenoxy)biphenyl
I
O
Cl

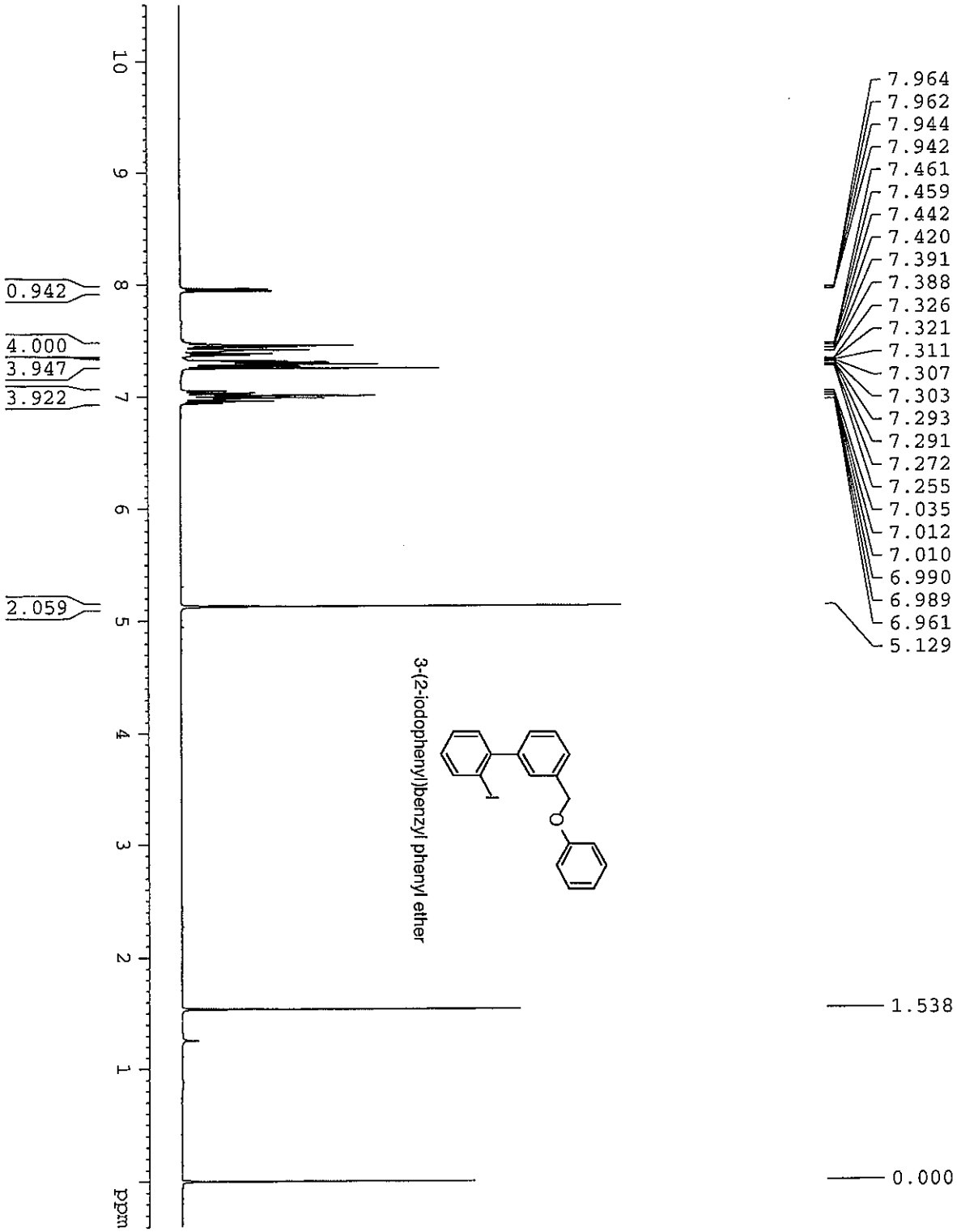

156.424
155.806
146.012
145.792
139.583
129.972
129.803
129.594
129.123
128.403
128.218
124.563
120.287
119.903
118.224
98.401
77.402
77.085
76.768
2-iodo-3'-(p-chlorophenoxy)biphenyl
I
O
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

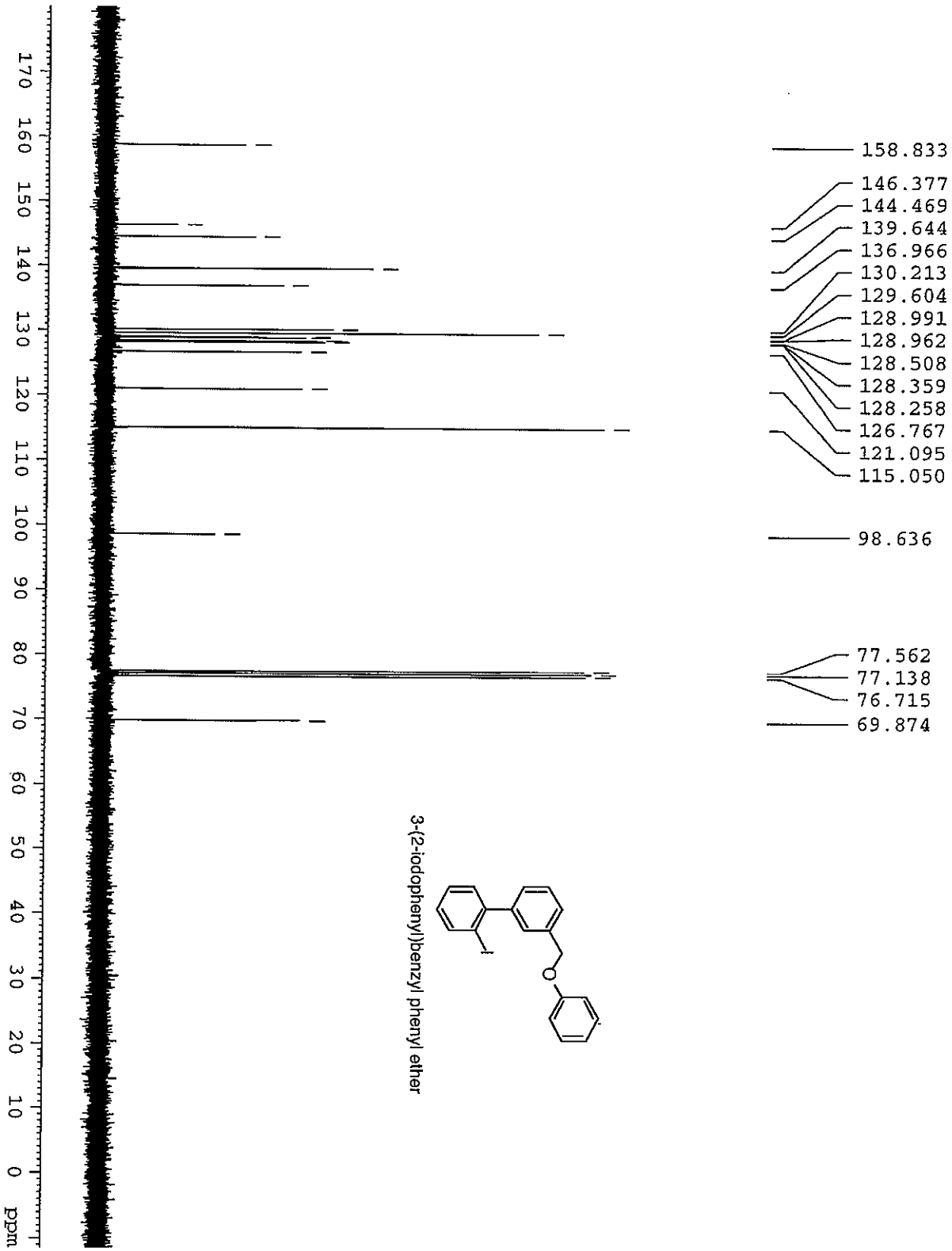

7.906
7.904
7.886
7.884
7.647
7.628
7.342
7.323
7.303
7.229
7.224
7.219
7.210
7.204
7.161
7.158
7.153
7.145
7.141
7.138
7.127
7.113
7.111
7.093
7.092
6.996
6.981
6.977
6.546
6.539
5.339
1.000
1.015
3.163
7.258
1.071
1.001
2.146
10
9
8
7
6
5
4
3
2
1
ppm
1-[3-(2-iodophenyl)benzyl]indole
I
N
0.000

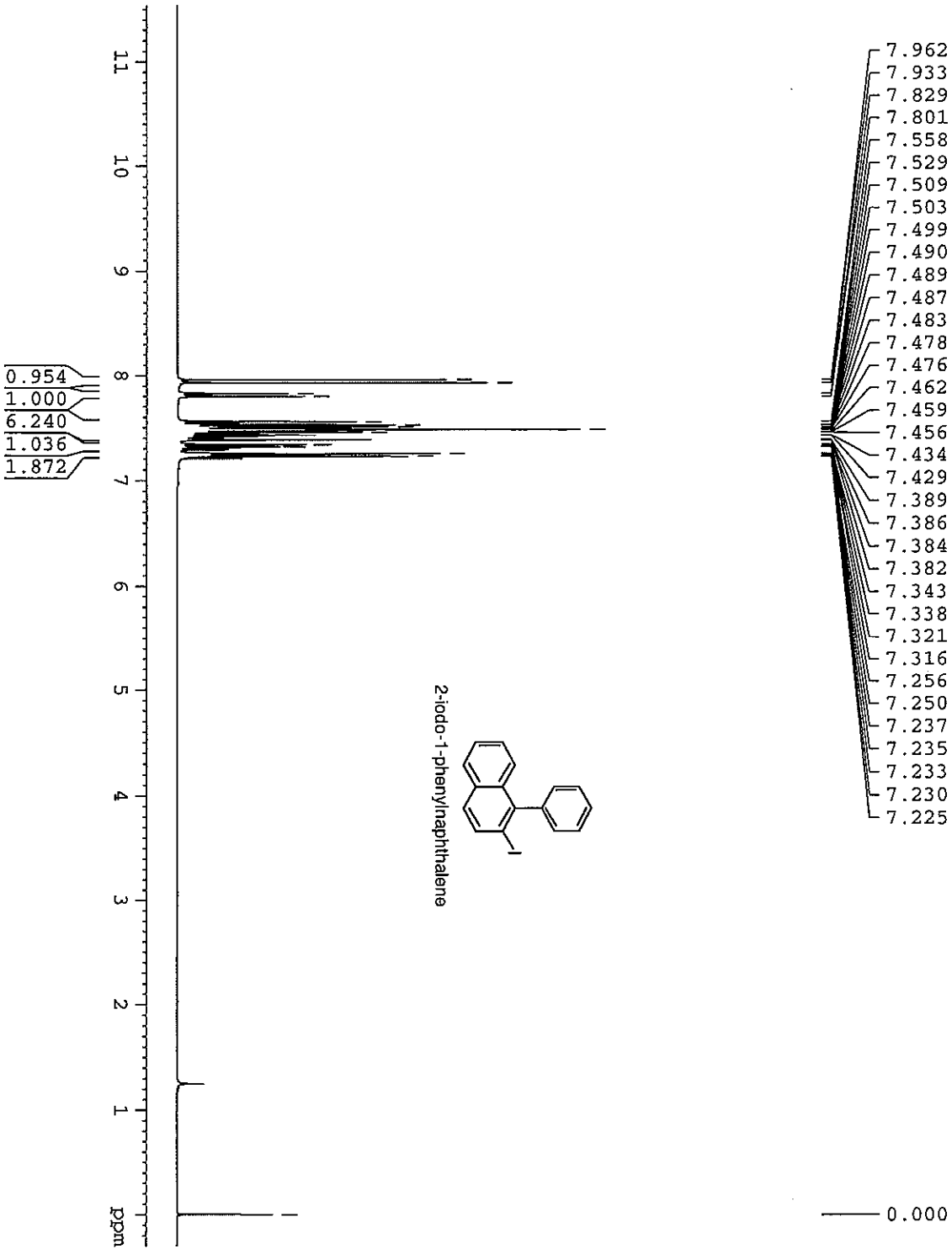

1-[3-(2-iodophenyl)benzyl]indole
146.105
144.614
139.641
137.371
136.388
130.097
129.004
128.862
128.625
128.595
128.395
128.238
128.025
126.210
121.800
121.068
119.643
109.938
101.852
98.591
77.457
77.140
76.822
50.147
200
180
160
140
120
100
80
60
40
20
ppm

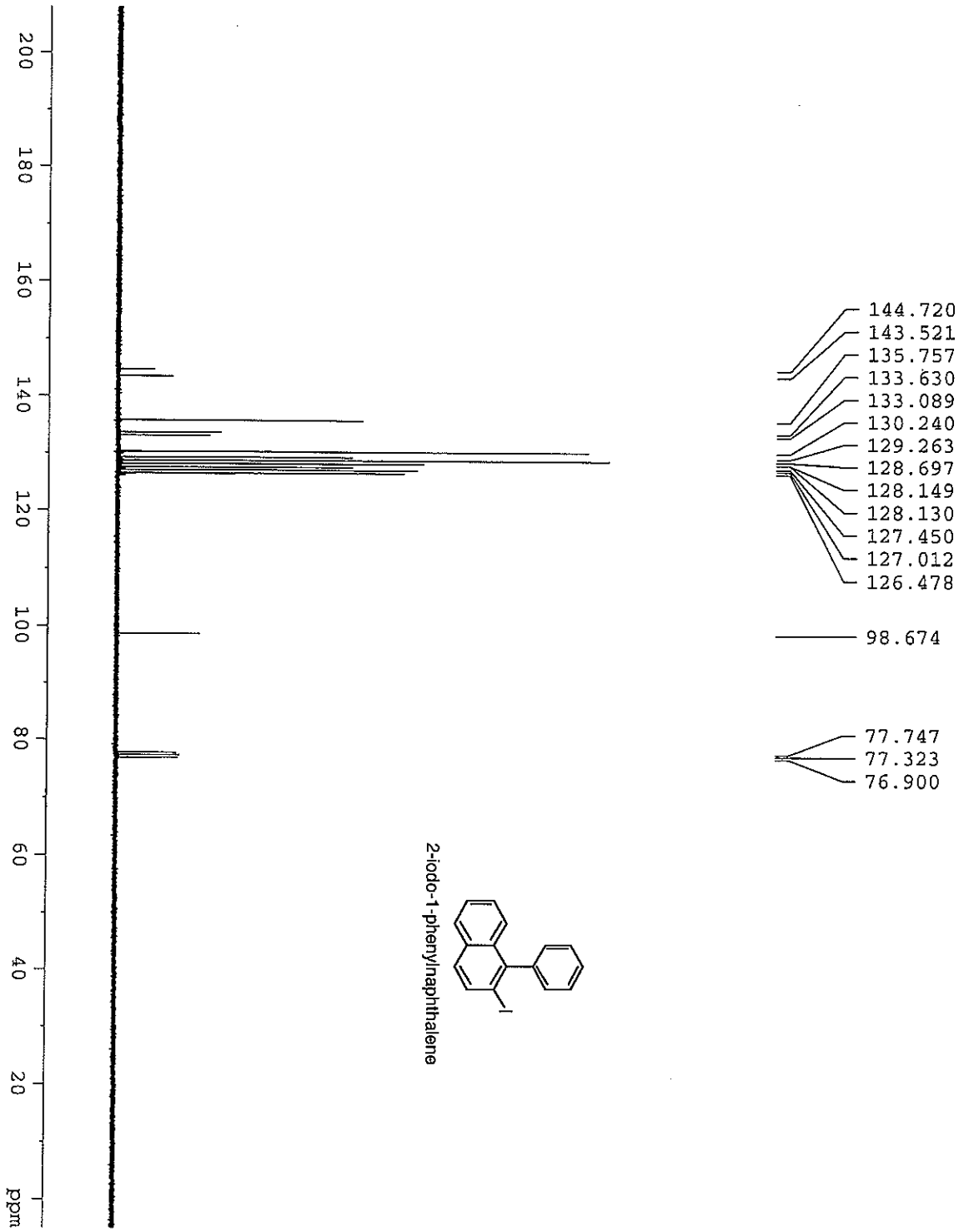

1-[3-(2-iodophenyl)benzyl]-3-methylindole
I
N
Me
0.934
1.000
3.070
6.203
0.994
0.955
1.985
2.898
7.898
7.895
7.584
7.582
7.565
7.564
7.344
7.341
7.338
7.325
7.323
7.319
7.307
7.288
7.268
7.243
7.239
7.229
7.223
7.220
7.200
7.162
7.159
7.142
7.121
7.120
7.115
7.112
7.102
7.101
7.098
7.096
6.993
6.990
6.989
6.924
6.923
5.293
2.330
2.328
1.511
0.000
ppm

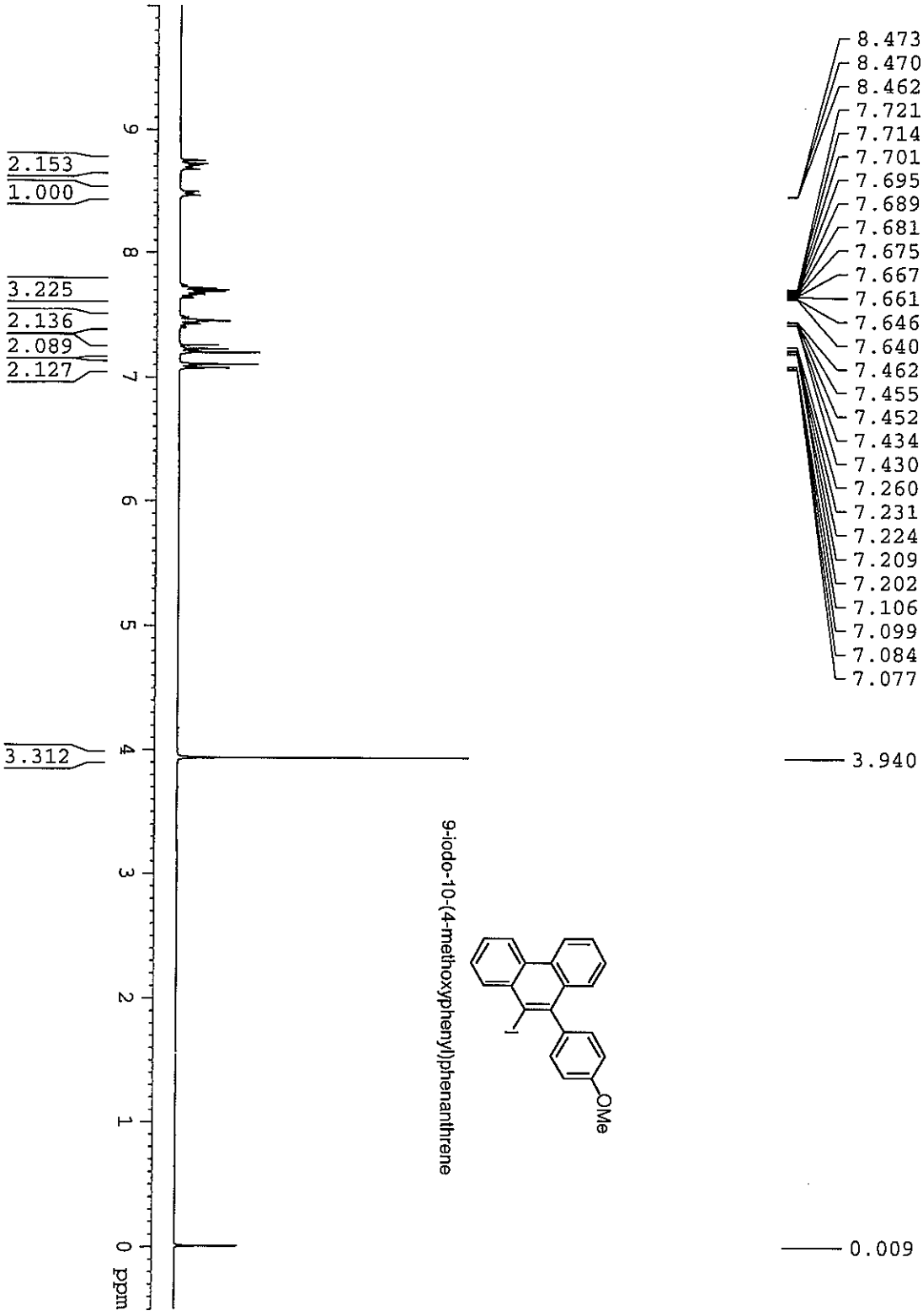

146.356
144.737
139.836
137.936
136.909
130.335
129.273
129.195
128.745
128.726
128.442
128.205
126.419
126.213
121.936
119.340
119.106
111.188
109.919
98.845
77.698
77.382
77.063
50.059
10.066
1-[3-(2-iodophenyl)benzyl]-3-methylindole
I
N
Me
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

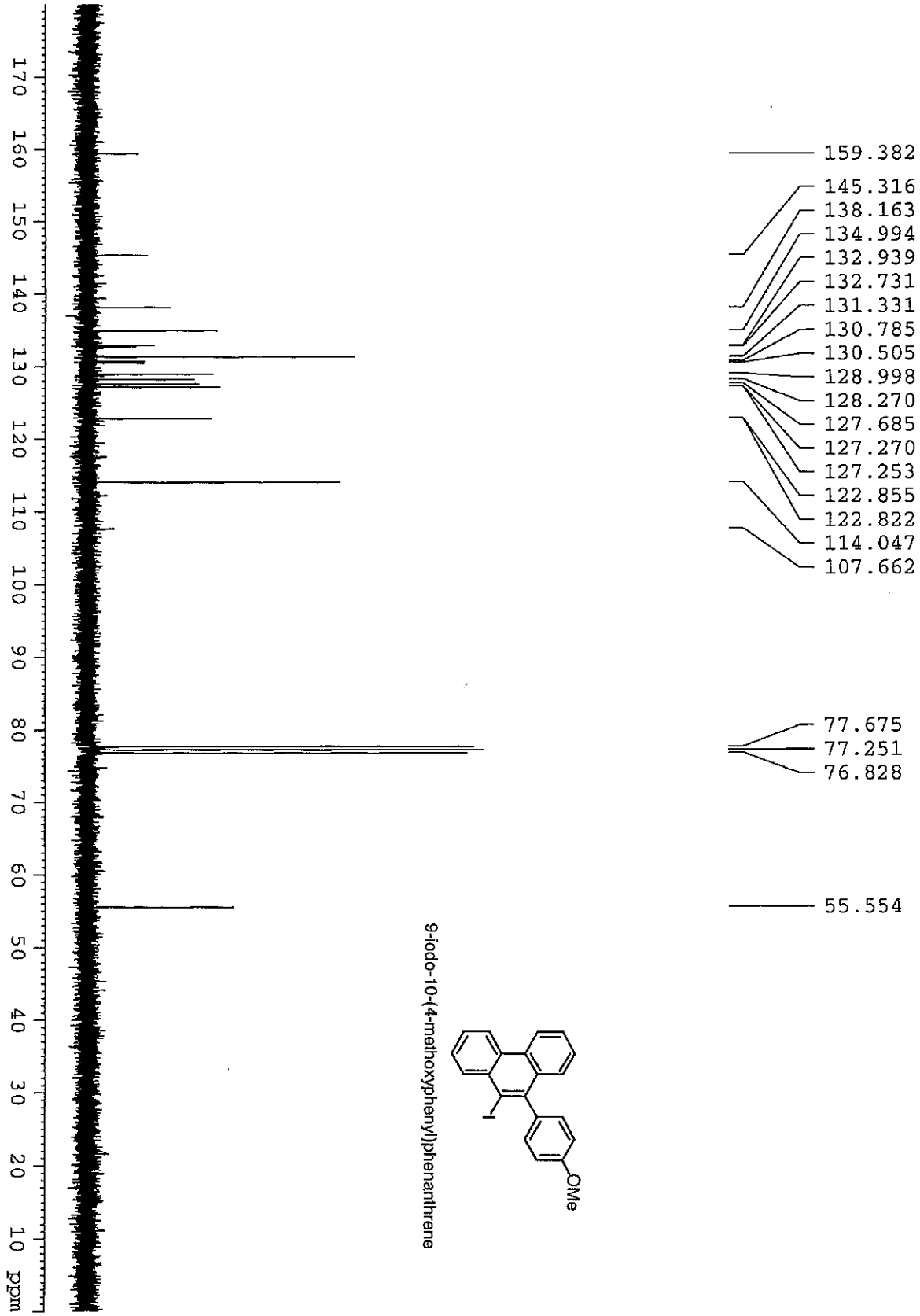

7.964
7.962
7.944
7.942
7.461
7.459
7.442
7.420
7.391
7.388
7.326
7.321
7.311
7.307
7.303
7.293
7.291
7.272
7.255
7.035
7.012
7.010
6.990
6.989
6.961
5.129
1.538
0.000
0.942
4.000
3.947
3.922
2.059
10
9
8
7
6
5
4
3
2
1
ppm
3-(2-iodophenyl)benzyl phenyl ether
I
O


158.833
146.377
144.469
139.644
136.966
130.213
129.604
128.991
128.962
128.508
128.359
128.258
126.767
121.095
115.050
98.636
77.562
77.138
76.715
69.874
3-(2-iodophenyl)benzyl phenyl ether
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


0.954
1.000
6.240
1.036
1.872
7.962
7.933
7.829
7.801
7.558
7.529
7.509
7.503
7.499
7.490
7.489
7.487
7.483
7.478
7.476
7.462
7.459
7.456
7.434
7.429
7.389
7.386
7.384
7.382
7.343
7.338
7.321
7.316
7.256
7.250
7.237
7.235
7.233
7.230
7.225
0.000
2-iodo-1-phenylnaphthalene
ppm


200
180
160
140
120
100
80
60
40
20
ppm
144.720
143.521
135.757
133.630
133.089
130.240
129.263
128.697
128.149
128.130
127.450
127.012
126.478
98.674
77.747
77.323
76.900
2-iodo-1-phenylnaphthalene
I


8.473
8.470
8.462
7.721
7.714
7.701
7.695
7.689
7.681
7.675
7.667
7.661
7.646
7.640
7.462
7.455
7.452
7.434
7.430
7.260
7.231
7.224
7.209
7.202
7.106
7.099
7.084
7.077
3.940
0.009
2.153
1.000
3.225
2.136
2.089
2.127
3.312
9
8
7
6
5
4
3
2
1
0
ppm
9-iodo-10-(4-methoxyphenyl)phenanthrene
I
OMe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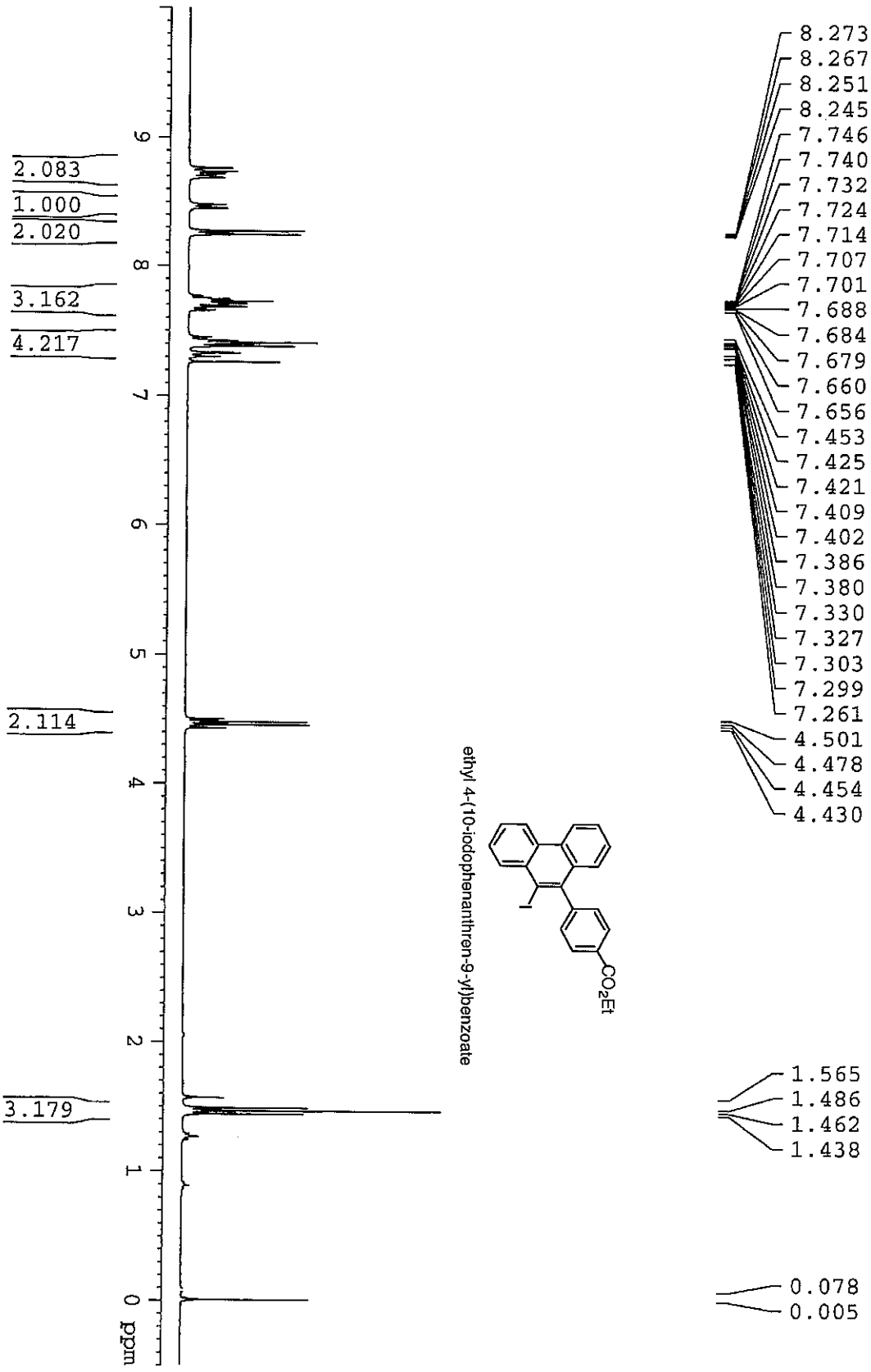
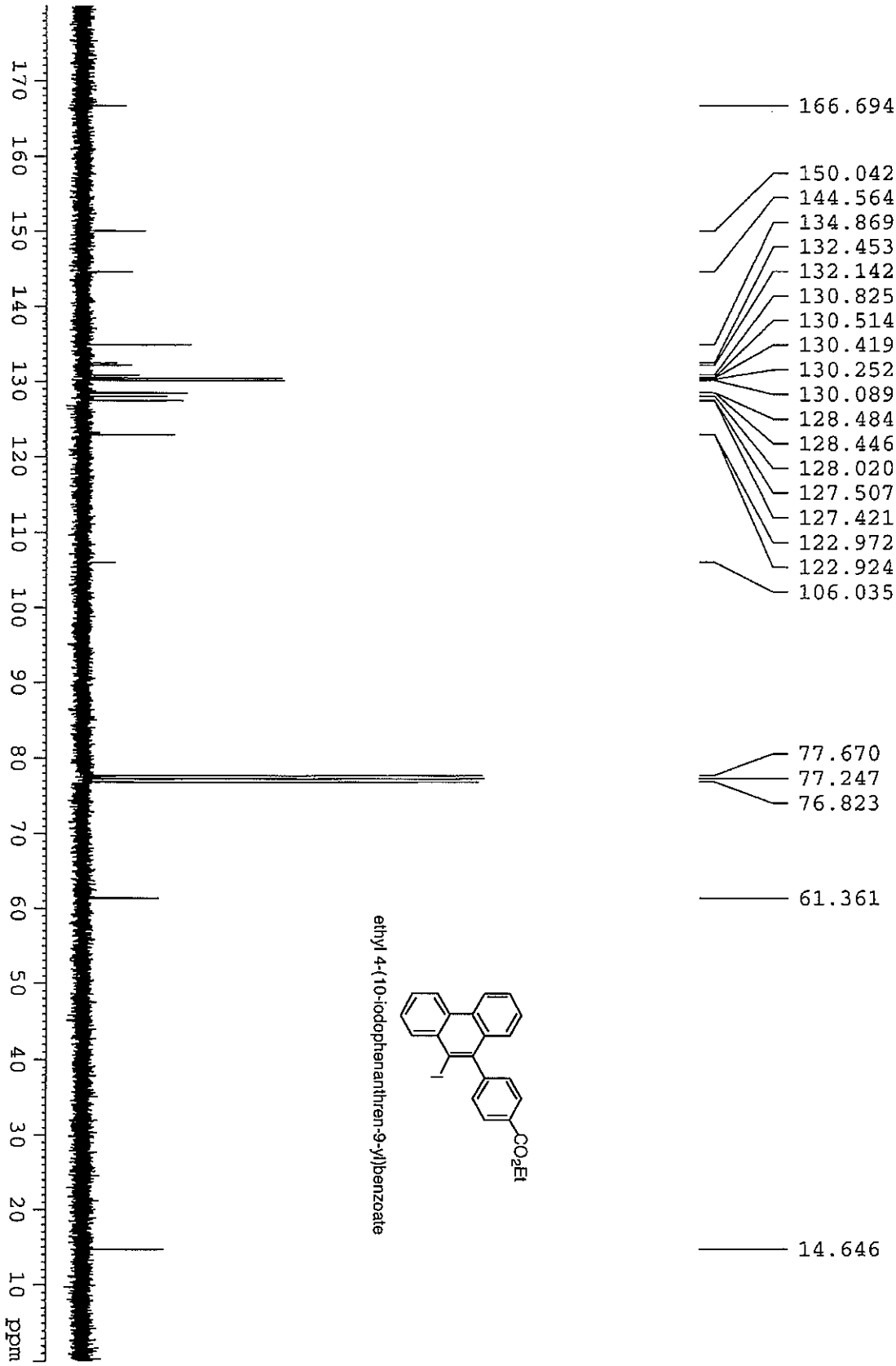
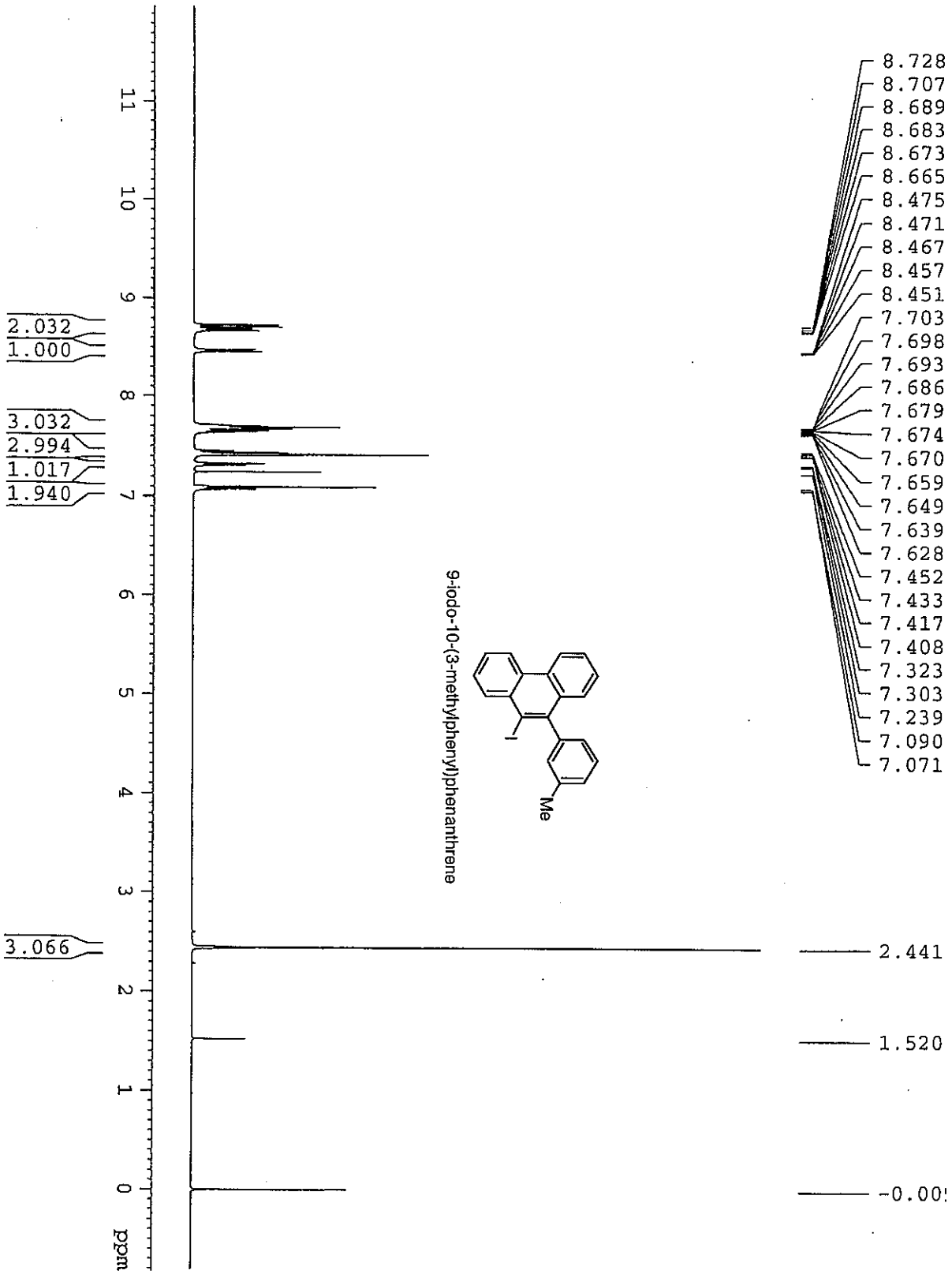
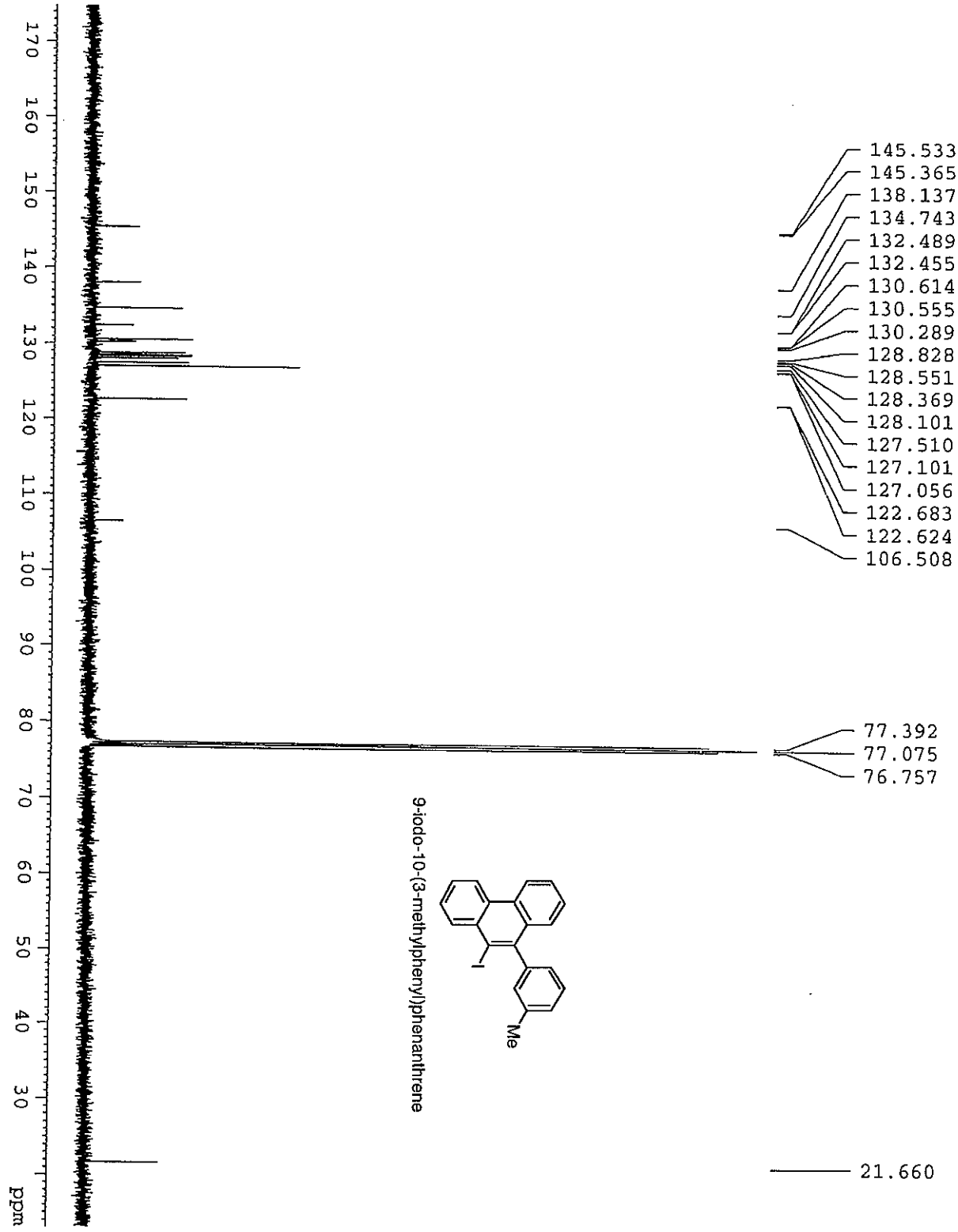
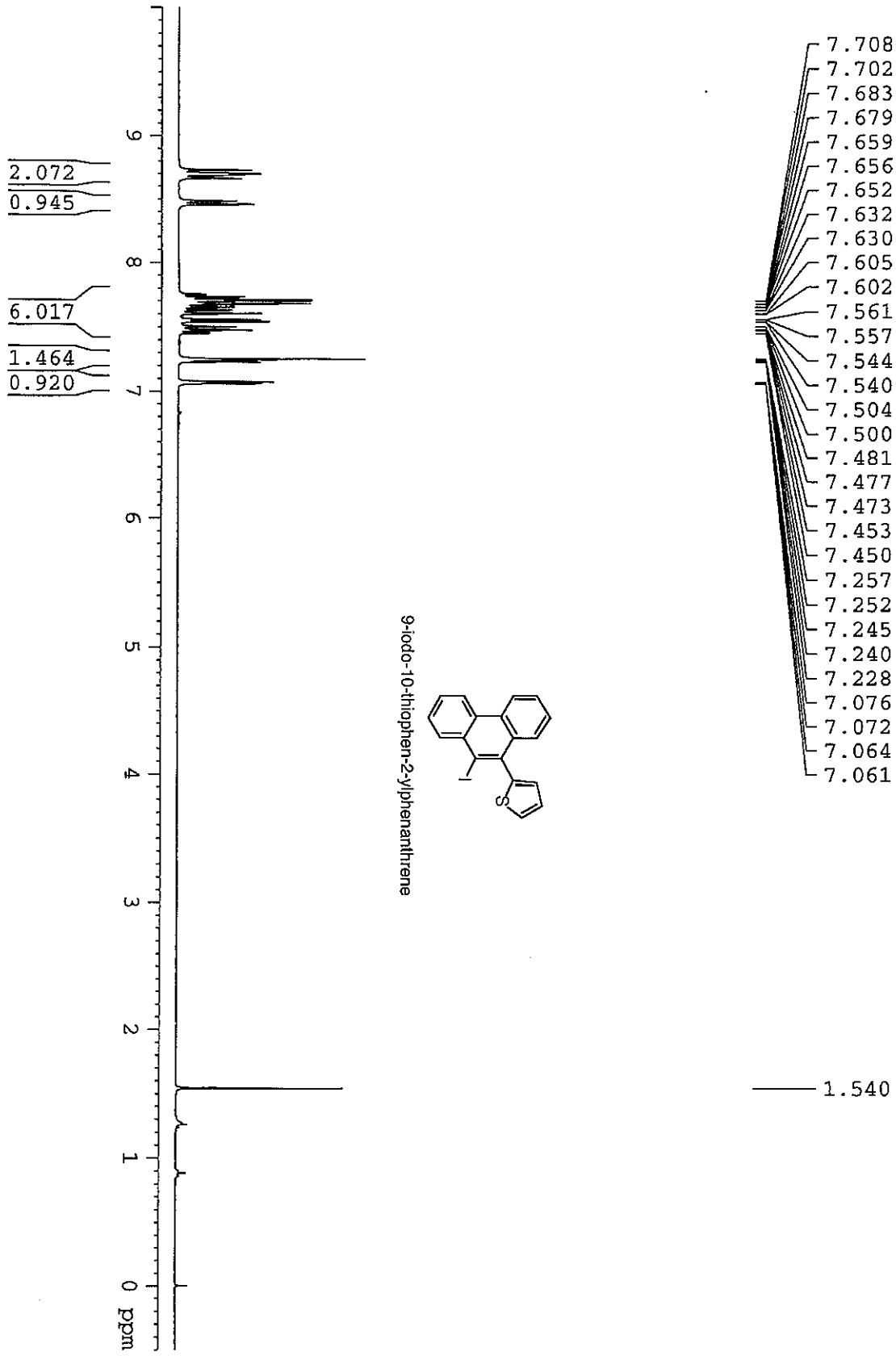
145.316
138.163
134.994
132.939
132.731
131.331
130.785
130.505
128.998
128.270
127.685
127.270
127.253
122.855
122.822
114.047
107.662
77.675
77.251
76.828
55.554
9-iodo-10-(4-methoxyphenyl)phenanthrene
I
OMe
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

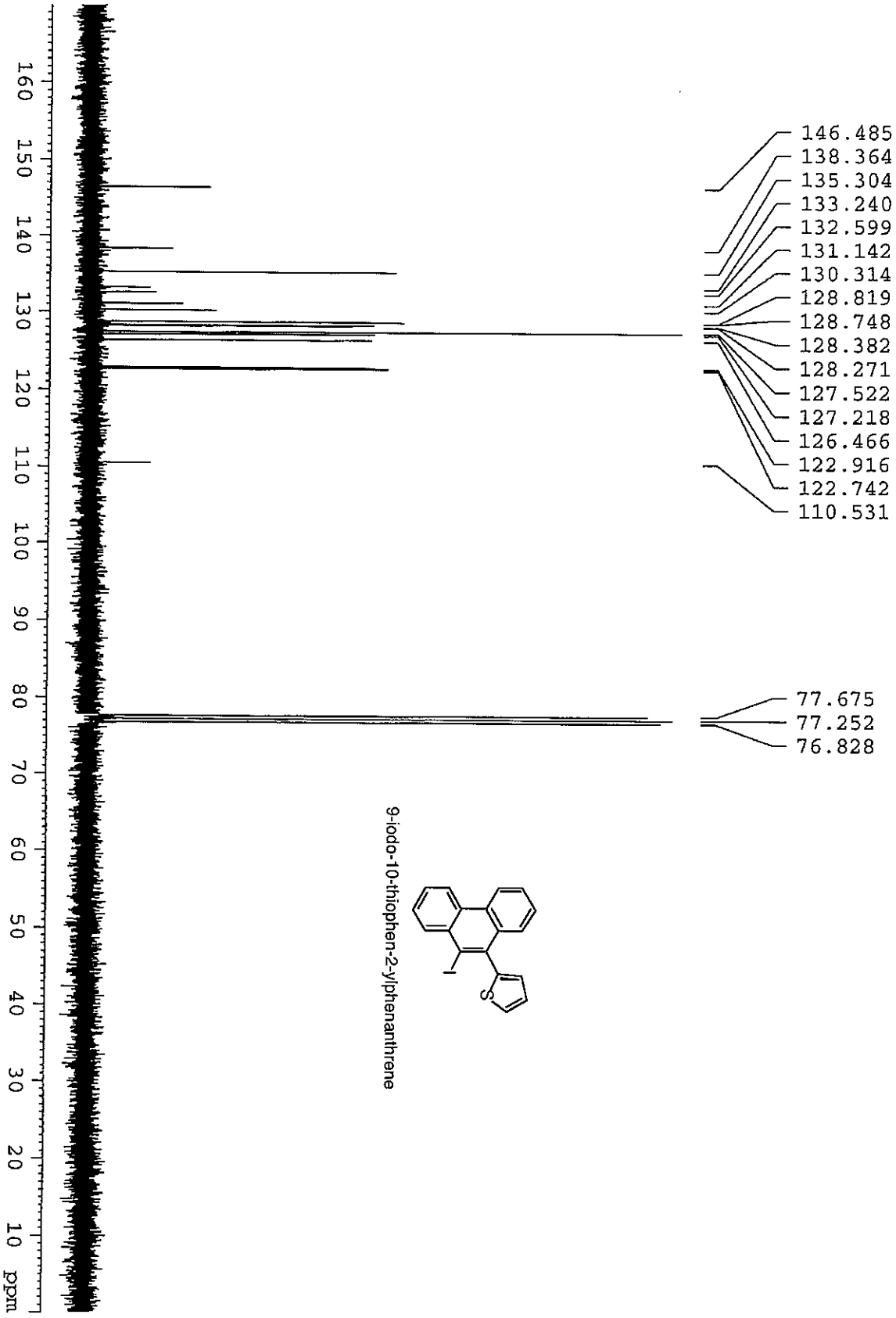

2.083
1.000
2.020
3.162
4.217
2.114
3.179
9
8
7
6
5
4
3
2
1
0
ppm
8.273
8.267
8.251
8.245
7.746
7.740
7.732
7.724
7.714
7.707
7.701
7.688
7.684
7.679
7.660
7.656
7.453
7.425
7.421
7.409
7.402
7.386
7.380
7.330
7.327
7.303
7.299
7.261
4.501
4.478
4.454
4.430
1.565
1.486
1.462
1.438
0.078
0.005
ethyl 4-(10-iodophenanthren-9-yl)benzoate
I
CO2Et

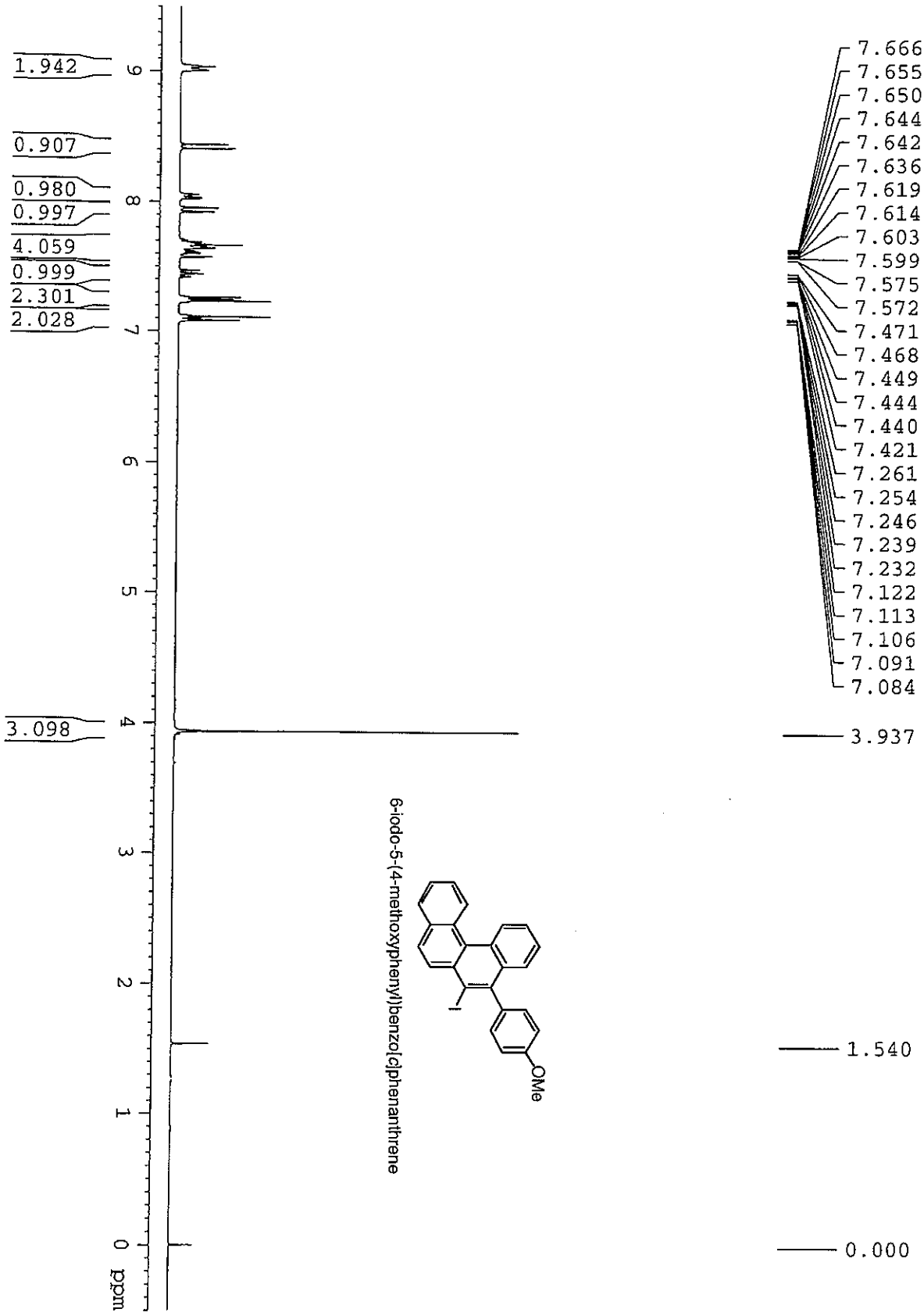

166.694
150.042
144.564
134.869
132.453
132.142
130.825
130.514
130.419
130.252
130.089
128.484
128.446
128.020
127.507
127.421
122.972
122.924
106.035
77.670
77.247
76.823
61.361
14.646
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
ethyl 4-(10-iodophenanthren-9-yl)benzoate
CO2Et

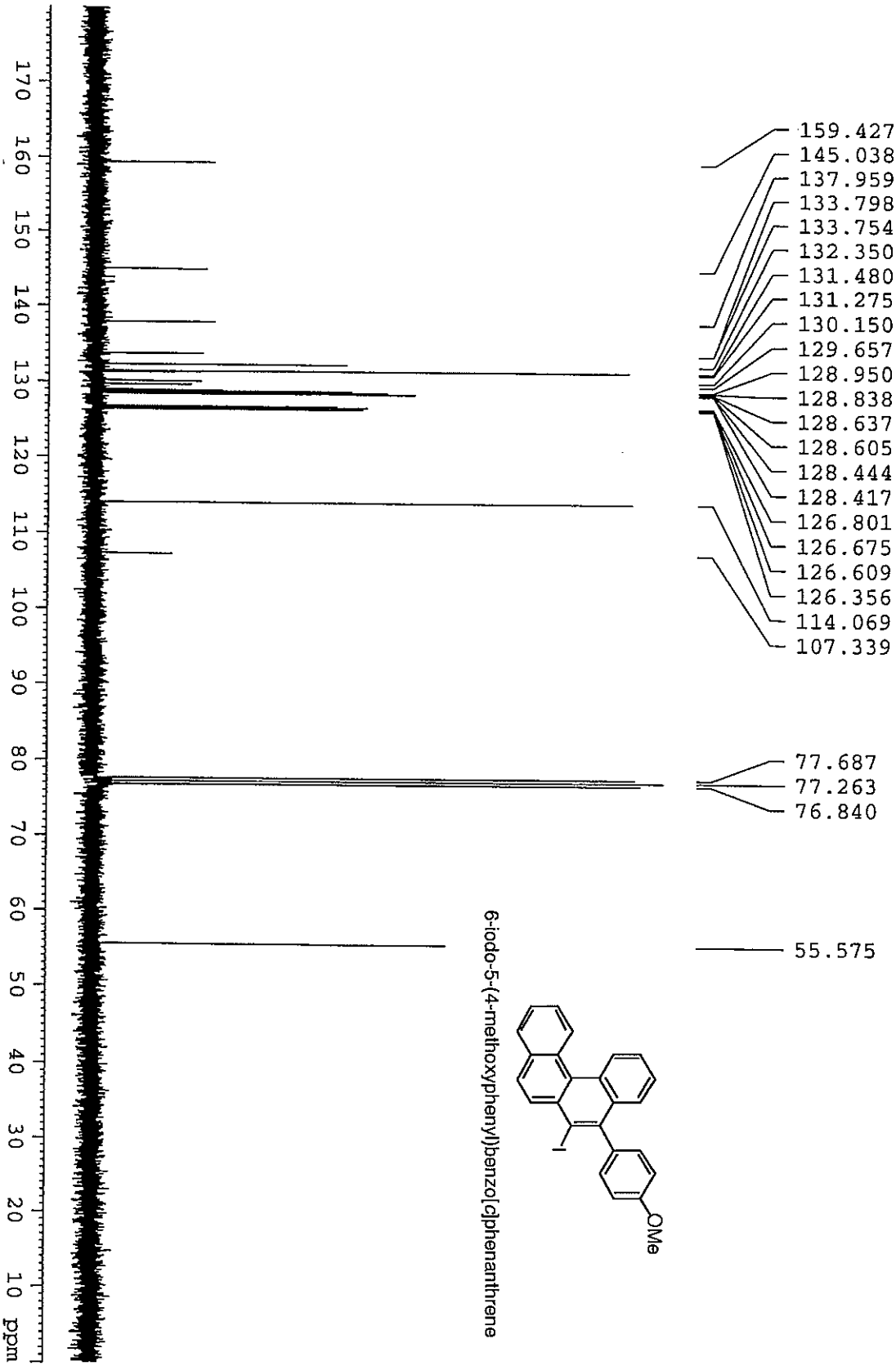

8.728
8.707
8.689
8.683
8.673
8.665
8.475
8.471
8.467
8.457
8.451
7.703
7.698
7.693
7.686
7.679
7.674
7.670
7.659
7.649
7.639
7.628
7.452
7.433
7.417
7.408
7.323
7.303
7.239
7.090
7.071
2.441
1.520
-0.00
2.032
1.000
3.032
2.994
1.017
1.940
3.066
9-iodo-10-(3-methylphenyl)phenanthrene
Me
ppm

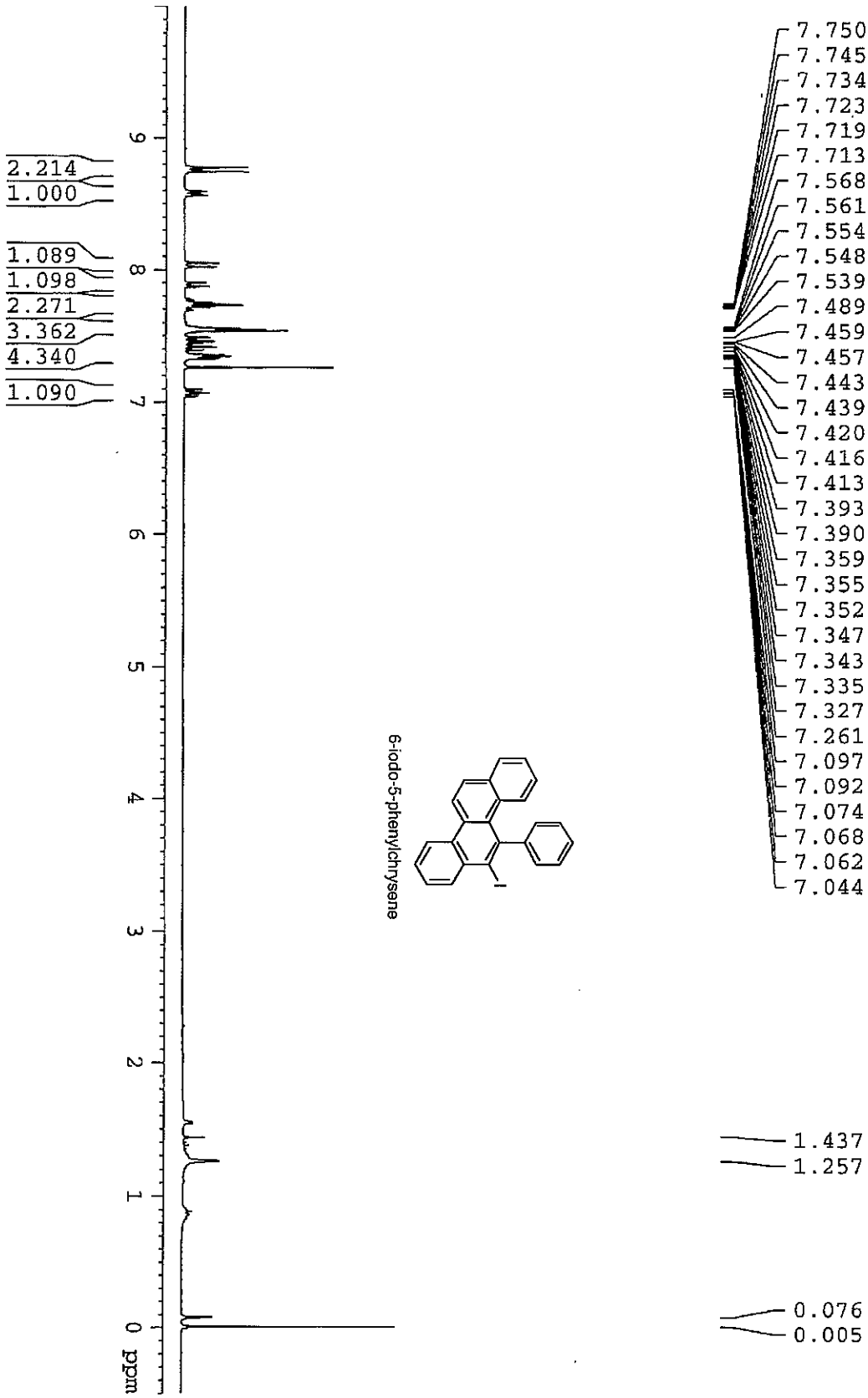

145.533
145.365
138.137
134.743
132.489
132.455
130.614
130.555
130.289
128.828
128.551
128.369
128.101
127.510
127.101
127.056
122.683
122.624
106.508
77.392
77.075
76.757
21.660
9-iodo-10-(3-methylphenyl)phenanthrene
Me
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30

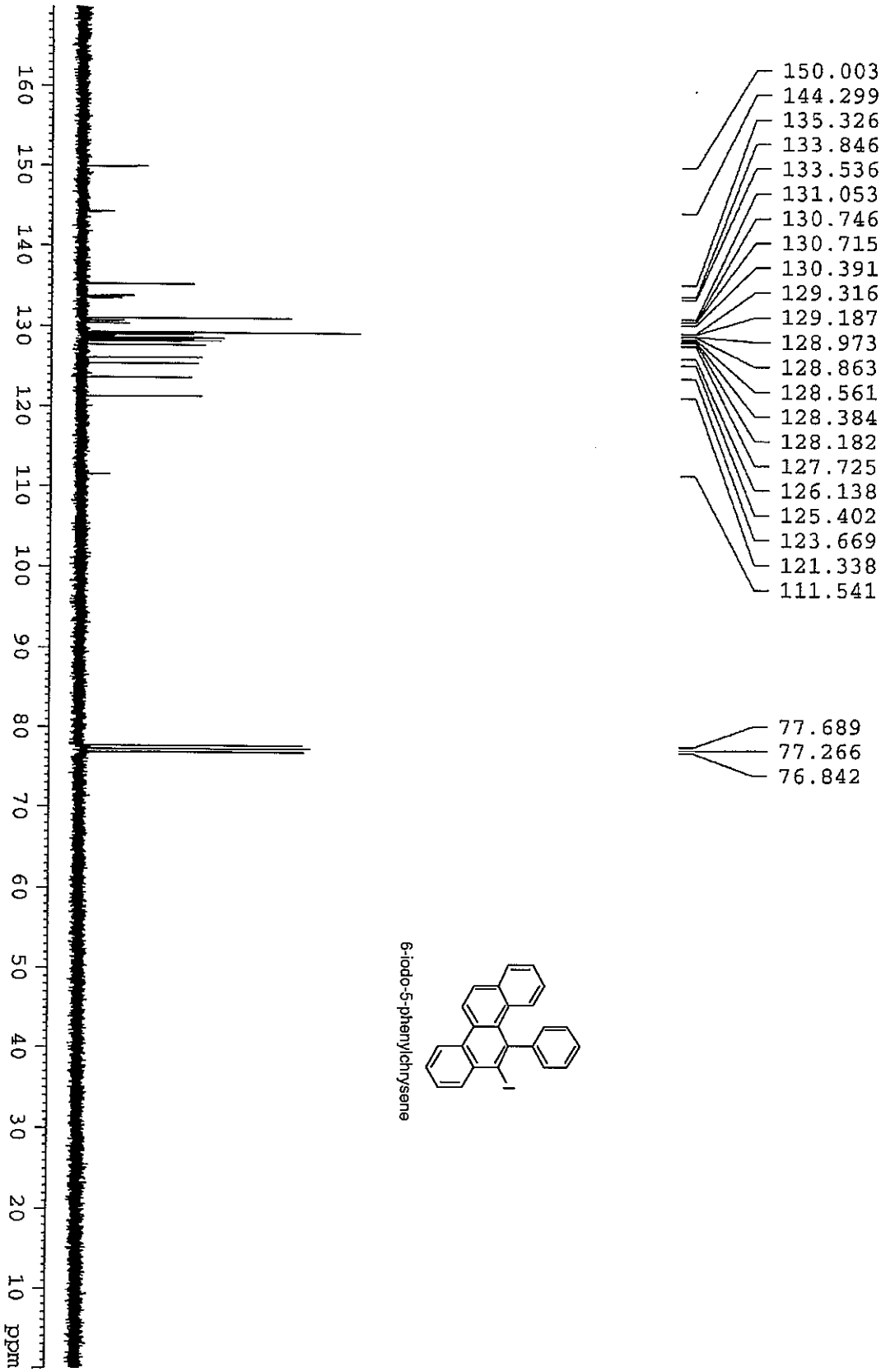

2.072
0.945
6.017
1.464
0.920
9
8
7
6
5
4
3
2
1
0
ppm
9-iodo-10-thiophen-2-ylphenanthrene
I
S
7.708
7.702
7.683
7.679
7.659
7.656
7.652
7.632
7.630
7.605
7.602
7.561
7.557
7.544
7.540
7.504
7.500
7.481
7.477
7.473
7.453
7.450
7.257
7.252
7.245
7.240
7.228
7.076
7.072
7.064
7.061
1.540

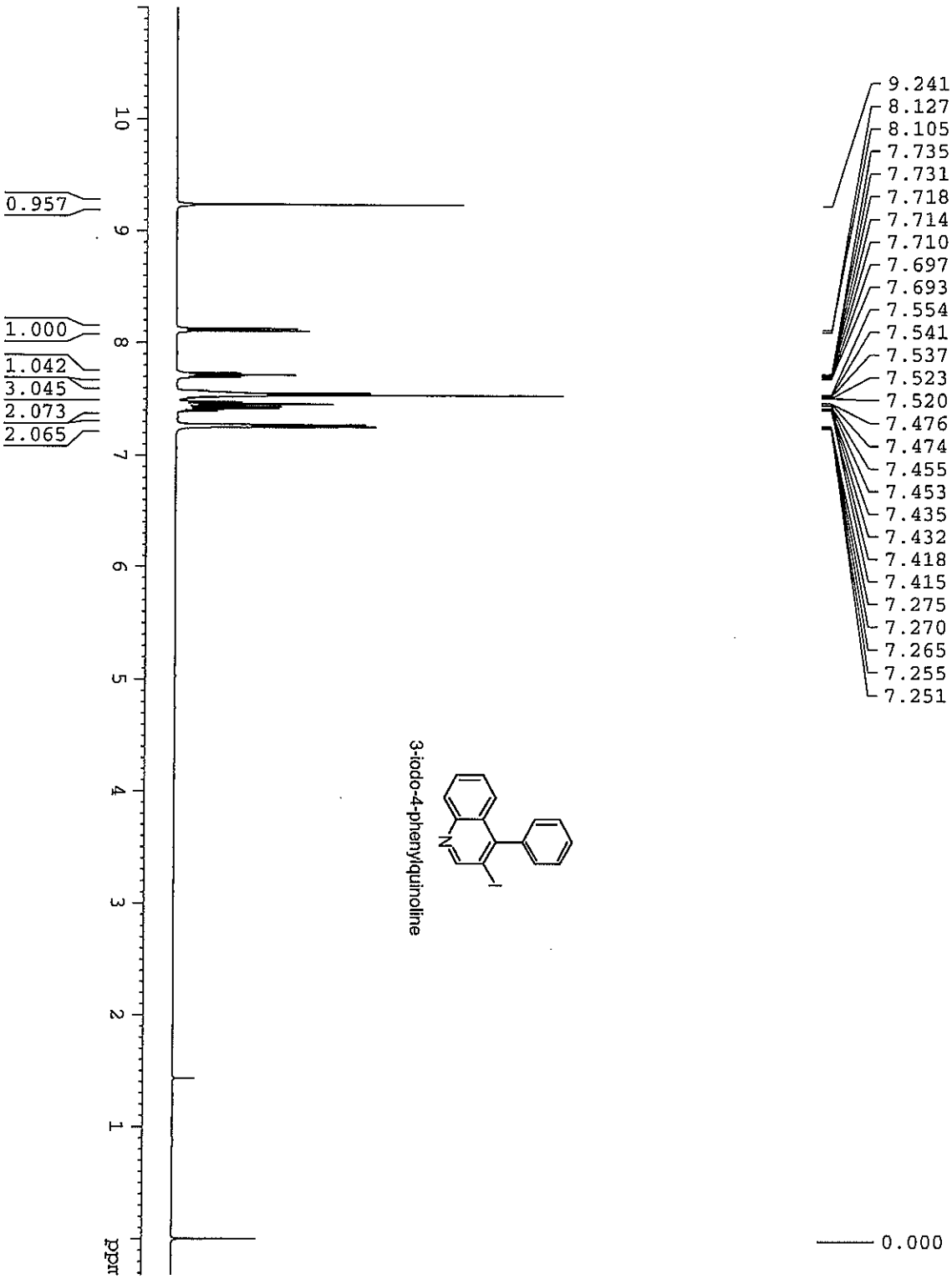

146.485
138.364
135.304
133.240
132.599
131.142
130.314
128.819
128.748
128.382
128.271
127.522
127.218
126.466
122.916
122.742
110.531
77.675
77.252
76.828
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
9-iodo-10-thiophen-2-ylphenanthrene
I
S

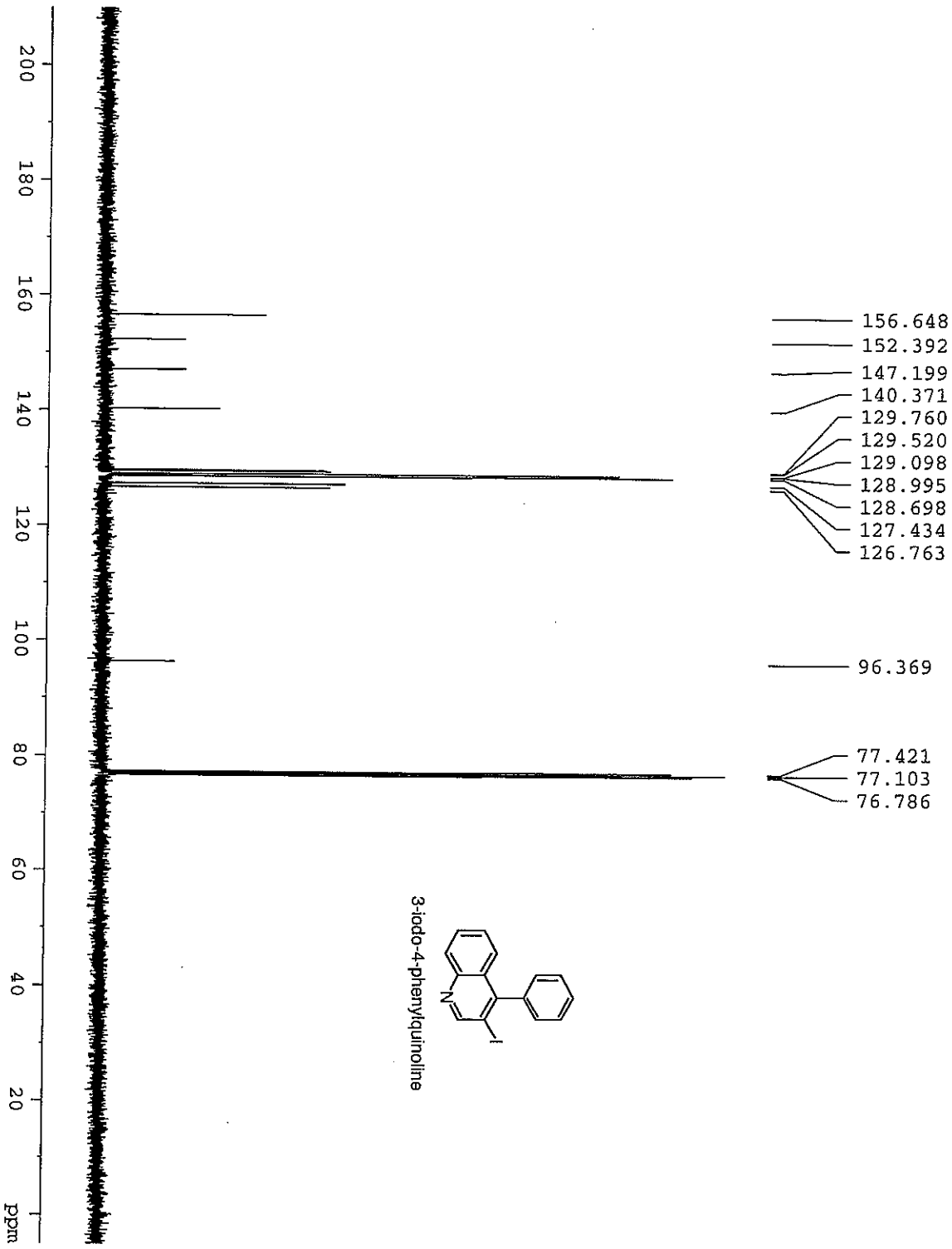

1.942
0.907
0.980
0.997
4.059
0.999
2.301
2.028
3.098
9
8
7
6
5
4
3
2
1
0
ppm
7.666
7.655
7.650
7.644
7.642
7.636
7.619
7.614
7.603
7.599
7.575
7.572
7.471
7.468
7.449
7.444
7.440
7.421
7.261
7.254
7.246
7.239
7.232
7.122
7.113
7.106
7.091
7.084
3.937
1.540
0.000
6-iodo-5-(4-methoxyphenyl)benzo[c]phenanthrene
OMe

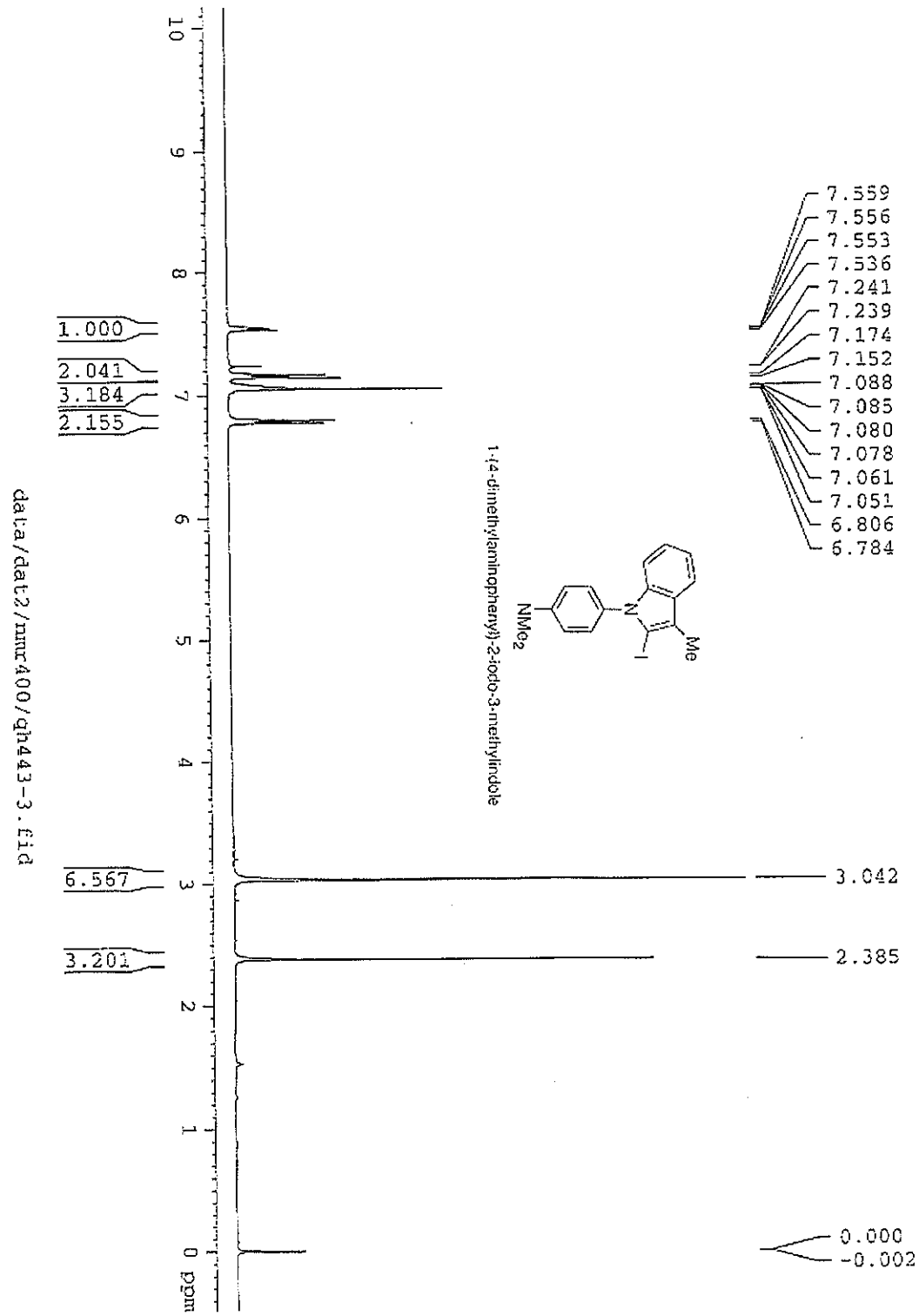

159.427
145.038
137.959
133.798
133.754
132.350
131.480
131.275
130.150
129.657
128.950
128.838
128.637
128.605
128.444
128.417
126.801
126.675
126.609
126.356
114.069
107.339
77.687
77.263
76.840
55.575
6-iodo-5-(4-methoxyphenyl)benzo[c]phenanthrene
I
OMe
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

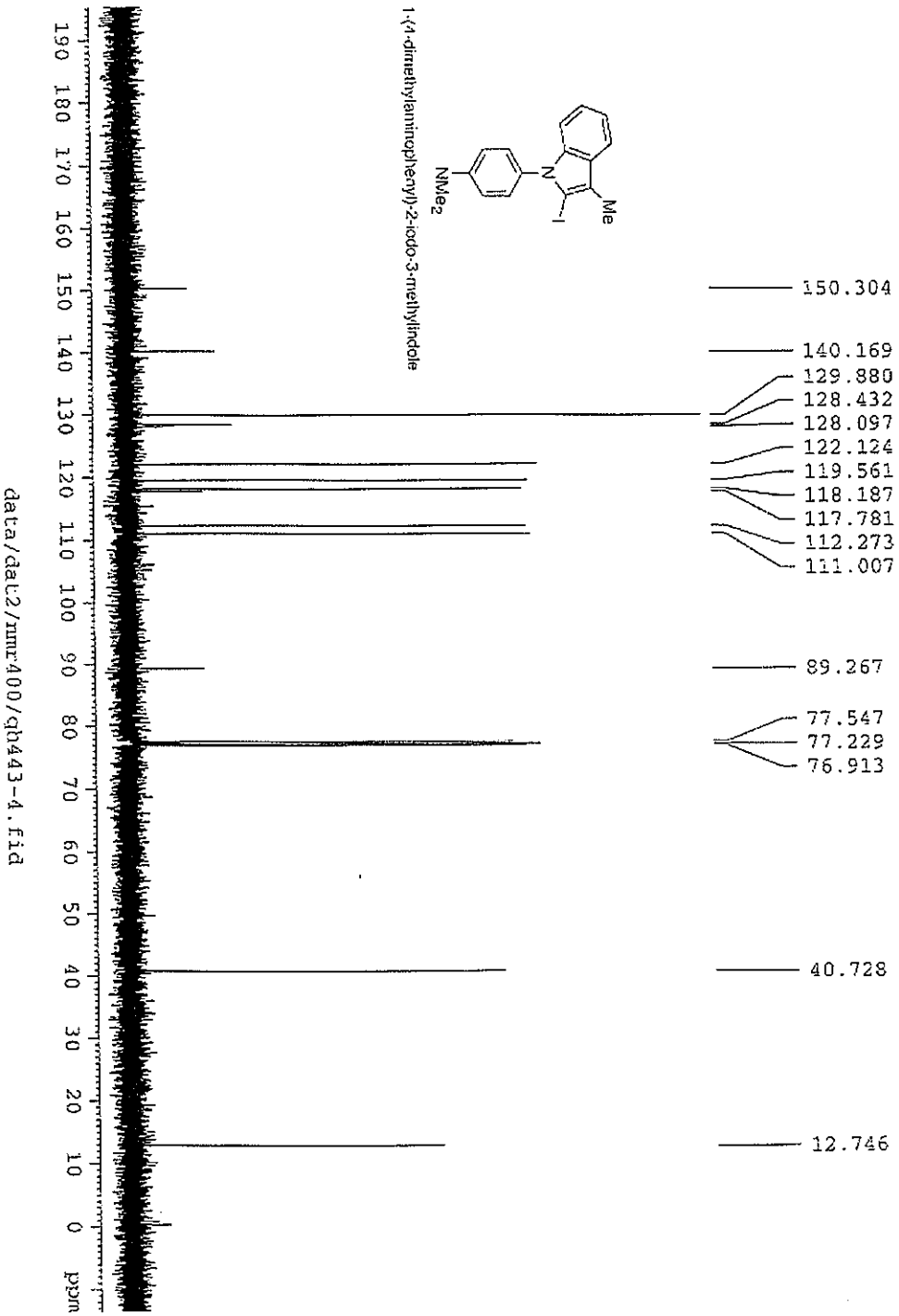

2.214
1.000
1.089
1.098
2.271
3.362
4.340
1.090
9
8
7
6
5
4
3
2
1
0 ppm
6-iodo-5-phenylchrysene
I
7.750
7.745
7.734
7.723
7.719
7.713
7.568
7.561
7.554
7.548
7.539
7.489
7.459
7.457
7.443
7.439
7.420
7.416
7.413
7.393
7.390
7.359
7.355
7.352
7.347
7.343
7.335
7.327
7.261
7.097
7.092
7.074
7.068
7.062
7.044
1.437
1.257
0.076
0.005

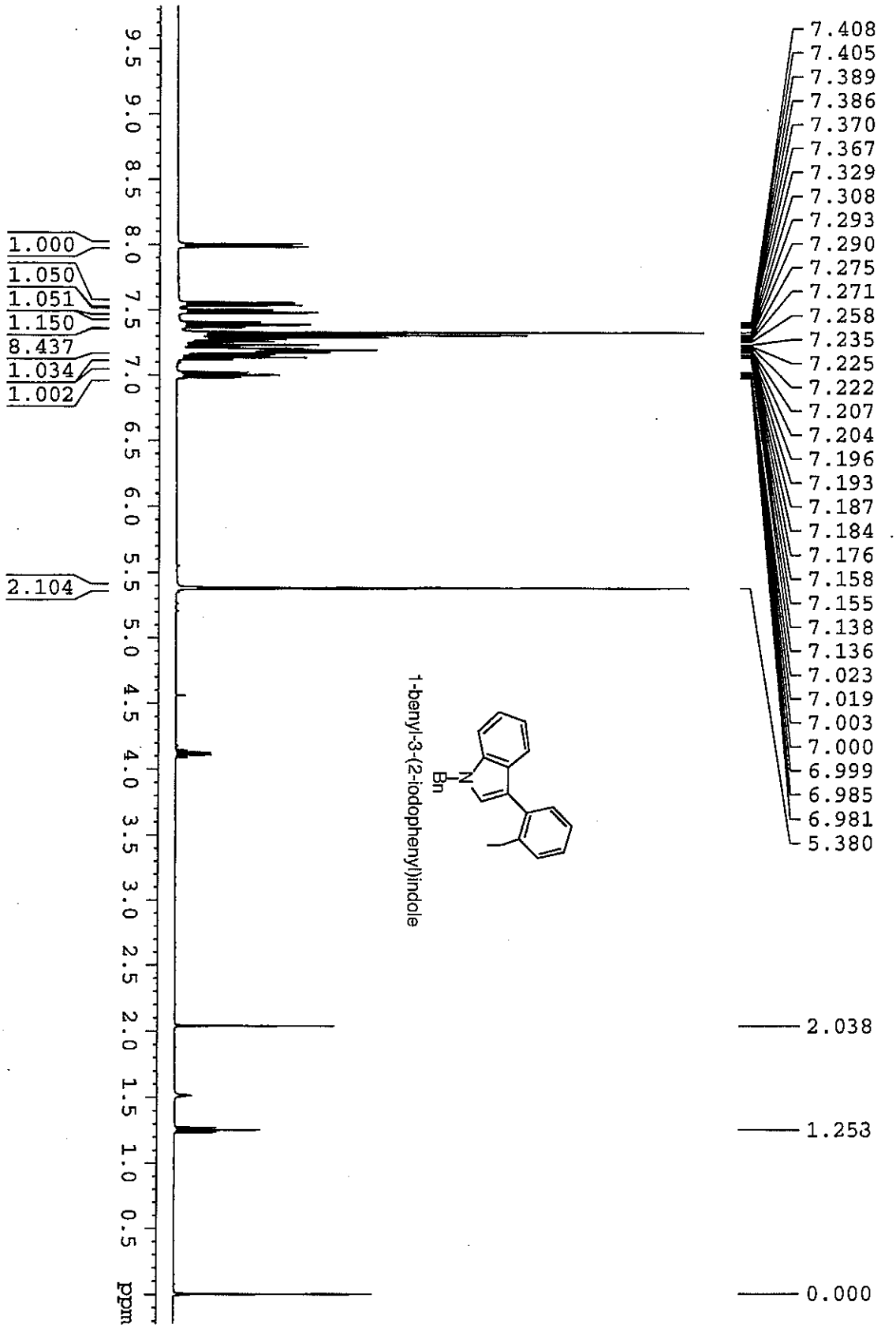

150.003
144.299
135.326
133.846
133.536
131.053
130.746
130.715
130.391
129.316
129.187
128.973
128.863
128.561
128.384
128.182
127.725
126.138
125.402
123.669
121.338
111.541
77.689
77.266
76.842
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
6-iodo-5-phenylchrysene

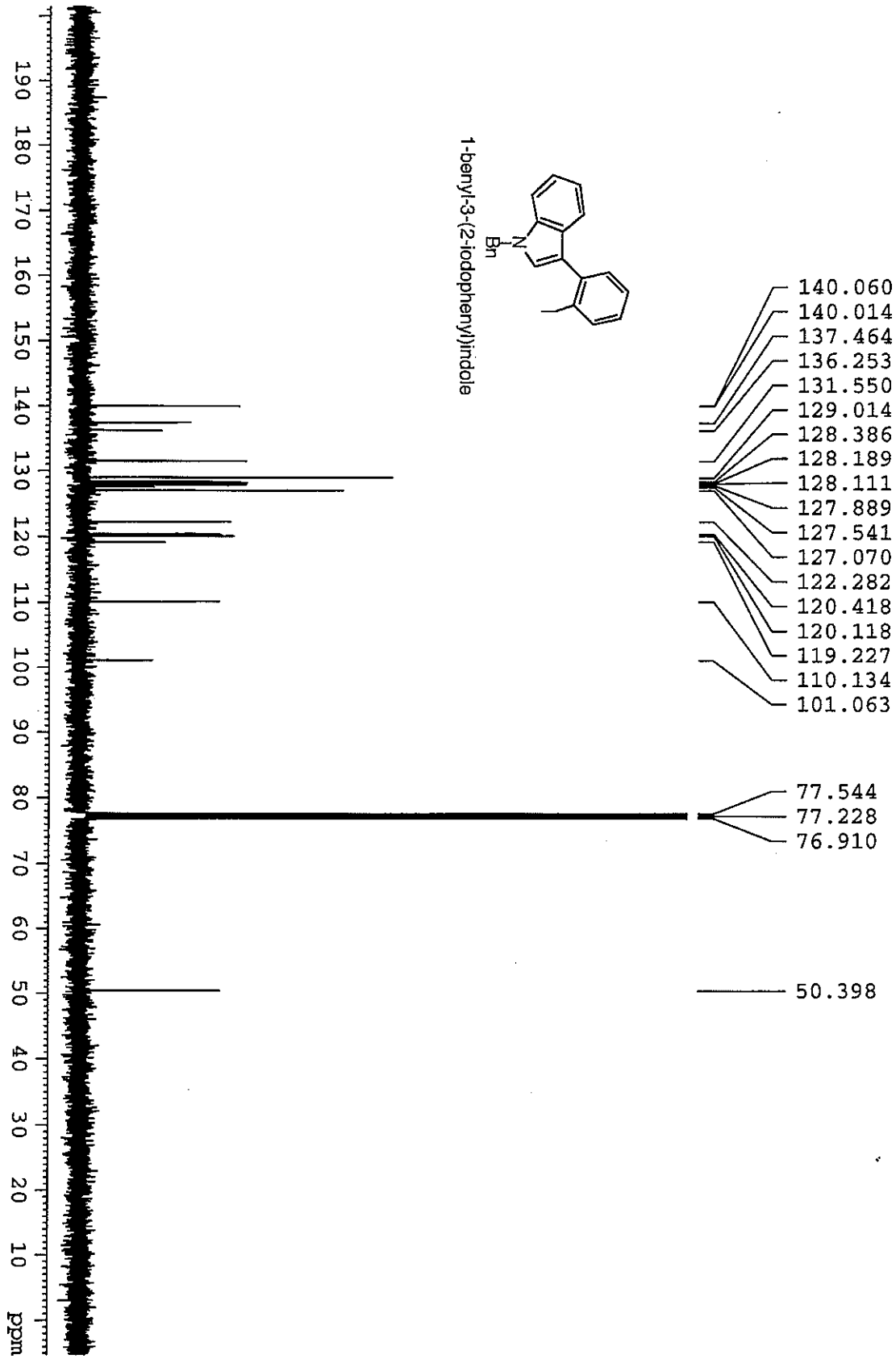

0.957
1.000
1.042
3.045
2.073
2.065
ppm
9.241
8.127
8.105
7.735
7.731
7.718
7.714
7.710
7.697
7.693
7.554
7.541
7.537
7.523
7.520
7.476
7.474
7.455
7.453
7.435
7.432
7.418
7.415
7.275
7.270
7.265
7.255
7.251
0.000
3-iodo-4-phenylquinoline

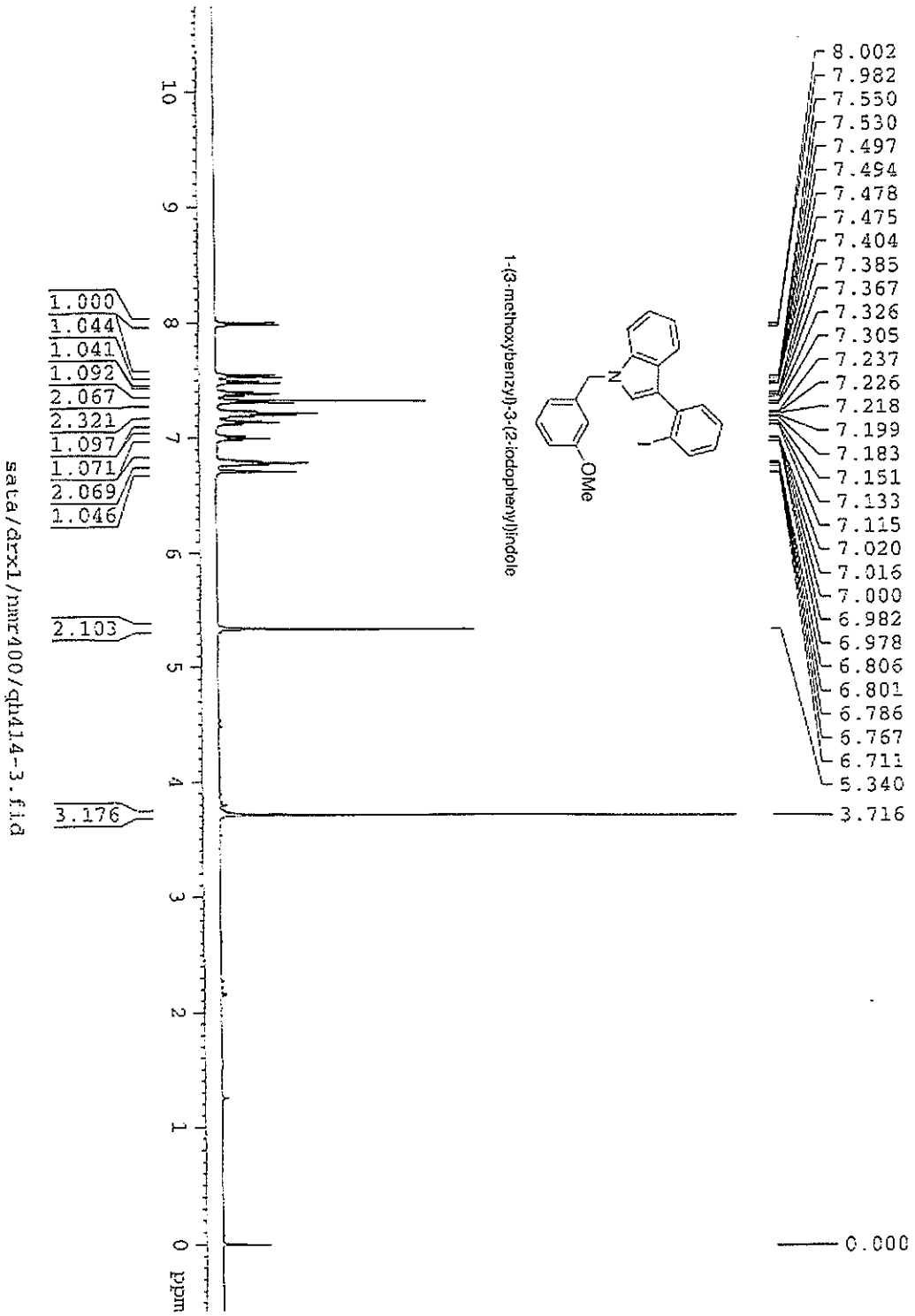

156.648
152.392
147.199
140.371
129.760
129.520
129.098
128.995
128.698
127.434
126.763
96.369
77.421
77.103
76.786
3-iodo-4-phenylquinoline
N
I
200
180
160
140
120
100
80
60
40
20
ppm

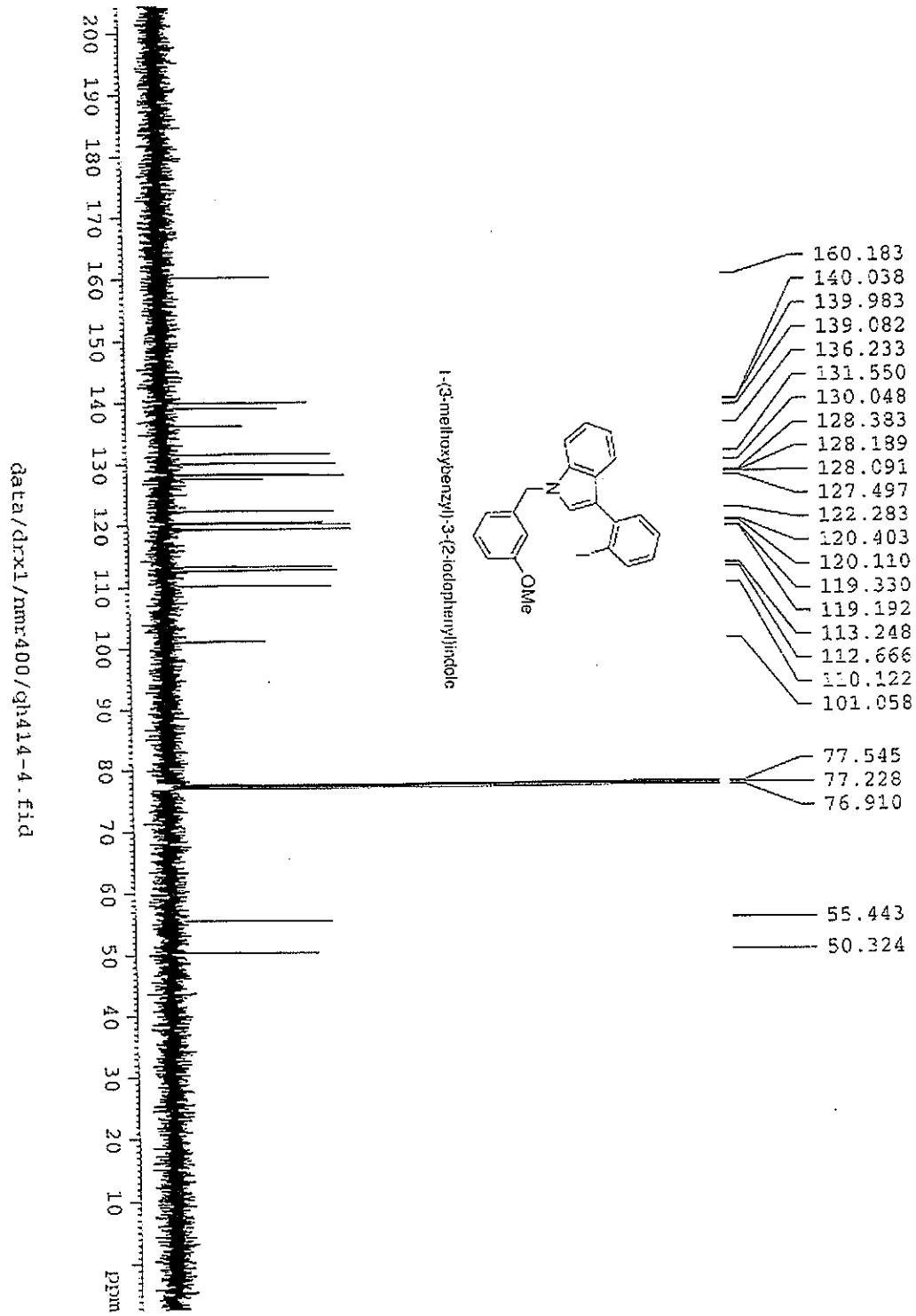

data/dat2/nmr400/qh443-3.fid
1-(4-dimethylaminophenyl)-2-iodo-3-methylindole
NMe2
Me
I
7.559
7.556
7.553
7.536
7.241
7.239
7.174
7.152
7.088
7.085
7.080
7.078
7.061
7.051
6.806
6.784
1.000
2.041
3.184
2.155
6.567
3.201
3.042
2.385
0.000
-0.002
10
9
8
7
6
5
4
3
2
1
0 ppm

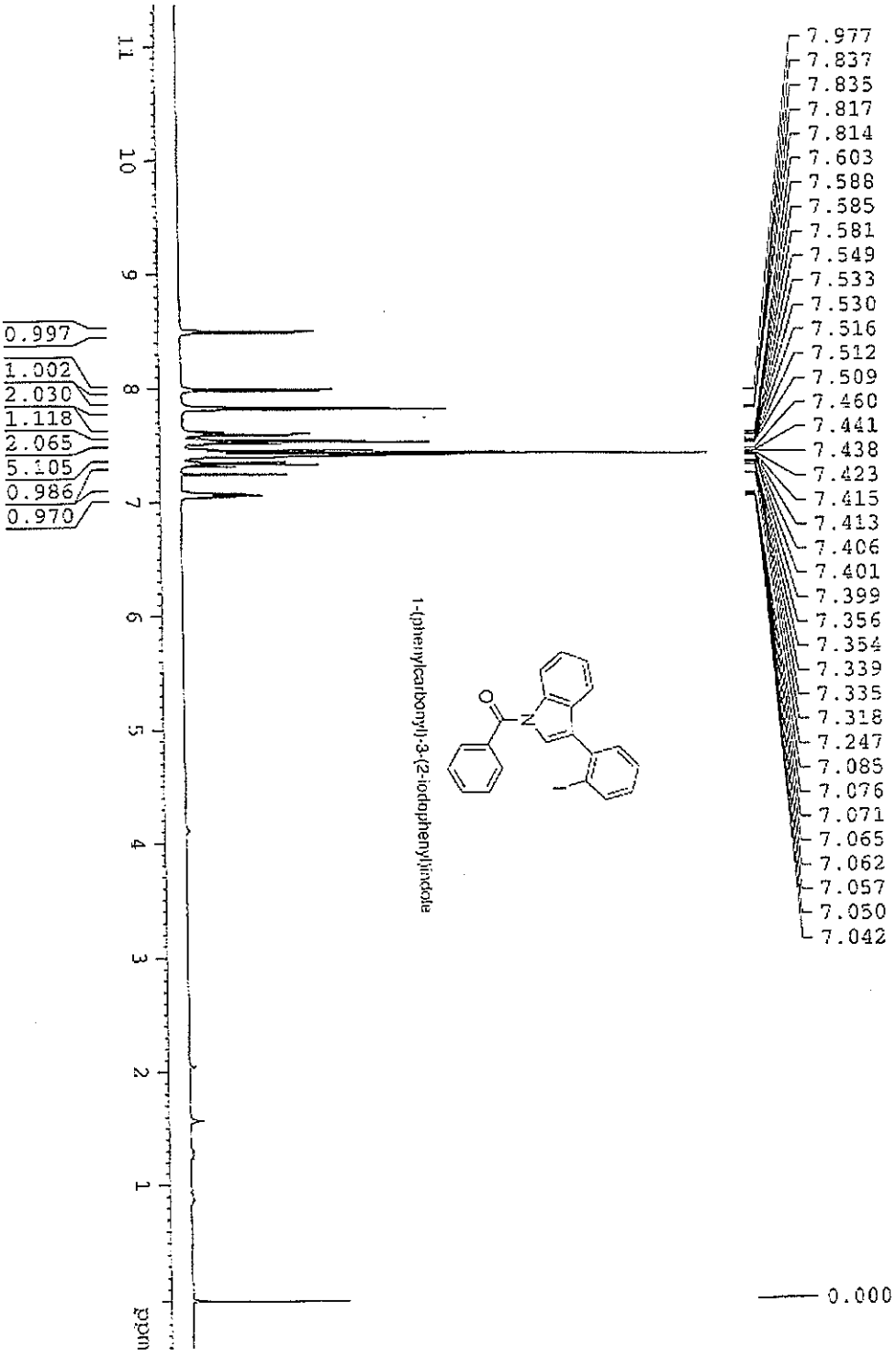

1-(4-dimethylaminophenyl)-2-iodo-3-methylindole
NMe2
N
I
Me
150.304
140.169
129.880
128.432
128.097
122.124
119.561
118.187
117.781
112.273
111.007
89.267
77.547
77.229
76.913
40.728
12.746
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/data2/nmr400/qb443-4.fid

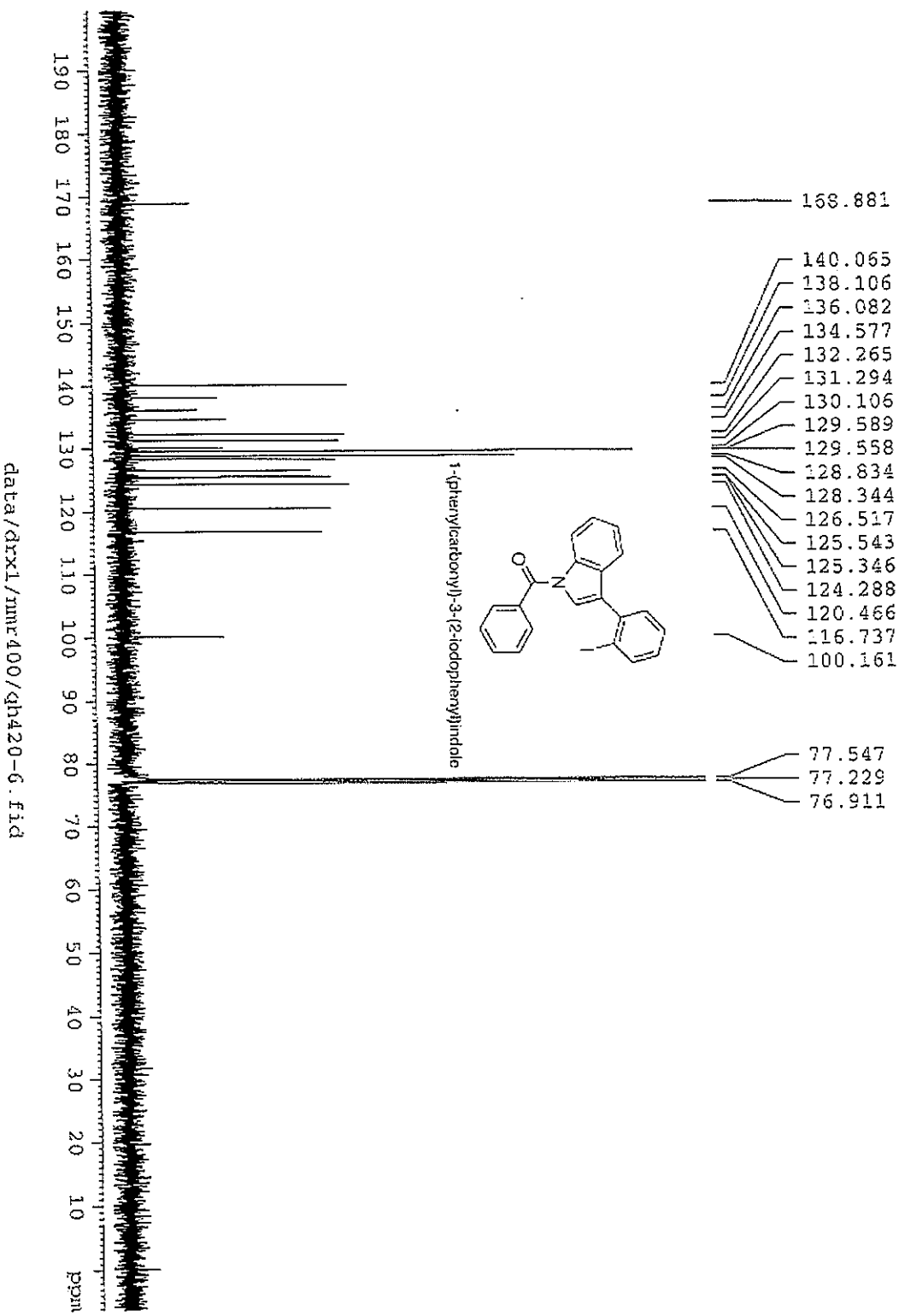

7.408
7.405
7.389
7.386
7.370
7.367
7.329
7.308
7.293
7.290
7.275
7.271
7.258
7.235
7.225
7.222
7.207
7.204
7.196
7.193
7.187
7.184
7.176
7.158
7.155
7.138
7.136
7.023
7.019
7.003
7.000
6.999
6.985
6.981
5.380
1.000
1.050
1.051
1.150
8.437
1.034
1.002
2.104
2.038
1.253
0.000
1-benyl-3-(2-iodophenyl)indole
Bn
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm

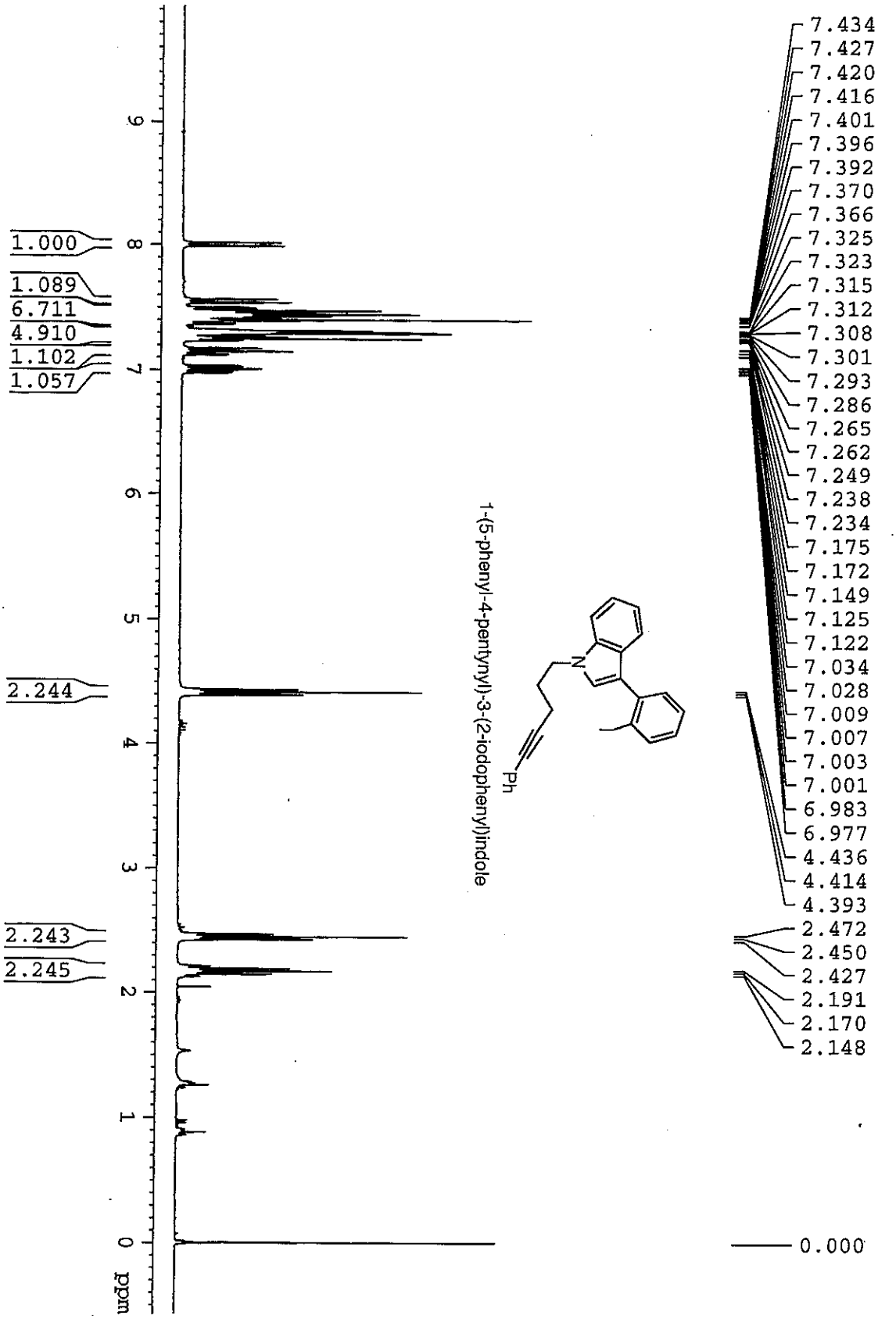

1-benyl-3-(2-iodophenyl)indole
Bn
140.060
140.014
137.464
136.253
131.550
129.014
128.386
128.189
128.111
127.889
127.541
127.070
122.282
120.418
120.118
119.227
110.134
101.063
77.544
77.228
76.910
50.398
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

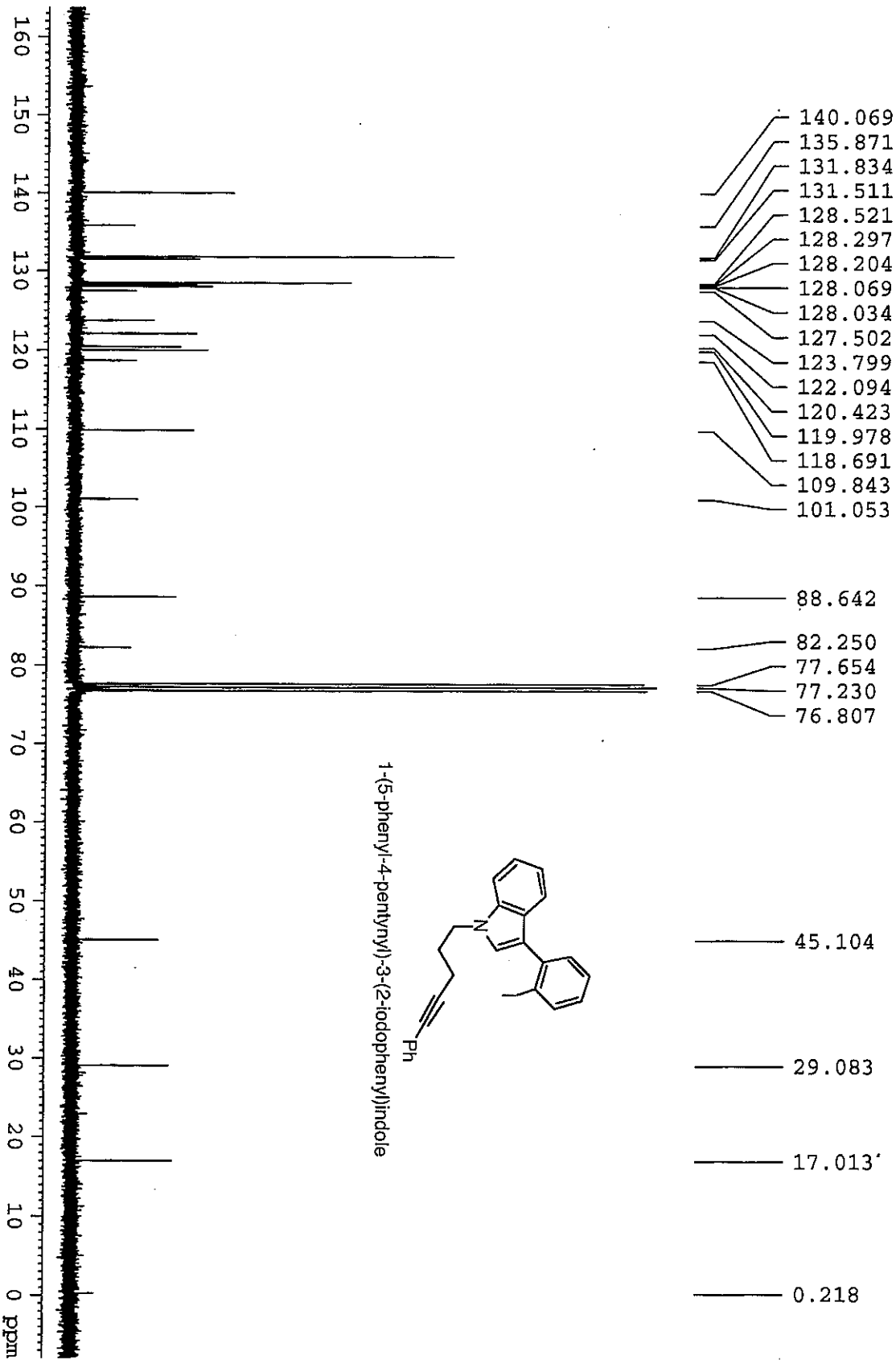

8.002
7.982
7.550
7.530
7.497
7.494
7.478
7.475
7.404
7.385
7.367
7.326
7.305
7.237
7.226
7.218
7.199
7.183
7.151
7.133
7.115
7.020
7.016
7.000
6.982
6.978
6.806
6.801
6.786
6.767
6.711
5.340
3.716
0.000
1.000
1.044
1.041
1.092
2.067
2.321
1.097
1.071
2.069
1.046
2.103
3.176
1-(3-methoxybenzyl)-3-(2-iodophenyl)indole
OMe
N
I
10
9
8
7
6
5
4
3
2
1
0
ppm
sata/drx1/nmr400/qh414-3.fid

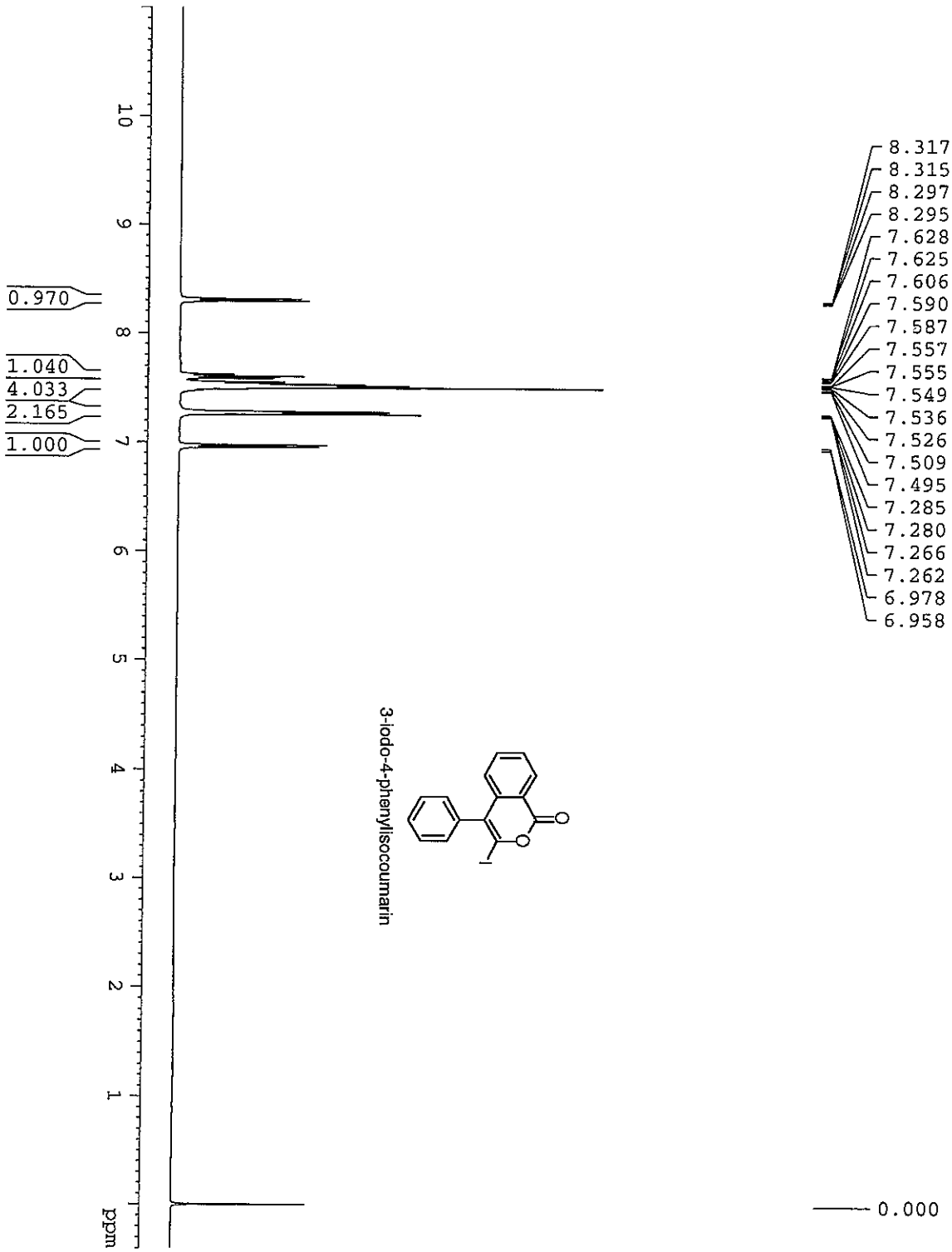

160.183
140.038
139.983
139.082
136.233
131.550
130.048
128.383
128.189
128.091
127.497
122.283
120.403
120.110
119.330
119.192
113.248
112.666
110.122
101.058
77.545
77.228
76.910
55.443
50.324
1-(3-methoxybenzyl)-3-(2-iodophenyl)indole
OMe
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh414-4.fid

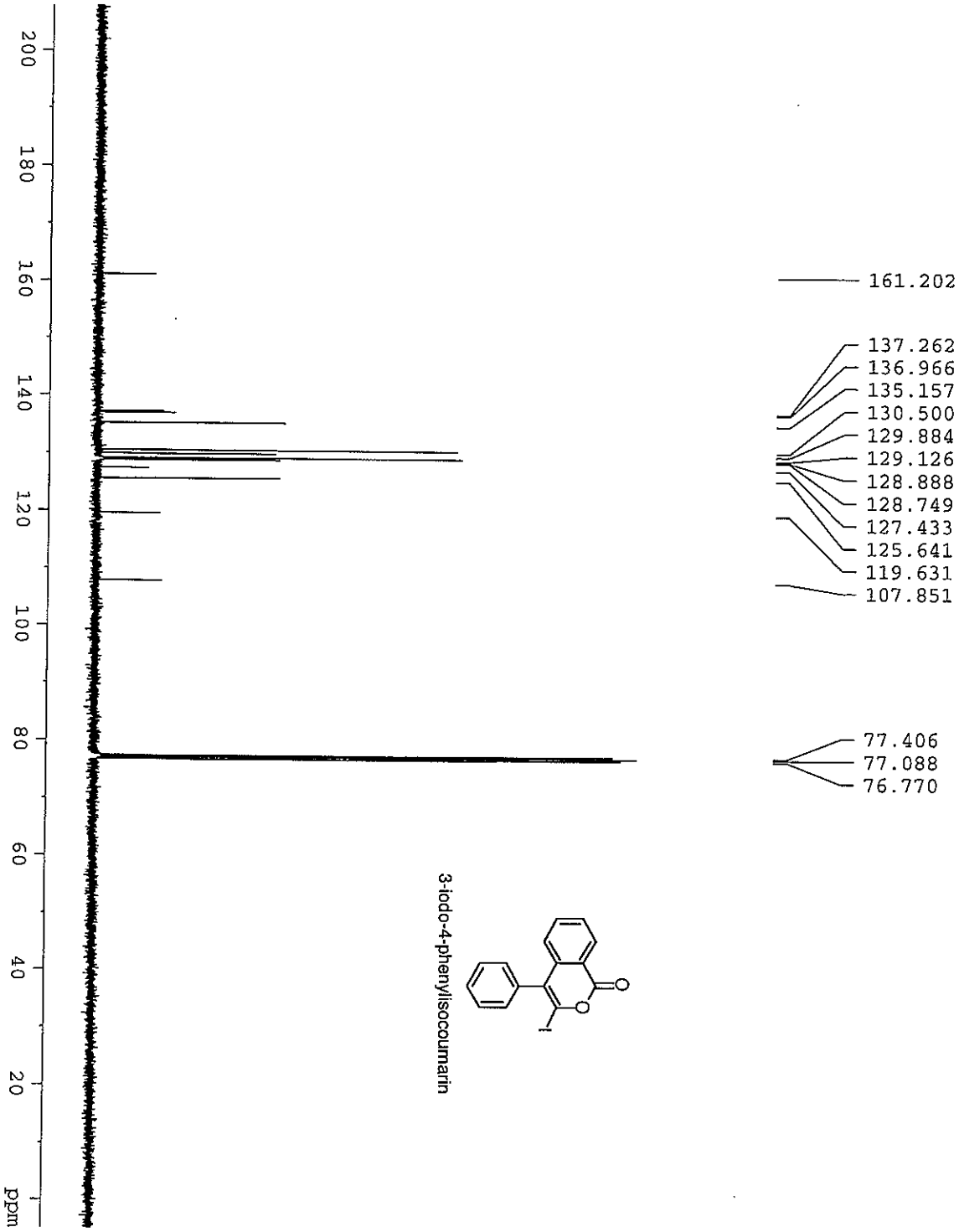

7.977
7.837
7.835
7.817
7.814
7.603
7.588
7.585
7.581
7.549
7.533
7.530
7.516
7.512
7.509
7.460
7.441
7.438
7.423
7.415
7.413
7.406
7.401
7.399
7.356
7.354
7.339
7.335
7.318
7.247
7.085
7.076
7.071
7.065
7.062
7.057
7.050
7.042
0.997
1.002
2.030
1.118
2.065
5.105
0.986
0.970
1-(phenylcarbonyl)-3-(2-iodophenyl)indole
0.000
ppm
data/drx1/nmr400/qh420-5.fid

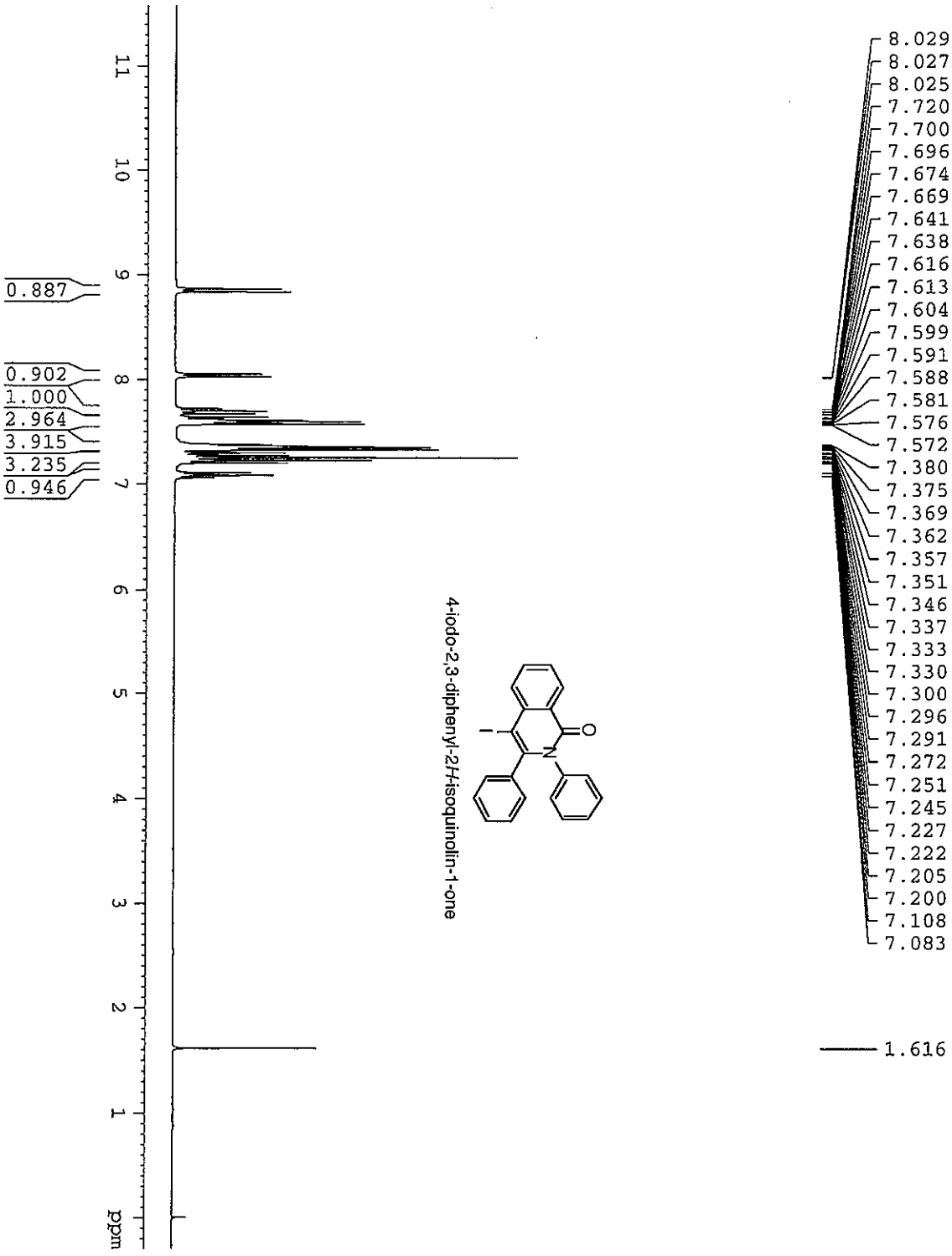

168.881
140.065
138.106
136.082
134.577
132.265
131.294
130.106
129.589
129.558
128.834
128.344
126.517
125.543
125.346
124.288
120.466
116.737
100.161
77.547
77.229
76.911
1-(phenylcarbonyl)-3-(2-iodophenyl)indole
data/drx1/nmr400/qh420-6.fid
ppm

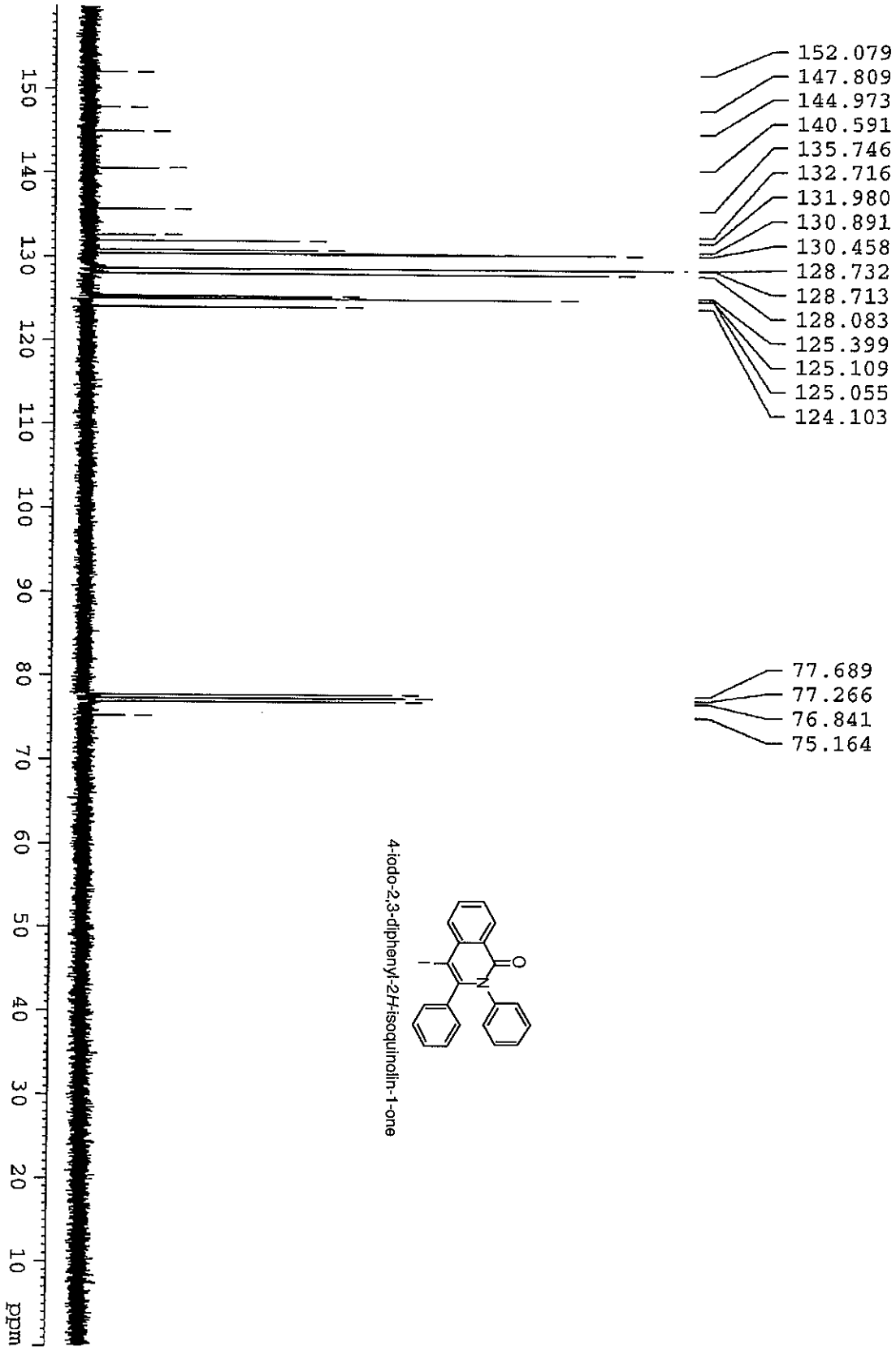

1-(5-phenyl-4-pentynyl)-3-(2-iodophenyl)indole
Ph
N
1.000
1.089
6.711
4.910
1.102
1.057
2.244
2.243
2.245
ppm
0
1
2
3
4
5
6
7
8
9
7.434
7.427
7.420
7.416
7.401
7.396
7.392
7.370
7.366
7.325
7.323
7.315
7.312
7.308
7.301
7.293
7.286
7.265
7.262
7.249
7.238
7.234
7.175
7.172
7.149
7.125
7.122
7.034
7.028
7.009
7.007
7.003
7.001
6.983
6.977
4.436
4.414
4.393
2.472
2.450
2.427
2.191
2.170
2.148
0.000

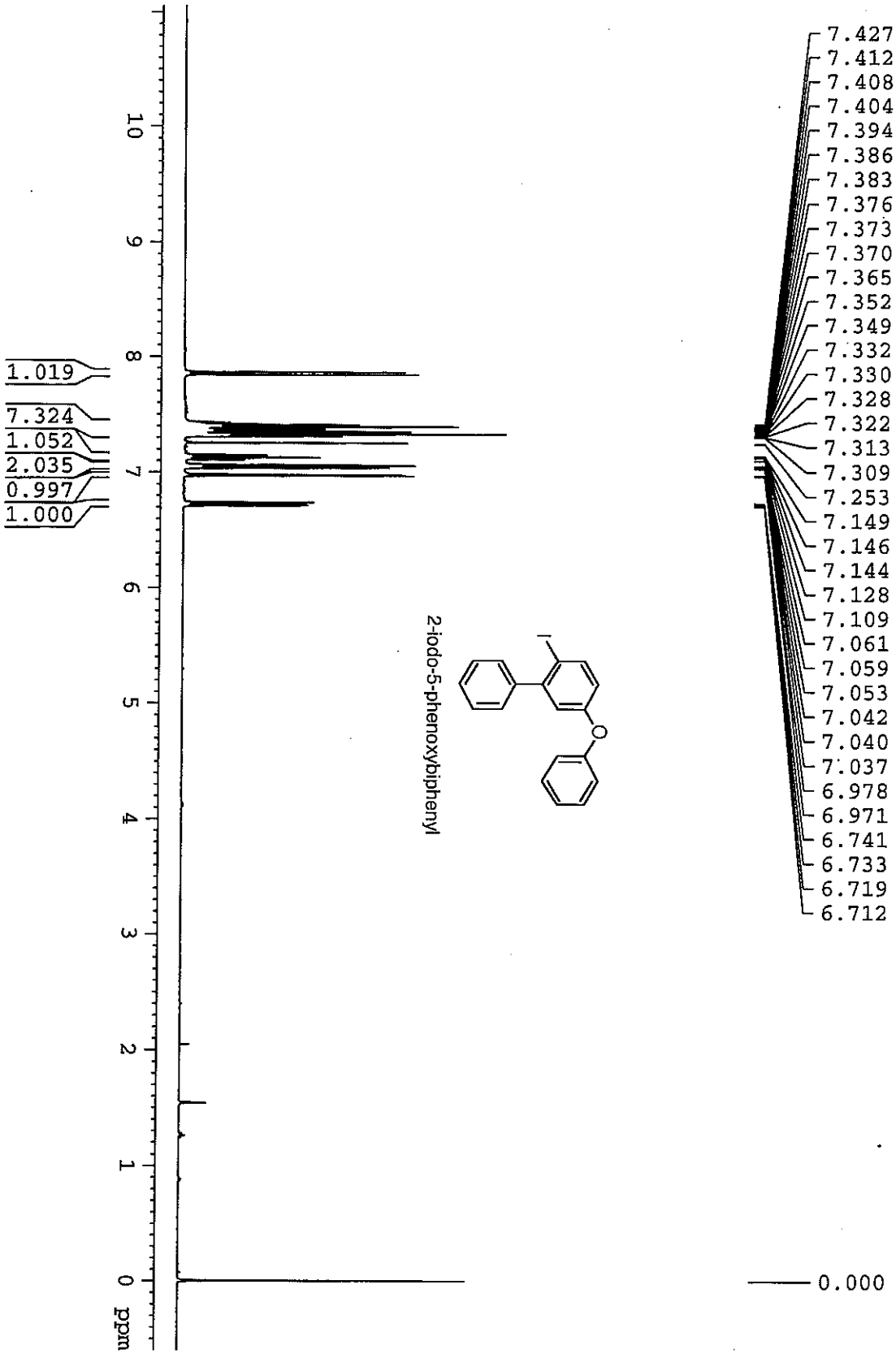

140.069
135.871
131.834
131.511
128.521
128.297
128.204
128.069
128.034
127.502
123.799
122.094
120.423
119.978
118.691
109.843
101.053
88.642
82.250
77.654
77.230
76.807
45.104
29.083
17.013
0.218
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
1-(5-phenyl-4-pentynyl)-3-(2-iodophenyl)indole
N
Ph

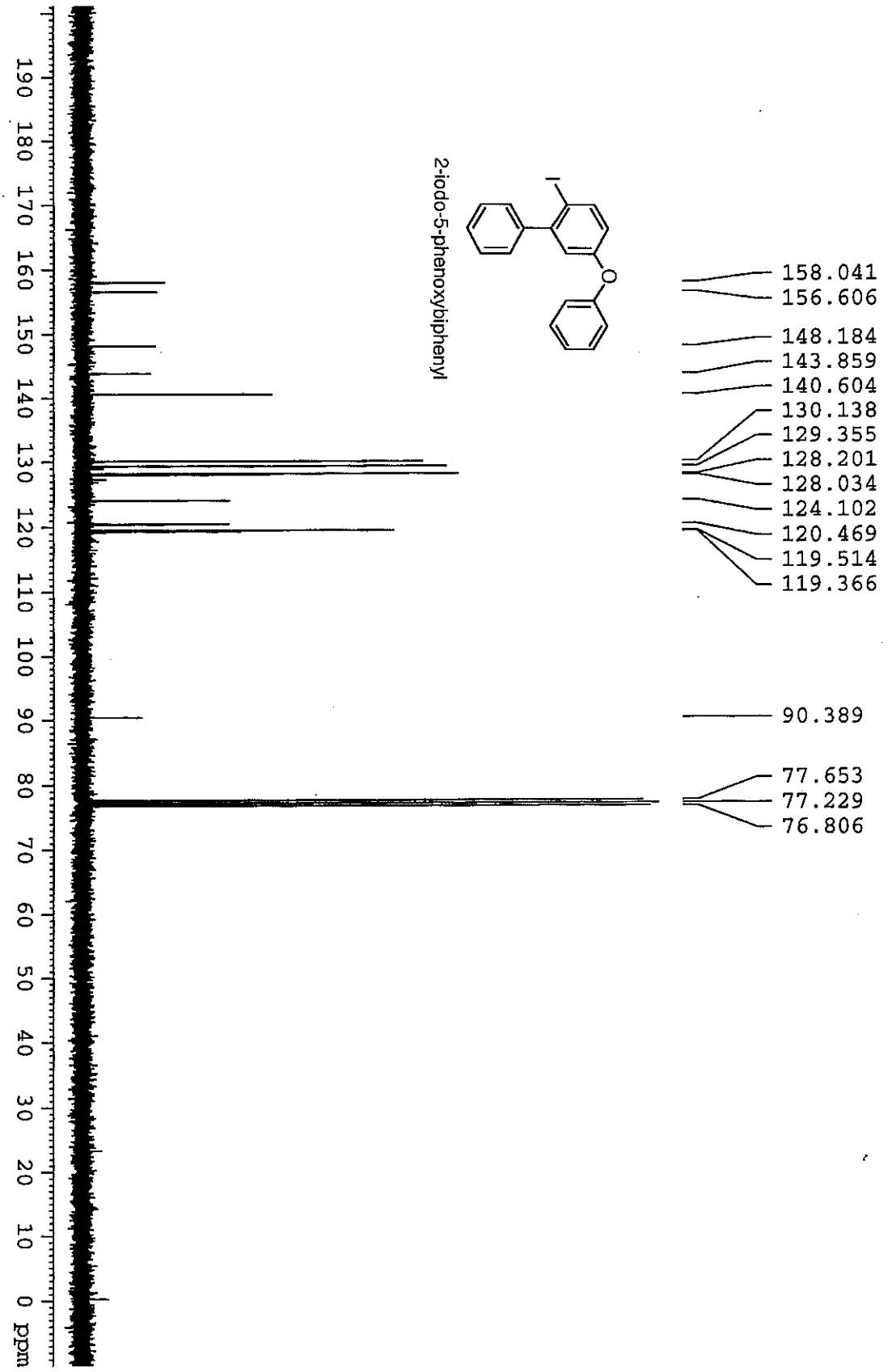

0.970
1.040
4.033
2.165
1.000
10
9
8
7
6
5
4
3
2
1
ppm
8.317
8.315
8.297
8.295
7.628
7.625
7.606
7.590
7.587
7.557
7.555
7.549
7.536
7.526
7.509
7.495
7.285
7.280
7.266
7.262
6.978
6.958
0.000
3-iodo-4-phenylisocoumarin
O
O
I

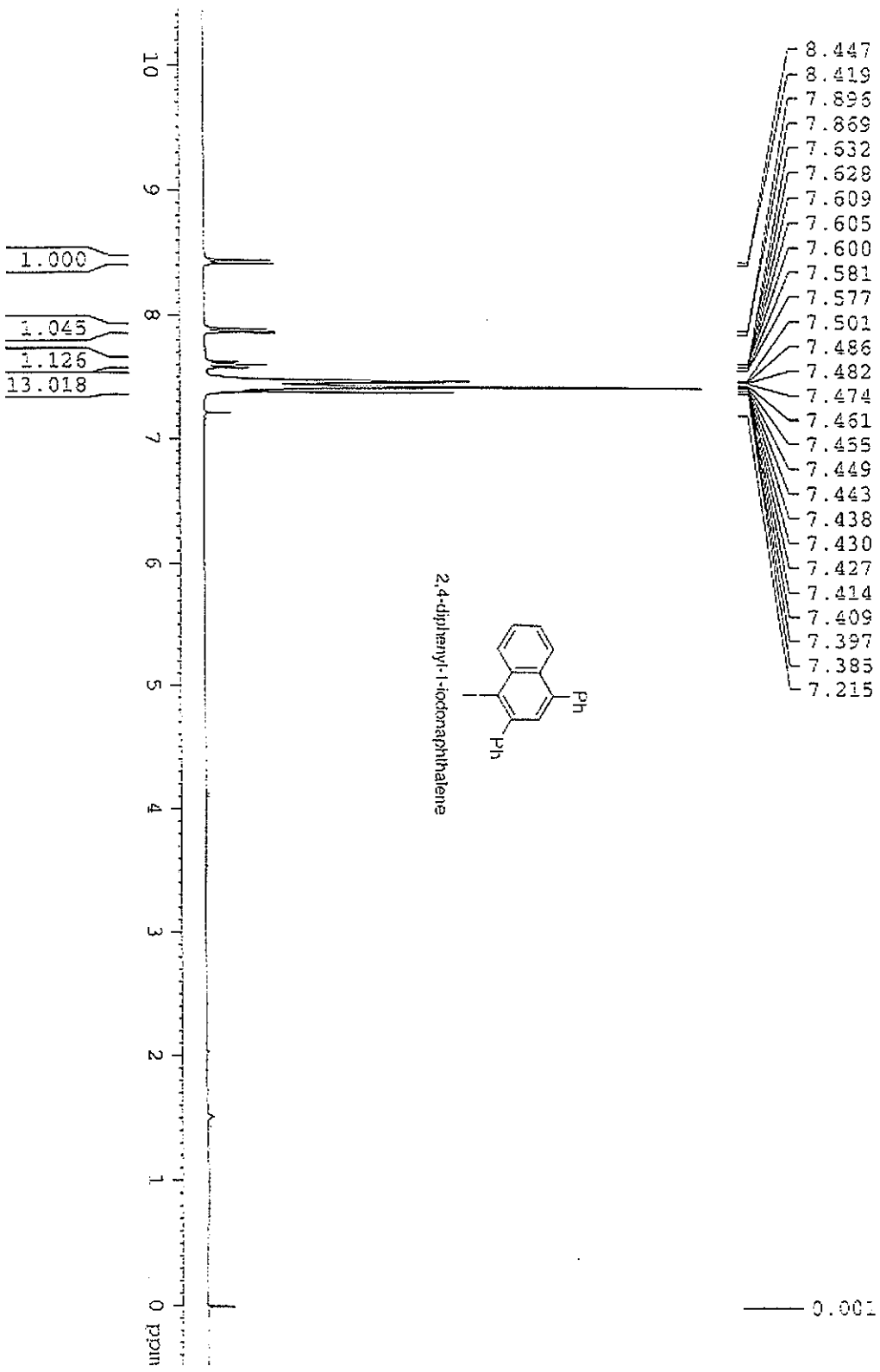

161.202
137.262
136.966
135.157
130.500
129.884
129.126
128.888
128.749
127.433
125.641
119.631
107.851
77.406
77.088
76.770
200
180
160
140
120
100
80
60
40
20
ppm
3-iodo-4-phenylisocoumarin

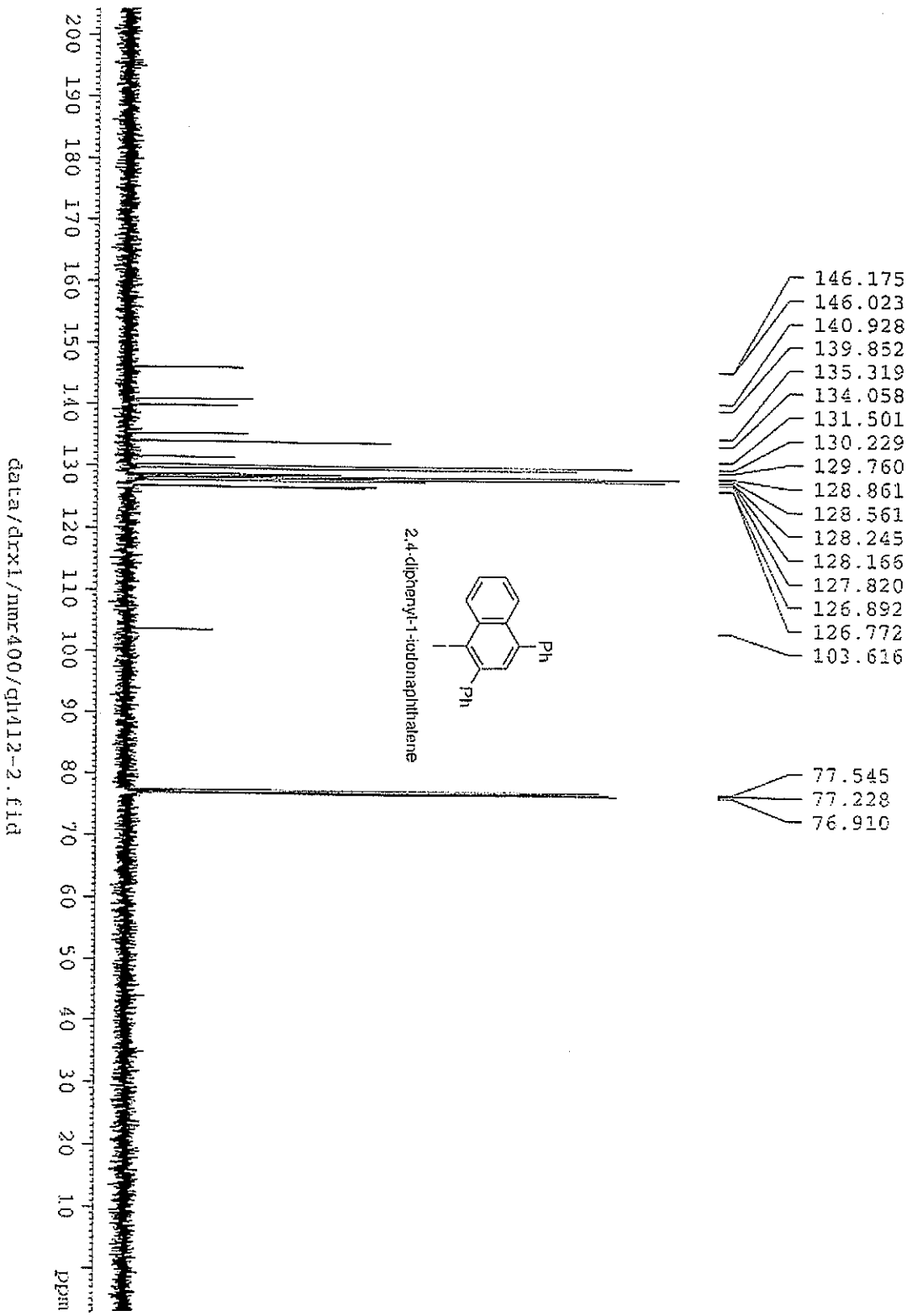

0.887
0.902
1.000
2.964
3.915
3.235
0.946
11
10
9
8
7
6
5
4
3
2
1
ppm
4-iodo-2,3-diphenyl-2H-isoquinolin-1-one
O
I
N
8.029
8.027
8.025
7.720
7.700
7.696
7.674
7.669
7.641
7.638
7.616
7.613
7.604
7.599
7.591
7.588
7.581
7.576
7.572
7.380
7.375
7.369
7.362
7.357
7.351
7.346
7.337
7.333
7.330
7.300
7.296
7.291
7.272
7.251
7.245
7.227
7.222
7.205
7.200
7.108
7.083
1.616

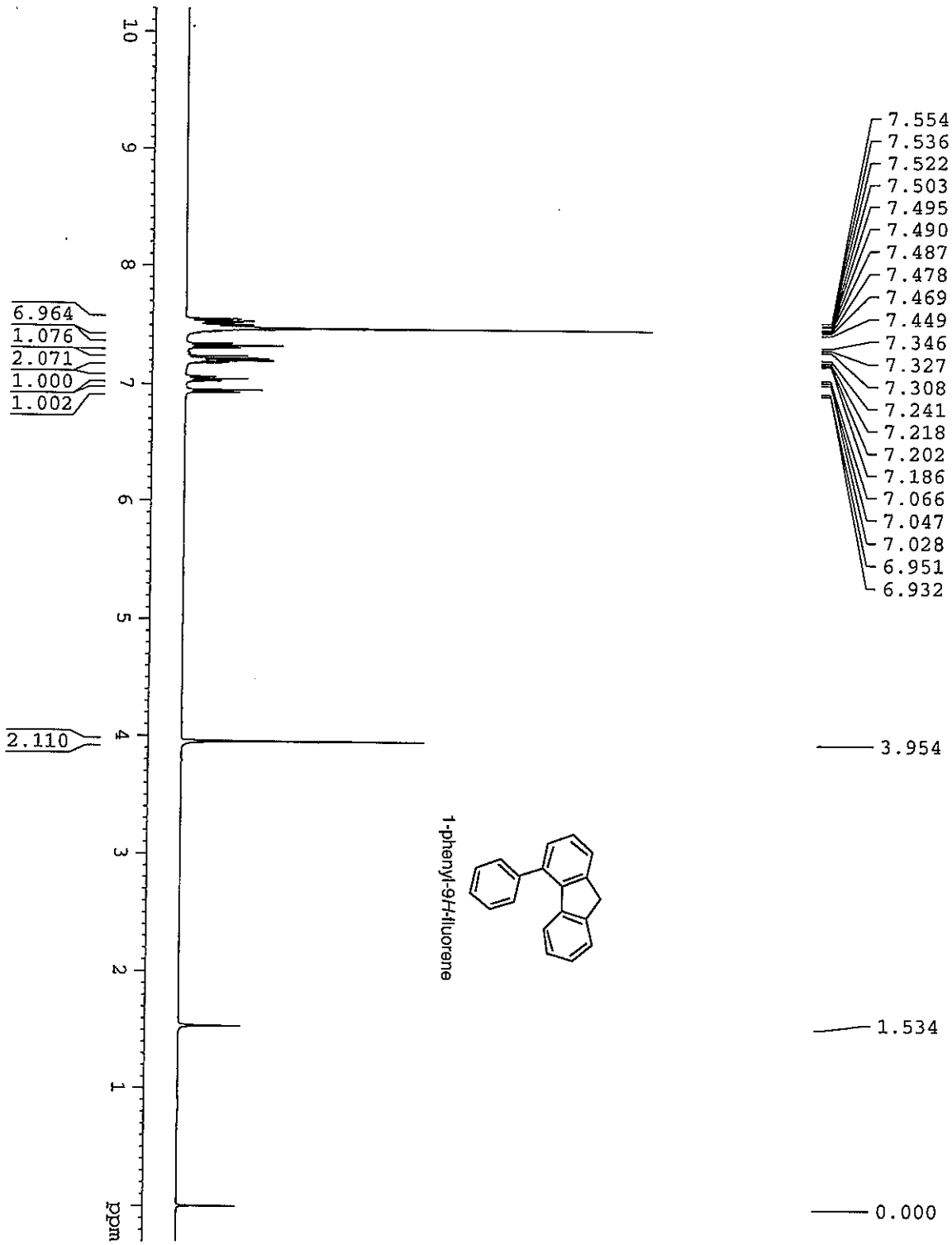

152.079
147.809
144.973
140.591
135.746
132.716
131.980
130.891
130.458
128.732
128.713
128.083
125.399
125.109
125.055
124.103
77.689
77.266
76.841
75.164
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
4-iodo-2,3-diphenyl-2H-isoquinolin-1-one
I
O
N

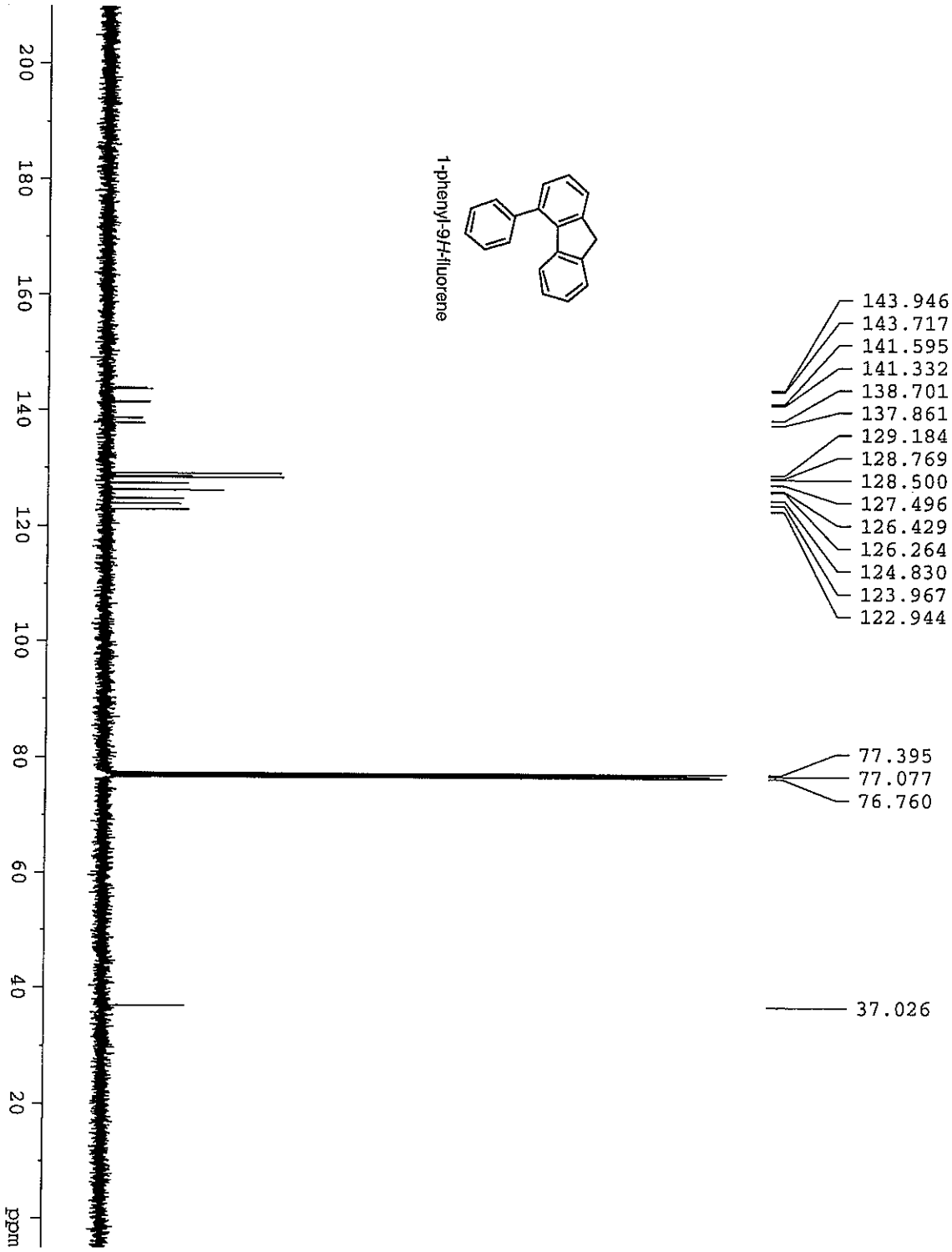

1.019
7.324
1.052
2.035
0.997
1.000
10
9
8
7
6
5
4
3
2
1
0
ppm
2-iodo-5-phenoxybiphenyl
I
O
7.427
7.412
7.408
7.404
7.394
7.386
7.383
7.376
7.373
7.370
7.365
7.352
7.349
7.332
7.330
7.328
7.322
7.313
7.309
7.253
7.149
7.146
7.144
7.128
7.109
7.061
7.059
7.053
7.042
7.040
7.037
6.978
6.971
6.741
6.733
6.719
6.712
0.000

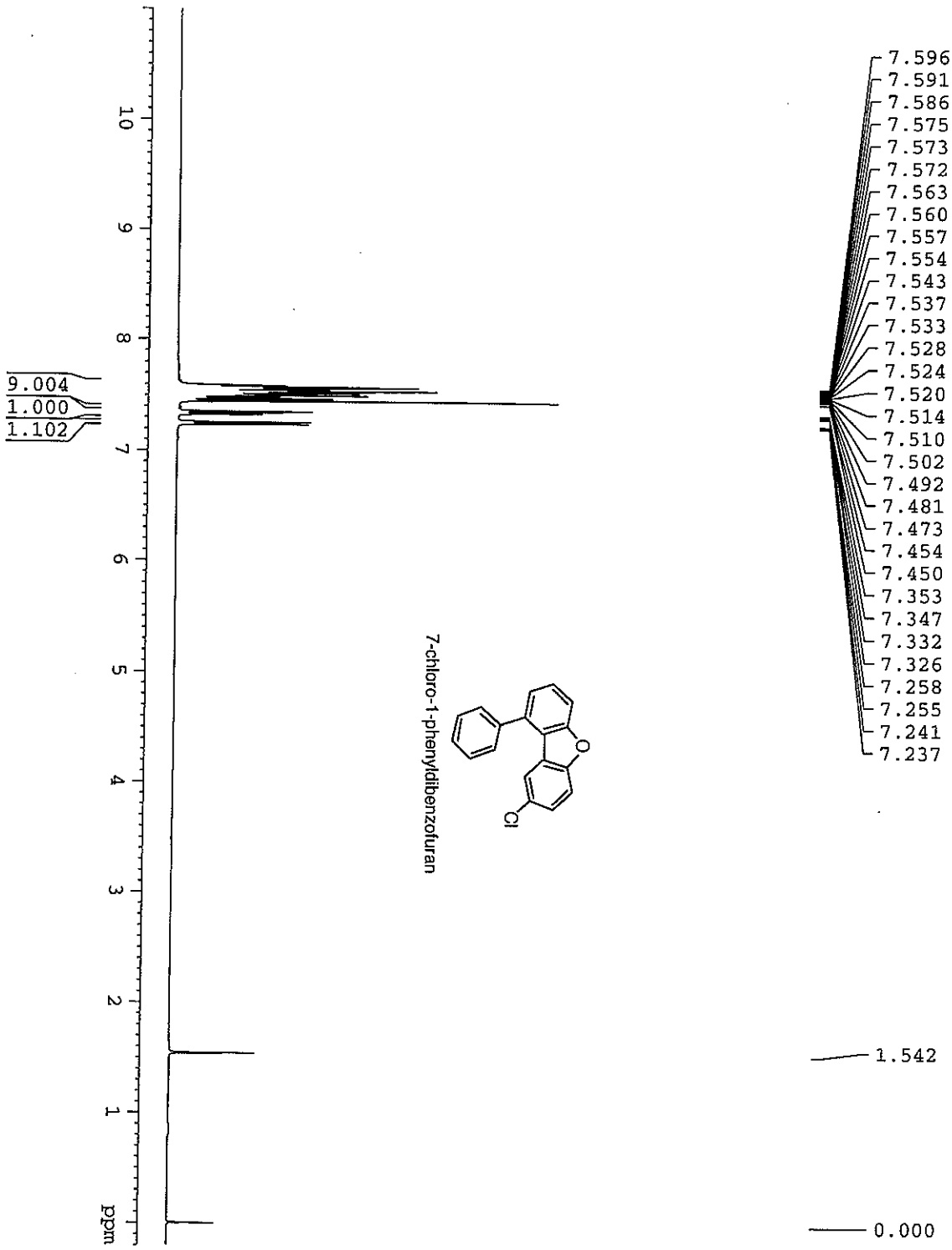

2-iodo-5-phenoxybiphenyl
158.041
156.606
148.184
143.859
140.604
130.138
129.355
128.201
128.034
124.102
120.469
119.514
119.366
90.389
77.653
77.229
76.806
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

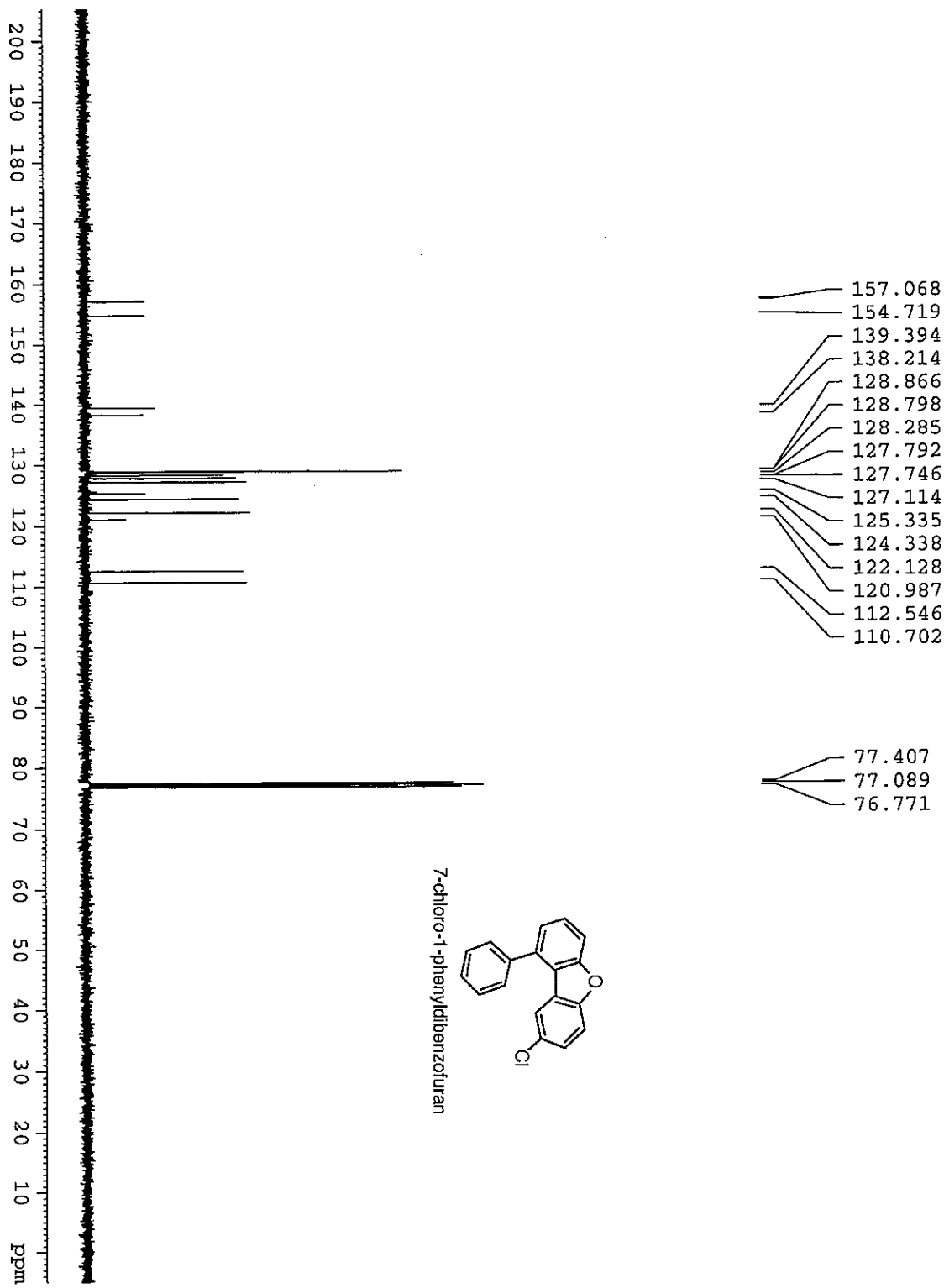

8.447
8.419
7.896
7.869
7.632
7.628
7.609
7.605
7.600
7.581
7.577
7.501
7.486
7.482
7.474
7.461
7.455
7.449
7.443
7.438
7.430
7.427
7.414
7.409
7.397
7.385
7.215
1.000
1.045
1.125
13.018
Ph
Ph
2,4-diphenyl-1-iodonaphthalene
0.001
ppm
data/dat2/nmr300/qh412-1.fid

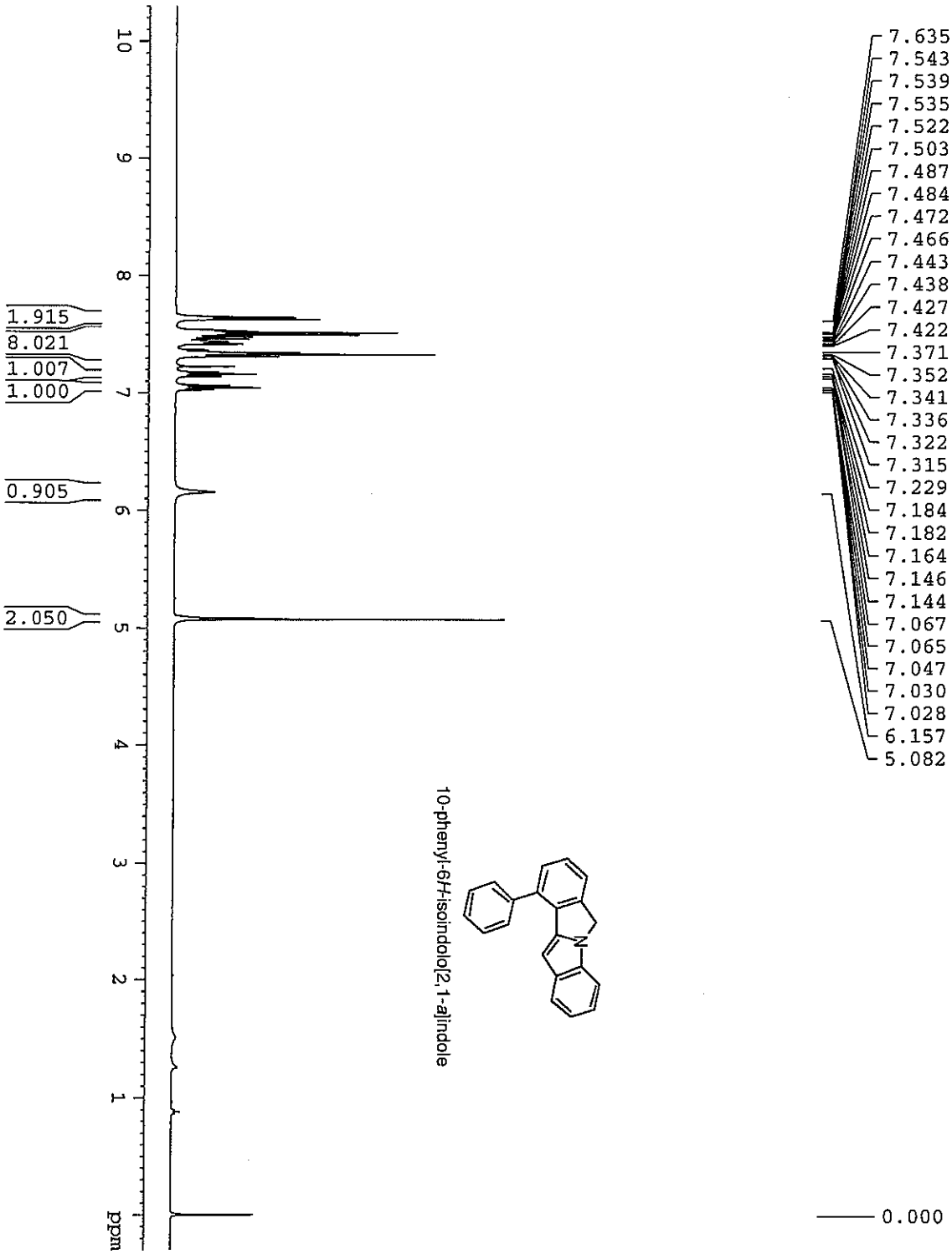

146.175
146.023
140.928
139.852
135.319
134.058
131.501
130.229
129.760
128.861
128.561
128.245
128.166
127.820
126.892
126.772
103.616
77.545
77.228
76.910
2,4-diphenyl-1-iodonaphthalene
Ph
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm
data/drxl/nmr400/qh412-2.fid

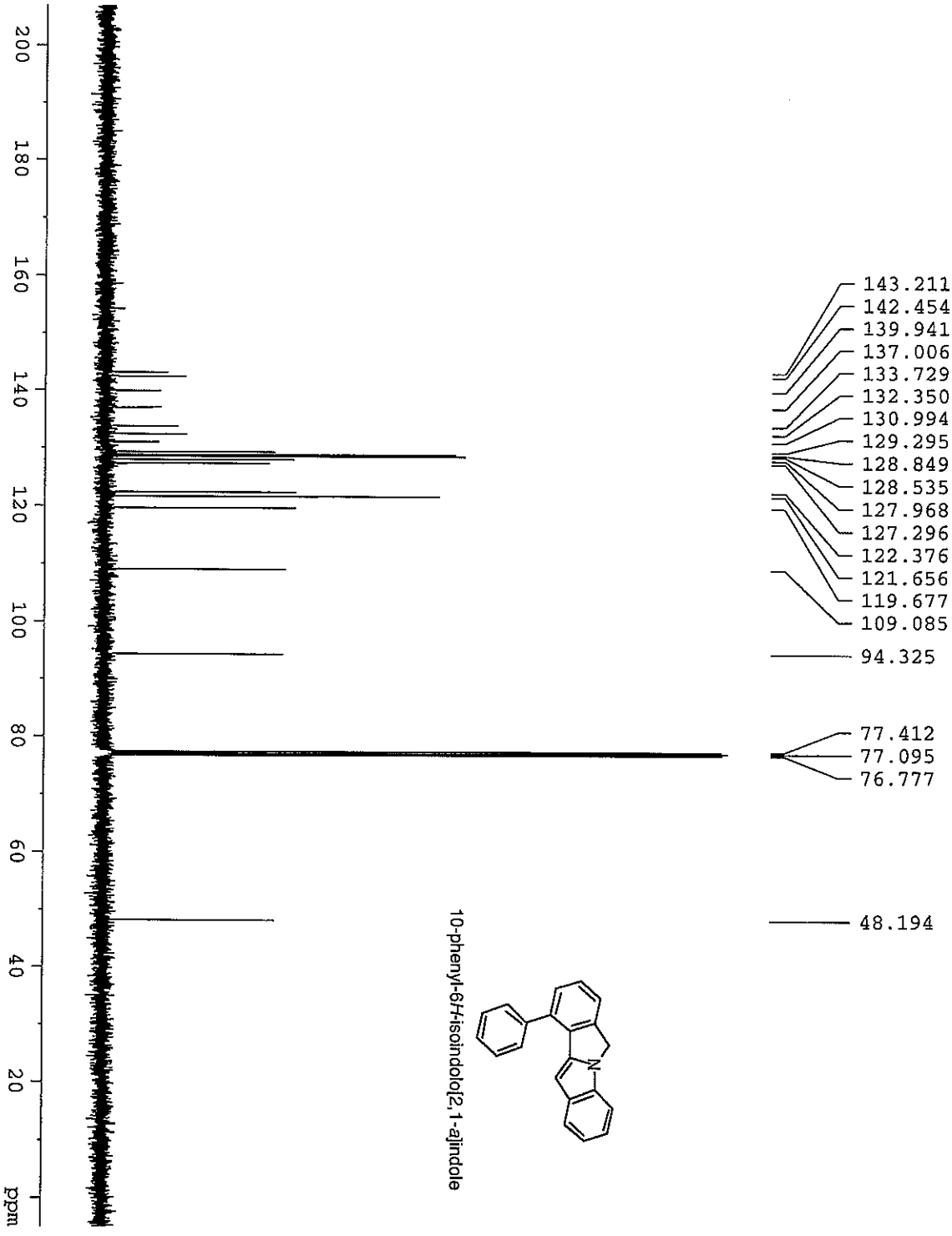

7.554
7.536
7.522
7.503
7.495
7.490
7.487
7.478
7.469
7.449
7.346
7.327
7.308
7.241
7.218
7.202
7.186
7.066
7.047
7.028
6.951
6.932
6.964
1.076
2.071
1.000
1.002
2.110
3.954
1.534
0.000
1-phenyl-9H-fluorene
ppm

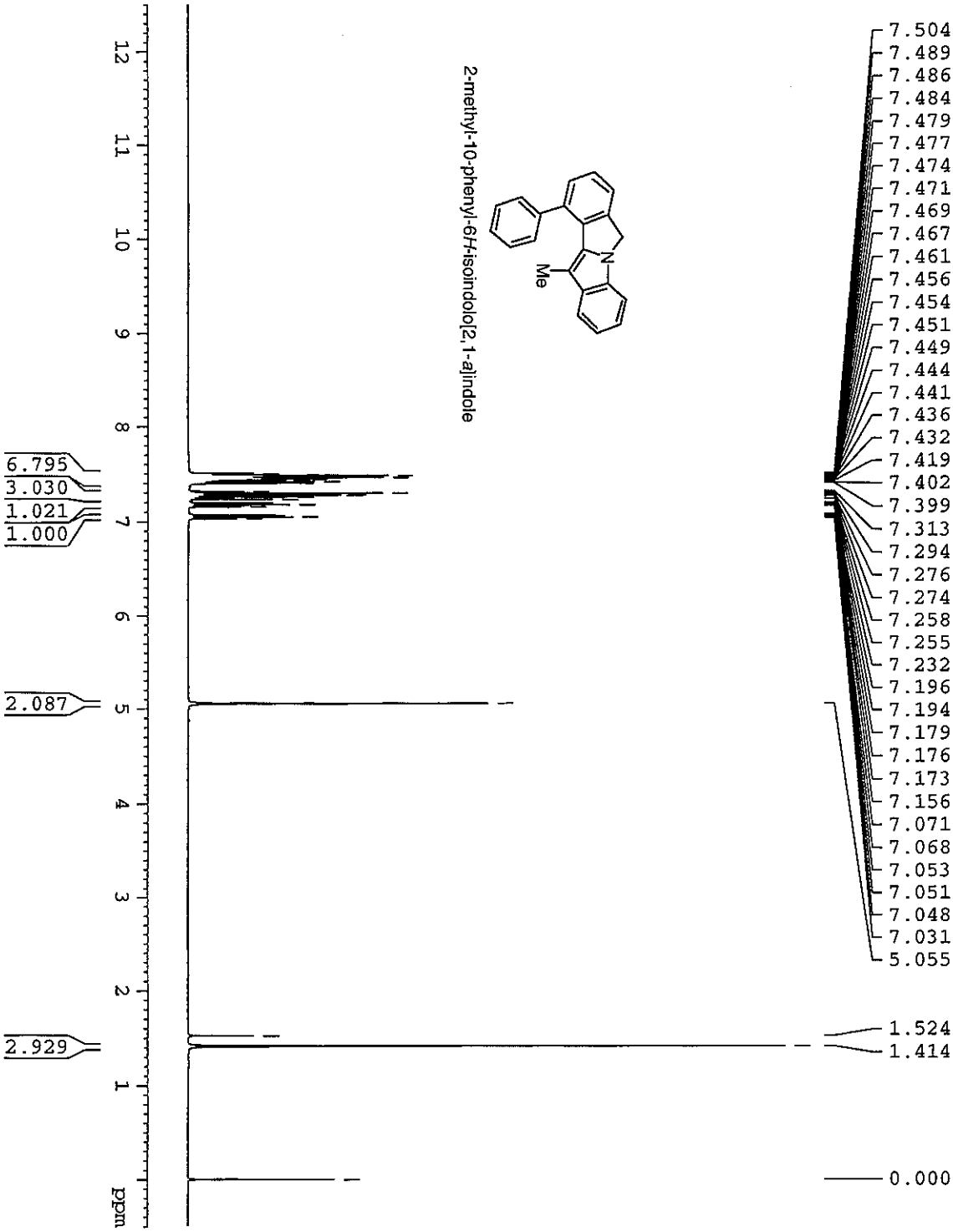

1-phenyl-9H-fluorene
143.946
143.717
141.595
141.332
138.701
137.861
129.184
128.769
128.500
127.496
126.429
126.264
124.830
123.967
122.944
77.395
77.077
76.760
37.026
200
180
160
140
120
100
80
60
40
20
ppm

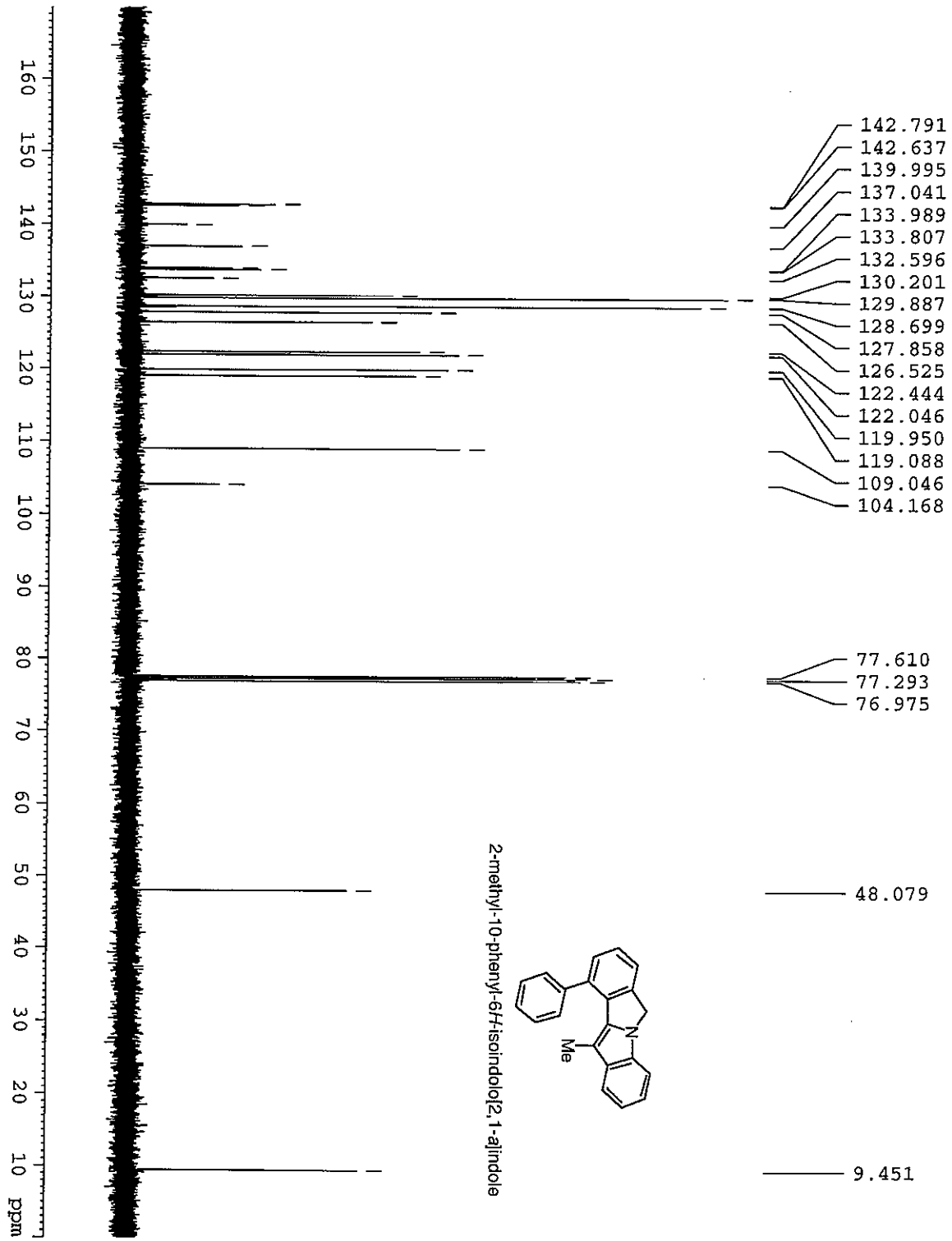

9.004
1.000
1.102
10
9
8
7
6
5
4
3
2
1
ppm
7-chloro-1-phenyldibenzofuran
O
Cl
7.596
7.591
7.586
7.575
7.573
7.572
7.563
7.560
7.557
7.554
7.543
7.537
7.533
7.528
7.524
7.520
7.514
7.510
7.502
7.492
7.481
7.473
7.454
7.450
7.353
7.347
7.332
7.326
7.258
7.255
7.241
7.237
1.542
0.000

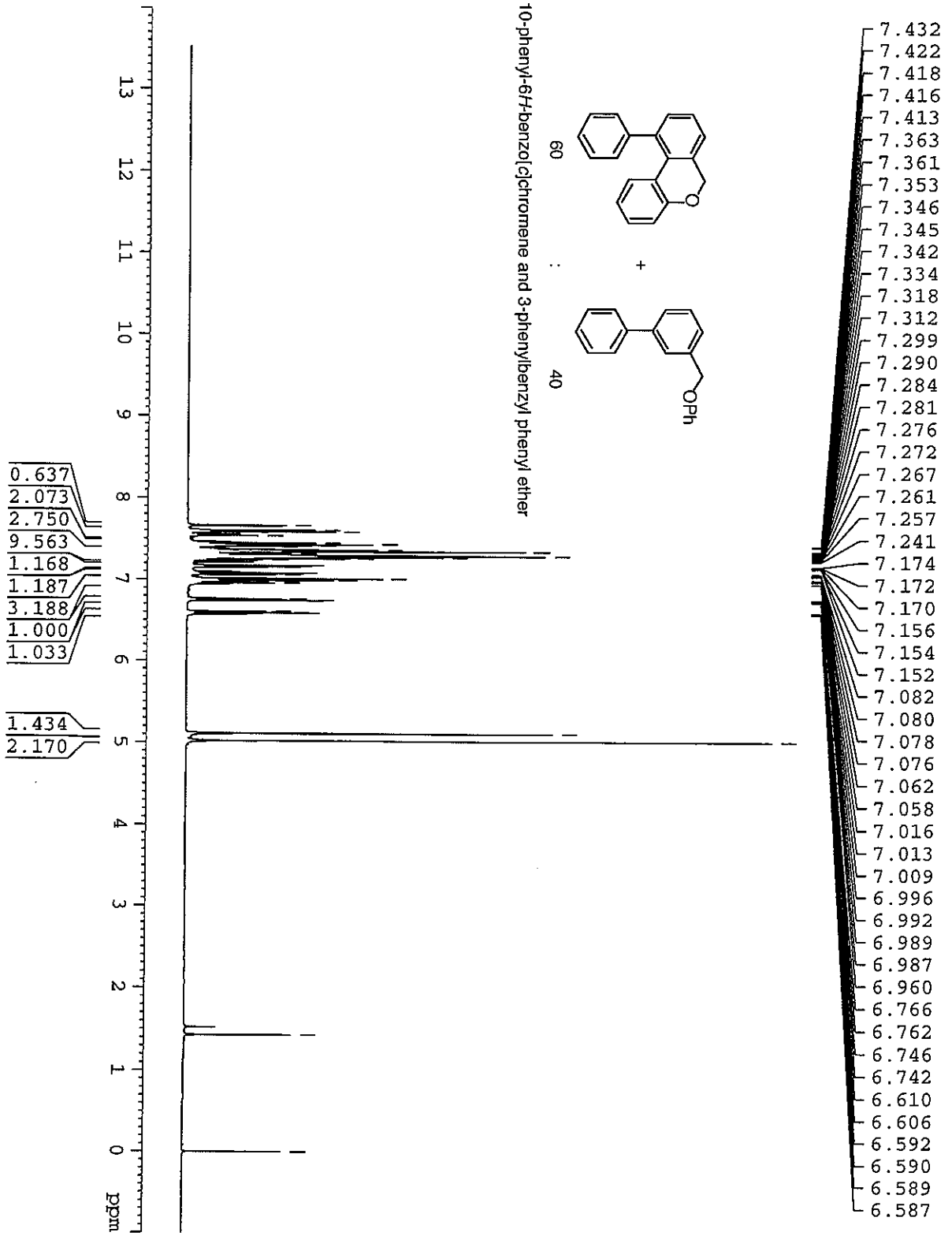

157.068
154.719
139.394
138.214
128.866
128.798
128.285
127.792
127.746
127.114
125.335
124.338
122.128
120.987
112.546
110.702
77.407
77.089
76.771
7-chloro-1-phenyldibenzofuran
Cl
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

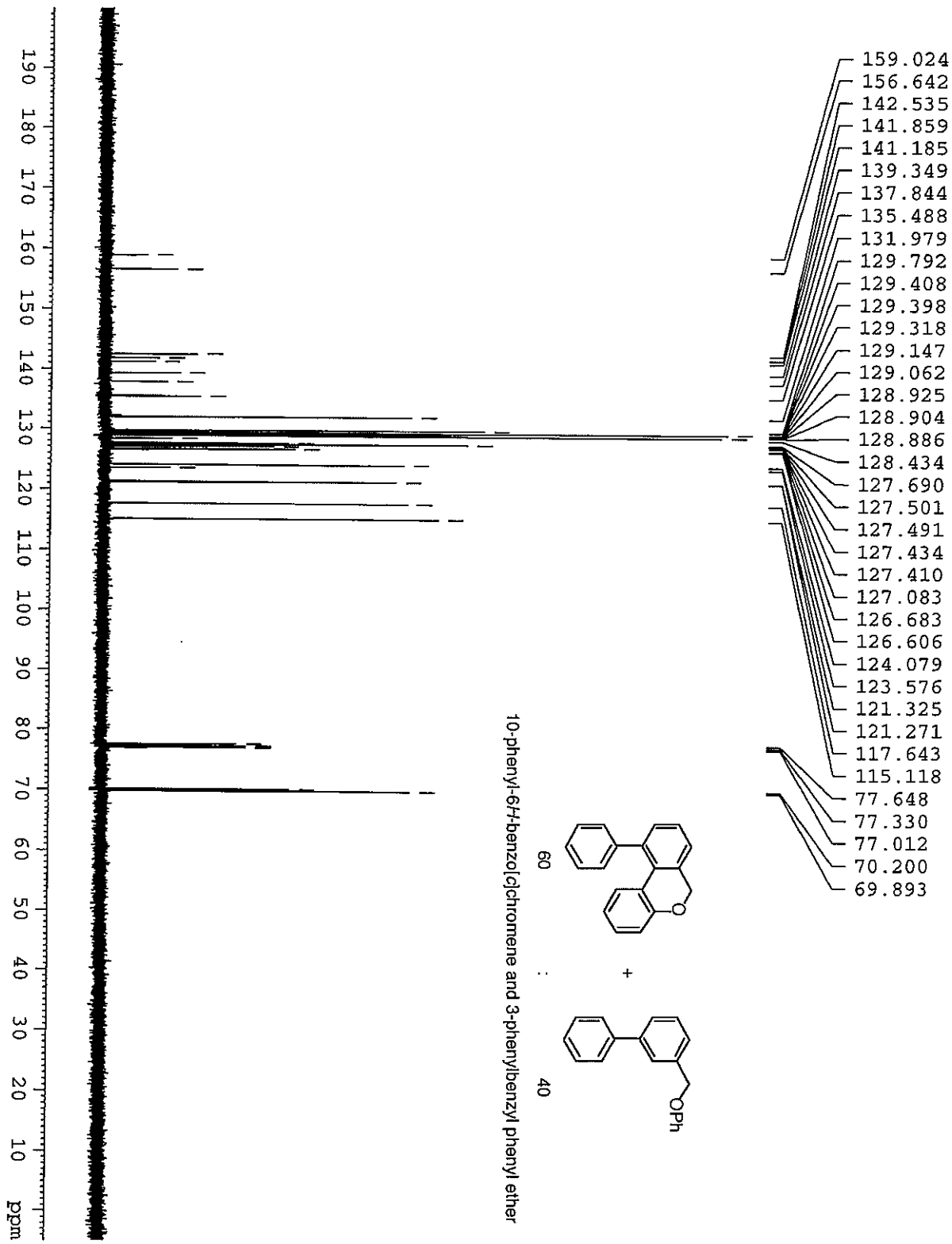

10
9
8
7
6
5
4
3
2
1
ppm
1.915
8.021
1.007
1.000
0.905
2.050
7.635
7.543
7.539
7.535
7.522
7.503
7.487
7.484
7.472
7.466
7.443
7.438
7.427
7.422
7.371
7.352
7.341
7.336
7.322
7.315
7.229
7.184
7.182
7.164
7.146
7.144
7.067
7.065
7.047
7.030
7.028
6.157
5.082
0.000
10-phenyl-6H-isoindolo[2,1-a]indole
N

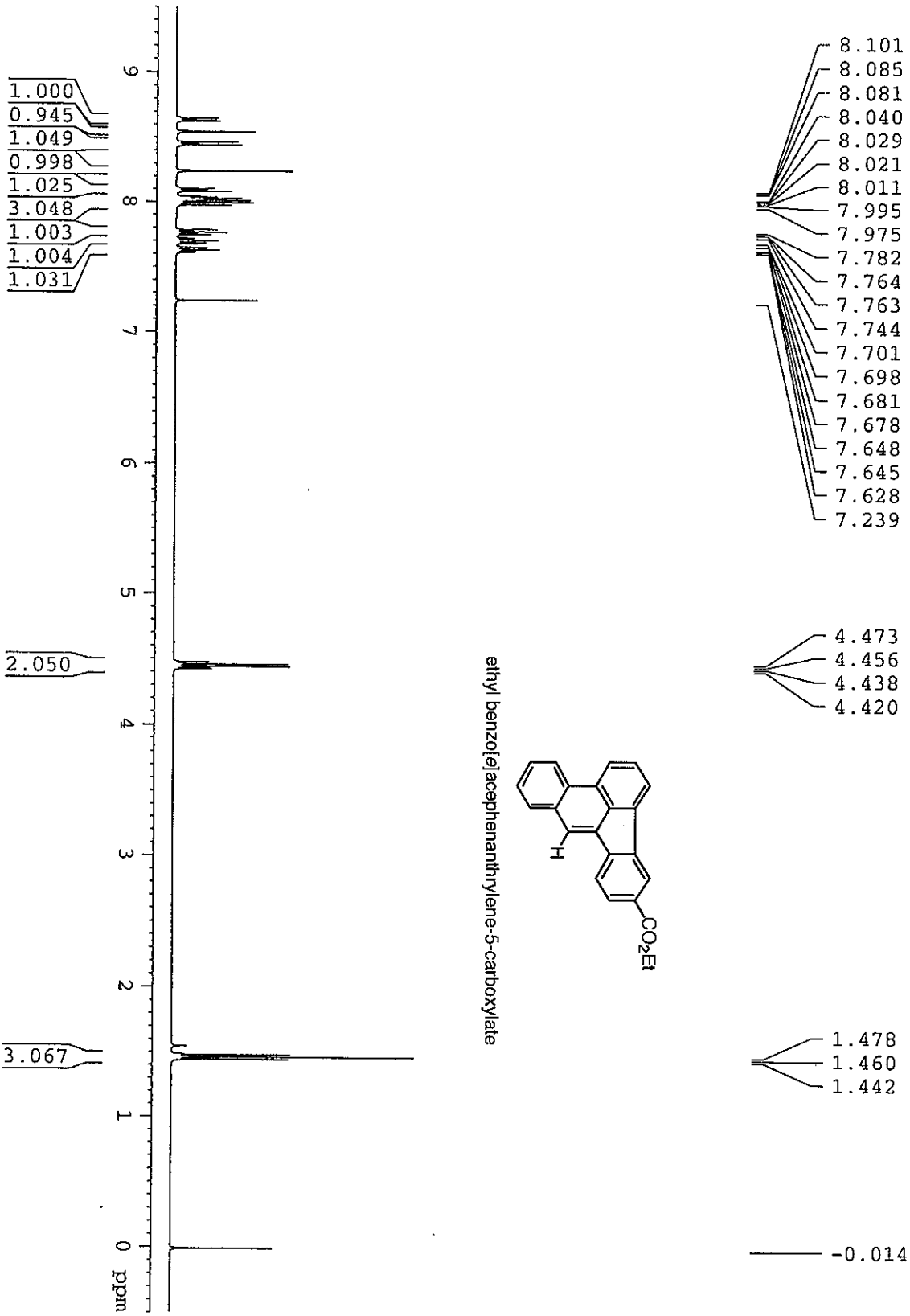

143.211
142.454
139.941
137.006
133.729
132.350
130.994
129.295
128.849
128.535
127.968
127.296
122.376
121.656
119.677
109.085
94.325
77.412
77.095
76.777
48.194
200
180
160
140
120
100
80
60
40
20
ppm
10-phenyl-6H-isoindolo[2,1-a]indole
N

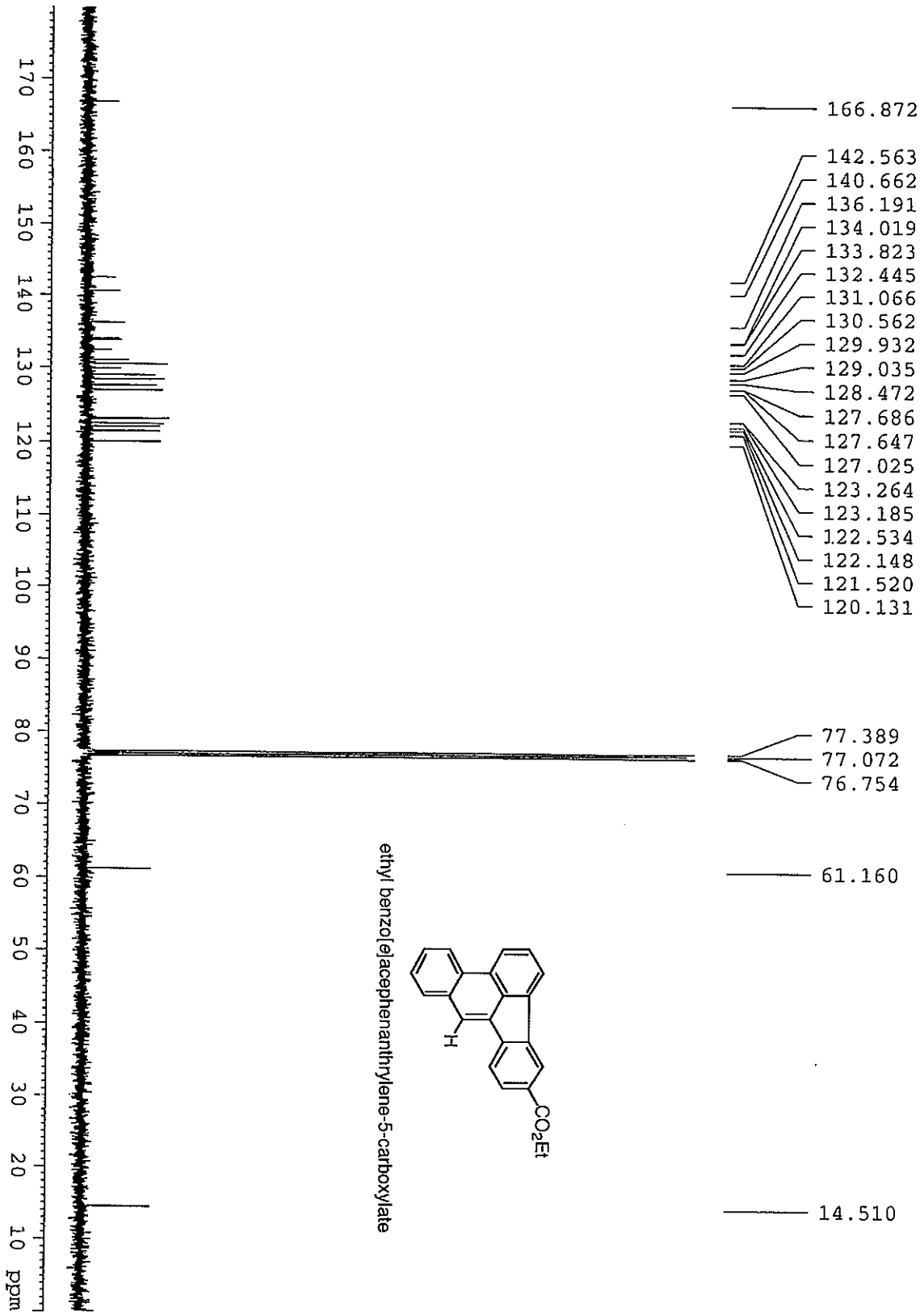

2-methyl-10-phenyl-6H-isoindolo[2,1-a]indole
Me
N
7.504
7.489
7.486
7.484
7.479
7.477
7.474
7.471
7.469
7.467
7.461
7.456
7.454
7.451
7.449
7.444
7.441
7.436
7.432
7.419
7.402
7.399
7.313
7.294
7.276
7.274
7.258
7.255
7.232
7.196
7.194
7.179
7.176
7.173
7.156
7.071
7.068
7.053
7.051
7.048
7.031
5.055
1.524
1.414
0.000
6.795
3.030
1.021
1.000
2.087
2.929
ppm

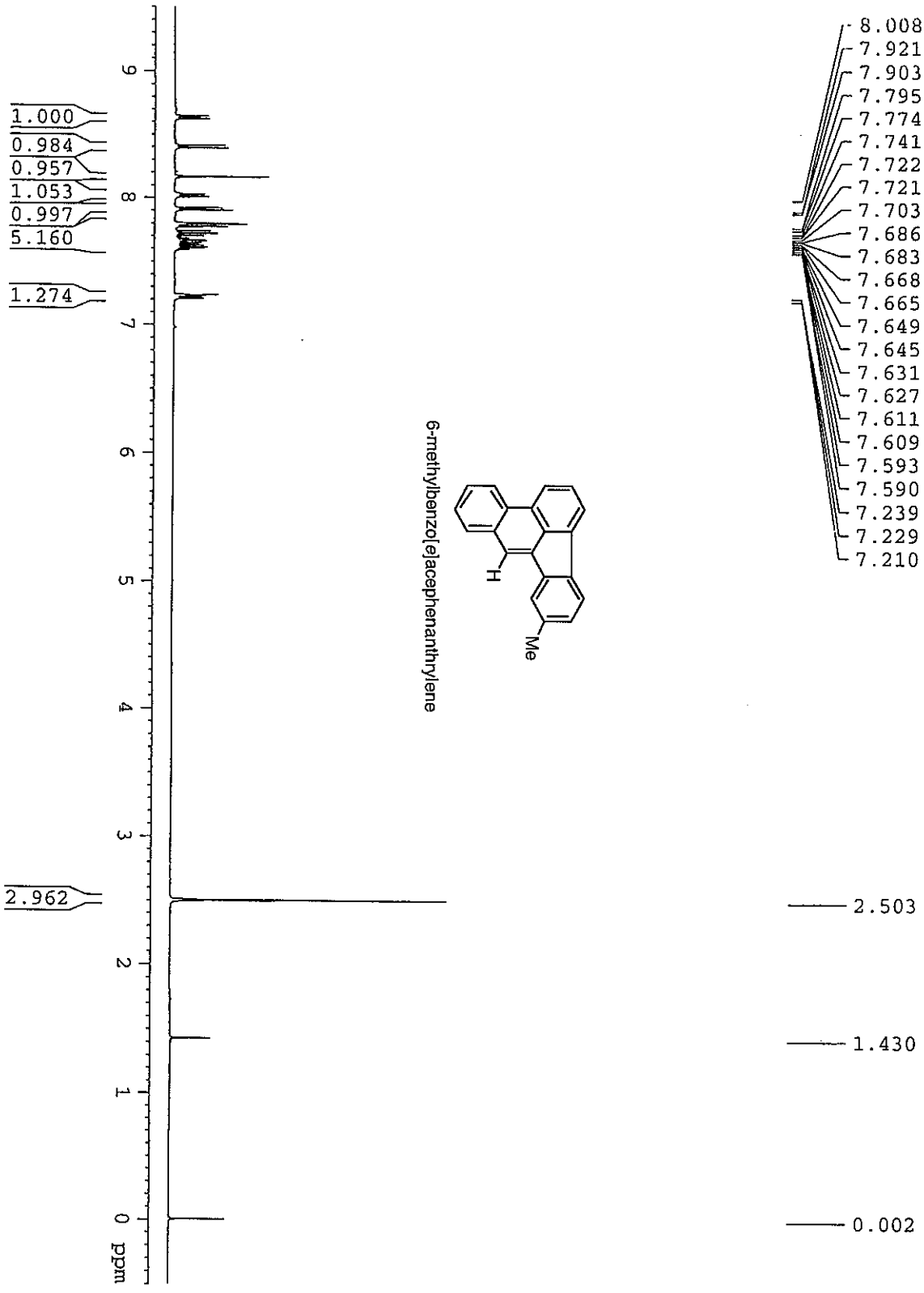

142.791
142.637
139.995
137.041
133.989
133.807
132.596
130.201
129.887
128.699
127.858
126.525
122.444
122.046
119.950
119.088
109.046
104.168
77.610
77.293
76.975
48.079
9.451
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
2-methyl-10-phenyl-6H-isoindolo[2,1-a]indole
Me
N

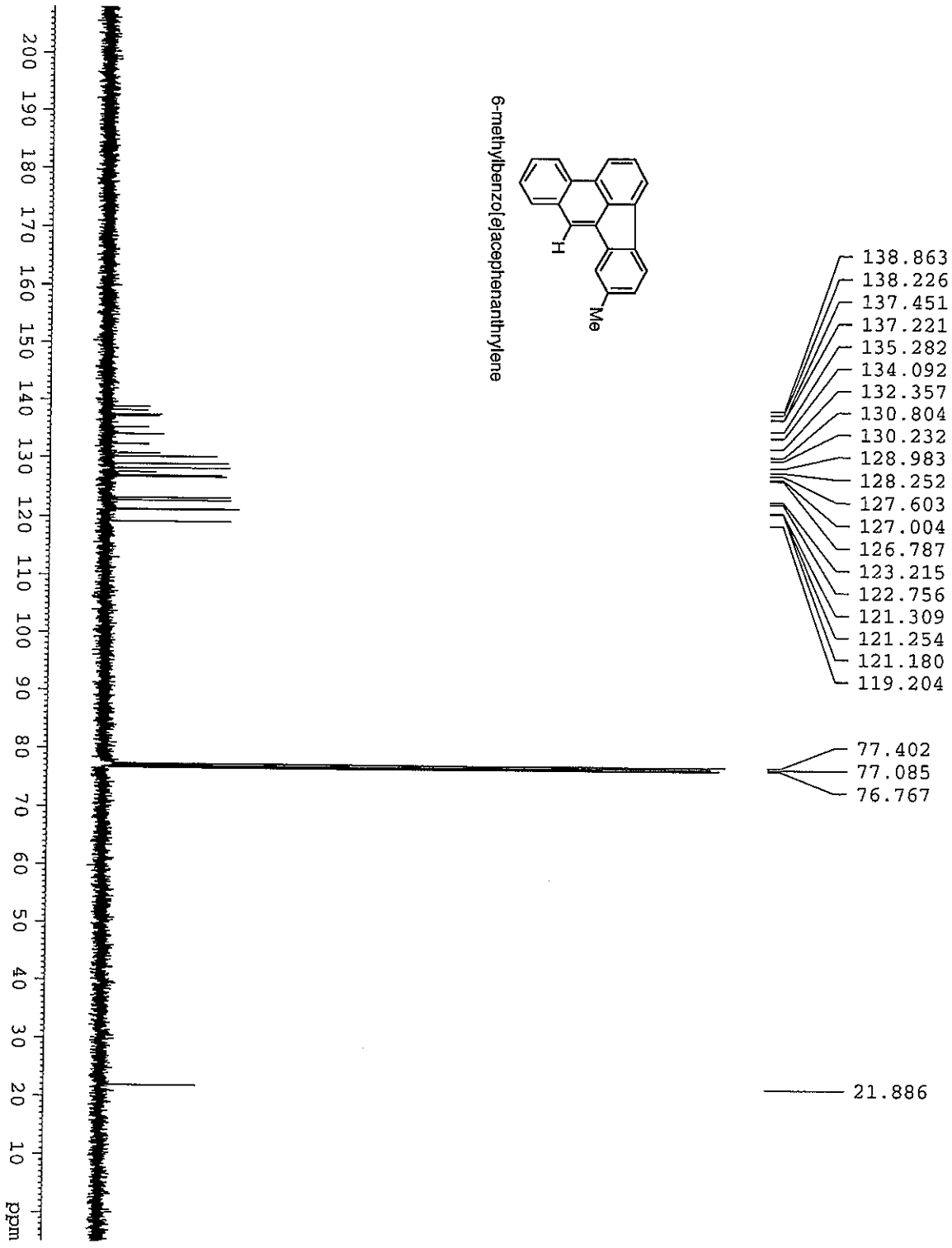

10-phenyl-6*H*-benzo[*c*]chromene and 3-phenylbenzyl phenyl ether
OPh
0.637
2.073
2.750
9.563
1.168
1.187
3.188
1.000
1.033
1.434
2.170
7.432
7.422
7.418
7.416
7.413
7.363
7.361
7.353
7.346
7.345
7.342
7.334
7.318
7.312
7.299
7.290
7.284
7.281
7.276
7.272
7.267
7.261
7.257
7.241
7.174
7.172
7.170
7.156
7.154
7.152
7.082
7.080
7.078
7.076
7.062
7.058
7.016
7.013
7.009
6.996
6.992
6.989
6.987
6.960
6.766
6.762
6.746
6.742
6.610
6.606
6.592
6.590
6.589
6.587
ppm

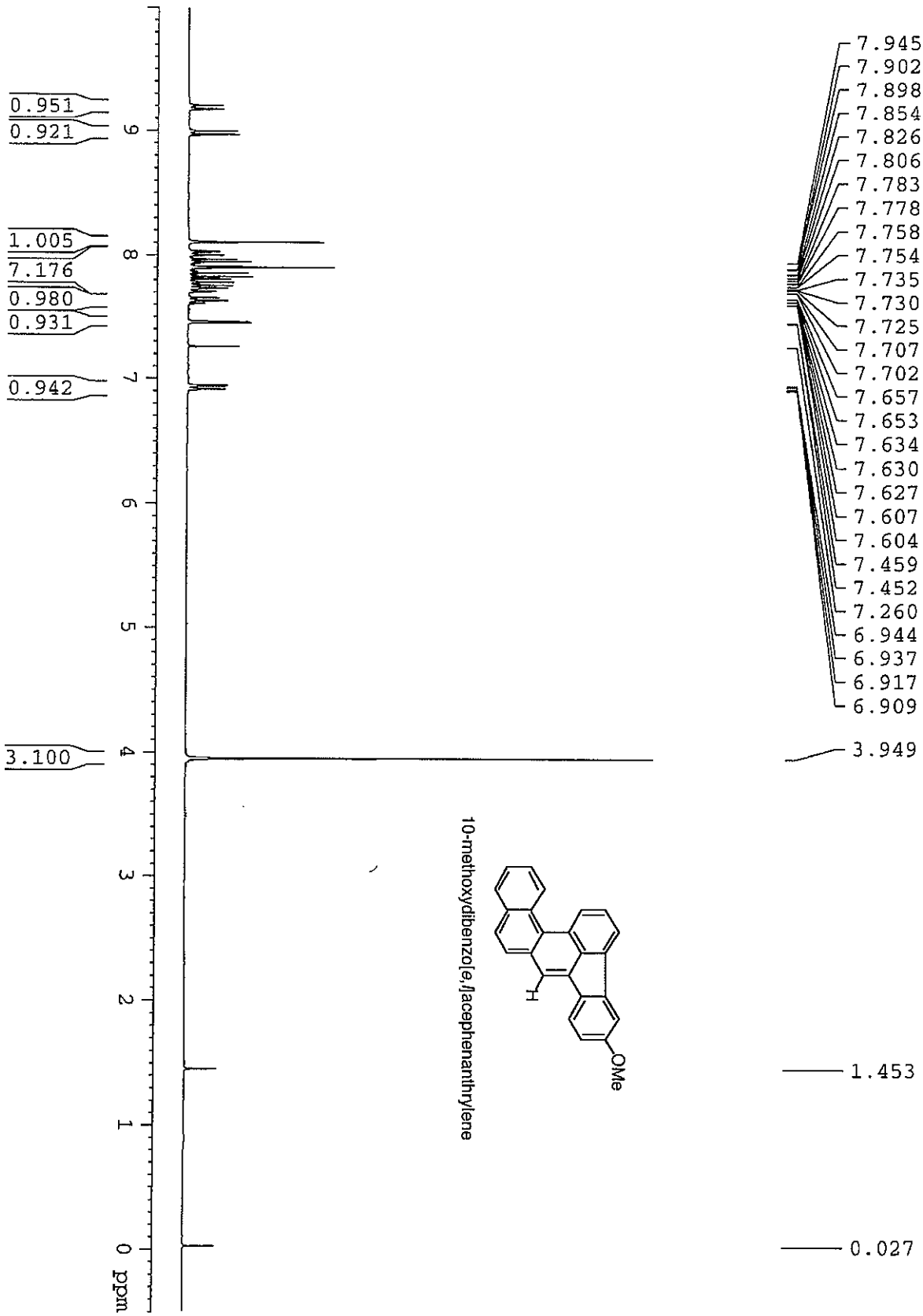

159.024
156.642
142.535
141.859
141.185
139.349
137.844
135.488
131.979
129.792
129.408
129.398
129.318
129.147
129.062
128.925
128.904
128.886
128.434
127.690
127.501
127.491
127.434
127.410
127.083
126.683
126.606
124.079
123.576
121.325
121.271
117.643
115.118
77.648
77.330
77.012
70.200
69.893
OPh
10-phenyl-6H-benzo[c]chromene and 3-phenylbenzyl phenyl ether
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

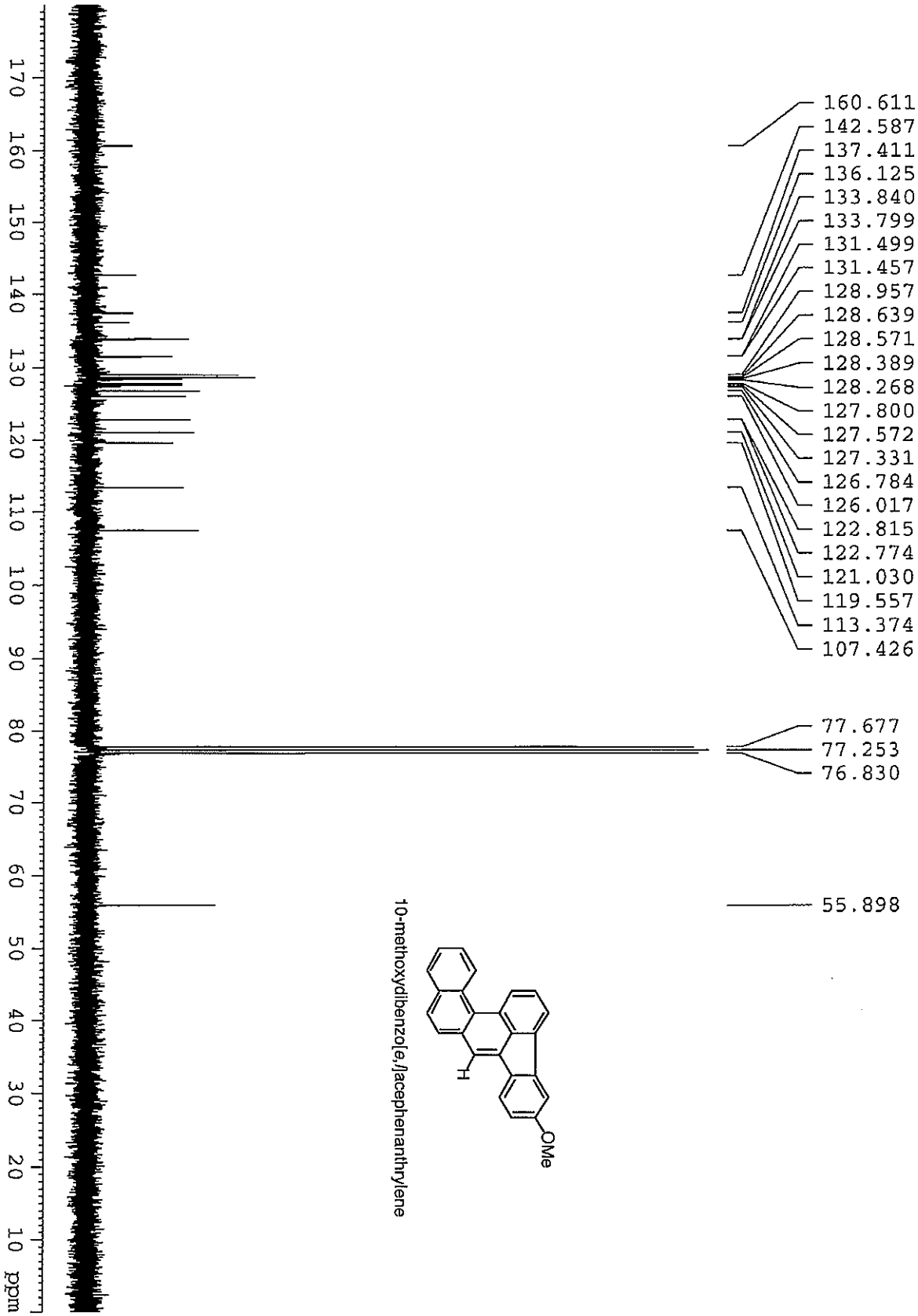

1.000
0.945
1.049
0.998
1.025
3.048
1.003
1.004
1.031
2.050
3.067
9
8
7
6
5
4
3
2
1
0
ppm
8.101
8.085
8.081
8.040
8.029
8.021
8.011
7.995
7.975
7.782
7.764
7.763
7.744
7.701
7.698
7.681
7.678
7.648
7.645
7.628
7.239
4.473
4.456
4.438
4.420
1.478
1.460
1.442
-0.014
ethyl benzo[e]acephenanthrylene-5-carboxylate
H
CO2Et

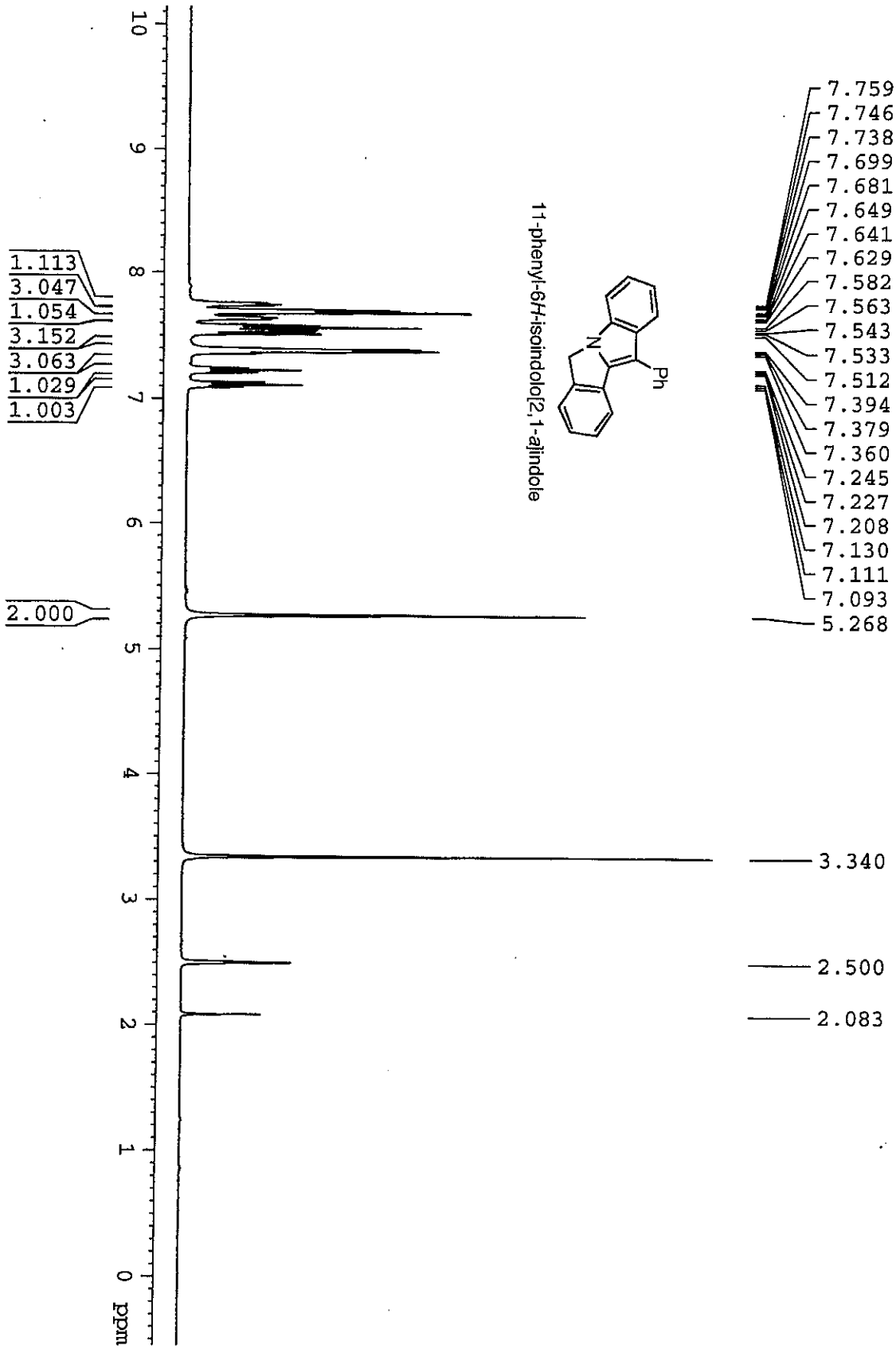

166.872
142.563
140.662
136.191
134.019
133.823
132.445
131.066
130.562
129.932
129.035
128.472
127.686
127.647
127.025
123.264
123.185
122.534
122.148
121.520
120.131
77.389
77.072
76.754
61.160
14.510
ethyl benzo[e]acephenanthrylene-5-carboxylate
H
CO2Et
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

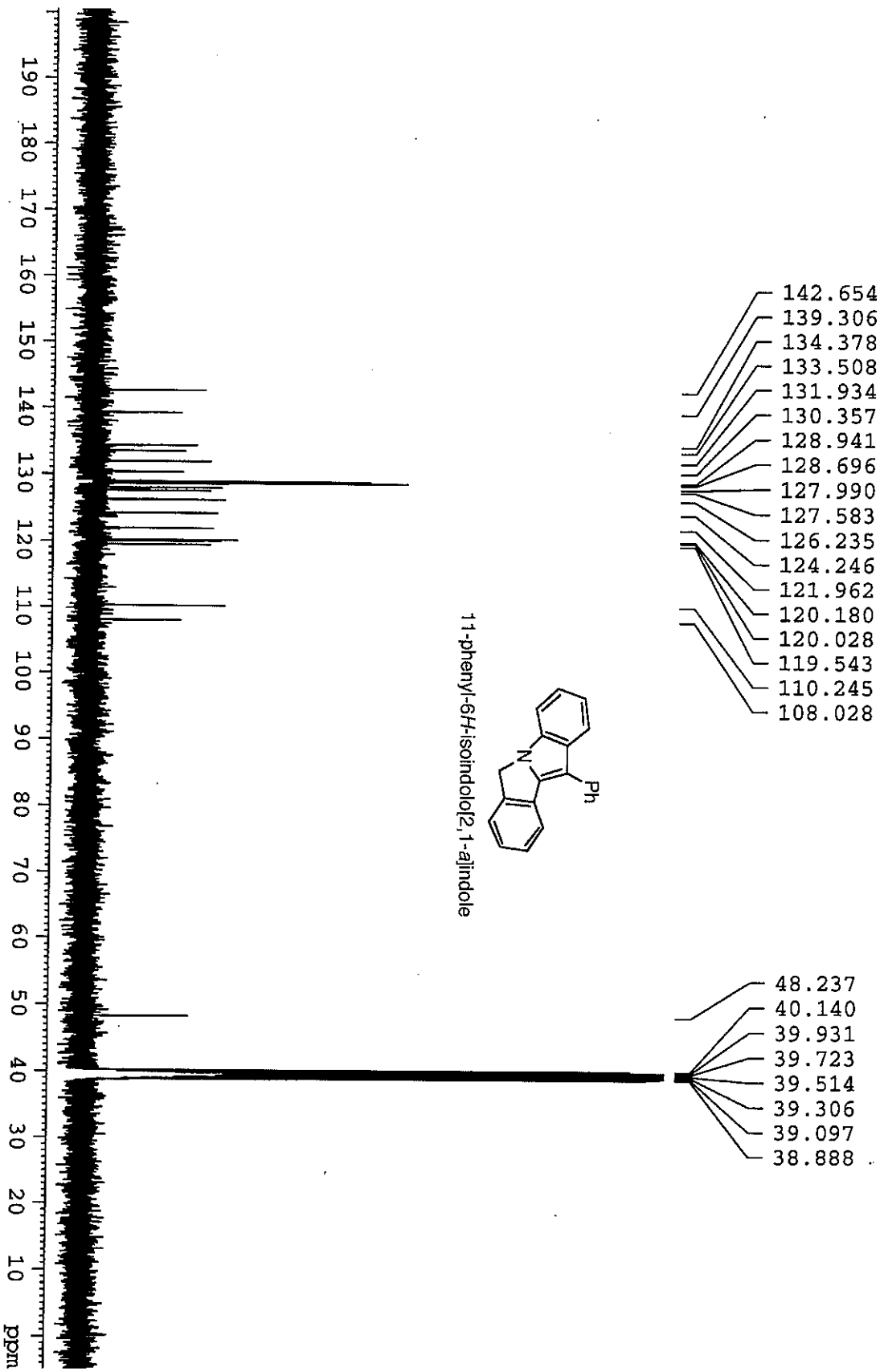

8.008
7.921
7.903
7.795
7.774
7.741
7.722
7.721
7.703
7.686
7.683
7.668
7.665
7.649
7.645
7.631
7.627
7.611
7.609
7.593
7.590
7.239
7.229
7.210
1.000
0.984
0.957
1.053
0.997
5.160
1.274
2.962
2.503
1.430
0.002
6-methylbenzo[e]acephenanthrylene
H
Me
ppm

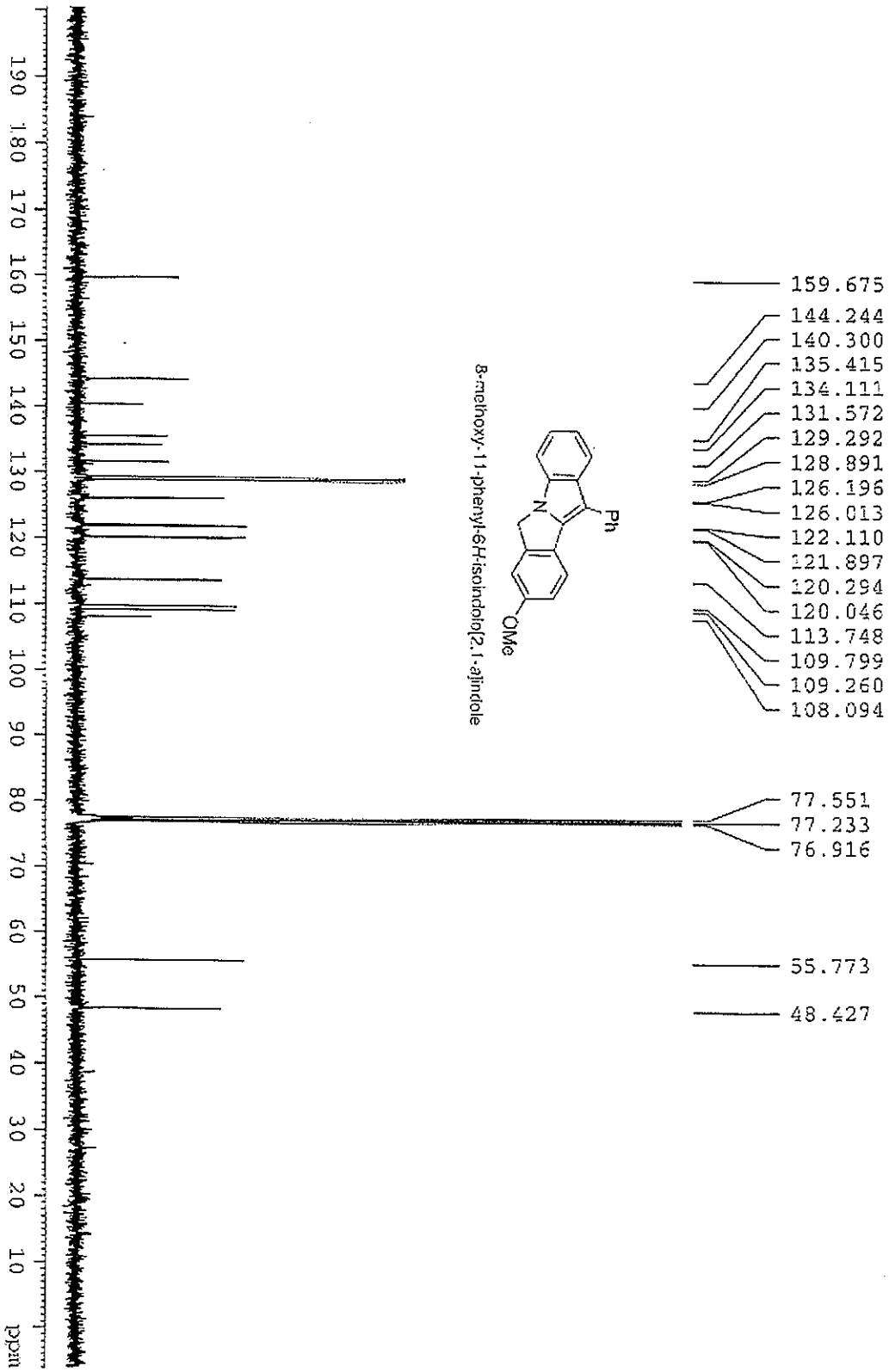

6-methylbenzo[e]acephenanthrylene
H
Me
138.863
138.226
137.451
137.221
135.282
134.092
132.357
130.804
130.232
128.983
128.252
127.603
127.004
126.787
123.215
122.756
121.309
121.254
121.180
119.204
77.402
77.085
76.767
21.886
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

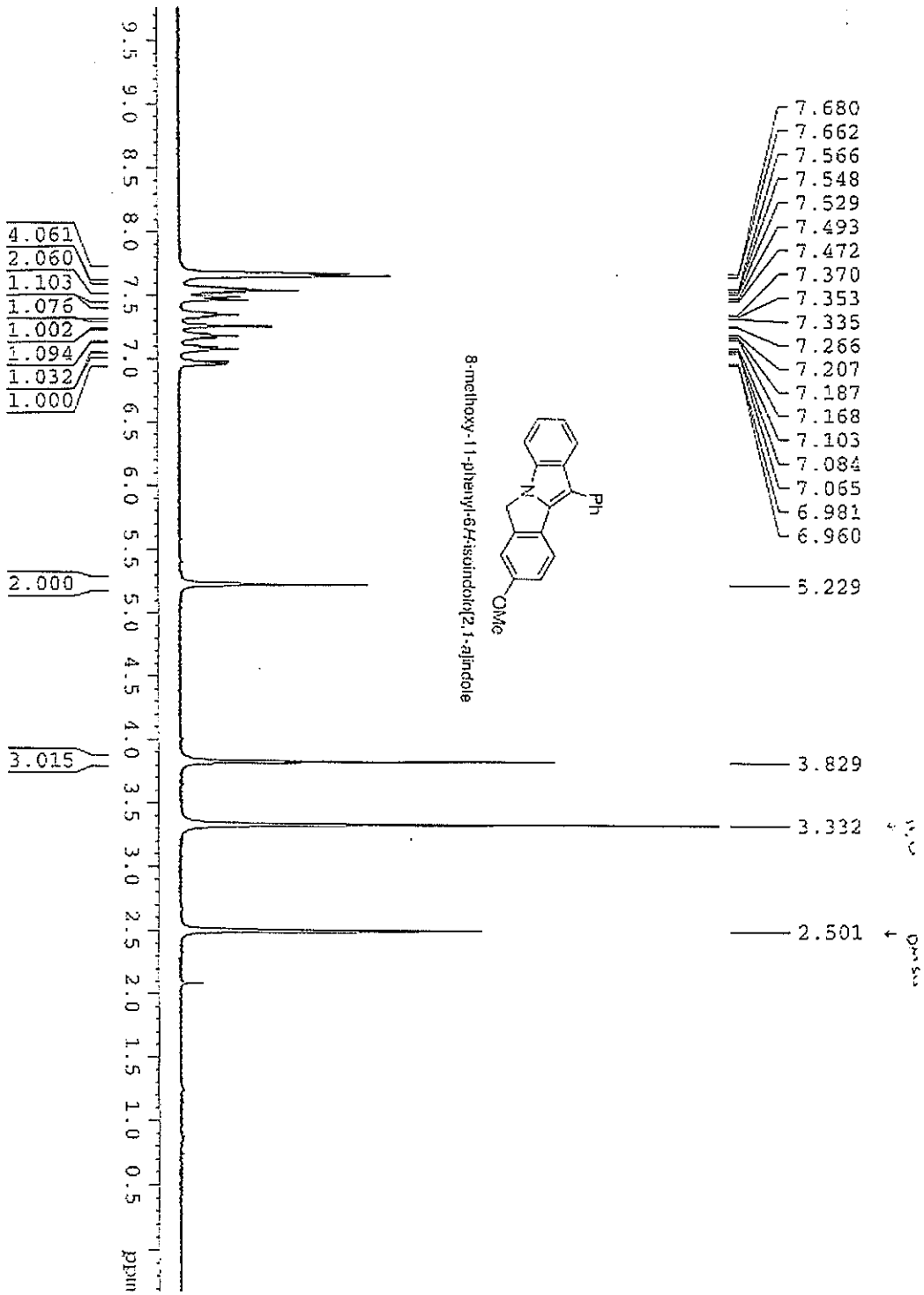

0.951
0.921
1.005
7.176
0.980
0.931
0.942
3.100
9
8
7
6
5
4
3
2
1
0 ppm
7.945
7.902
7.898
7.854
7.826
7.806
7.783
7.778
7.758
7.754
7.735
7.730
7.725
7.707
7.702
7.657
7.653
7.634
7.630
7.627
7.607
7.604
7.459
7.452
7.260
6.944
6.937
6.917
6.909
3.949
1.453
0.027
10-methoxydibenzo[e,l]acephenanthrylene
H
OMe

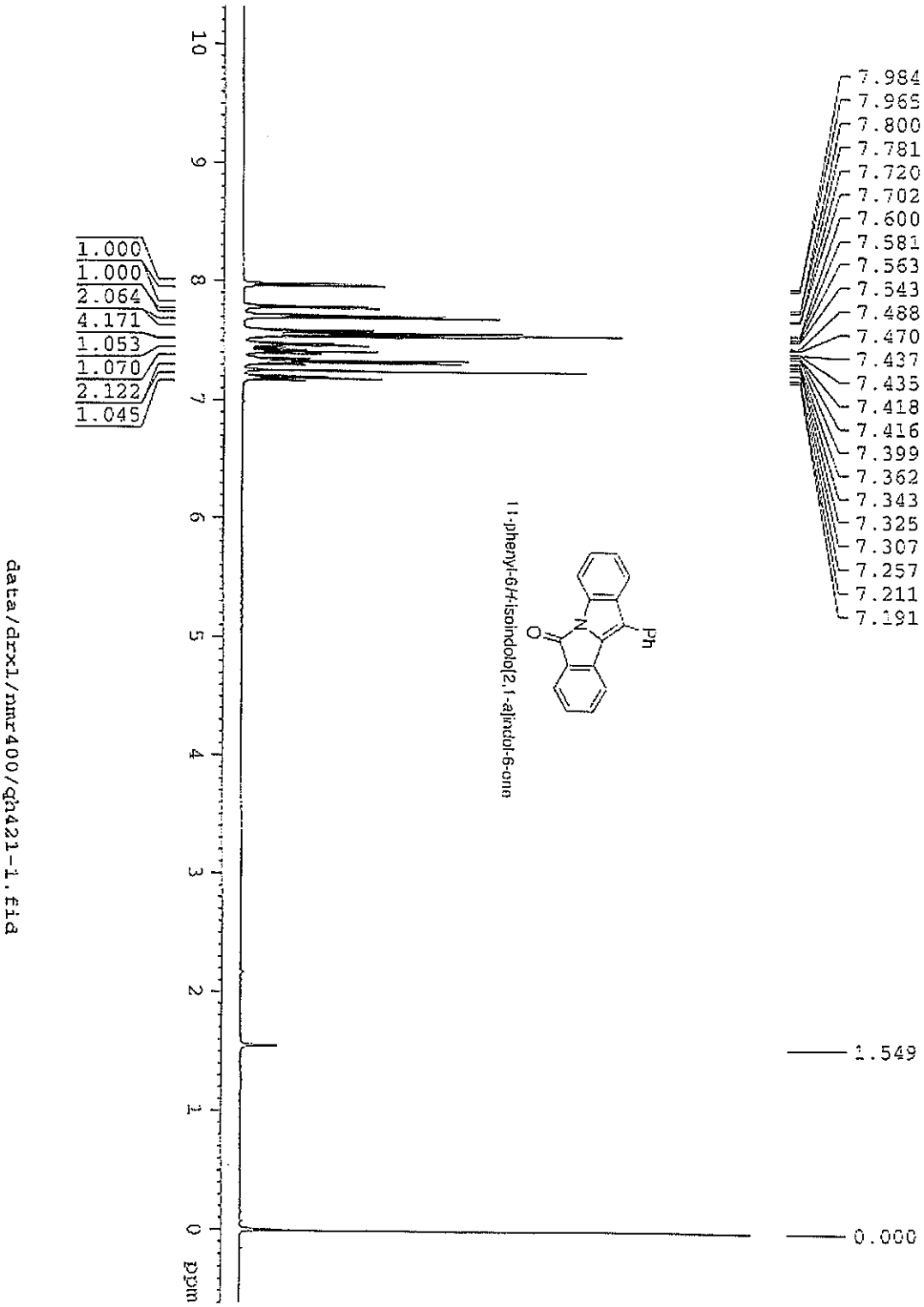

160.611
142.587
137.411
136.125
133.840
133.799
131.499
131.457
128.957
128.639
128.571
128.389
128.268
127.800
127.572
127.331
126.784
126.017
122.815
122.774
121.030
119.557
113.374
107.426
77.677
77.253
76.830
55.898
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
10-methoxydibenzo[e,fl]acephenanthrylene
H
OMe

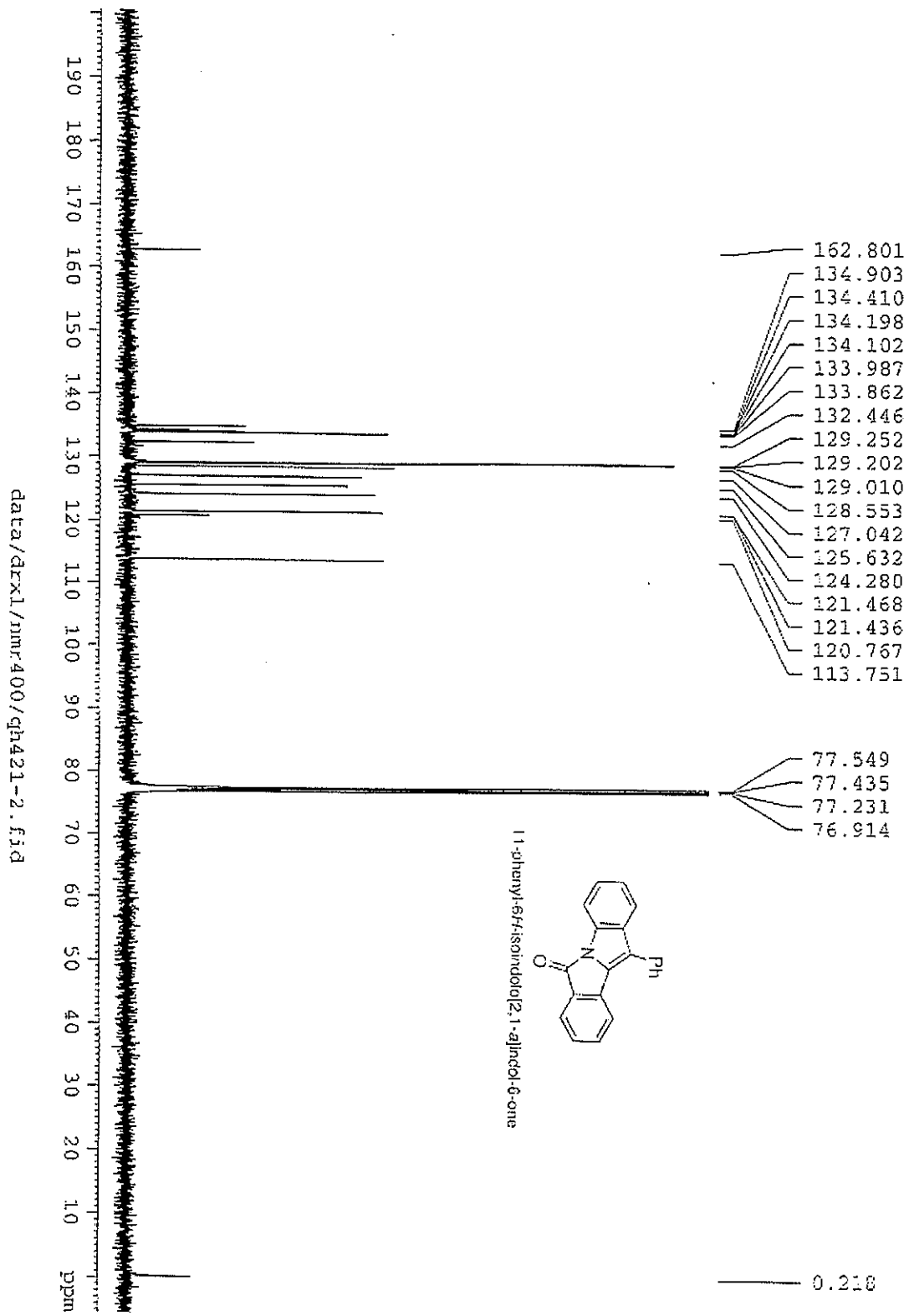

11-phenyl-6H-isoindolo[2,1-a]indole
Ph
N
7.759
7.746
7.738
7.699
7.681
7.649
7.641
7.629
7.582
7.563
7.543
7.533
7.512
7.394
7.379
7.360
7.245
7.227
7.208
7.130
7.111
7.093
5.268
3.340
2.500
2.083
1.113
3.047
1.054
3.152
3.063
1.029
1.003
2.000
10
9
8
7
6
5
4
3
2
1
0
ppm

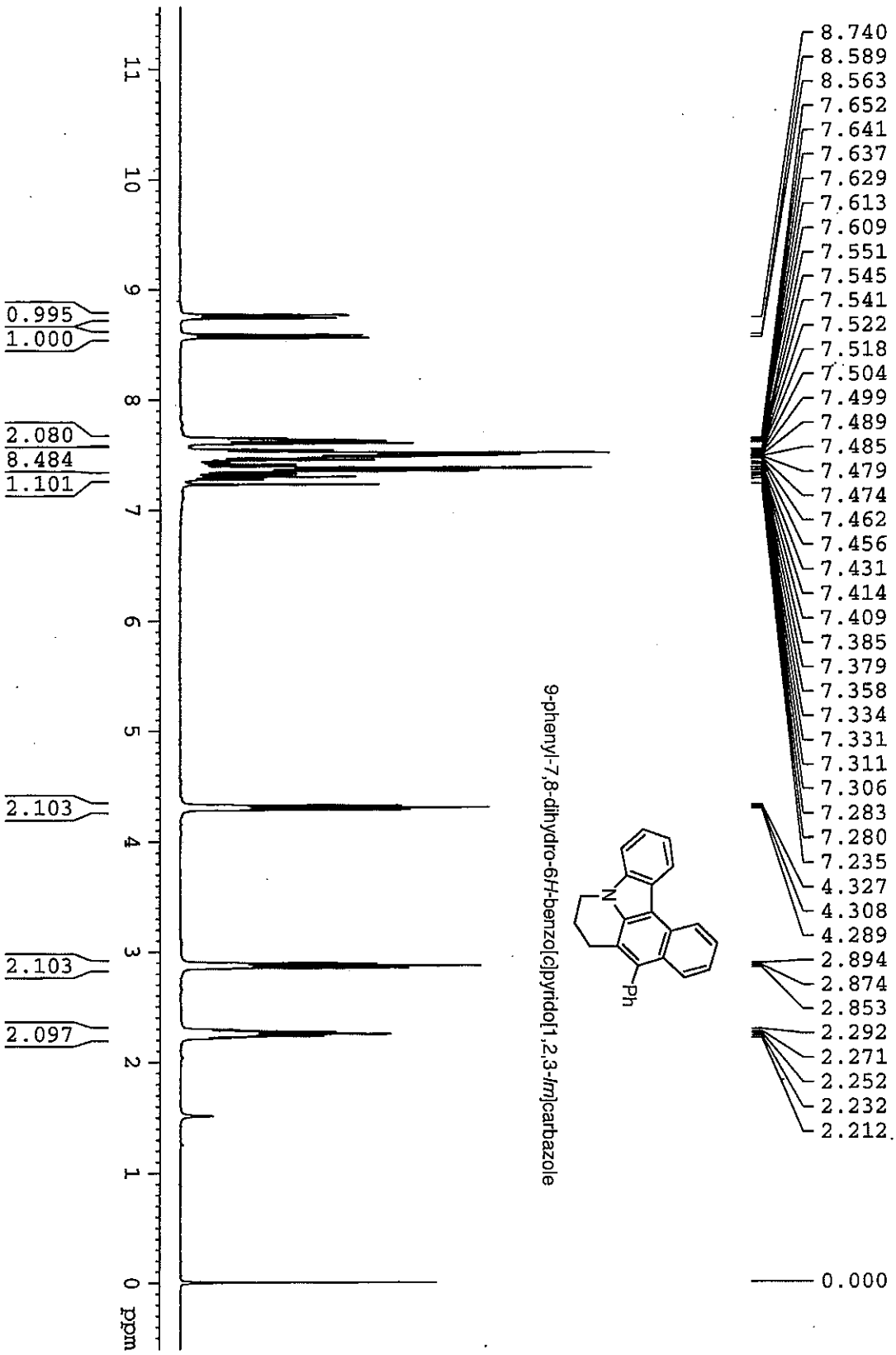

142.654
139.306
134.378
133.508
131.934
130.357
128.941
128.696
127.990
127.583
126.235
124.246
121.962
120.180
120.028
119.543
110.245
108.028
48.237
40.140
39.931
39.723
39.514
39.306
39.097
38.888
11-phenyl-6H-isoindolo[2,1-a]indole
Ph
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

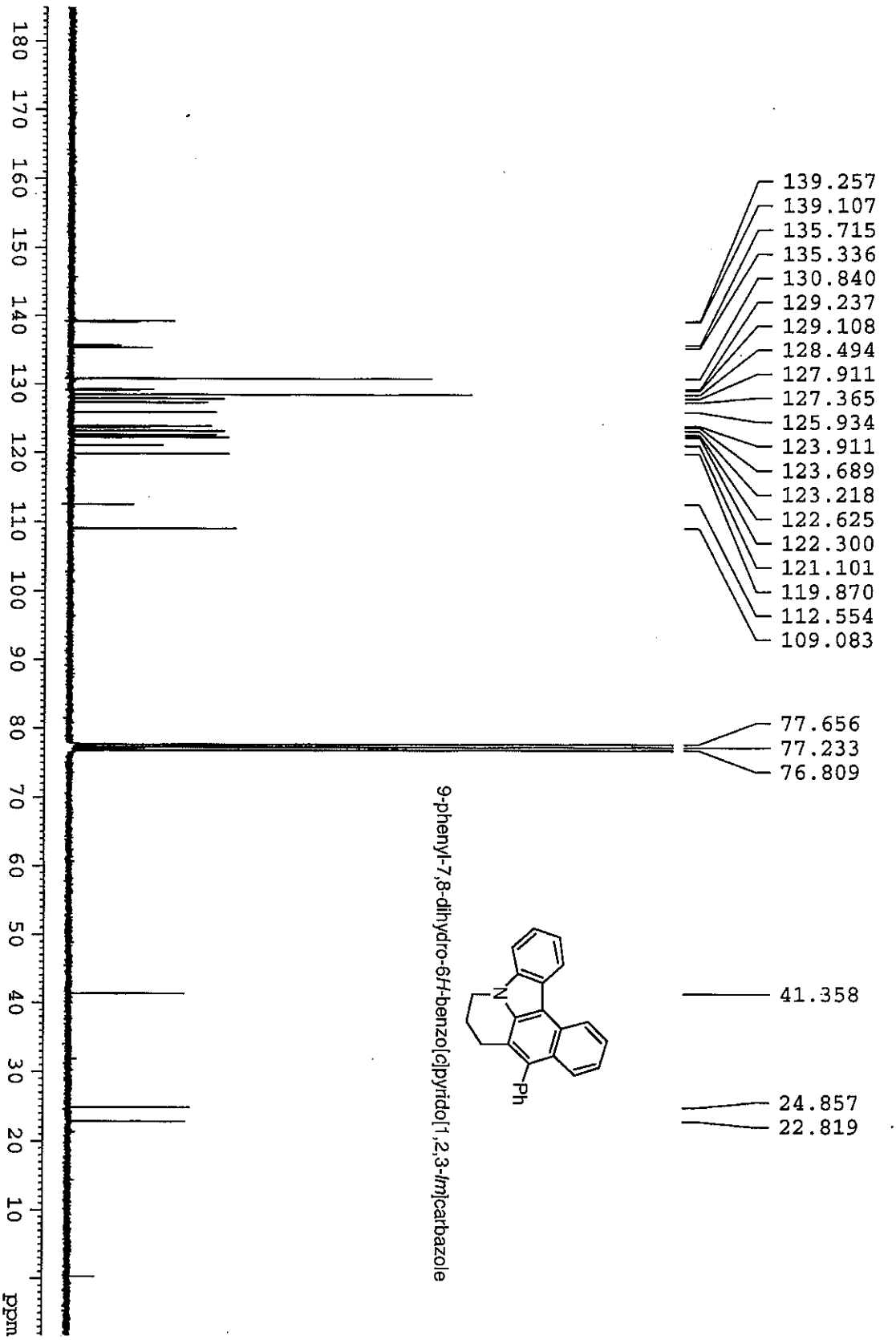

159.675
144.244
140.300
135.415
134.111
131.572
129.292
128.891
126.196
126.013
122.110
121.897
120.294
120.046
113.748
109.799
109.260
108.094
77.551
77.233
76.916
55.773
48.427
8-methoxy-11-phenyl-6H-isoindolo[2,1-a]indole
Ph
OMe
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/gh416-2.fid

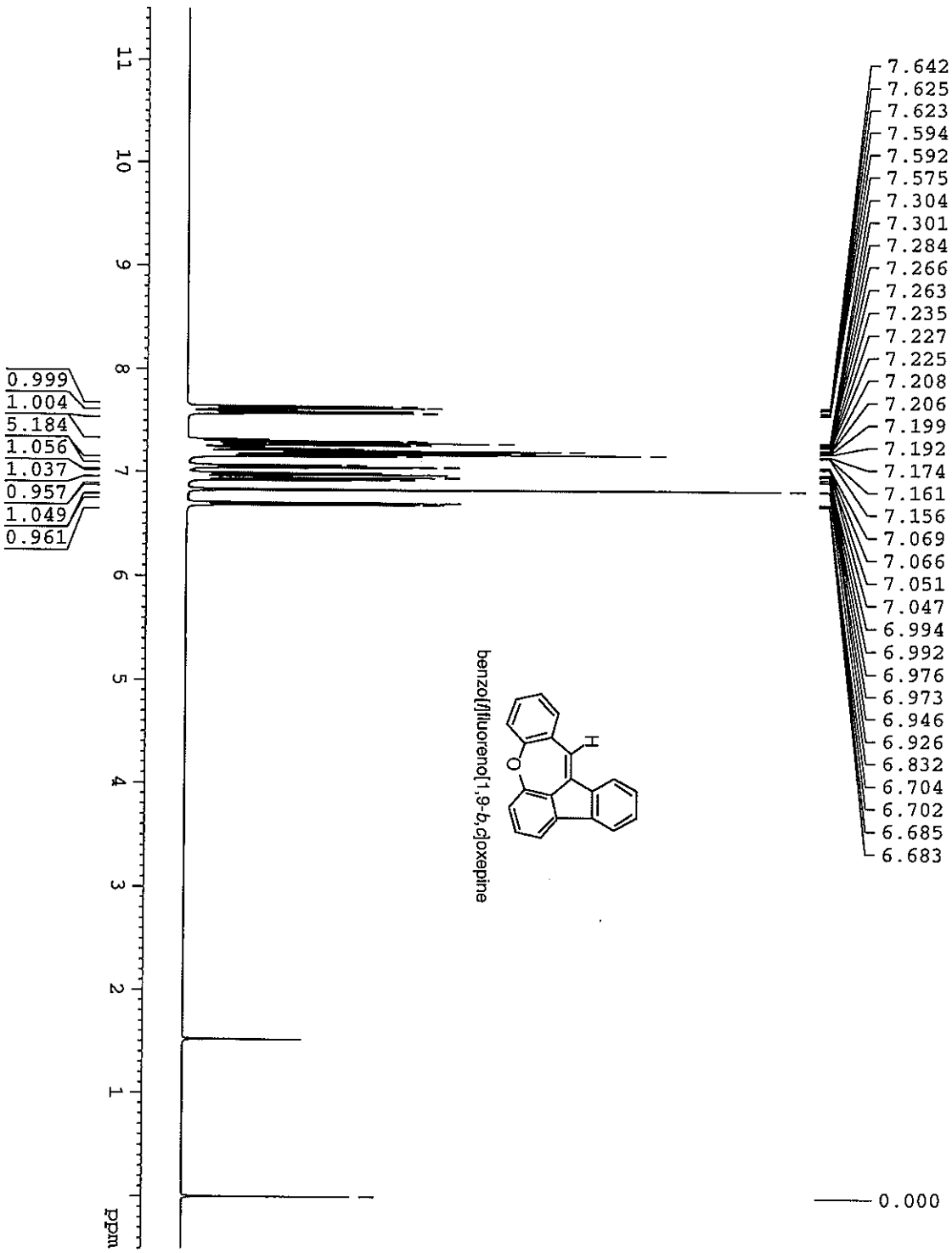

7.680
7.662
7.566
7.548
7.529
7.493
7.472
7.370
7.353
7.335
7.266
7.207
7.187
7.168
7.103
7.084
7.065
6.981
6.960
5.229
3.829
3.332
2.501
4.061
2.060
1.103
1.076
1.002
1.094
1.032
1.000
2.000
3.015
8-methoxy-11-phenyl-6H-isoindolo[2,1-a]indole
Ph
OMe
N
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
data/drx1/nmr400/gb416-5.fid

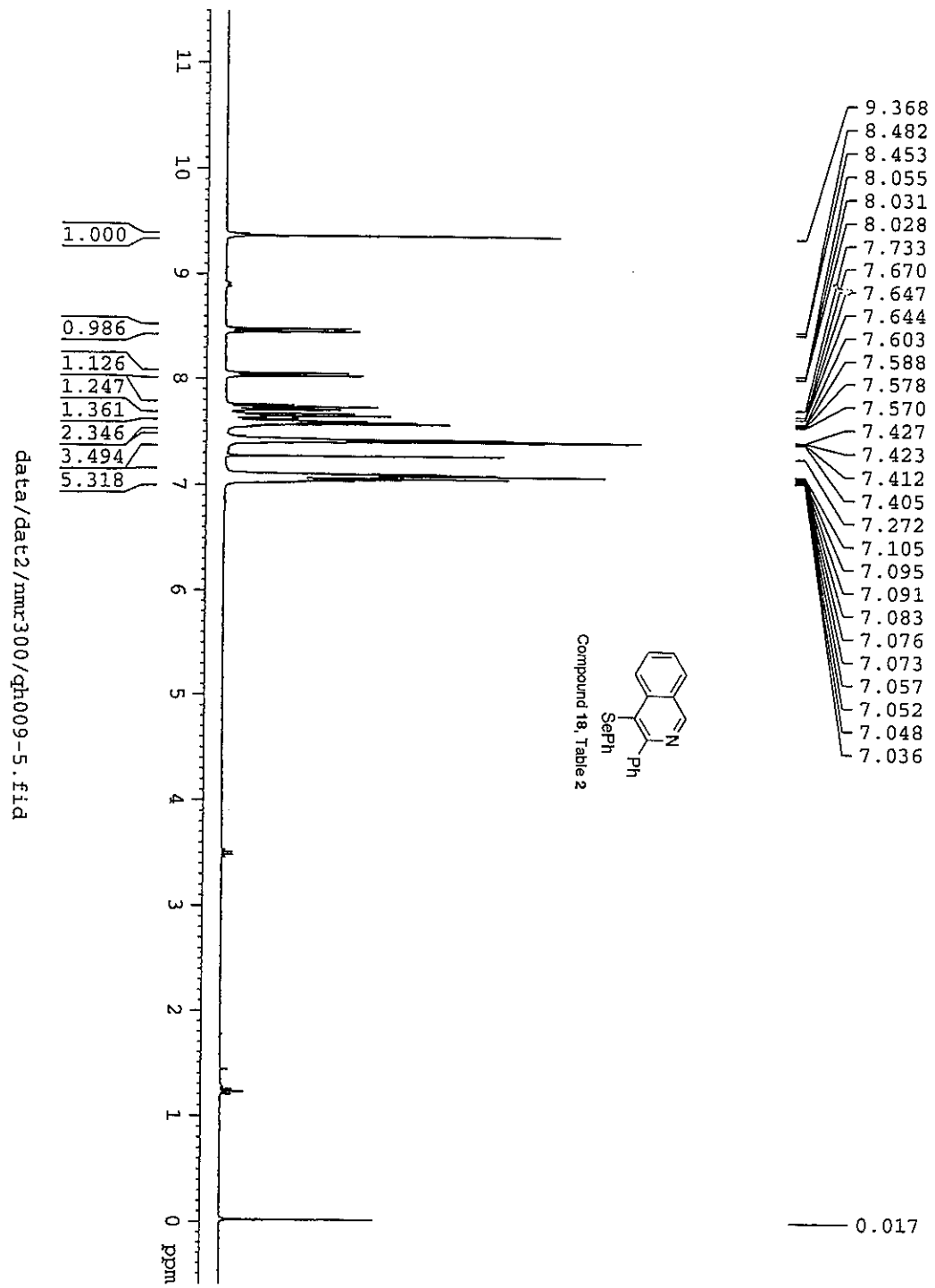

7.984
7.965
7.800
7.781
7.720
7.702
7.600
7.581
7.563
7.543
7.488
7.470
7.437
7.435
7.418
7.416
7.399
7.362
7.343
7.325
7.307
7.257
7.211
7.191
1.549
0.000
1.000
1.000
2.064
4.171
1.053
1.070
2.122
1.045
ppm
11-phenyl-6H-isoindolo[2,1-a]indol-6-one
Ph
O
N
data/drxl/nmr400/qh421-1.fid

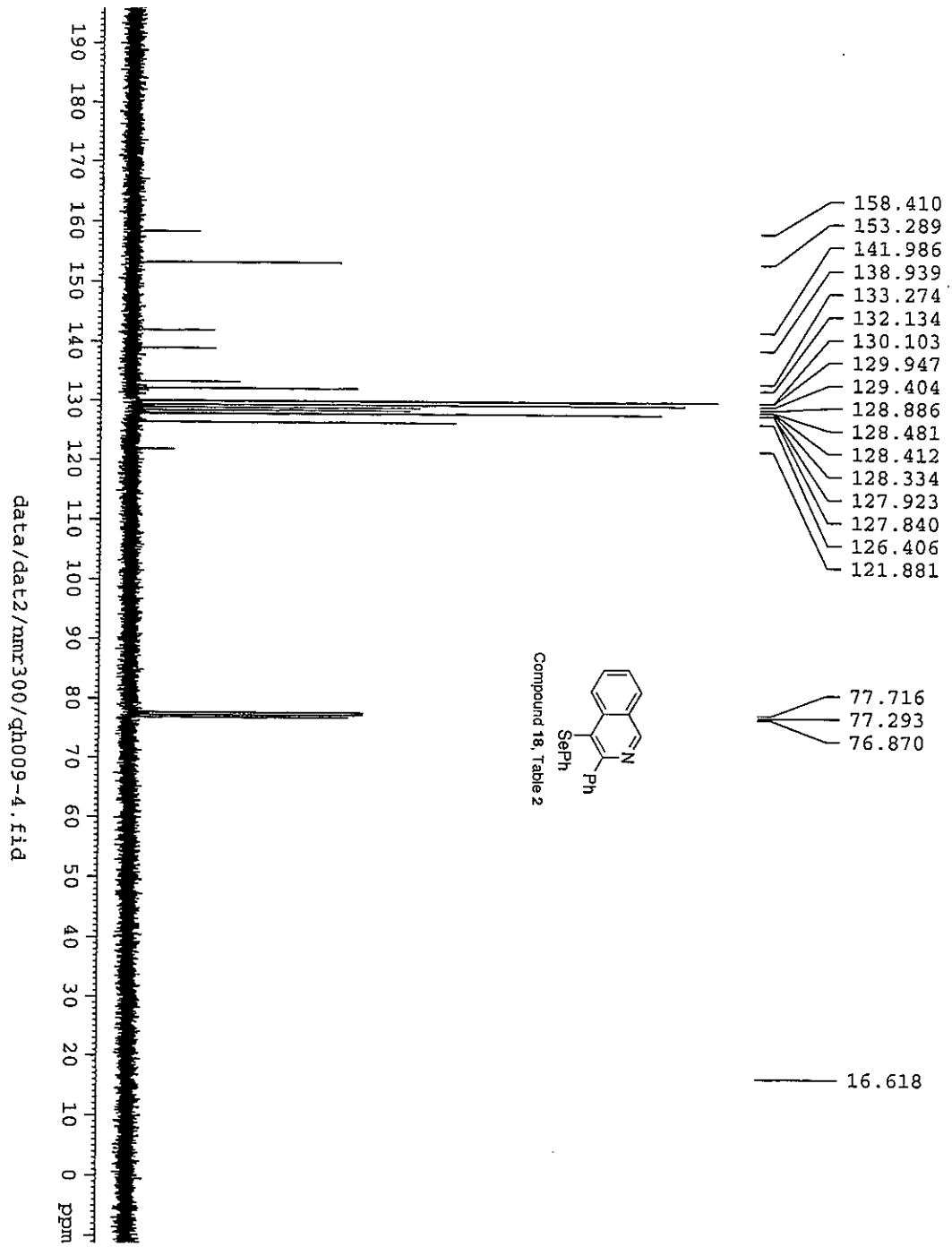

162.801
134.903
134.410
134.198
134.102
133.987
133.862
132.446
129.252
129.202
129.010
128.553
127.042
125.632
124.280
121.468
121.436
120.767
113.751
77.549
77.435
77.231
76.914
0.218
11-phenyl-6H-isoindolo[2,1-a]indol-6-one
O
N
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dcxl/nmr400/qh421-2.fid

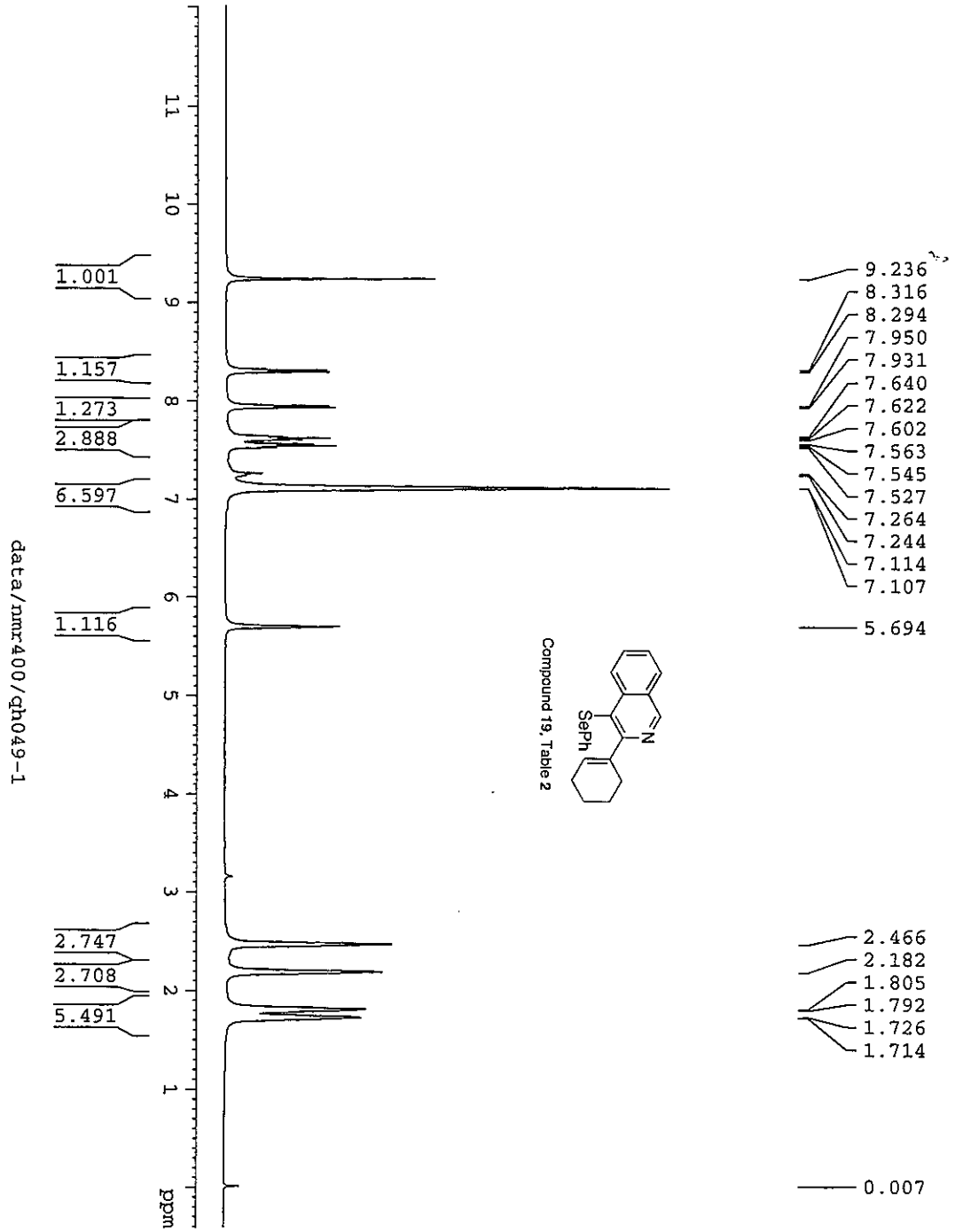

8.740
8.589
8.563
7.652
7.641
7.637
7.629
7.613
7.609
7.551
7.545
7.541
7.522
7.518
7.504
7.499
7.489
7.485
7.479
7.474
7.462
7.456
7.431
7.414
7.409
7.385
7.379
7.358
7.334
7.331
7.311
7.306
7.283
7.280
7.235
4.327
4.308
4.289
2.894
2.874
2.853
2.292
2.271
2.252
2.232
2.212
0.000
0.995
1.000
2.080
8.484
1.101
2.103
2.103
2.097
ppm
11
10
9
8
7
6
5
4
3
2
1
0
N
Ph
9-phenyl-7,8-dihydro-6H-benzo[c]pyrido[1,2,3-lm]carbazole

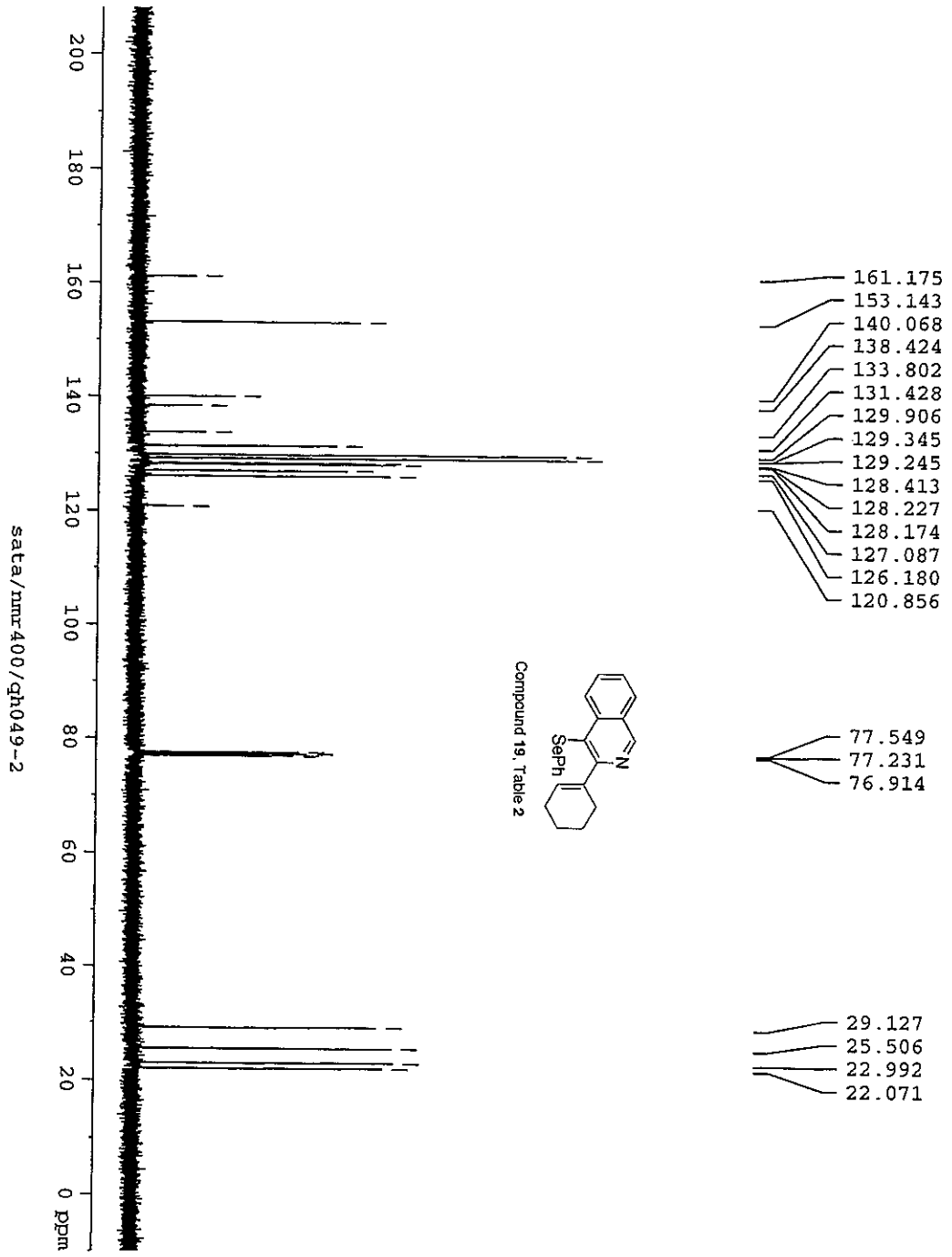

139.257
139.107
135.715
135.336
130.840
129.237
129.108
128.494
127.911
127.365
125.934
123.911
123.689
123.218
122.625
122.300
121.101
119.870
112.554
109.083
77.656
77.233
76.809
41.358
24.857
22.819
9-phenyl-7,8-dihydro-6H-benzo[c]pyrido[1,2,3-lm]carbazole
N
Ph
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

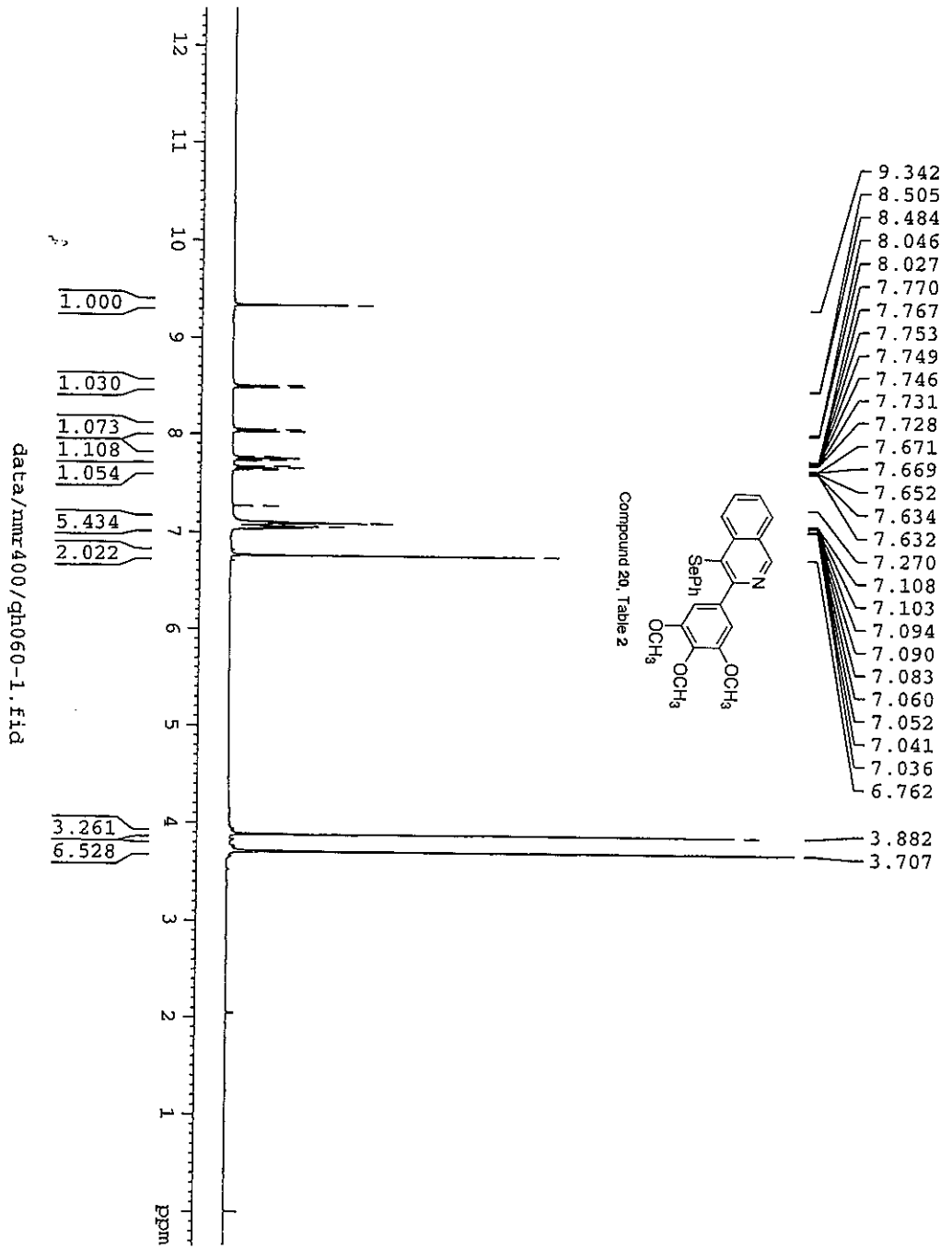

7.642
7.625
7.623
7.594
7.592
7.575
7.304
7.301
7.284
7.266
7.263
7.235
7.227
7.225
7.208
7.206
7.199
7.192
7.174
7.161
7.156
7.069
7.066
7.051
7.047
6.994
6.992
6.976
6.973
6.946
6.926
6.832
6.704
6.702
6.685
6.683
0.999
1.004
5.184
1.056
1.037
0.957
1.049
0.961
0.000
benzo[j]fluoreno[1,9-b,c]oxepine
H
O
ppm

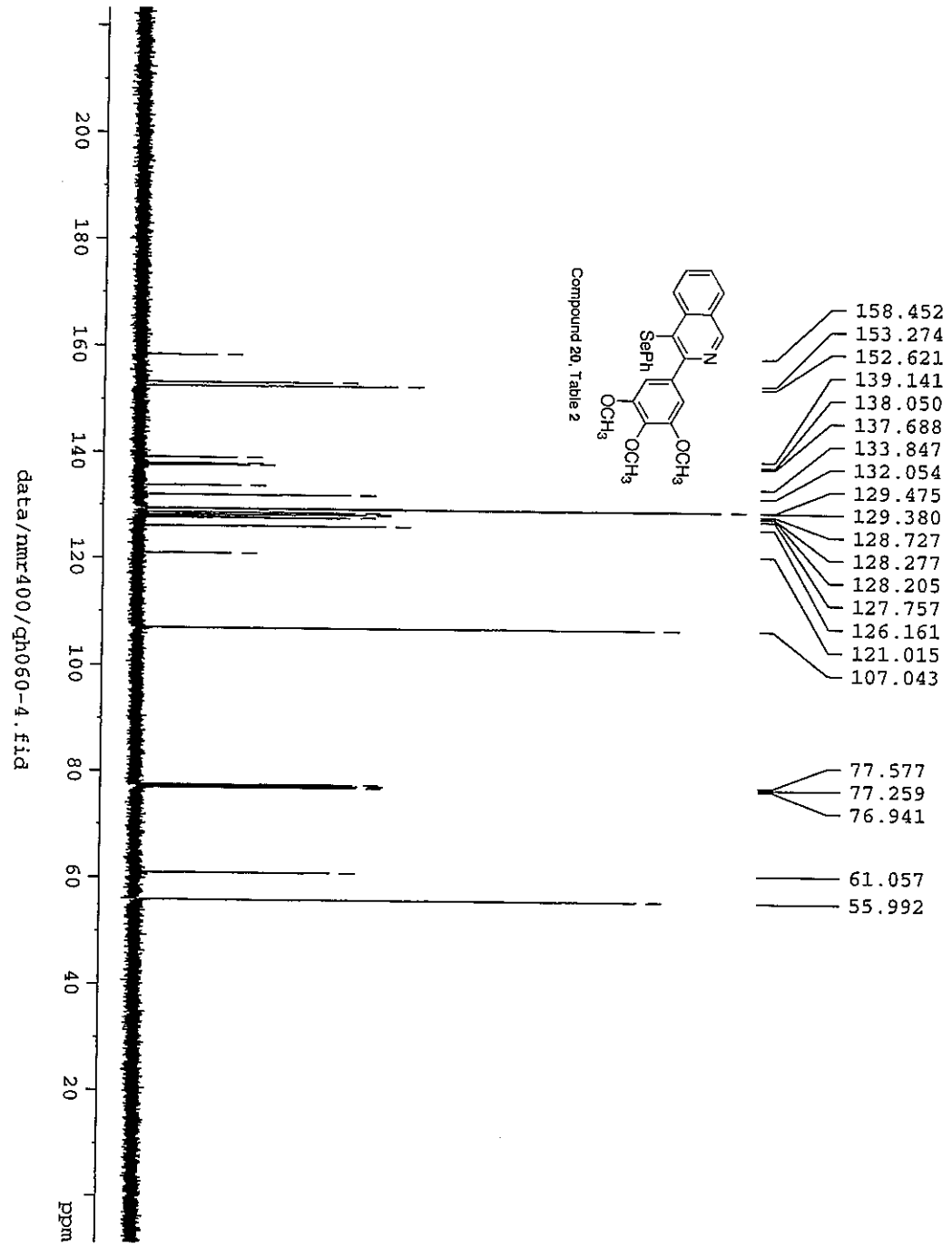

9.368
8.482
8.453
8.055
8.031
8.028
7.733
7.670
7.647
7.644
7.603
7.588
7.578
7.570
7.427
7.423
7.412
7.405
7.272
7.105
7.095
7.091
7.083
7.076
7.073
7.057
7.052
7.048
7.036
1.000
0.986
1.126
1.247
1.361
2.346
3.494
5.318
SePh
Ph
N
Compound 18, Table 2
0.017
ppm
data/dat2/nmr300/qh009-5.fid

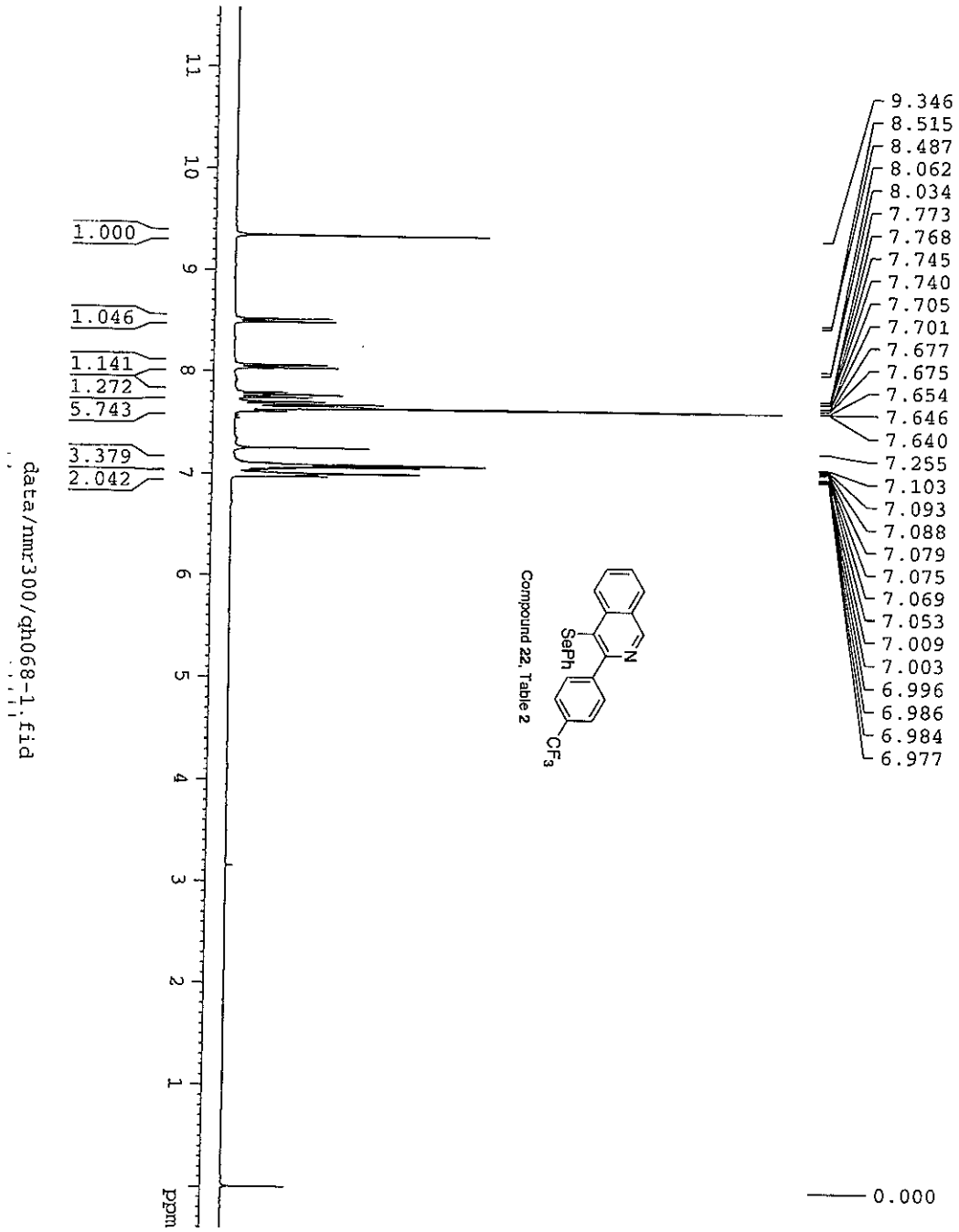

158.410
153.289
141.986
138.939
133.274
132.134
130.103
129.947
129.404
128.886
128.481
128.412
128.334
127.923
127.840
126.406
121.881
77.716
77.293
76.870
16.618
SePh
Ph
N
Compound 18, Table 2
data/dat2/nmr300/qh009-4.fid
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

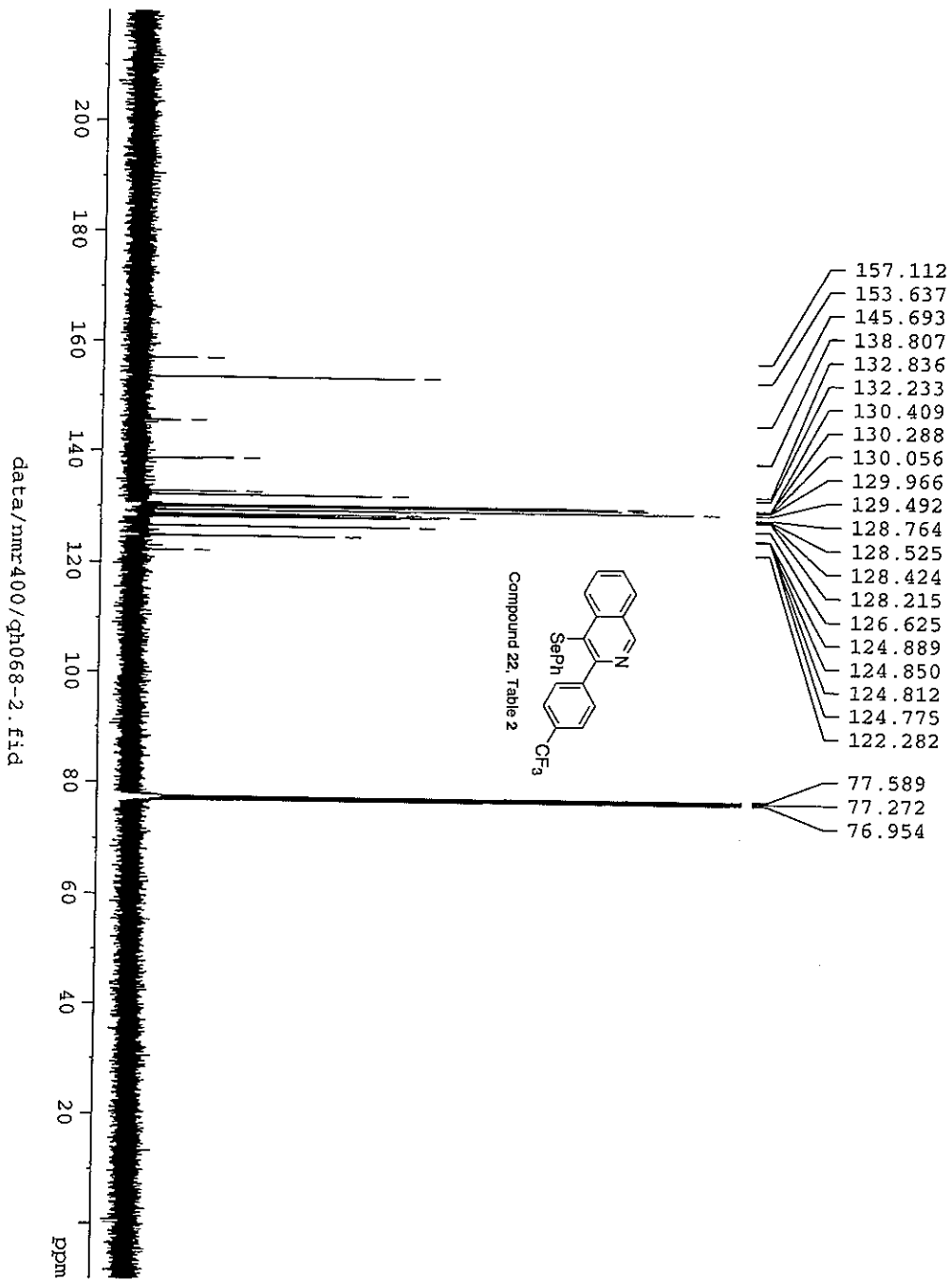

data/nmr400/qh049-1
Compound 19, Table 2
SePh
N
1.001
1.157
1.273
2.888
6.597
1.116
2.747
2.708
5.491
9.236
8.316
8.294
7.950
7.931
7.640
7.622
7.602
7.563
7.545
7.527
7.264
7.244
7.114
7.107
5.694
2.466
2.182
1.805
1.792
1.726
1.714
0.007
ppm

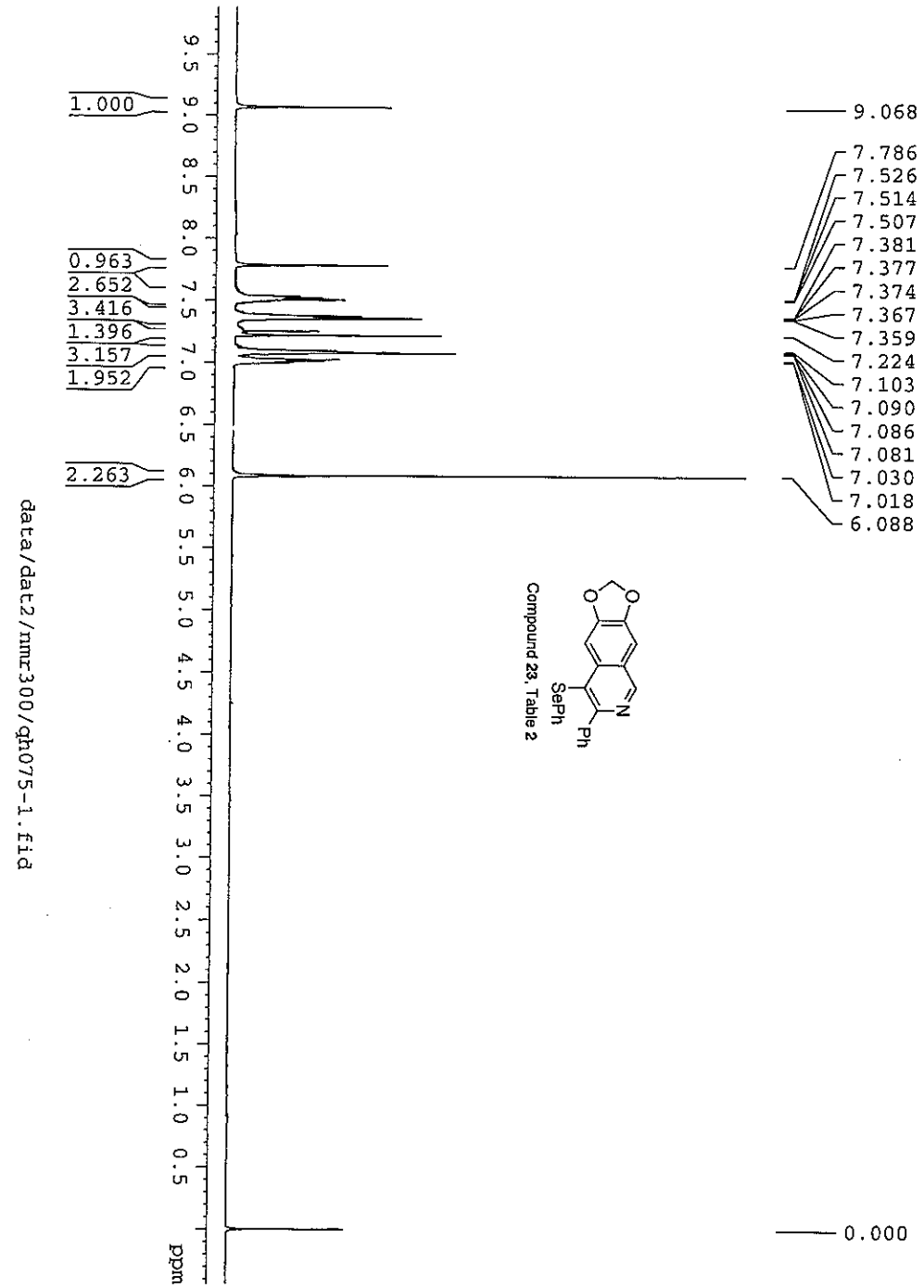

sata/nmr400/qh049-2
200
180
160
140
120
100
80
60
40
20
0 ppm
161.175
153.143
140.068
138.424
133.802
131.428
129.906
129.345
129.245
128.413
128.227
128.174
127.087
126.180
120.856
77.549
77.231
76.914
29.127
25.506
22.992
22.071
SePh
N
Compound 19, Table 2

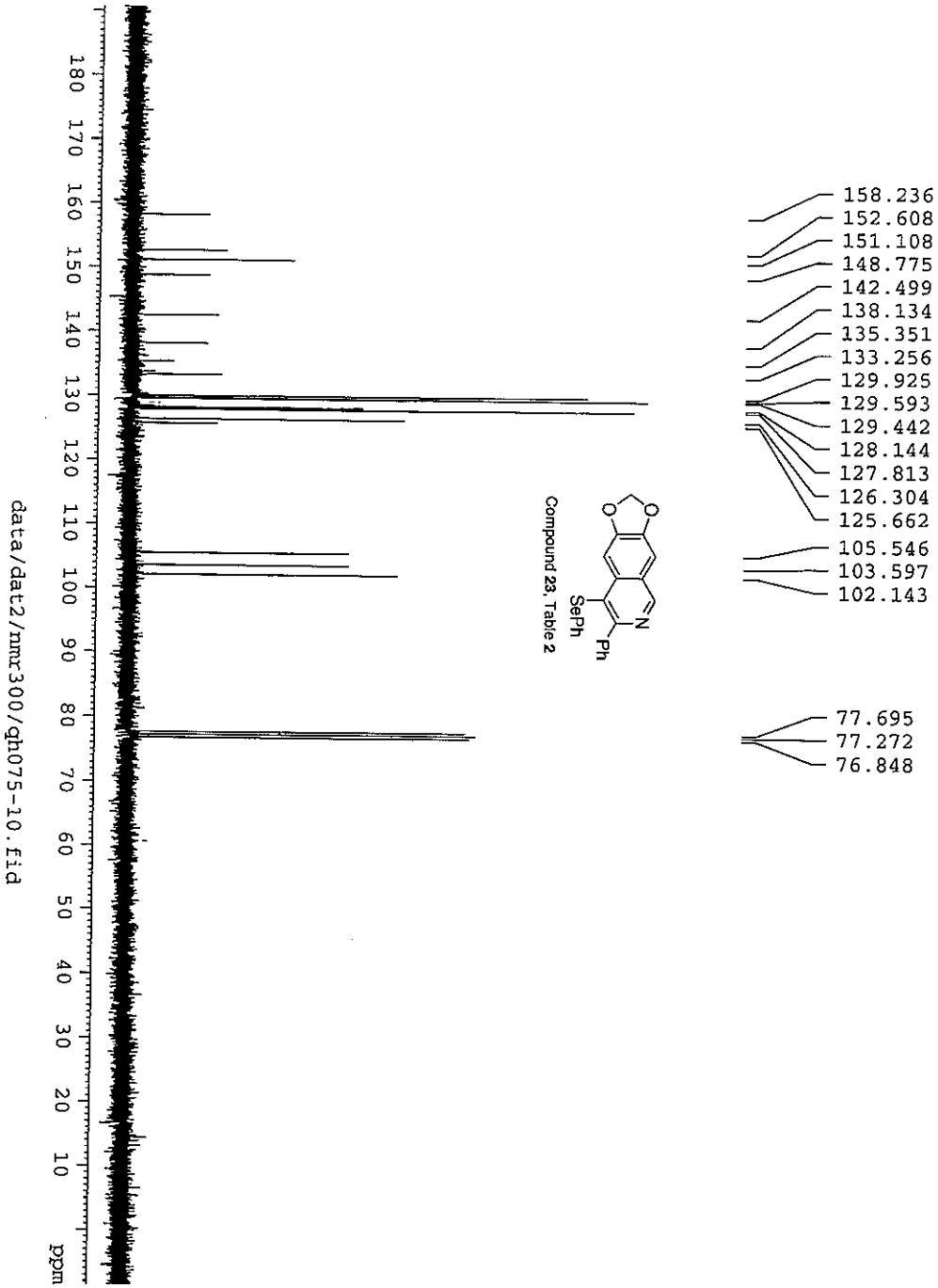

9.342
8.505
8.484
8.046
8.027
7.770
7.767
7.753
7.749
7.746
7.731
7.728
7.671
7.669
7.652
7.634
7.632
7.270
7.108
7.103
7.094
7.090
7.083
7.060
7.052
7.041
7.036
6.762
3.882
3.707
1.000
1.030
1.073
1.108
1.054
5.434
2.022
3.261
6.528
SePh
OCH3
OCH3
OCH3
N
Compound 20, Table 2
data/nmr400/qh060-1.fid
ppm

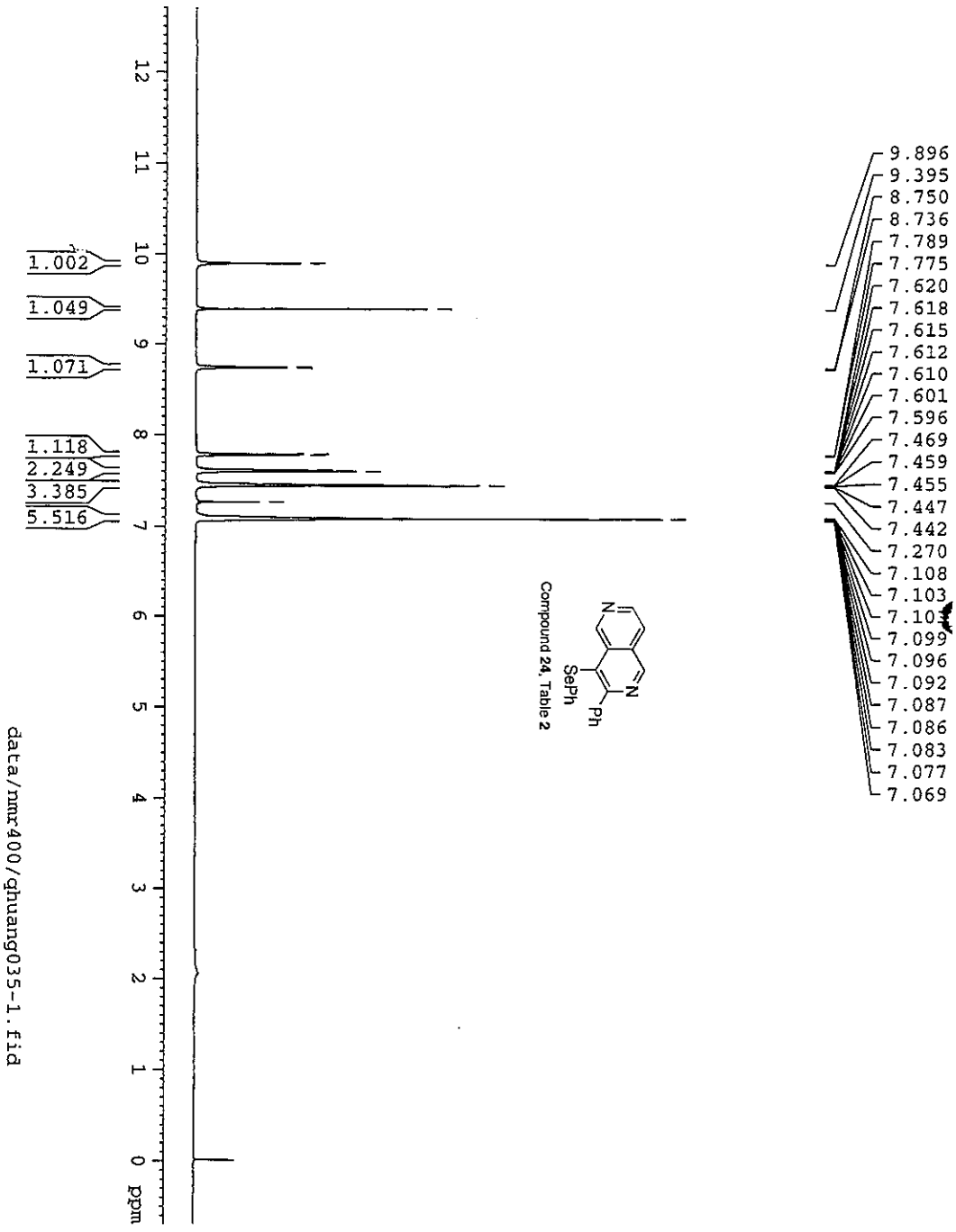

158.452
153.274
152.621
139.141
138.050
137.688
133.847
132.054
129.475
129.380
128.727
128.277
128.205
127.757
126.161
121.015
107.043
77.577
77.259
76.941
61.057
55.992
Compound 20, Table 2
SePh
N
OCH3
OCH3
OCH3
data/nmr400/qh060-4.fid
ppm
200
180
160
140
120
100
80
60
40
20

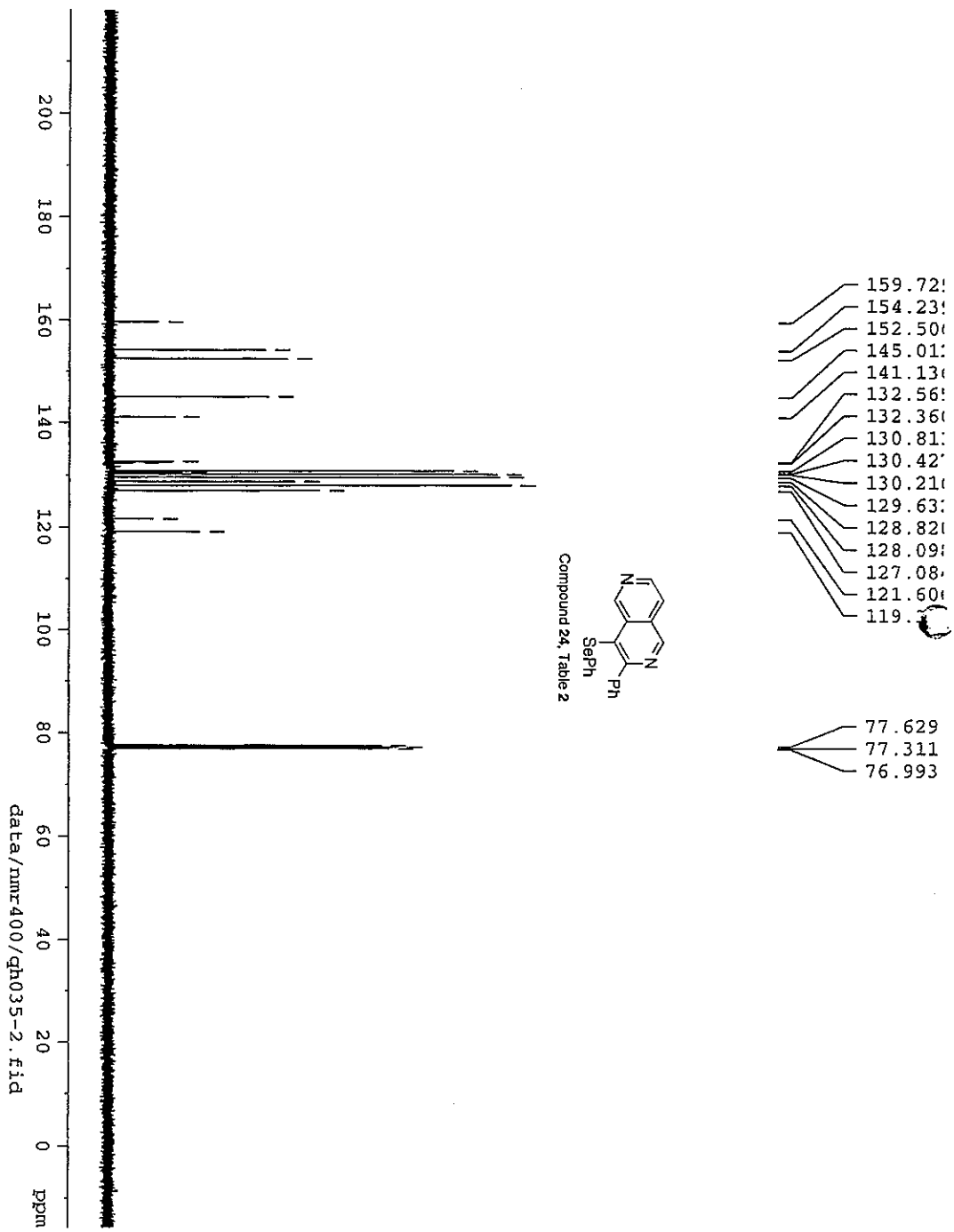

9.346
8.515
8.487
8.062
8.034
7.773
7.768
7.745
7.740
7.705
7.701
7.677
7.675
7.654
7.646
7.640
7.255
7.103
7.093
7.088
7.079
7.075
7.069
7.053
7.009
7.003
6.996
6.986
6.984
6.977
1.000
1.046
1.141
1.272
5.743
3.379
2.042
SePh
N
CF3
Compound 22, Table 2
0.000
ppm
data/nmr300/qh068-1.fid

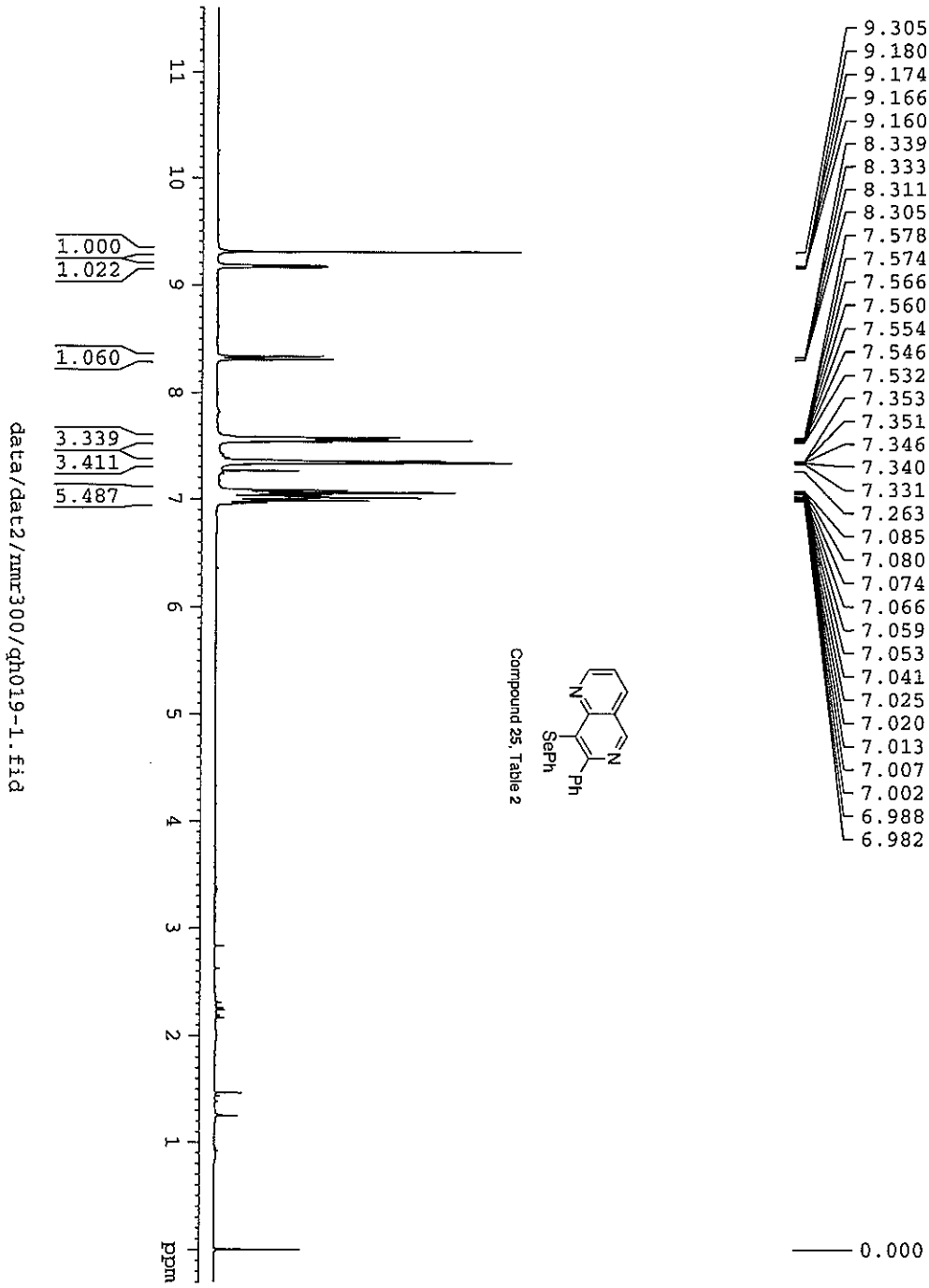

157.112
153.637
145.693
138.807
132.836
132.233
130.409
130.288
130.056
129.966
129.492
128.764
128.525
128.424
128.215
126.625
124.889
124.850
124.812
124.775
122.282
77.589
77.272
76.954
Compound 22, Table 2
SePh
N
CF3
200
180
160
140
120
100
80
60
40
20
ppm
data/nmr400/qh068-2.fid

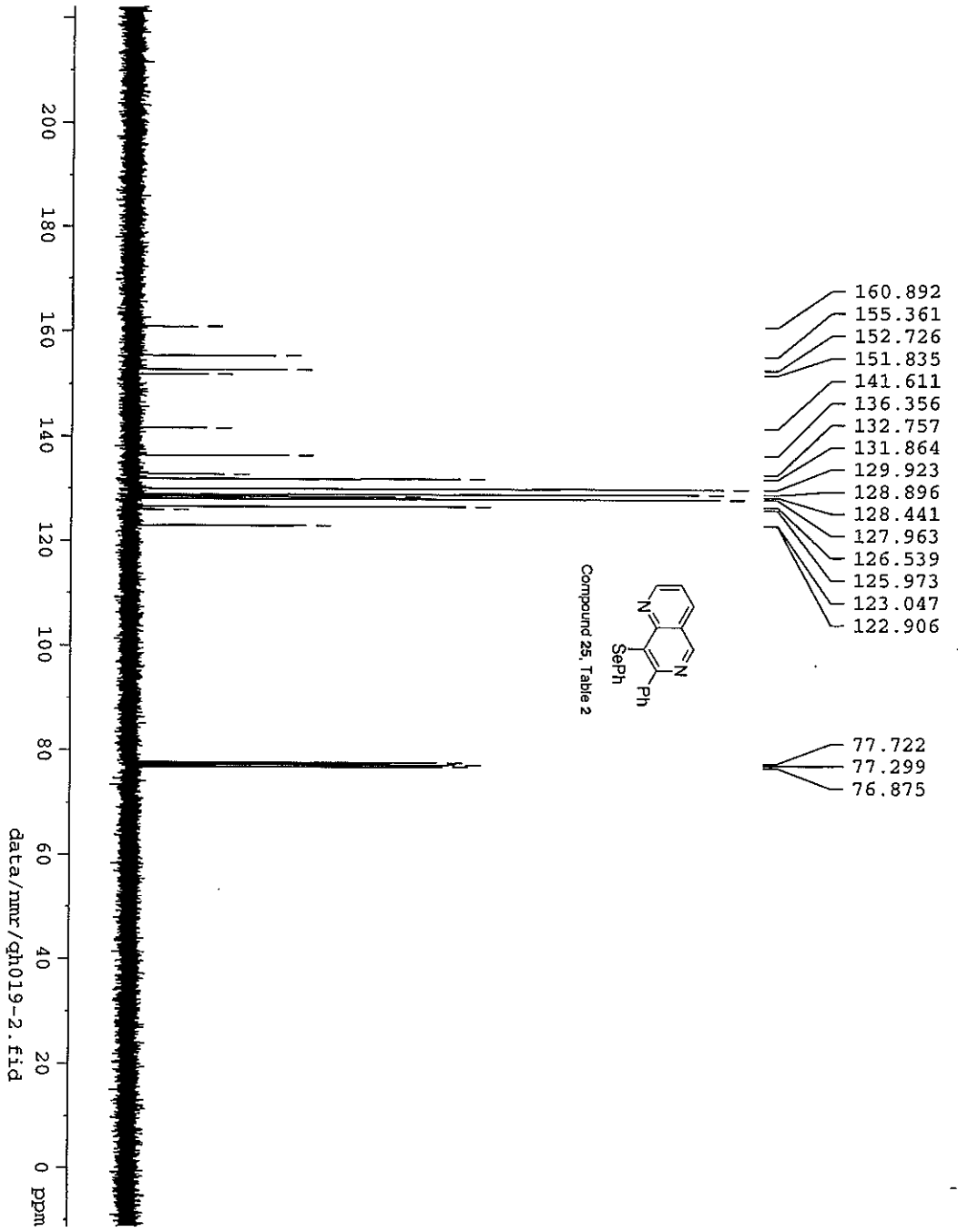

9.068
7.786
7.526
7.514
7.507
7.381
7.377
7.374
7.367
7.359
7.224
7.103
7.090
7.086
7.081
7.030
7.018
6.088
0.000
1.000
0.963
2.652
3.416
1.396
3.157
1.952
2.263
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
SePh
Ph
N
Compound 23, Table 2
data/dat2/nmr300/qh075-1.fid

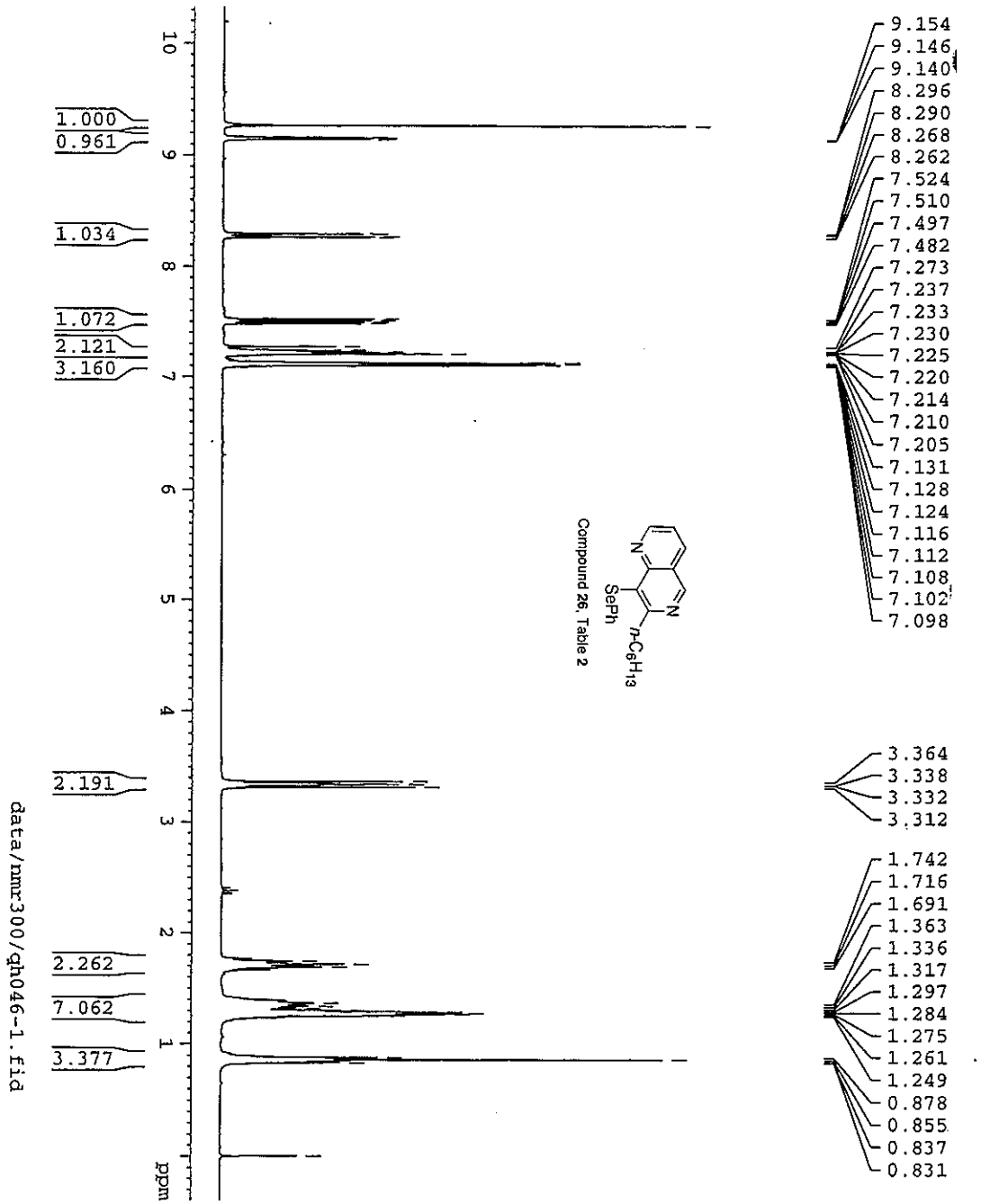

158.236
152.608
151.108
148.775
142.499
138.134
135.351
133.256
129.925
129.593
129.442
128.144
127.813
126.304
125.662
105.546
103.597
102.143
77.695
77.272
76.848
SePh
Ph
N
O
O
Compound 23, Table 2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm
data/dat2/nmr300/qh075-10.fid

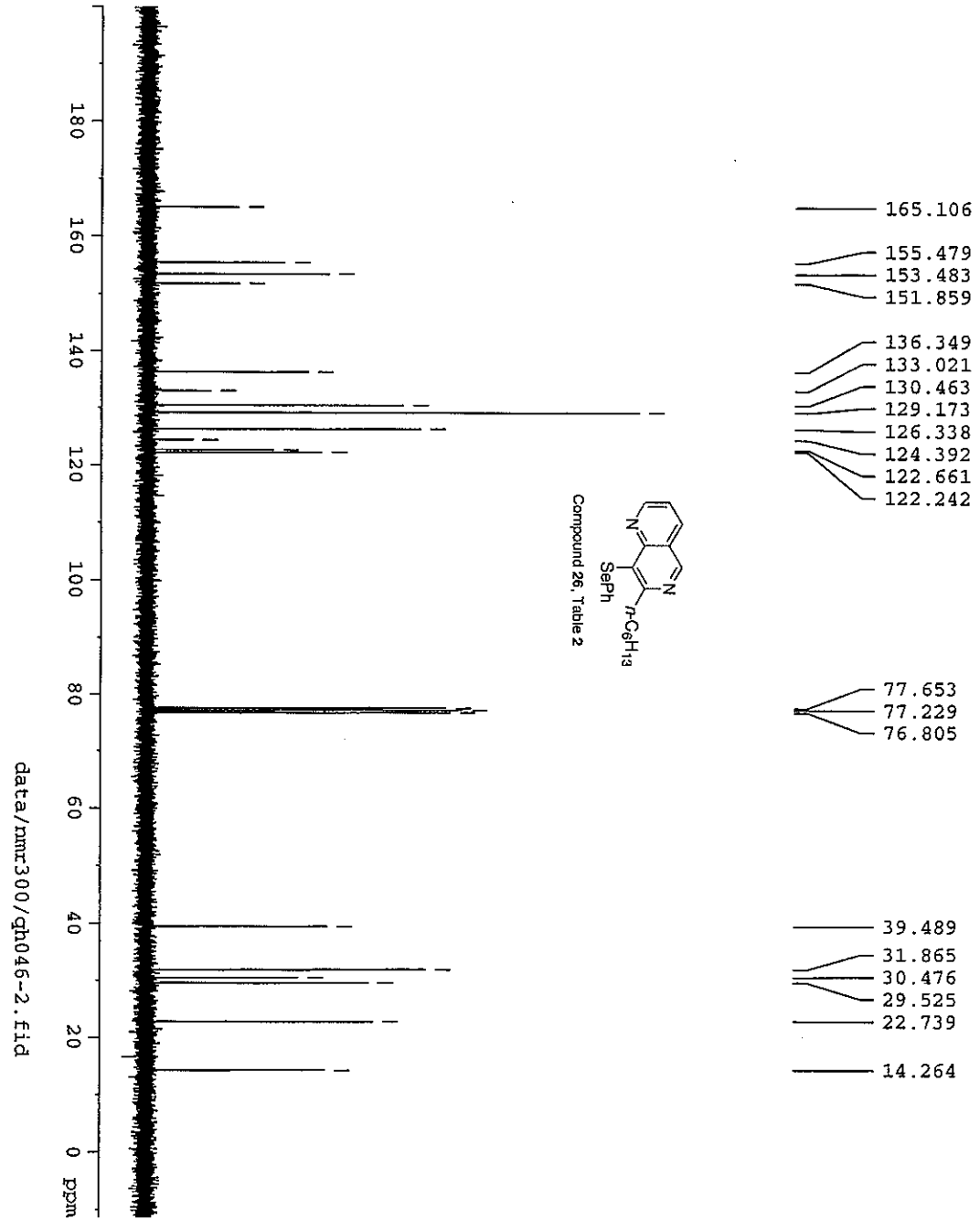

9.896
9.395
8.750
8.736
7.789
7.775
7.620
7.618
7.615
7.612
7.610
7.601
7.596
7.469
7.459
7.455
7.447
7.442
7.270
7.108
7.103
7.099
7.096
7.092
7.087
7.086
7.083
7.077
7.069
1.002
1.049
1.071
1.118
2.249
3.385
5.516
N
N
SePh
Ph
Compound 24, Table 2
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
data/nmr400/qhuang035-1.fid

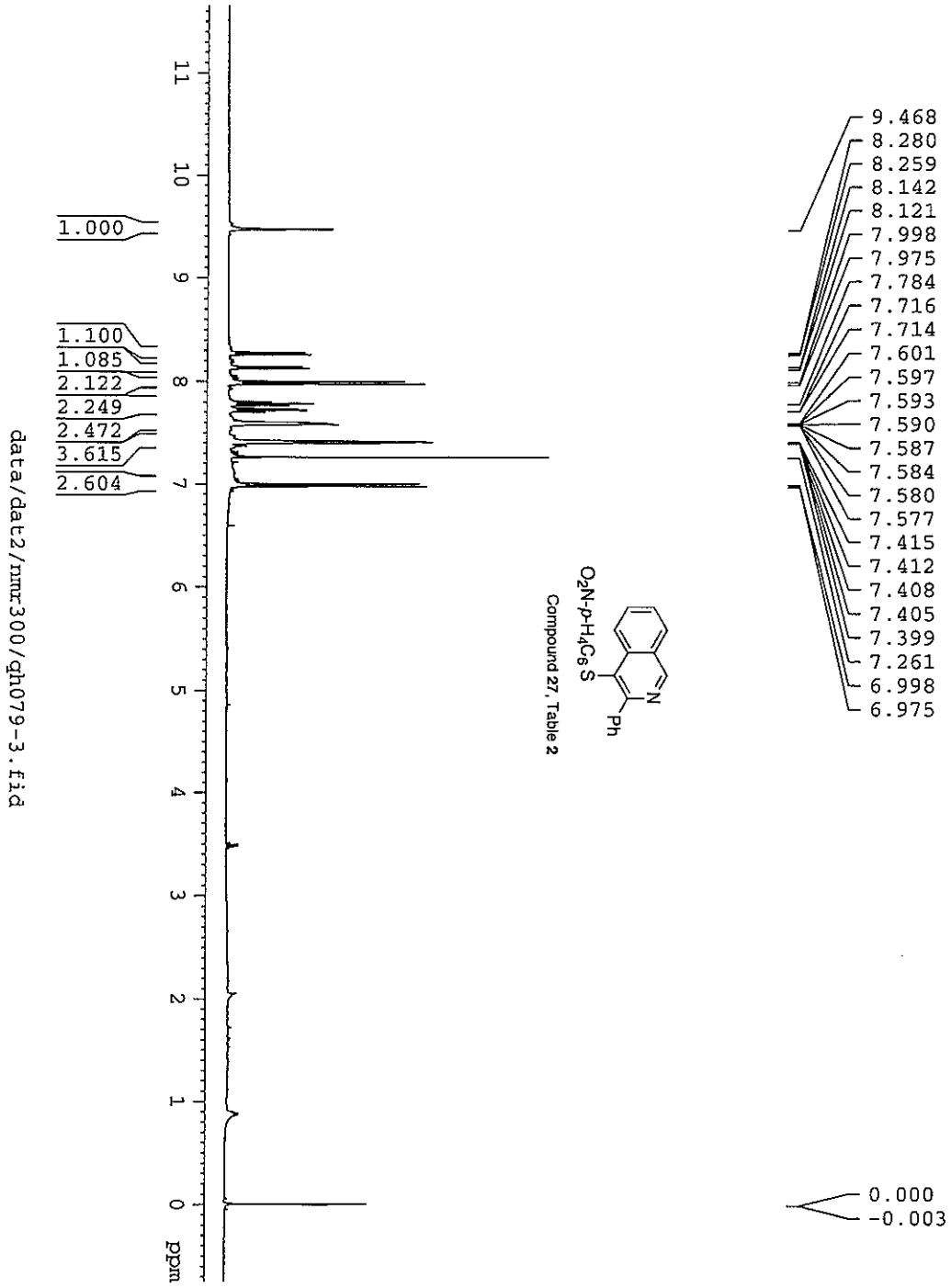

159.72
154.23
152.50
145.01
141.13
132.56
132.36
130.81
130.42
130.21
129.63
128.82
128.09
127.08
121.60
119.
77.629
77.311
76.993
N
N
SePh
Ph
Compound 24, Table 2
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh035-2.fid

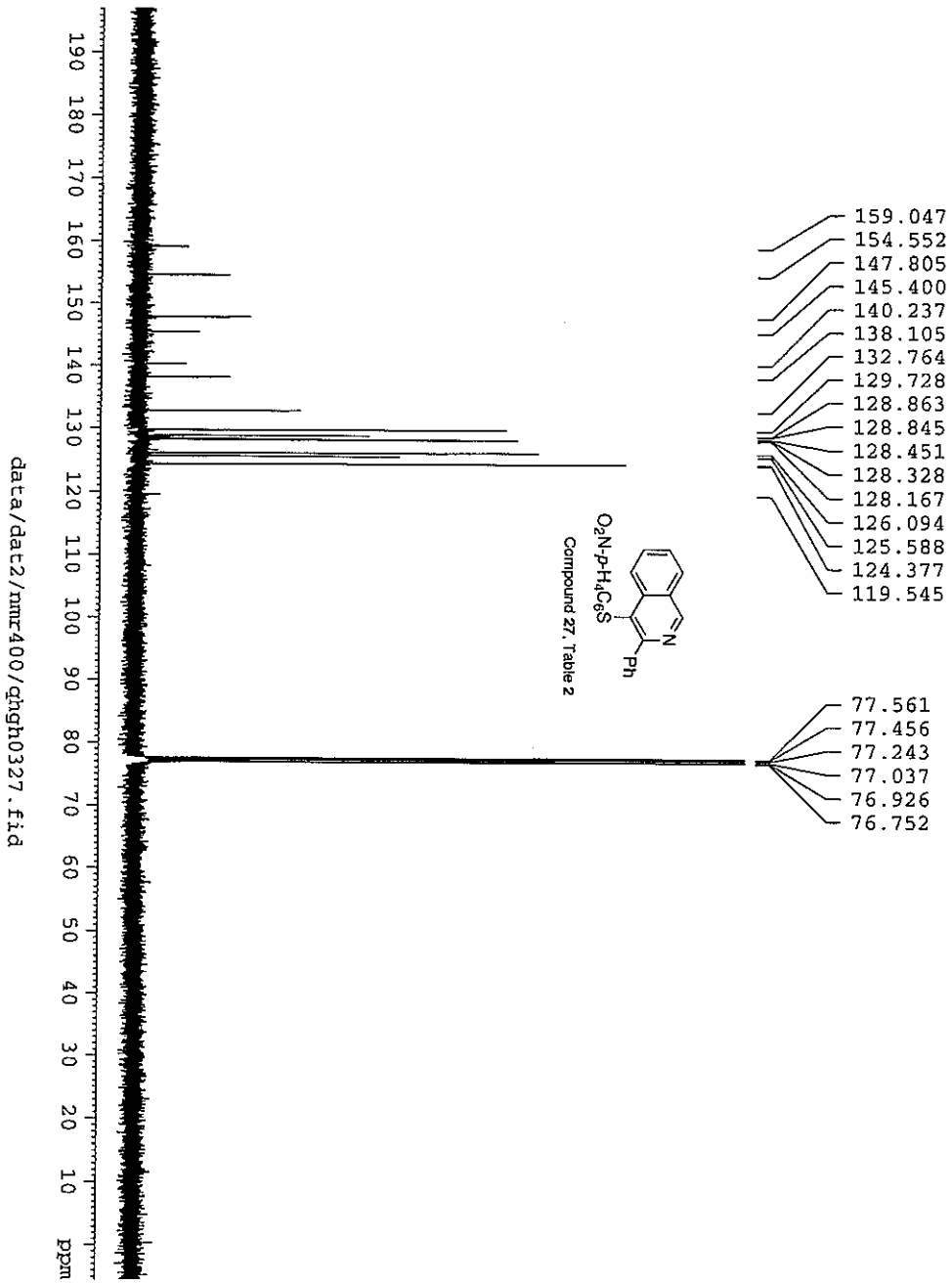

9.305
9.180
9.174
9.166
9.160
8.339
8.333
8.311
8.305
7.578
7.574
7.566
7.560
7.554
7.546
7.532
7.353
7.351
7.346
7.340
7.331
7.263
7.085
7.080
7.074
7.066
7.059
7.053
7.041
7.025
7.020
7.013
7.007
7.002
6.988
6.982
0.000
1.000
1.022
1.060
3.339
3.411
5.487
ppm
data/dat2/nmr300/qh019-1.fid
Compound 25, Table 2
N
N
SePh
Ph

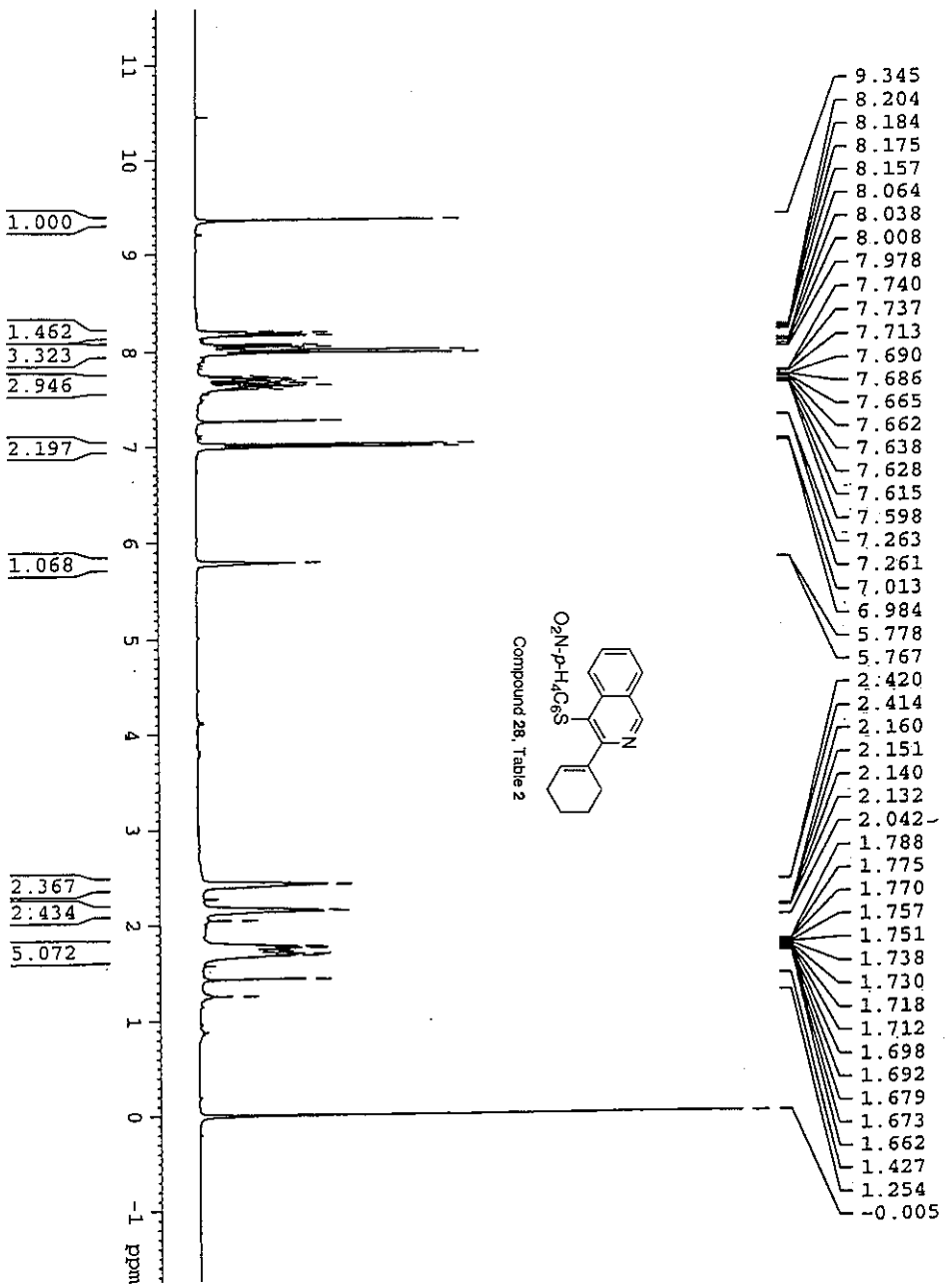

160.892
155.361
152.726
151.835
141.611
136.356
132.757
131.864
129.923
128.896
128.441
127.963
126.539
125.973
123.047
122.906
77.722
77.299
76.875
N
N
SePh
Ph
Compound 25, Table 2
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh019-2.fid

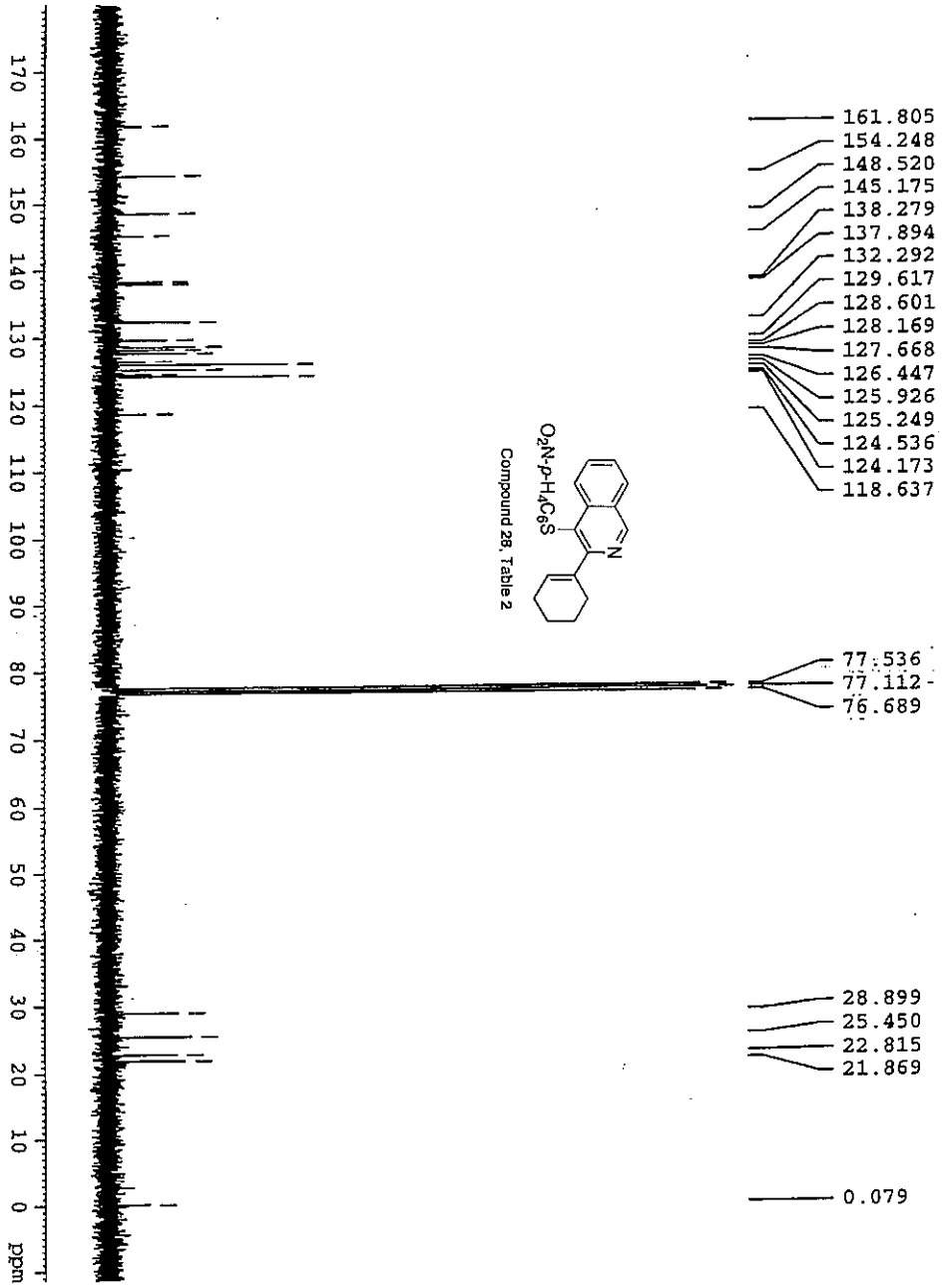

9.154
9.146
9.140
8.296
8.290
8.268
8.262
7.524
7.510
7.497
7.482
7.273
7.237
7.233
7.230
7.225
7.220
7.214
7.210
7.205
7.131
7.128
7.124
7.116
7.112
7.108
7.102
7.098
3.364
3.338
3.332
3.312
1.742
1.716
1.691
1.363
1.336
1.317
1.297
1.284
1.275
1.261
1.249
0.878
0.855
0.837
0.831
1.000
0.961
1.034
1.072
2.121
3.160
2.191
2.262
7.062
3.377
ppm
Compound 26, Table 2
SePh
n-C6H13
data/nmr300/qh046-1.fid

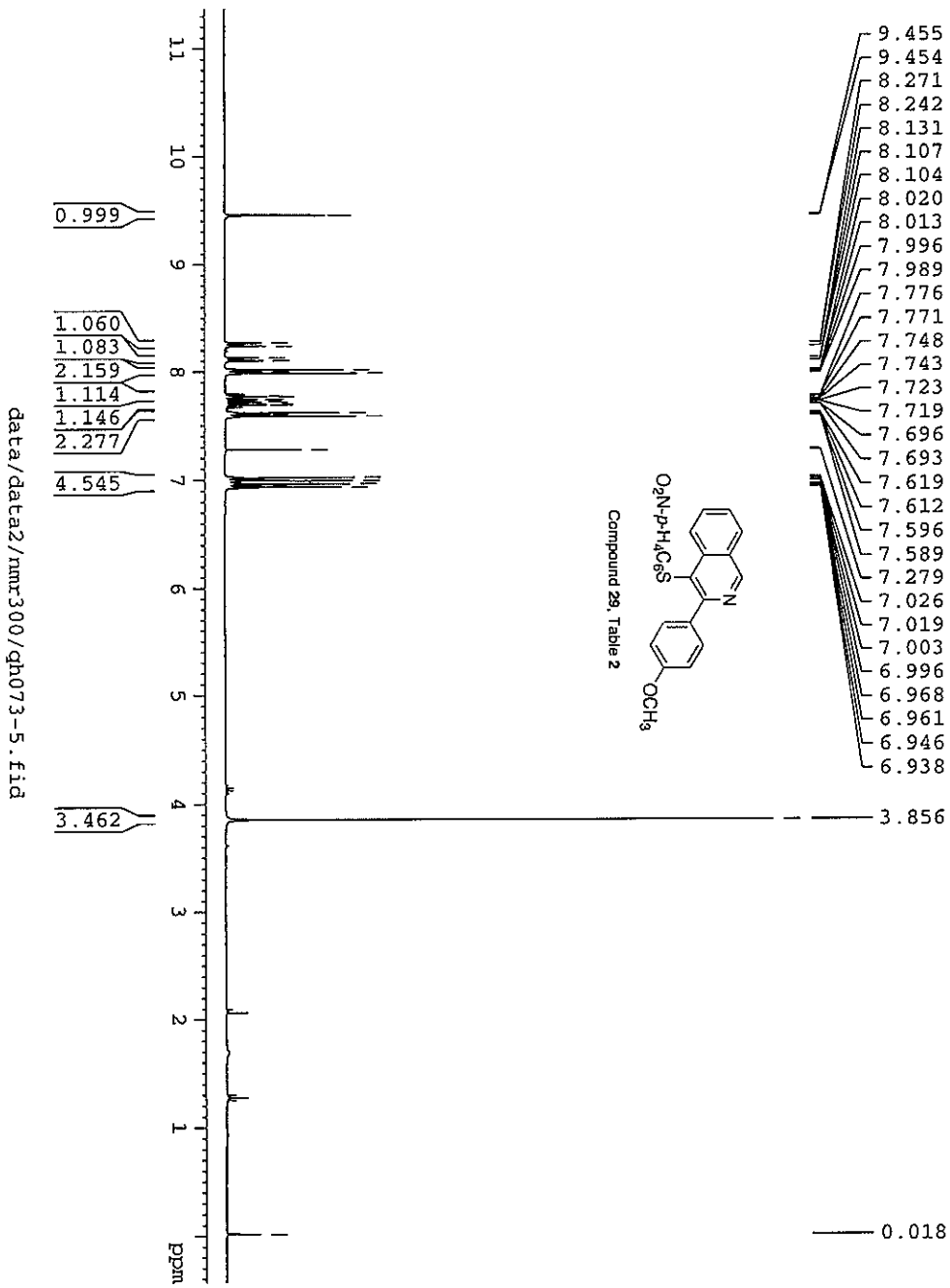

165.106
155.479
153.483
151.859
136.349
133.021
130.463
129.173
126.338
124.392
122.661
122.242
77.653
77.229
76.805
39.489
31.865
30.476
29.525
22.739
14.264
SePh
nC6H13
Compound 26, Table 2
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr300/qh046-2.fid

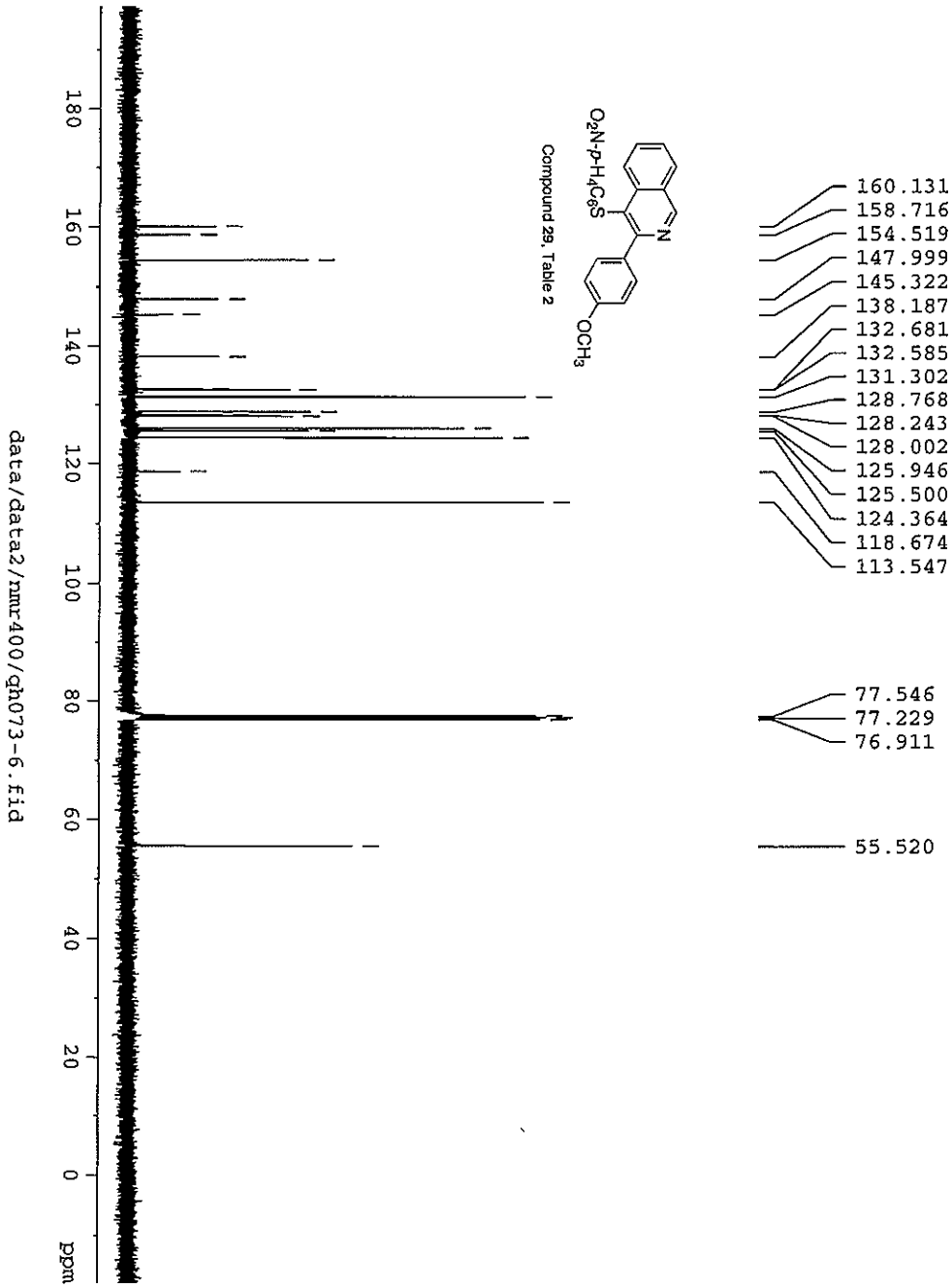

9.468
8.280
8.259
8.142
8.121
7.998
7.975
7.784
7.716
7.714
7.601
7.597
7.593
7.590
7.587
7.584
7.580
7.577
7.415
7.412
7.408
7.405
7.399
7.261
6.998
6.975
0.000
-0.003
1.000
1.100
1.085
2.122
2.249
2.472
3.615
2.604
O2N-p-H4C6 S
N
Ph
Compound 27, Table 2
data/dat2/nmr300/qh079-3.fid
ppm

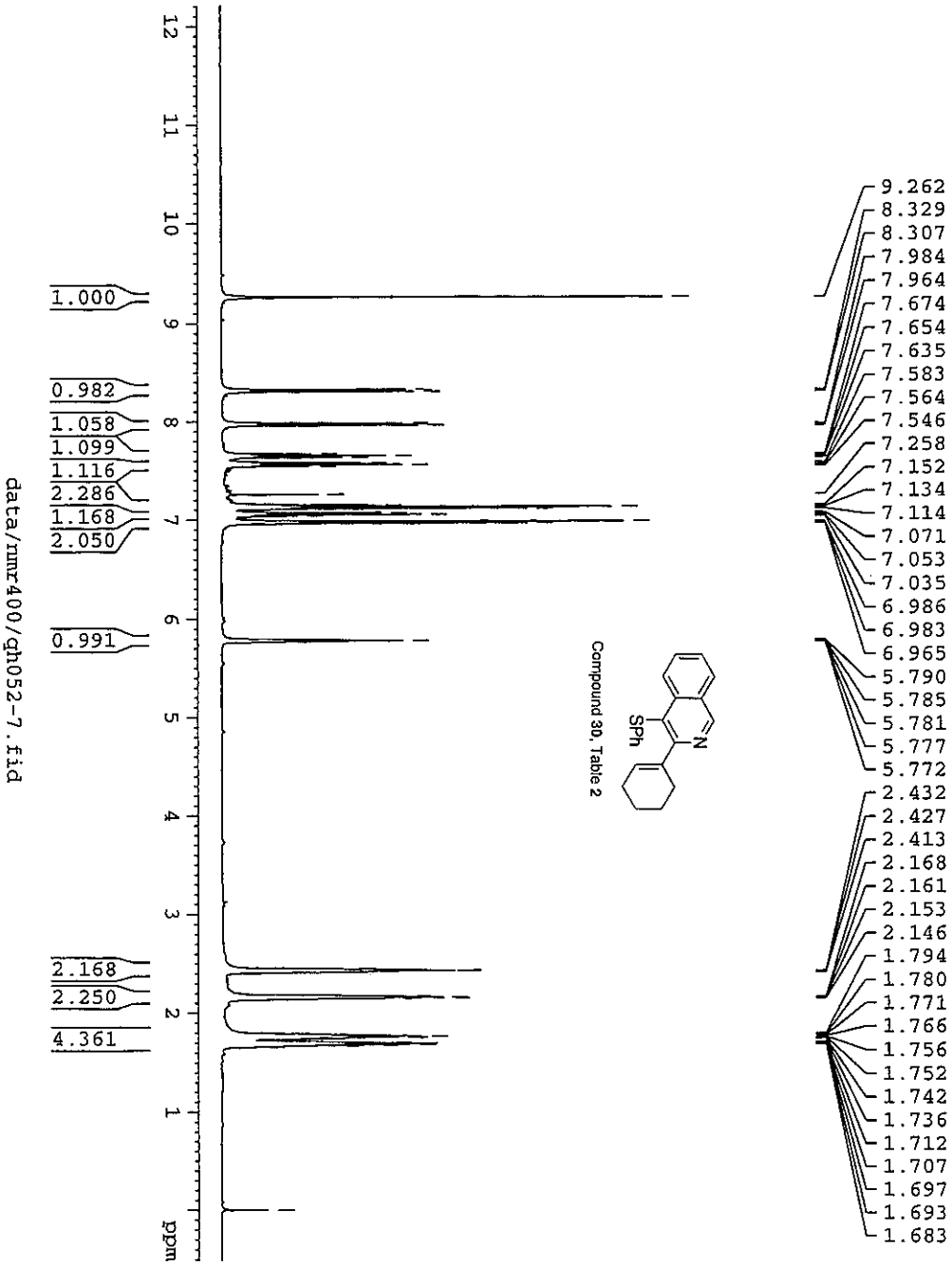

159.047
154.552
147.805
145.400
140.237
138.105
132.764
129.728
128.863
128.845
128.451
128.328
128.167
126.094
125.588
124.377
119.545
77.561
77.456
77.243
77.037
76.926
76.752
O2N-p-H4C6S
Ph
N
Compound 27, Table 2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr400/qhgh0327.fid

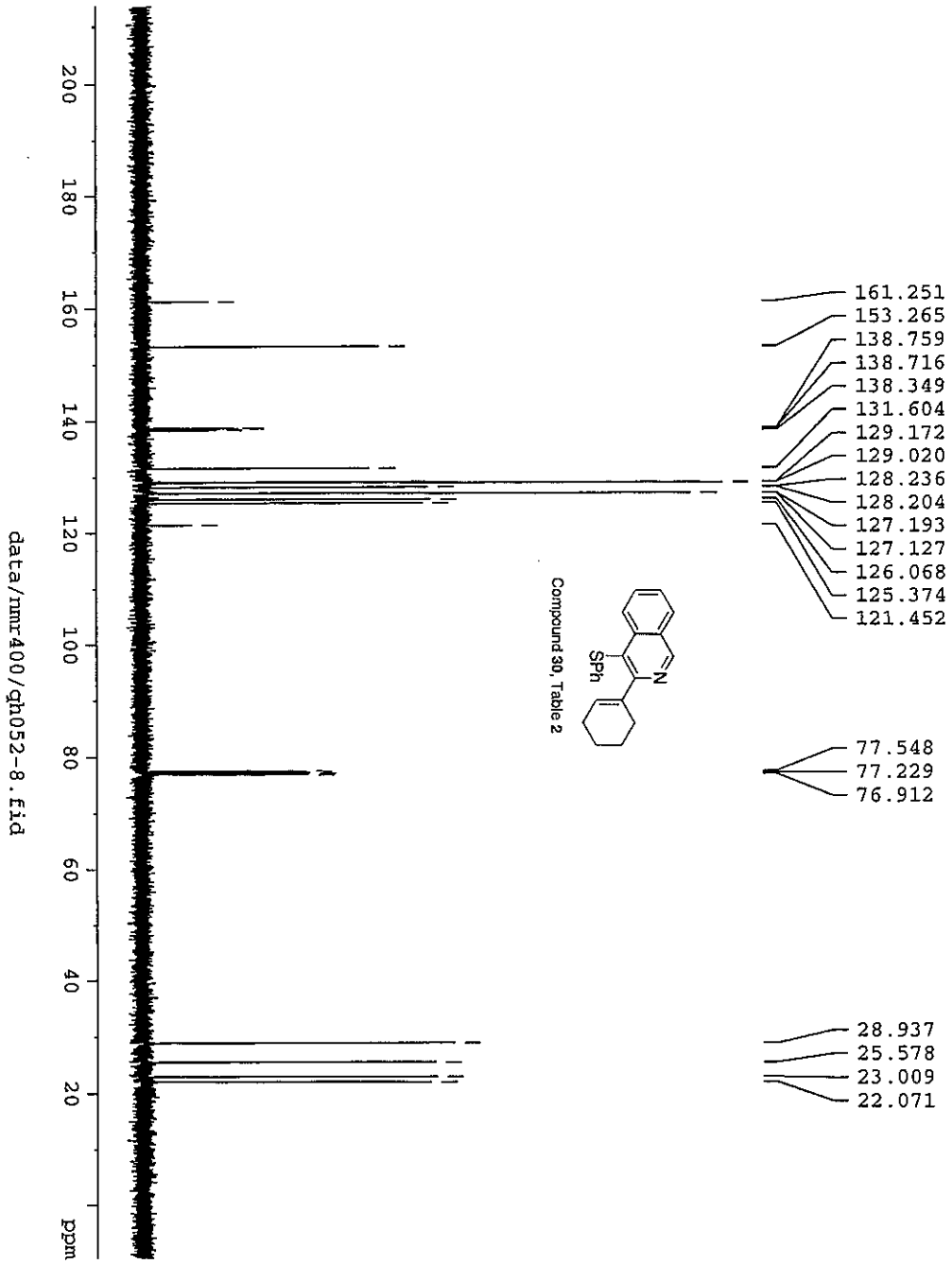

9.345
8.204
8.184
8.175
8.157
8.064
8.038
8.008
7.978
7.740
7.737
7.713
7.690
7.686
7.665
7.662
7.638
7.628
7.615
7.598
7.263
7.261
7.013
6.984
5.778
5.767
2.420
2.414
2.160
2.151
2.140
2.132
2.042
1.788
1.775
1.770
1.757
1.751
1.738
1.730
1.718
1.712
1.698
1.692
1.679
1.673
1.662
1.427
1.254
-0.005
O2N-p-H4C6S
N
Compound 28, Table 2
1.000
1.462
3.323
2.946
2.197
1.068
2.367
2.434
5.072
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm

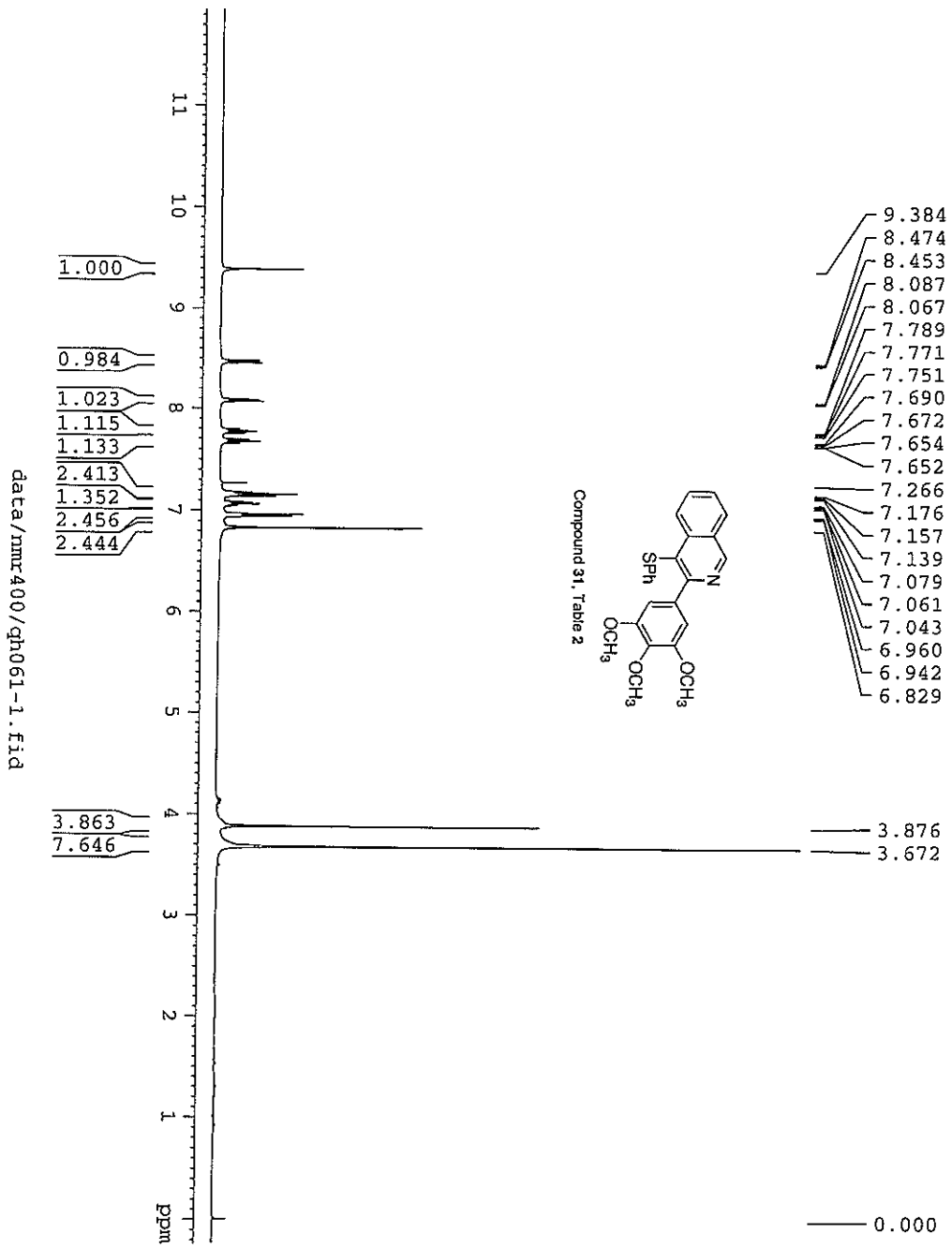

161.805
154.248
148.520
145.175
138.279
137.894
132.292
129.617
128.601
128.169
127.668
126.447
125.926
125.249
124.536
124.173
118.637
77.536
77.112
76.689
28.899
25.450
22.815
21.869
0.079
O2N-p-H4C6S
N
Compound 28, Table 2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

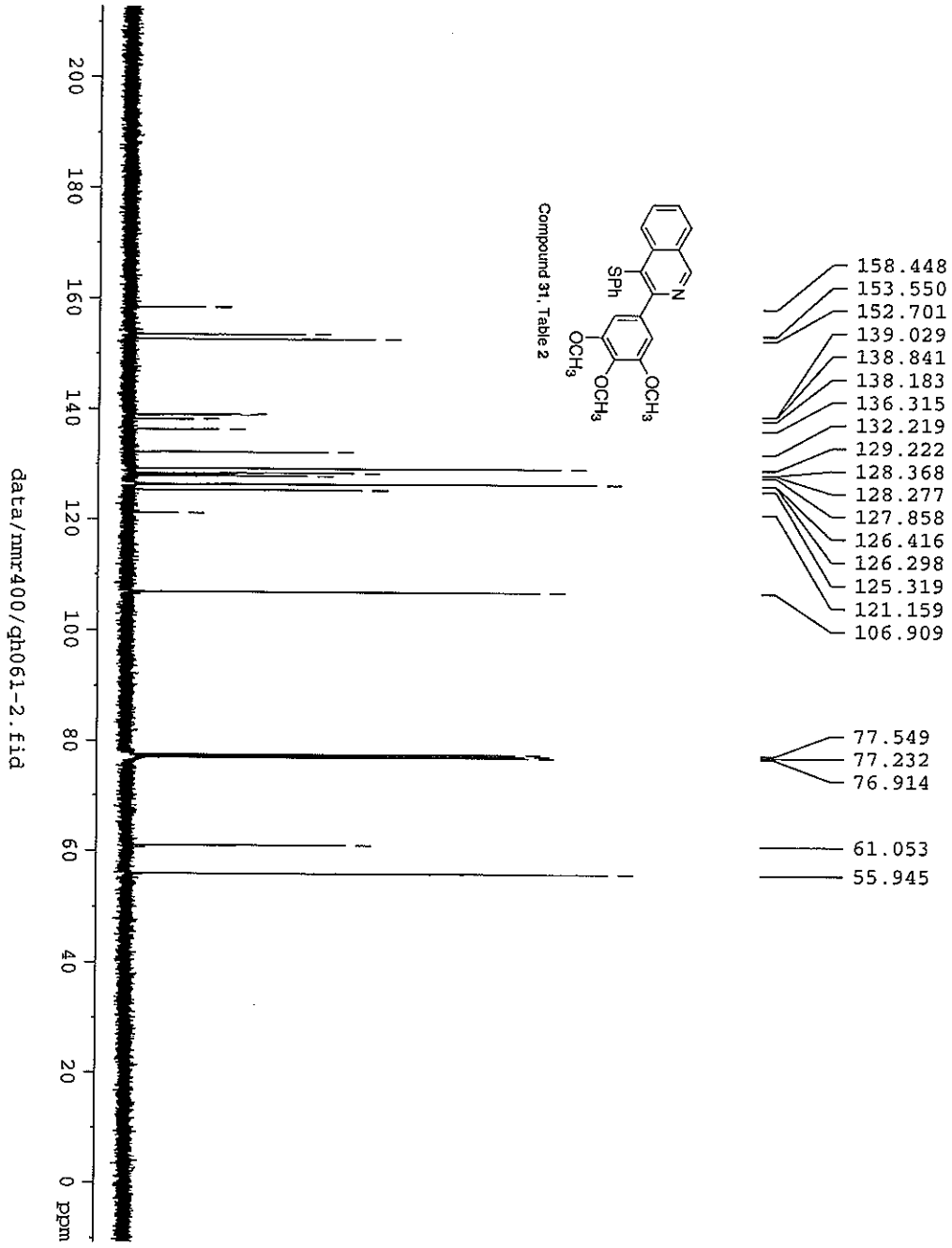

data/data2/nmr300/qh073-5.fid
0.999
1.060
1.083
2.159
1.114
1.146
2.277
4.545
3.462
9.455
9.454
8.271
8.242
8.131
8.107
8.104
8.020
8.013
7.996
7.989
7.776
7.771
7.748
7.743
7.723
7.719
7.696
7.693
7.619
7.612
7.596
7.589
7.279
7.026
7.019
7.003
6.996
6.968
6.961
6.946
6.938
3.856
0.018
ppm
O2N-p-H4C6S
OCH3
N
Compound 29, Table 2

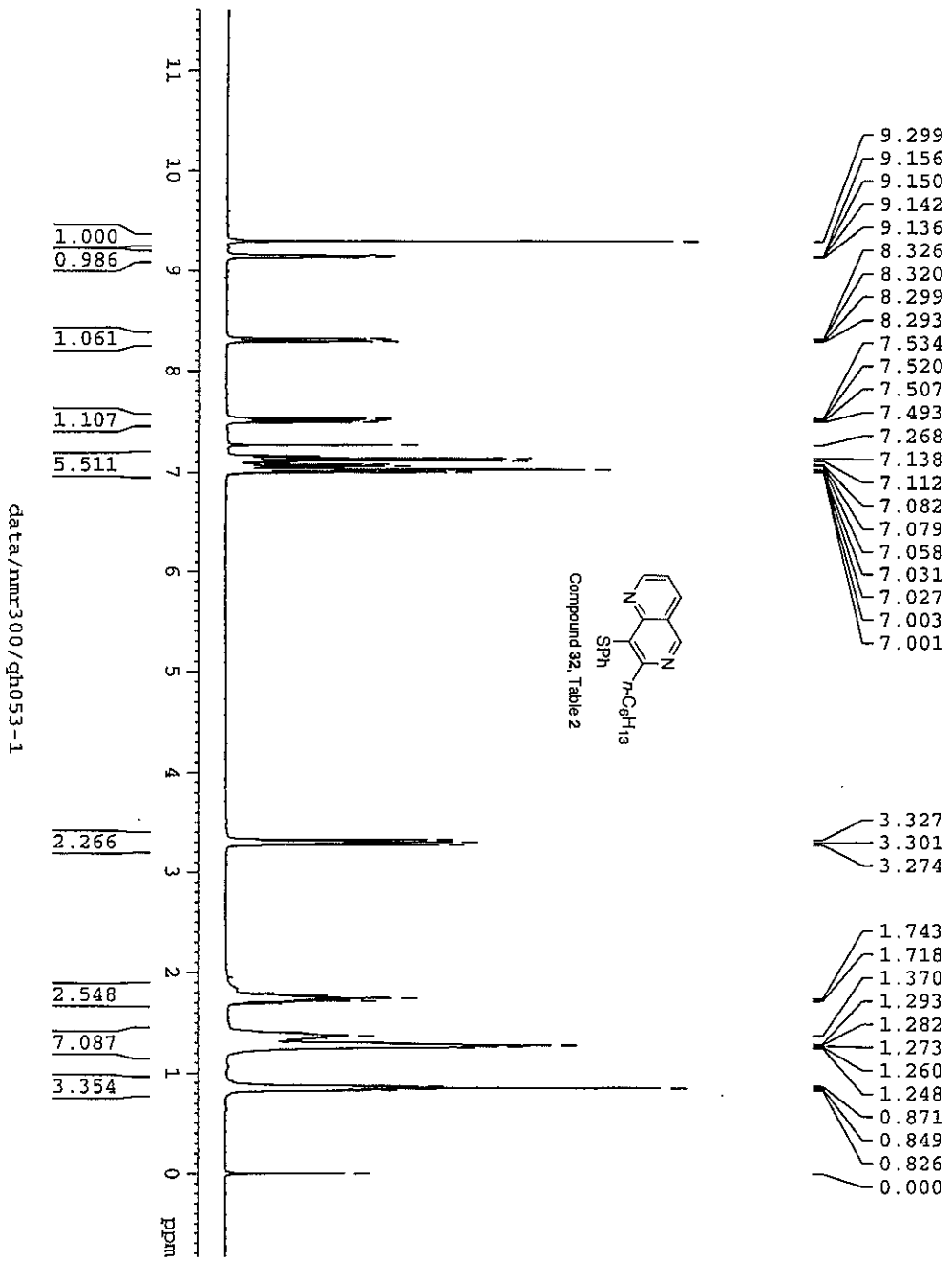

160.131
158.716
154.519
147.999
145.322
138.187
132.681
132.585
131.302
128.768
128.243
128.002
125.946
125.500
124.364
118.674
113.547
77.546
77.229
76.911
55.520
O2N-p-H4C6S
OCH3
N
Compound 29, Table 2
data/data2/nmr400/qh073-6.fid
180
160
140
120
100
80
60
40
20
0
ppm

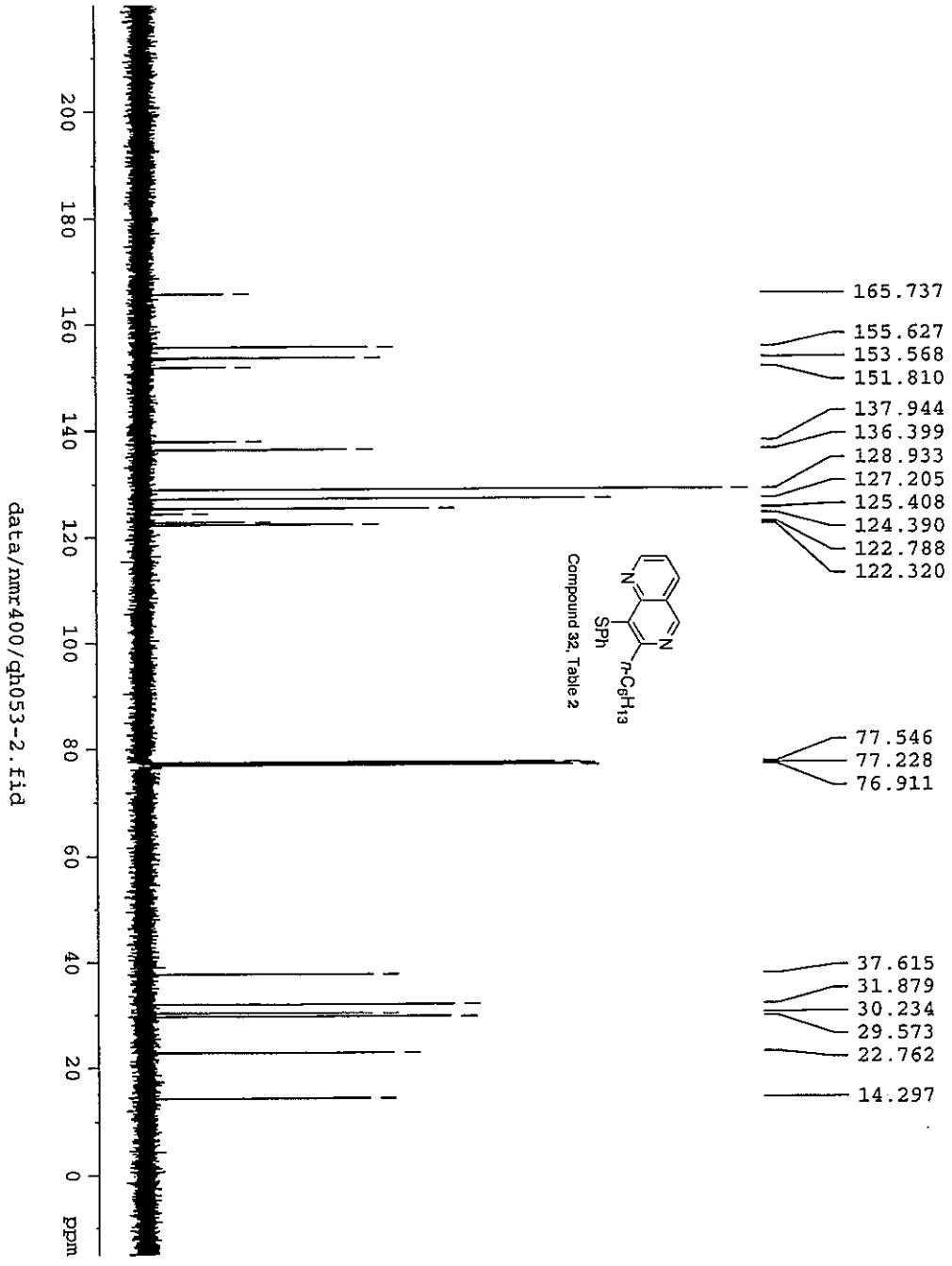

9.262
8.329
8.307
7.984
7.964
7.674
7.654
7.635
7.583
7.564
7.546
7.258
7.152
7.134
7.114
7.071
7.053
7.035
6.986
6.983
6.965
5.790
5.785
5.781
5.777
5.772
2.432
2.427
2.413
2.168
2.161
2.153
2.146
1.794
1.780
1.771
1.766
1.756
1.752
1.742
1.736
1.712
1.707
1.697
1.693
1.683
SPh
N
Compound 30, Table 2
1.000
0.982
1.058
1.099
1.116
2.286
1.168
2.050
0.991
2.168
2.250
4.361
12
11
10
9
8
7
6
5
4
3
2
1
ppm
data/nmr400/qh052-7.fid

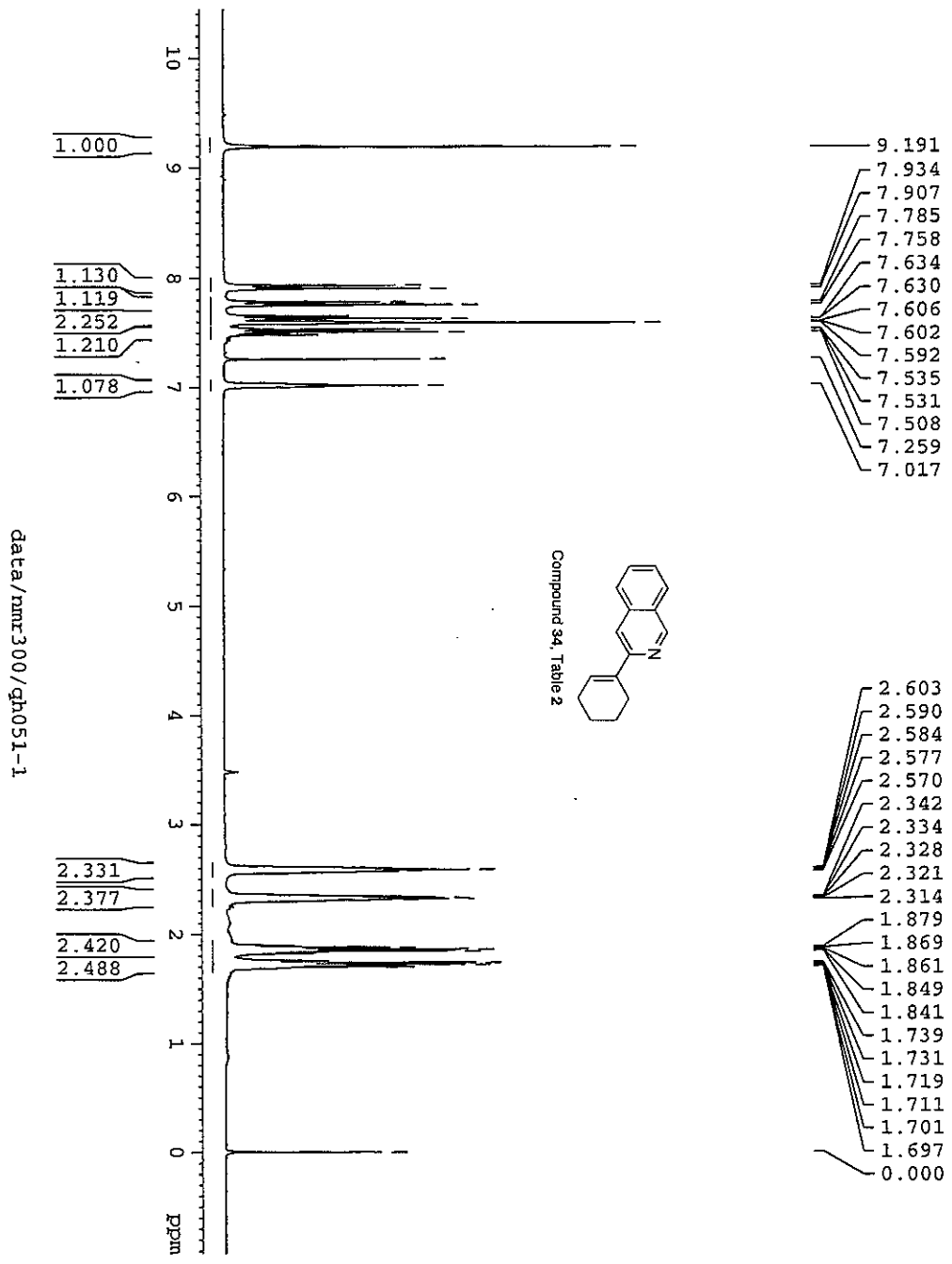

161.251
153.265
138.759
138.716
138.349
131.604
129.172
129.020
128.236
128.204
127.193
127.127
126.068
125.374
121.452
77.548
77.229
76.912
28.937
25.578
23.009
22.071
Compound 30, Table 2
SPh
N
200
180
160
140
120
100
80
60
40
20
ppm
data/nmr400/qh052-8.fid

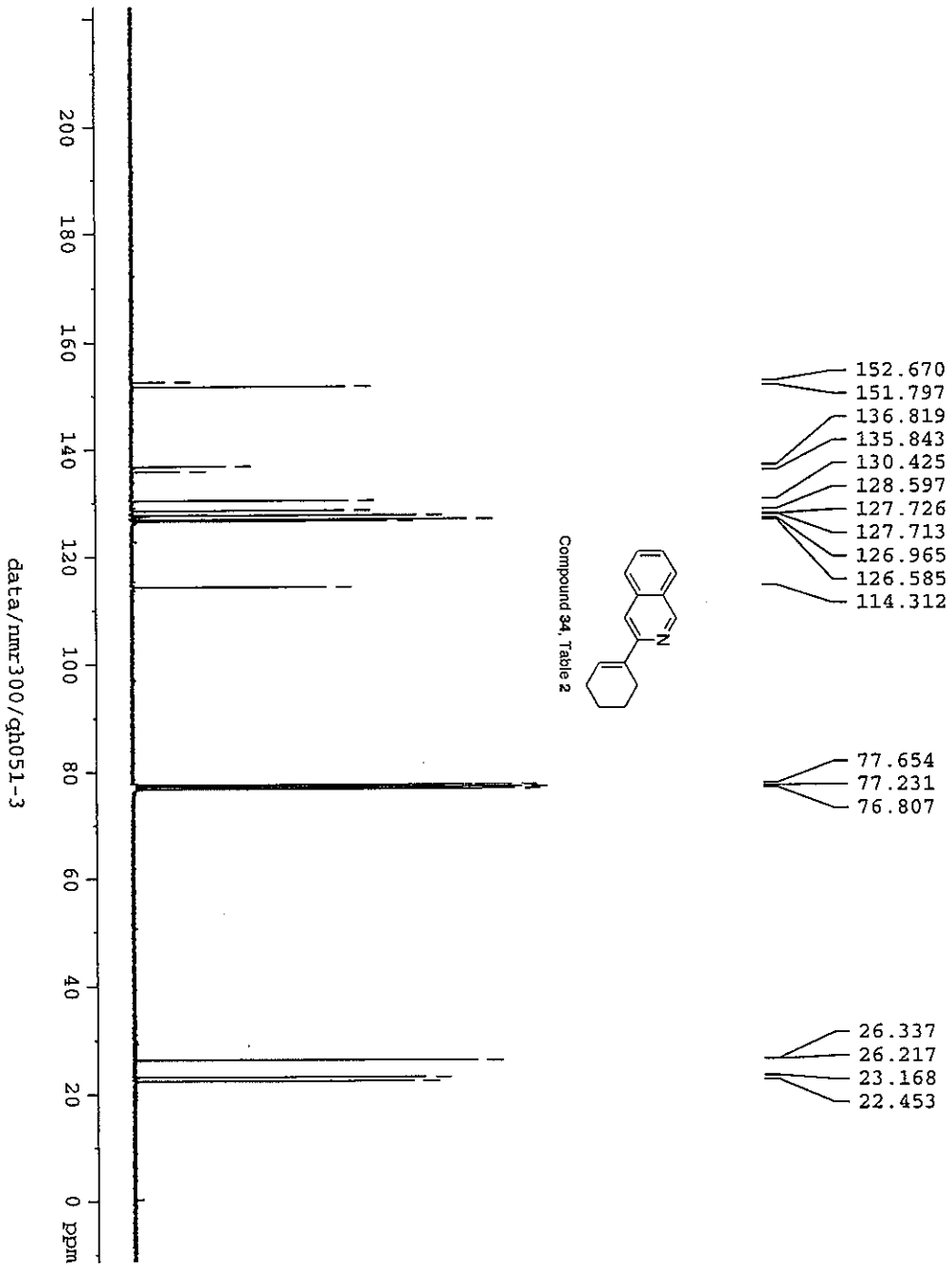

data/nmr400/qh061-1.fid
1.000
0.984
1.023
1.115
1.133
2.413
1.352
2.456
2.444
3.863
7.646
9.384
8.474
8.453
8.087
8.067
7.789
7.771
7.751
7.690
7.672
7.654
7.652
7.266
7.176
7.157
7.139
7.079
7.061
7.043
6.960
6.942
6.829
3.876
3.672
0.000
SPh
N
OCH3
OCH3
OCH3
Compound 31, Table 2
ppm

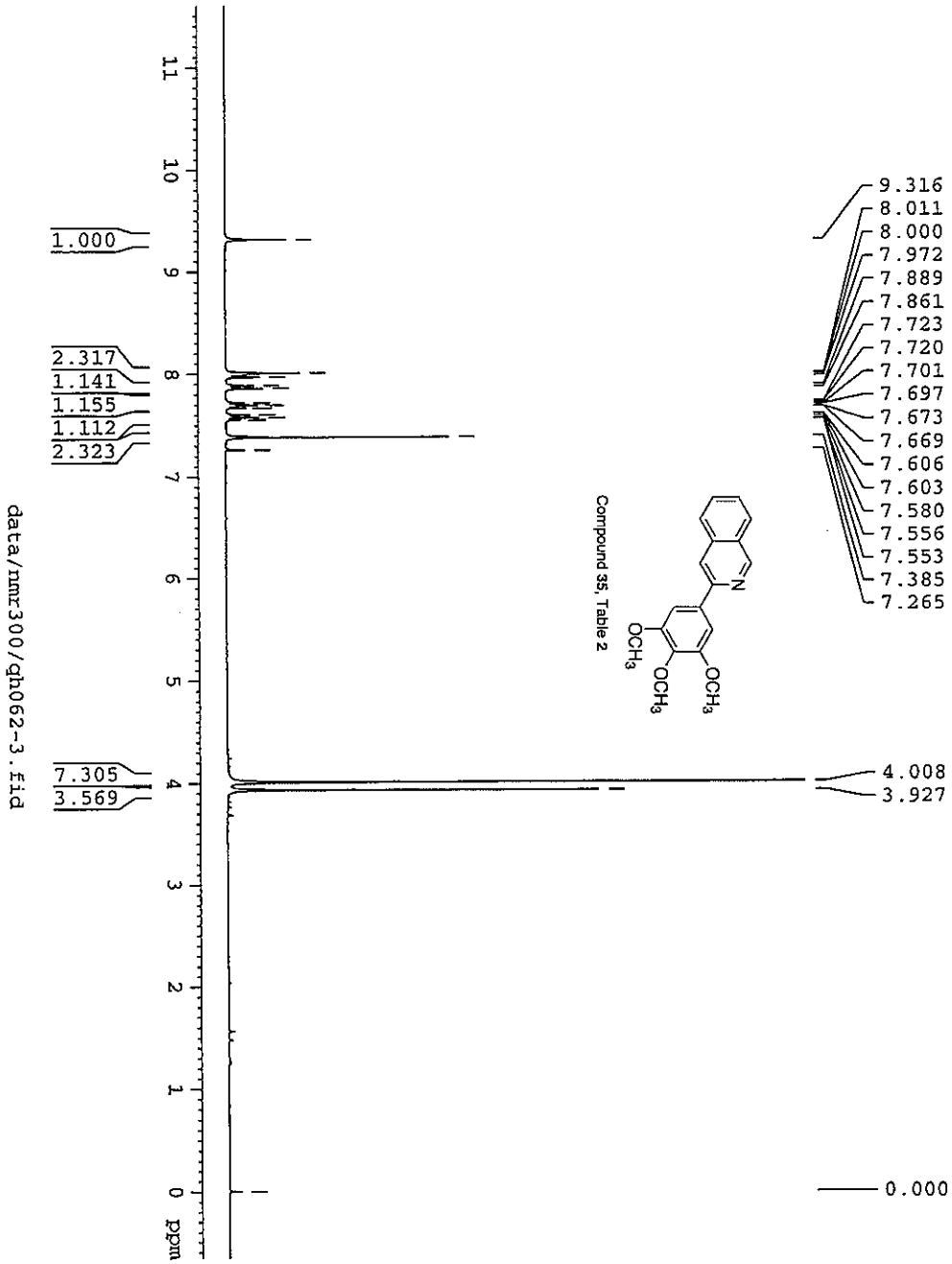

158.448
153.550
152.701
139.029
138.841
138.183
136.315
132.219
129.222
128.368
128.277
127.858
126.416
126.298
125.319
121.159
106.909
77.549
77.232
76.914
61.053
55.945
SPh
N
OCH3
OCH3
OCH3
Compound 31, Table 2
data/nmr400/qh061-2.fid
200
180
160
140
120
100
80
60
40
20
0 ppm

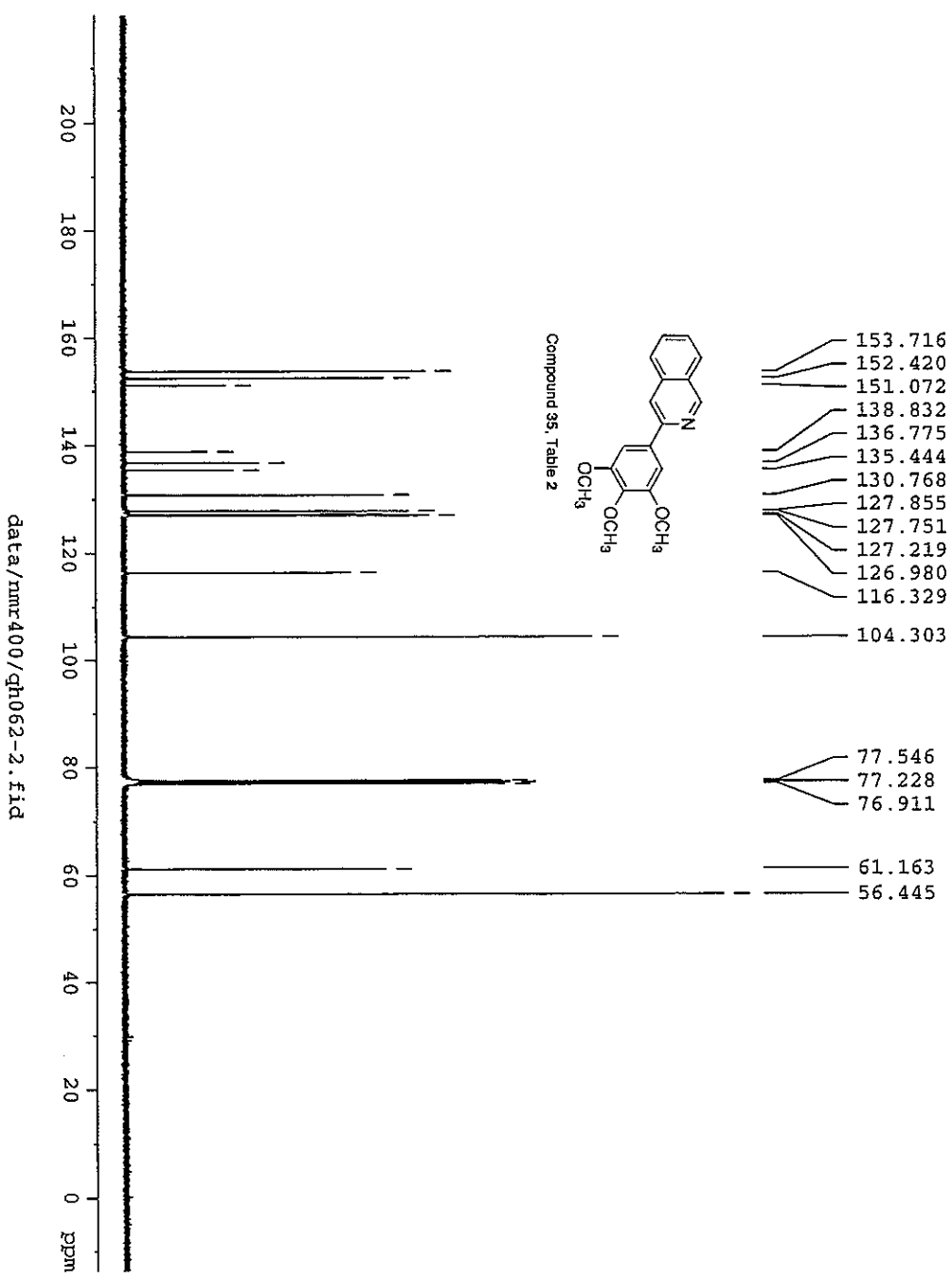

data/nmr300/qh053-1
1.000
0.986
1.061
1.107
5.511
2.266
2.548
7.087
3.354
ppm
SPh
n-C6H13
Compound 32, Table 2
9.299
9.156
9.150
9.142
9.136
8.326
8.320
8.299
8.293
7.534
7.520
7.507
7.493
7.268
7.138
7.112
7.082
7.079
7.058
7.031
7.027
7.003
7.001
3.327
3.301
3.274
1.743
1.718
1.370
1.293
1.282
1.273
1.260
1.248
0.871
0.849
0.826
0.000

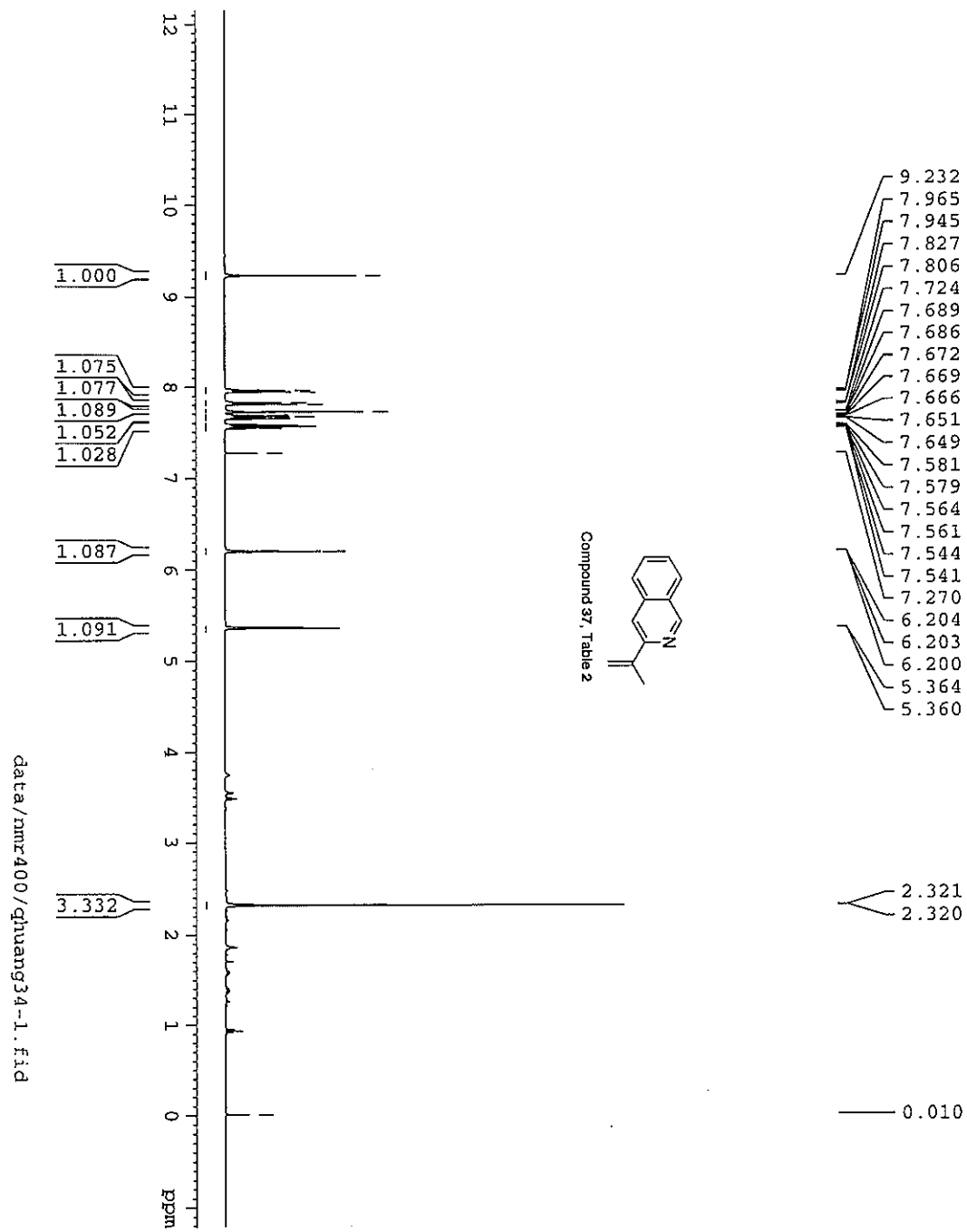

165.737
155.627
153.568
151.810
137.944
136.399
128.933
127.205
125.408
124.390
122.788
122.320
77.546
77.228
76.911
37.615
31.879
30.234
29.573
22.762
14.297
SPh
n-C6H13
Compound 32, Table 2
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh053-2.fid

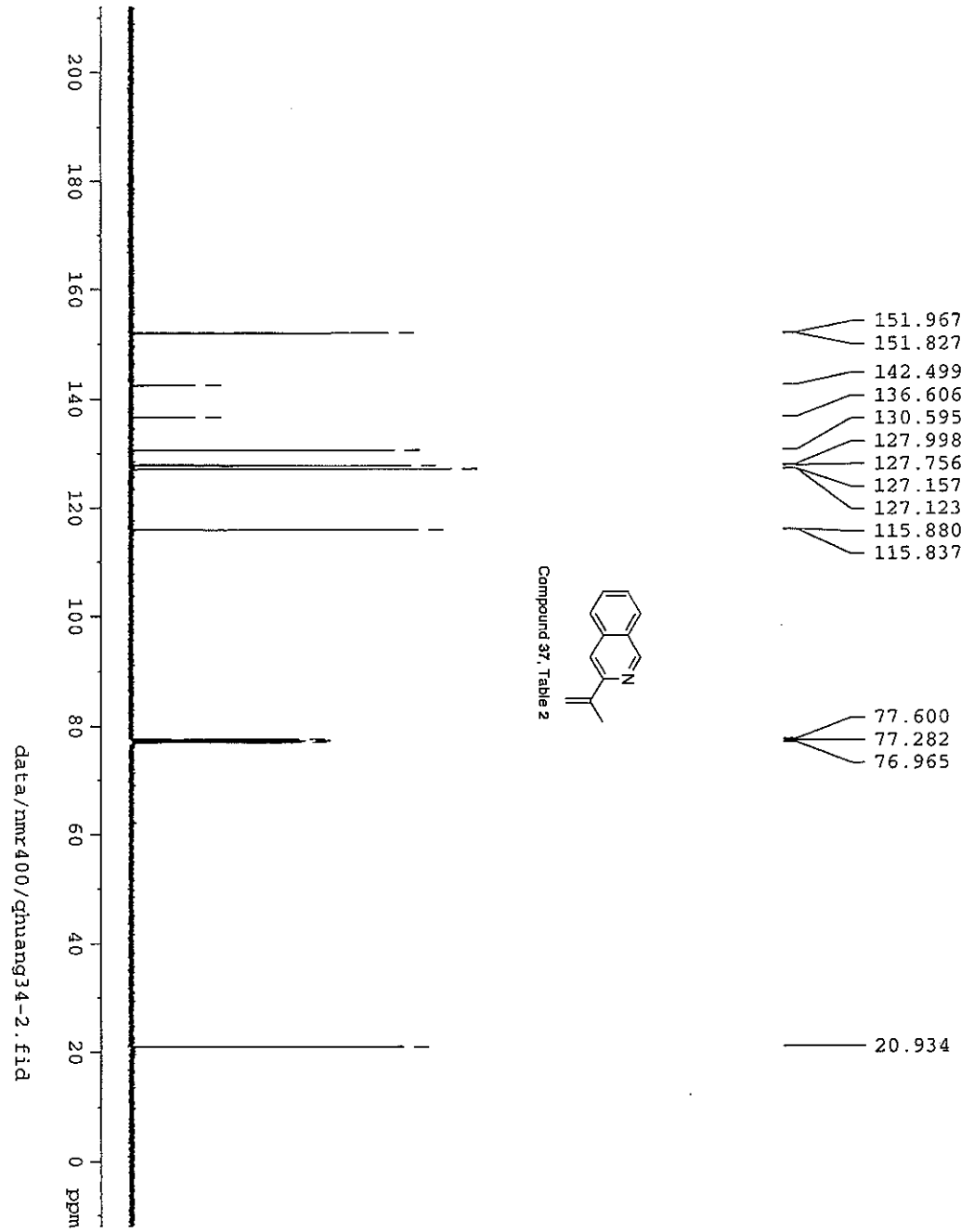

data/nmr300/qh051-1
1.000
1.130
1.119
2.252
1.210
1.078
2.331
2.377
2.420
2.488
ppm
Compound 34, Table 2
9.191
7.934
7.907
7.785
7.758
7.634
7.630
7.606
7.602
7.592
7.535
7.531
7.508
7.259
7.017
2.603
2.590
2.584
2.577
2.570
2.342
2.334
2.328
2.321
2.314
1.879
1.869
1.861
1.849
1.841
1.739
1.731
1.719
1.711
1.701
1.697
0.000

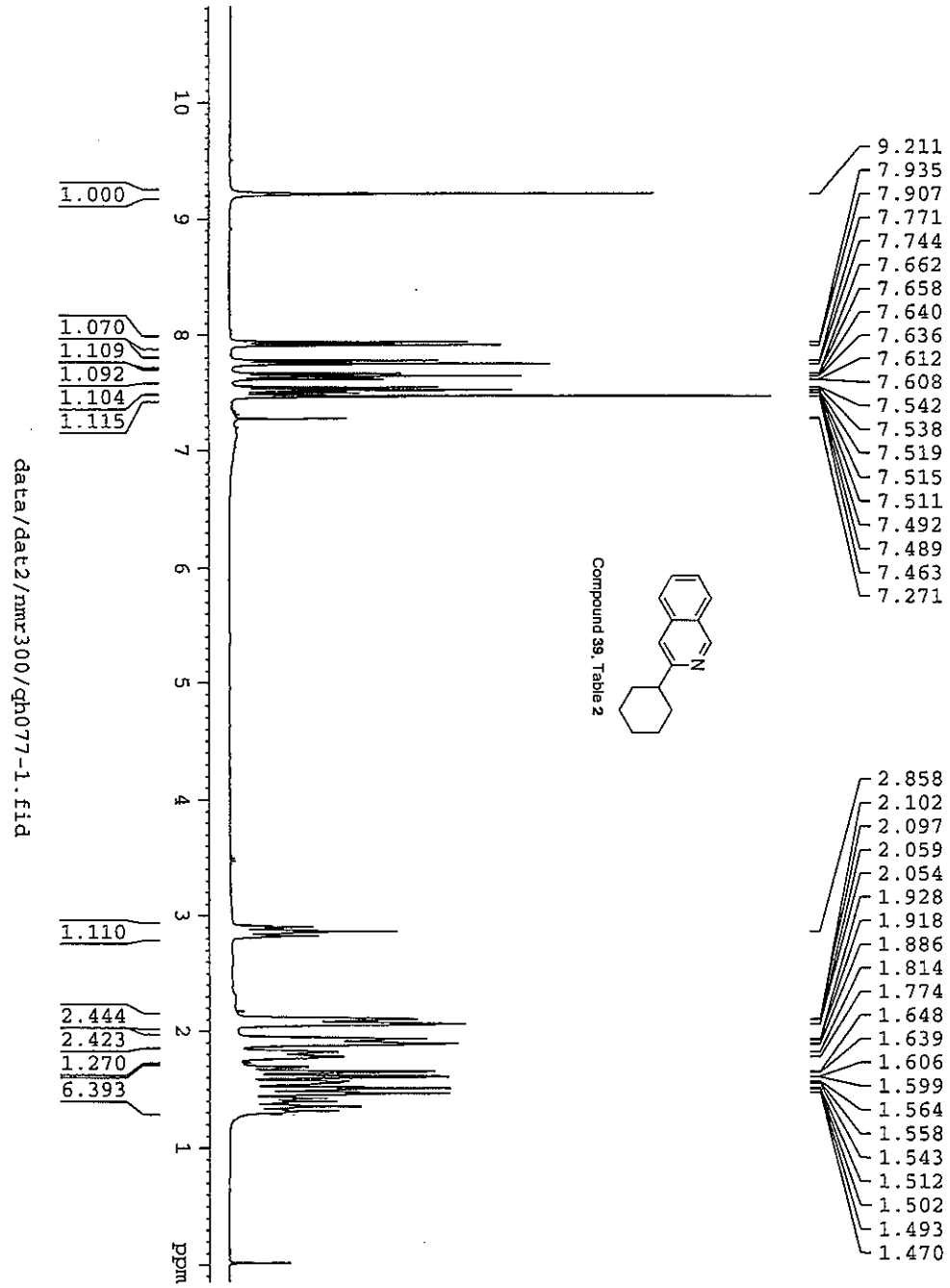

data/nmr300/qh051-3
200
180
160
140
120
100
80
60
40
20
0 ppm
Compound 34, Table 2
N
152.670
151.797
136.819
135.843
130.425
128.597
127.726
127.713
126.965
126.585
114.312
77.654
77.231
76.807
26.337
26.217
23.168
22.453

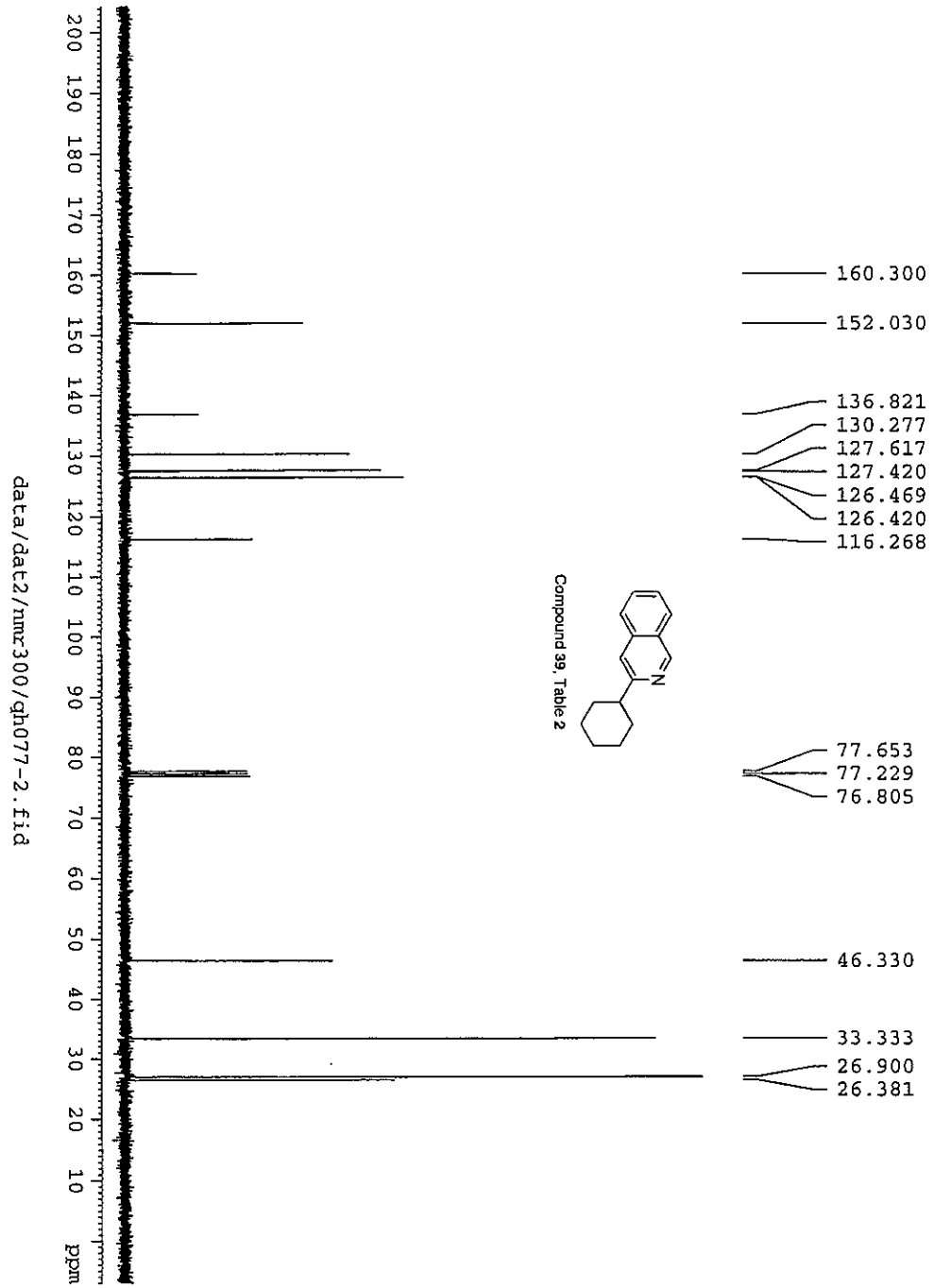

9.316
8.011
8.000
7.972
7.889
7.861
7.723
7.720
7.701
7.697
7.673
7.669
7.606
7.603
7.580
7.556
7.553
7.385
7.265
4.008
3.927
0.000
1.000
2.317
1.141
1.155
1.112
2.323
7.305
3.569
Compound 35, Table 2
OCH3
OCH3
OCH3
N
ppm
data/nmr300/qh062-3.fid

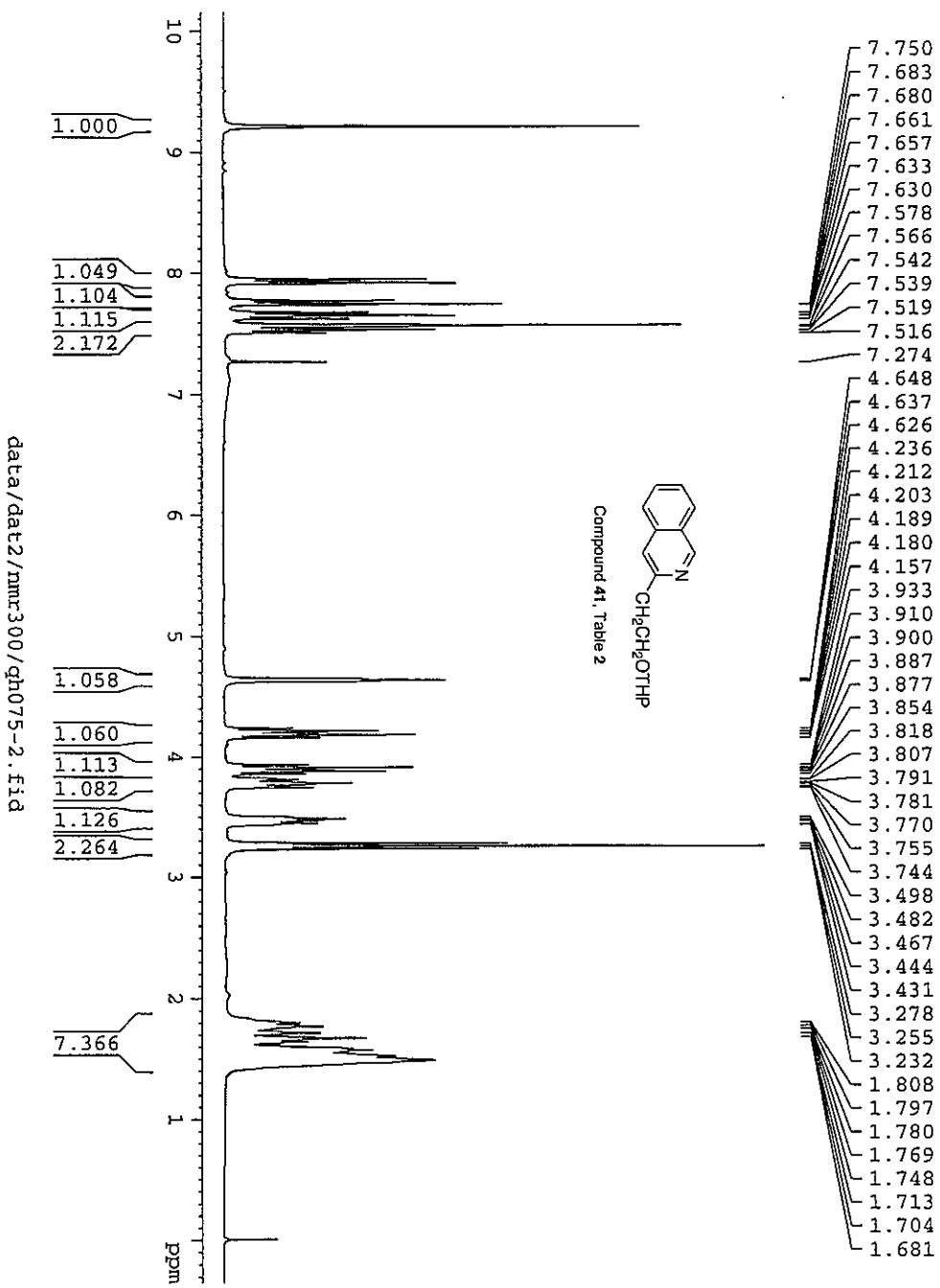

153.716
152.420
151.072
138.832
136.775
135.444
130.768
127.855
127.751
127.219
126.980
116.329
104.303
77.546
77.228
76.911
61.163
56.445
Compound 35, Table 2
OCH3
OCH3
OCH3
N
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh062-2.fid


9.232
7.965
7.945
7.827
7.806
7.724
7.689
7.686
7.672
7.669
7.666
7.651
7.649
7.581
7.579
7.564
7.561
7.544
7.541
7.270
6.204
6.203
6.200
5.364
5.360
2.321
2.320
0.010
1.000
1.075
1.077
1.089
1.052
1.028
1.087
1.091
3.332
Compound 37, Table 2
ppm
data/nmr400/qhuang34-1.fid


151.967
151.827
142.499
136.606
130.595
127.998
127.756
127.157
127.123
115.880
115.837
77.600
77.282
76.965
20.934
Compound 37, Table 2
N
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr400/qhuang34-2.fid


data/dat2/nmr300/qh077-1.fid
Compound 39, Table 2
9.211
7.935
7.907
7.771
7.744
7.662
7.658
7.640
7.636
7.612
7.608
7.542
7.538
7.519
7.515
7.511
7.492
7.489
7.463
7.271
2.858
2.102
2.097
2.059
2.054
1.928
1.918
1.886
1.814
1.774
1.648
1.639
1.606
1.599
1.564
1.558
1.543
1.512
1.502
1.493
1.470
1.000
1.070
1.109
1.092
1.104
1.115
1.110
2.444
2.423
1.270
6.393
ppm


160.300
152.030
136.821
130.277
127.617
127.420
126.469
126.420
116.268
77.653
77.229
76.805
46.330
33.333
26.900
26.381
Compound 39, Table 2
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh077-2.fid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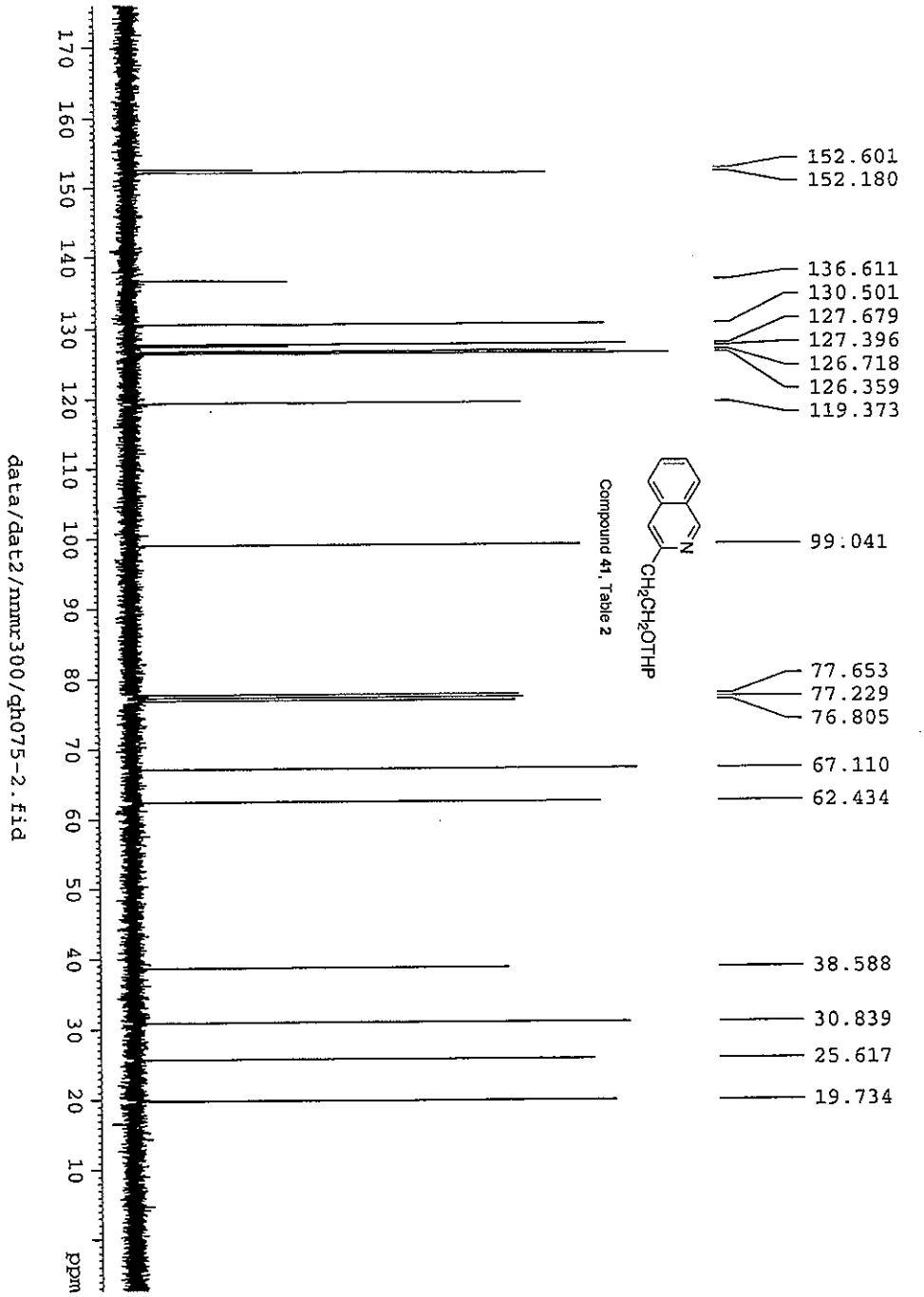
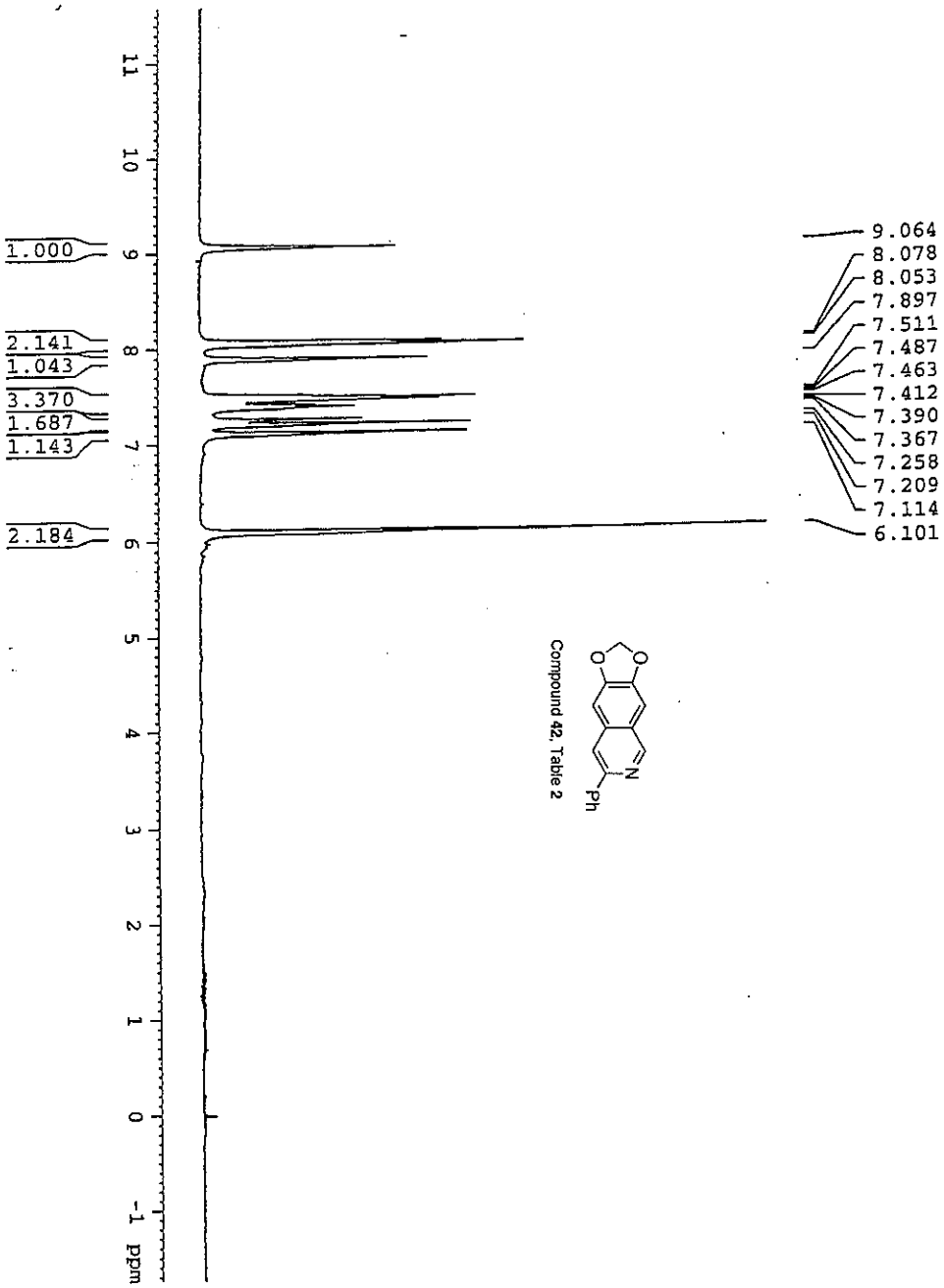
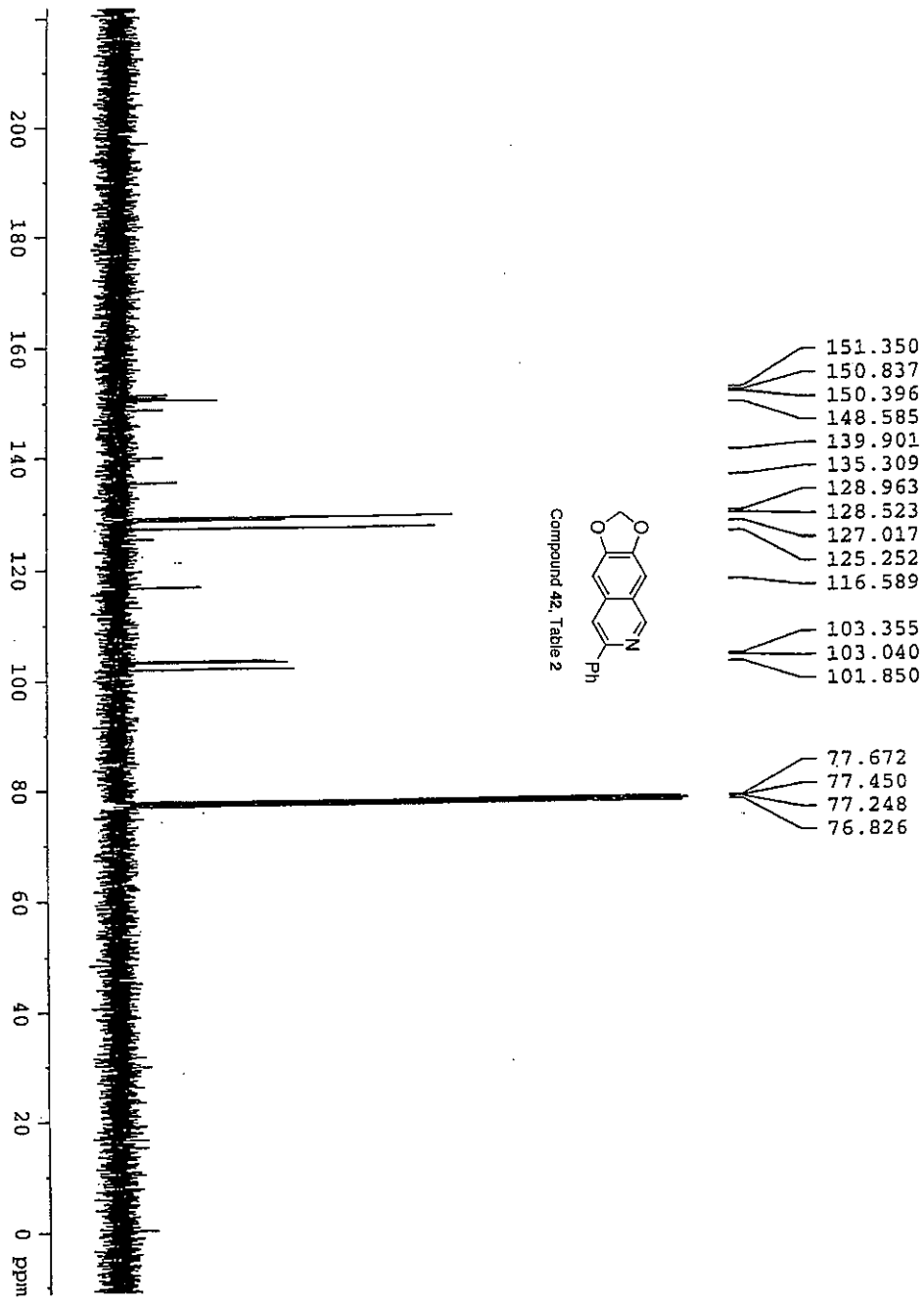
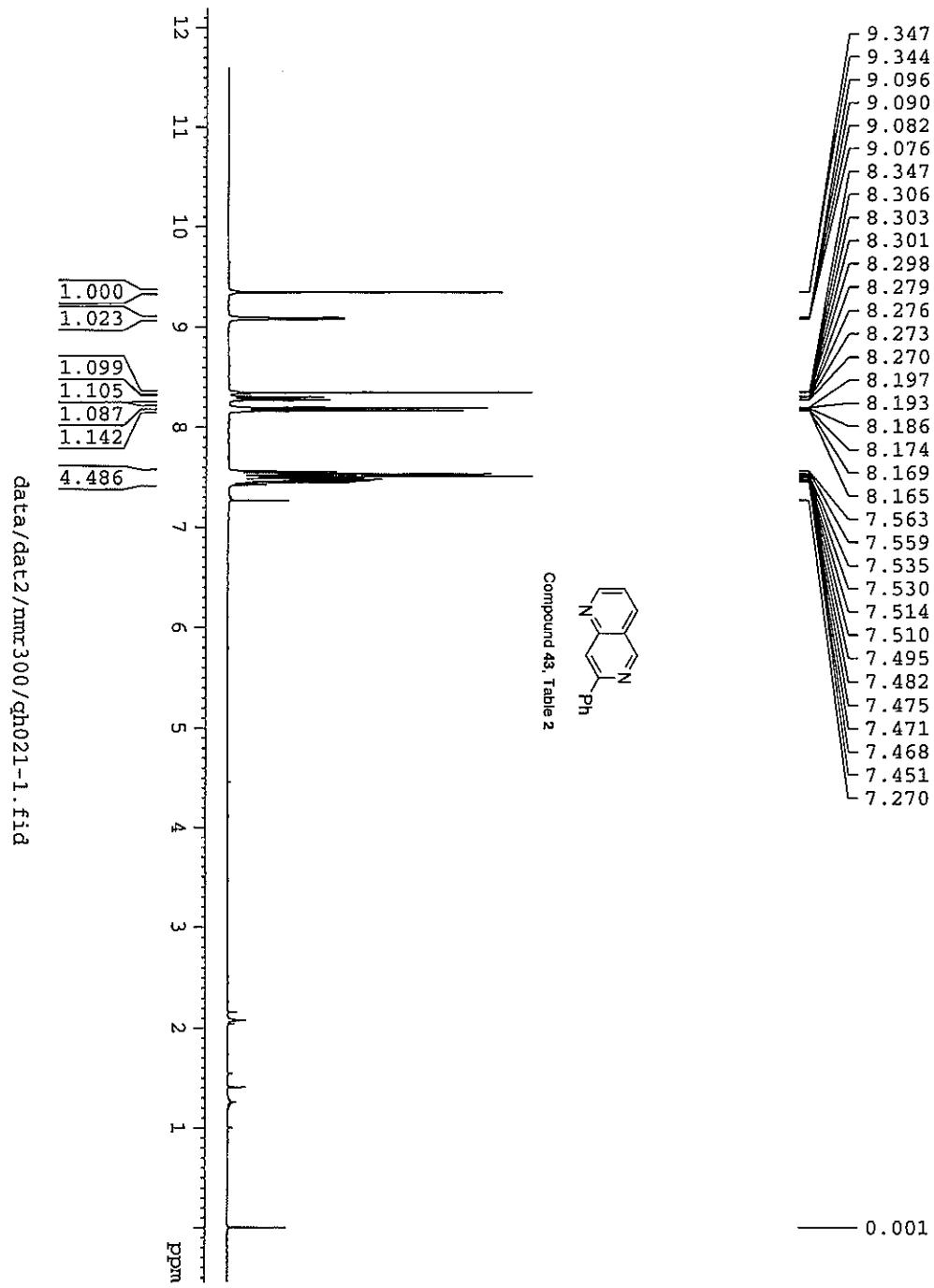
1.000
1.049
1.104
1.115
2.172
1.058
1.060
1.113
1.082
1.126
2.264
7.366
ppm
Compound 41, Table 2
CH2CH2OTHP
7.750
7.683
7.680
7.661
7.657
7.633
7.630
7.578
7.566
7.542
7.539
7.519
7.516
7.274
4.648
4.637
4.626
4.236
4.212
4.203
4.189
4.180
4.157
3.933
3.910
3.900
3.887
3.877
3.854
3.818
3.807
3.791
3.781
3.770
3.755
3.744
3.498
3.482
3.467
3.444
3.431
3.278
3.255
3.232
1.808
1.797
1.780
1.769
1.748
1.713
1.704
1.681

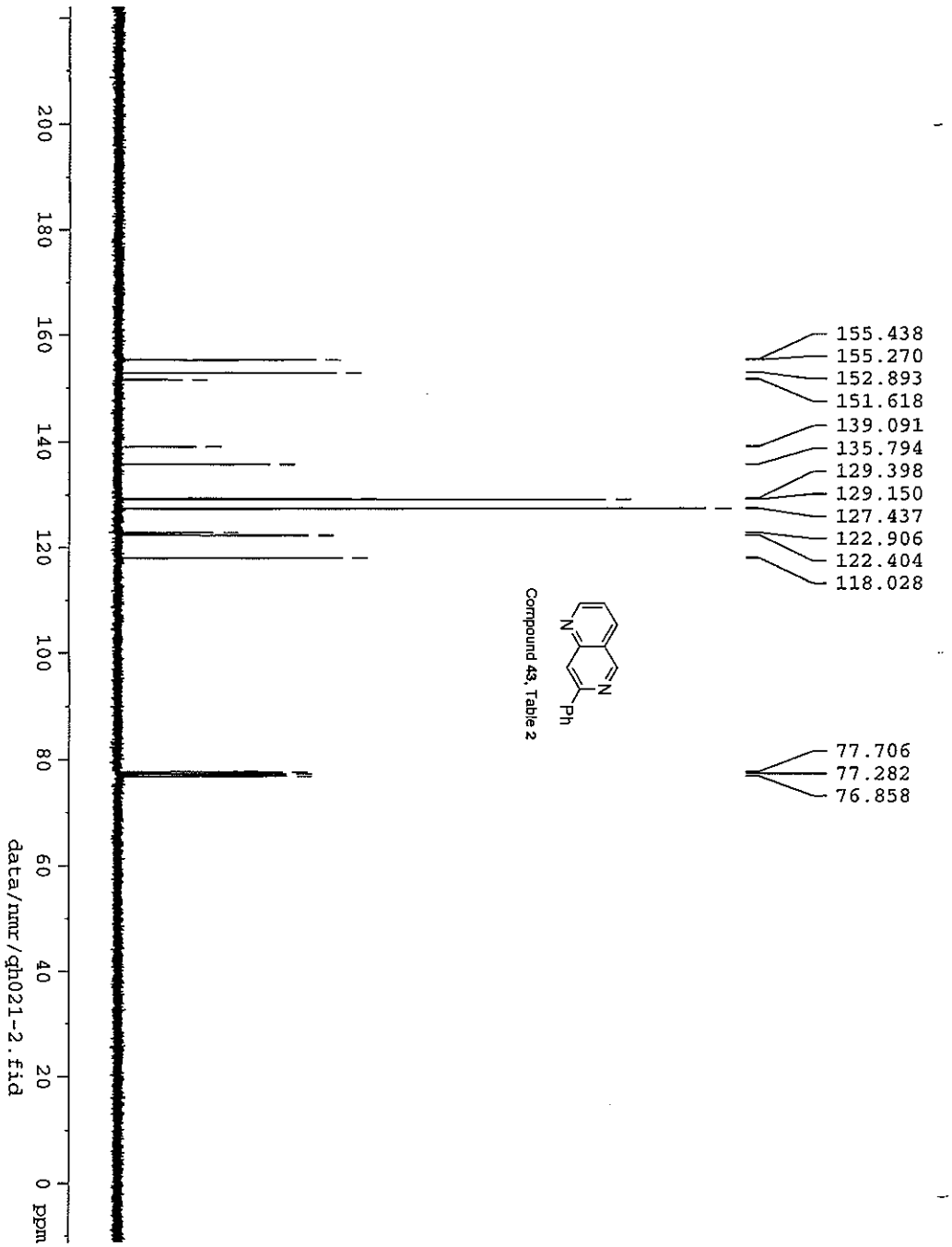

152.601
152.180
136.611
130.501
127.679
127.396
126.718
126.359
119.373
99.041
77.653
77.229
76.805
67.110
62.434
38.588
30.839
25.617
19.734
Compound 41, Table 2
CH2CH2OTHP
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmmr300/qh075-2.fid

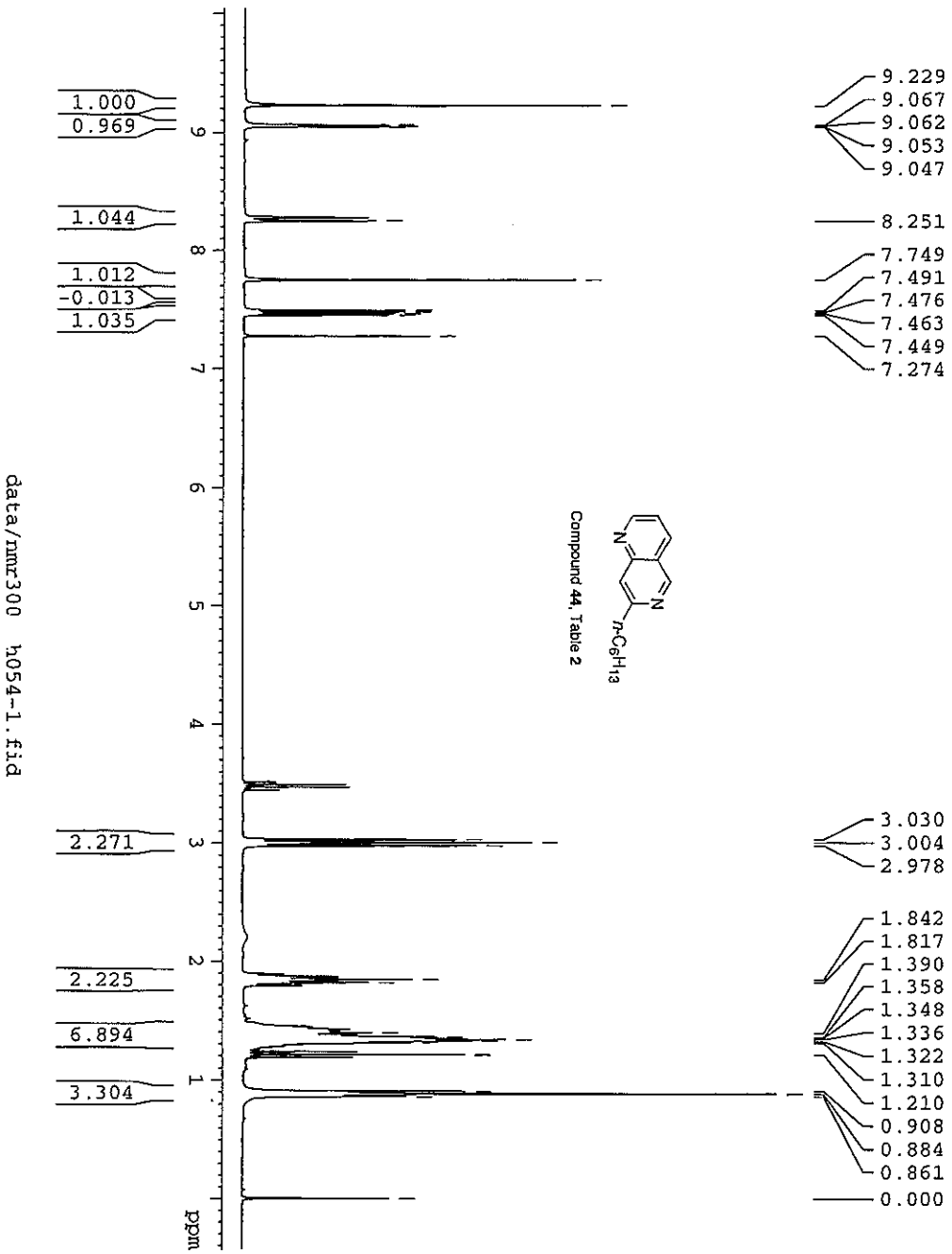

9.064
8.078
8.053
7.897
7.511
7.487
7.463
7.412
7.390
7.367
7.258
7.209
7.114
6.101
1.000
2.141
1.043
3.370
1.687
1.143
2.184
11
10
9
8
7
6
5
4
3
2
1
0
-1 ppm
Compound 42, Table 2
O
O
O
N
Ph

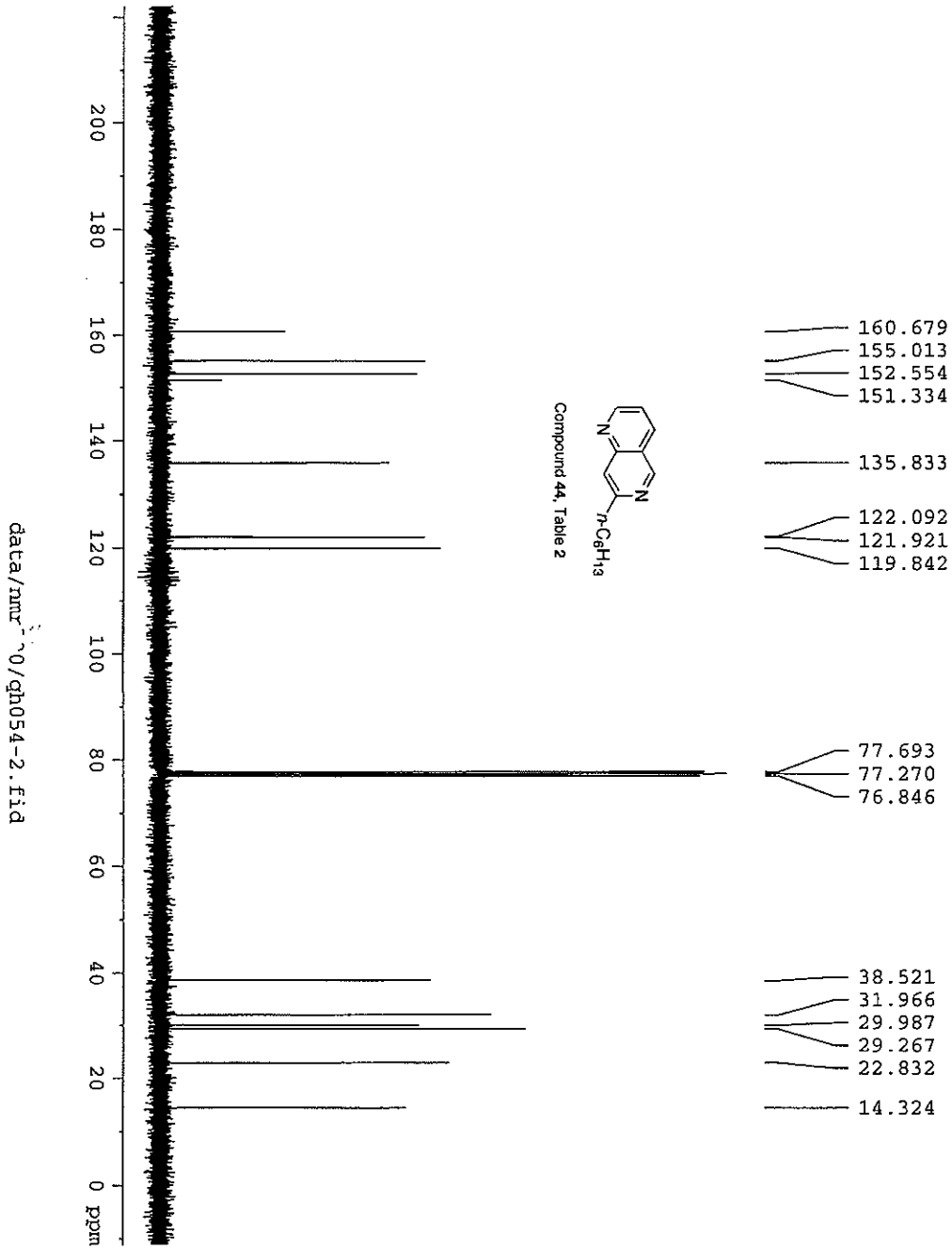
6e-1,+1

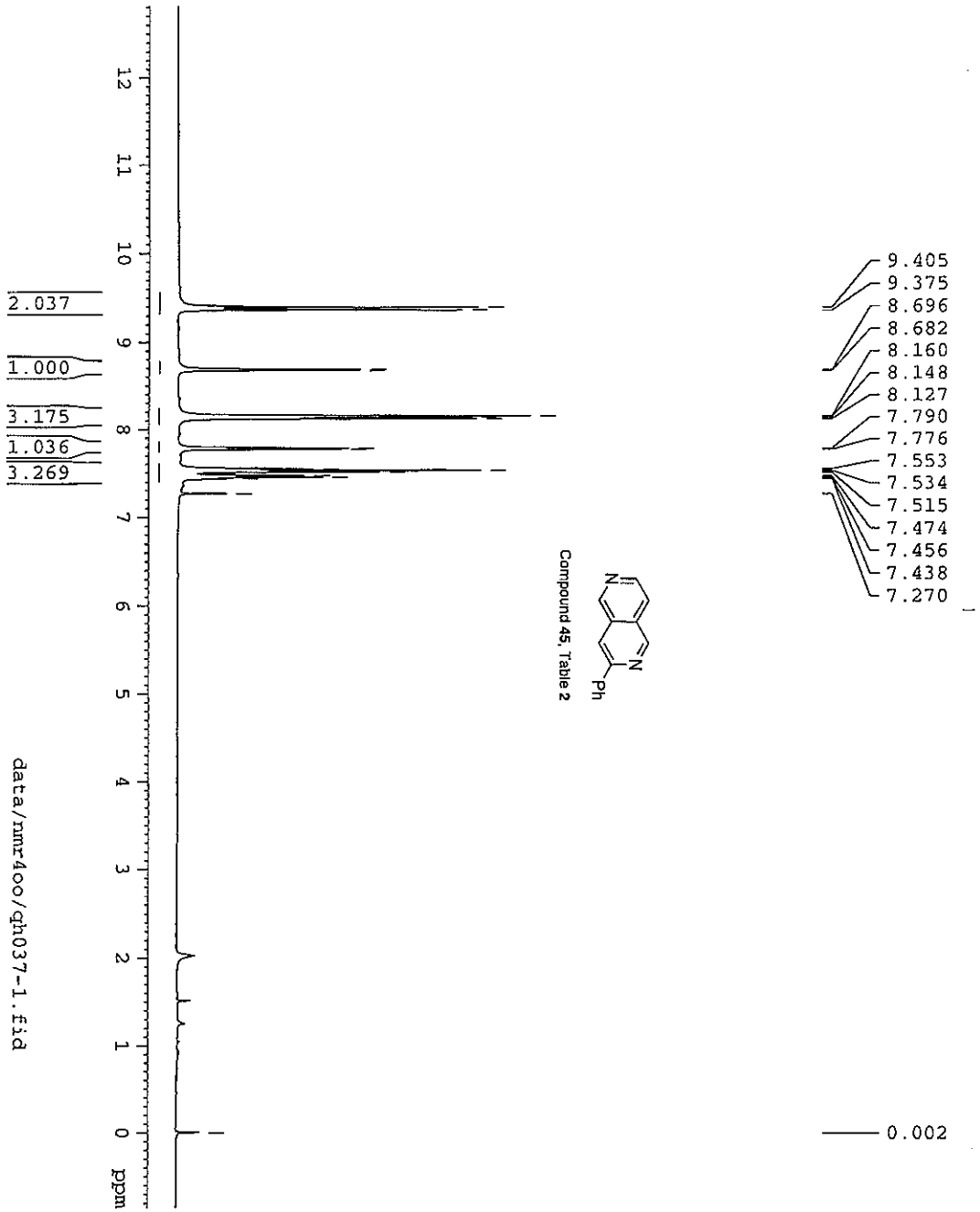

151.350
150.837
150.396
148.585
139.901
135.309
128.963
128.523
127.017
125.252
116.589
103.355
103.040
101.850
77.672
77.450
77.248
76.826
Compound 42, Table 2
Ph
N
O
O
200
180
160
140
120
100
80
60
40
20
0 ppm

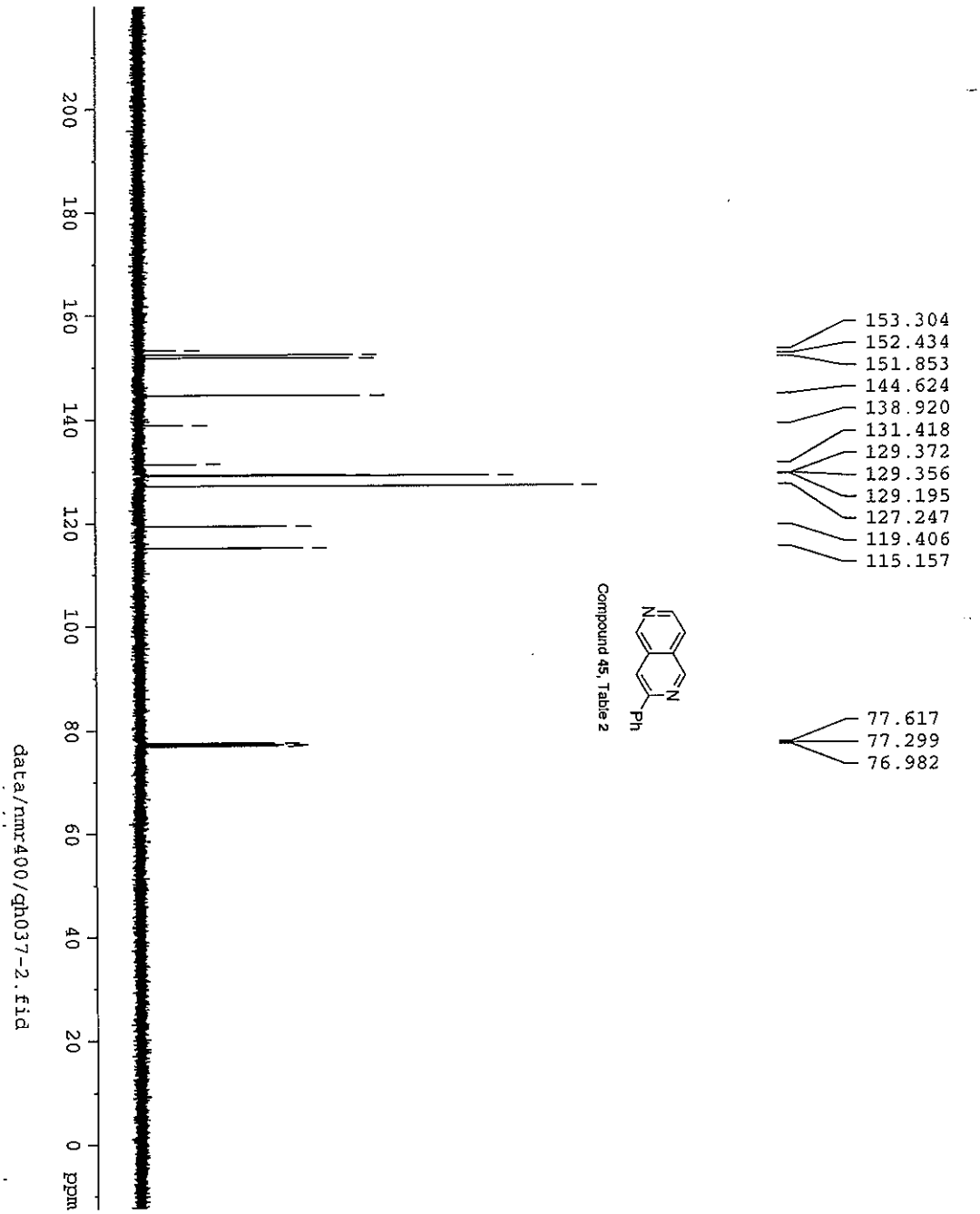

9.347
9.344
9.096
9.090
9.082
9.076
8.347
8.306
8.303
8.301
8.298
8.279
8.276
8.273
8.270
8.197
8.193
8.186
8.174
8.169
8.165
7.563
7.559
7.535
7.530
7.514
7.510
7.495
7.482
7.475
7.471
7.468
7.451
7.270
0.001
Compound 43, Table 2
Ph
N
N
1.000
1.023
1.099
1.105
1.087
1.142
4.486
12
11
10
9
8
7
6
5
4
3
2
1
ppm
data/dat2/nmr300/qh021-1.fid

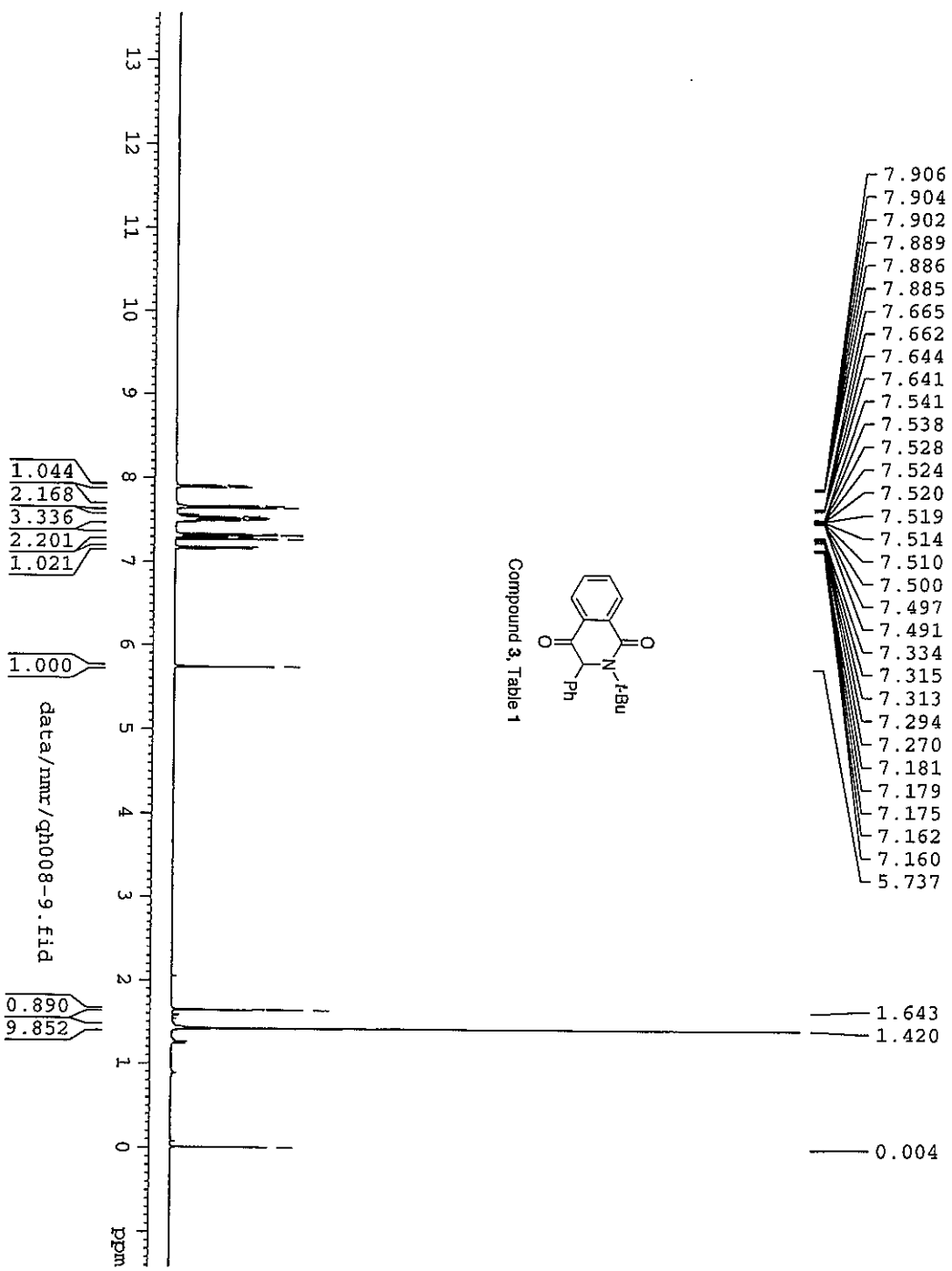

155.438
155.270
152.893
151.618
139.091
135.794
129.398
129.150
127.437
122.906
122.404
118.028
77.706
77.282
76.858
Compound 43, Table 2
N
N
Ph
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/qh021-2.fid

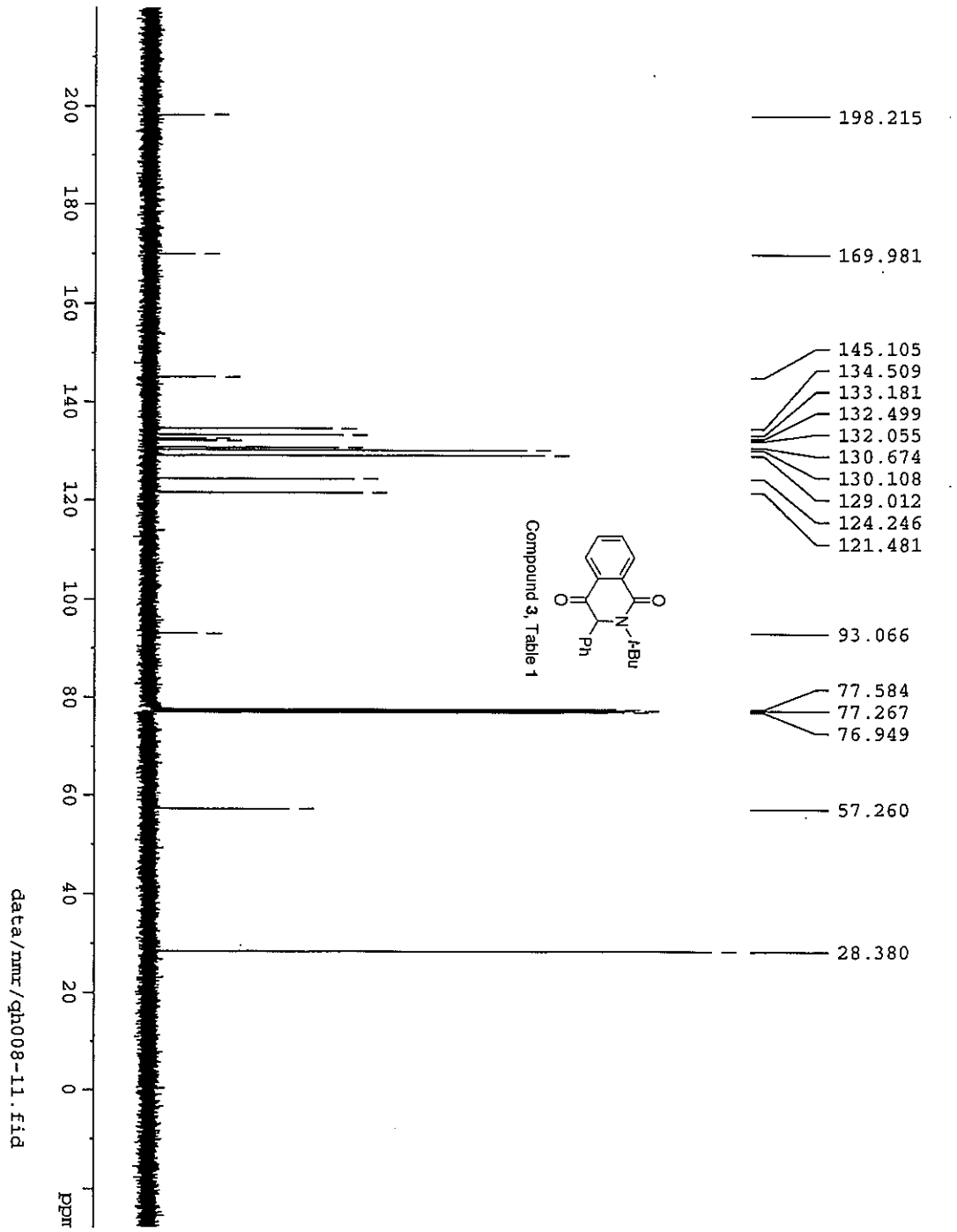

data/nmr300 h054-1.fid
Compound 44, Table 2
n-C6H13
ppm
1.000
0.969
1.044
1.012
-0.013
1.035
2.271
2.225
6.894
3.304
9.229
9.067
9.062
9.053
9.047
8.251
7.749
7.491
7.476
7.463
7.449
7.274
3.030
3.004
2.978
1.842
1.817
1.390
1.358
1.348
1.336
1.322
1.310
1.210
0.908
0.884
0.861
0.000


160.679
155.013
152.554
151.334
135.833
122.092
121.921
119.842
77.693
77.270
76.846
38.521
31.966
29.987
29.267
22.832
14.324
Compound 44, Table 2
n-C6H13
200
180
160
140
120
100
80
60
40
20
0 ppm
data/nmr/0/qh054-2.fid

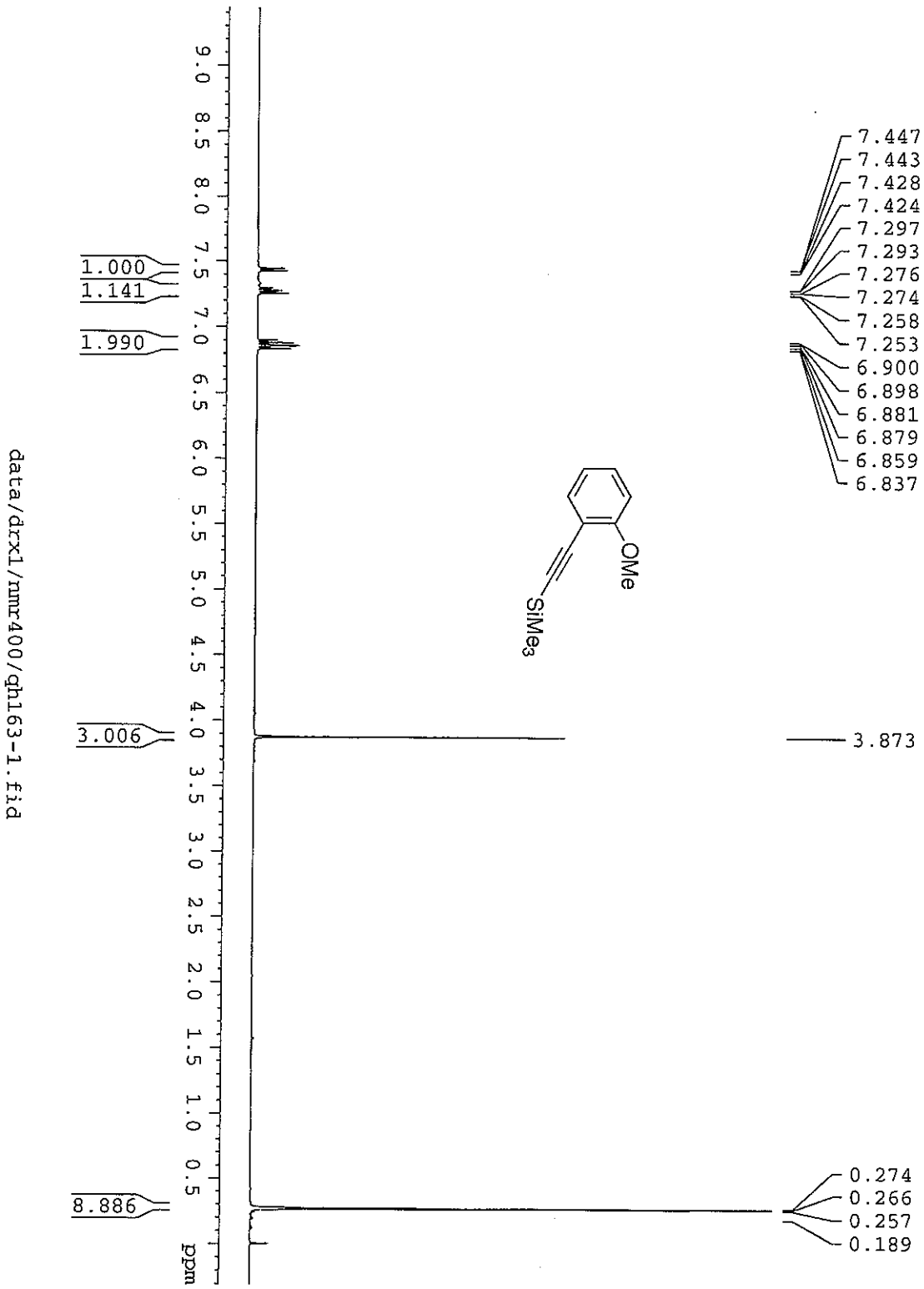

9.405
9.375
8.696
8.682
8.160
8.148
8.127
7.790
7.776
7.553
7.534
7.515
7.474
7.456
7.438
7.270
0.002
2.037
1.000
3.175
1.036
3.269
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
Compound 45, Table 2
N
N
Ph
data/nmr400/qh037-1.fid

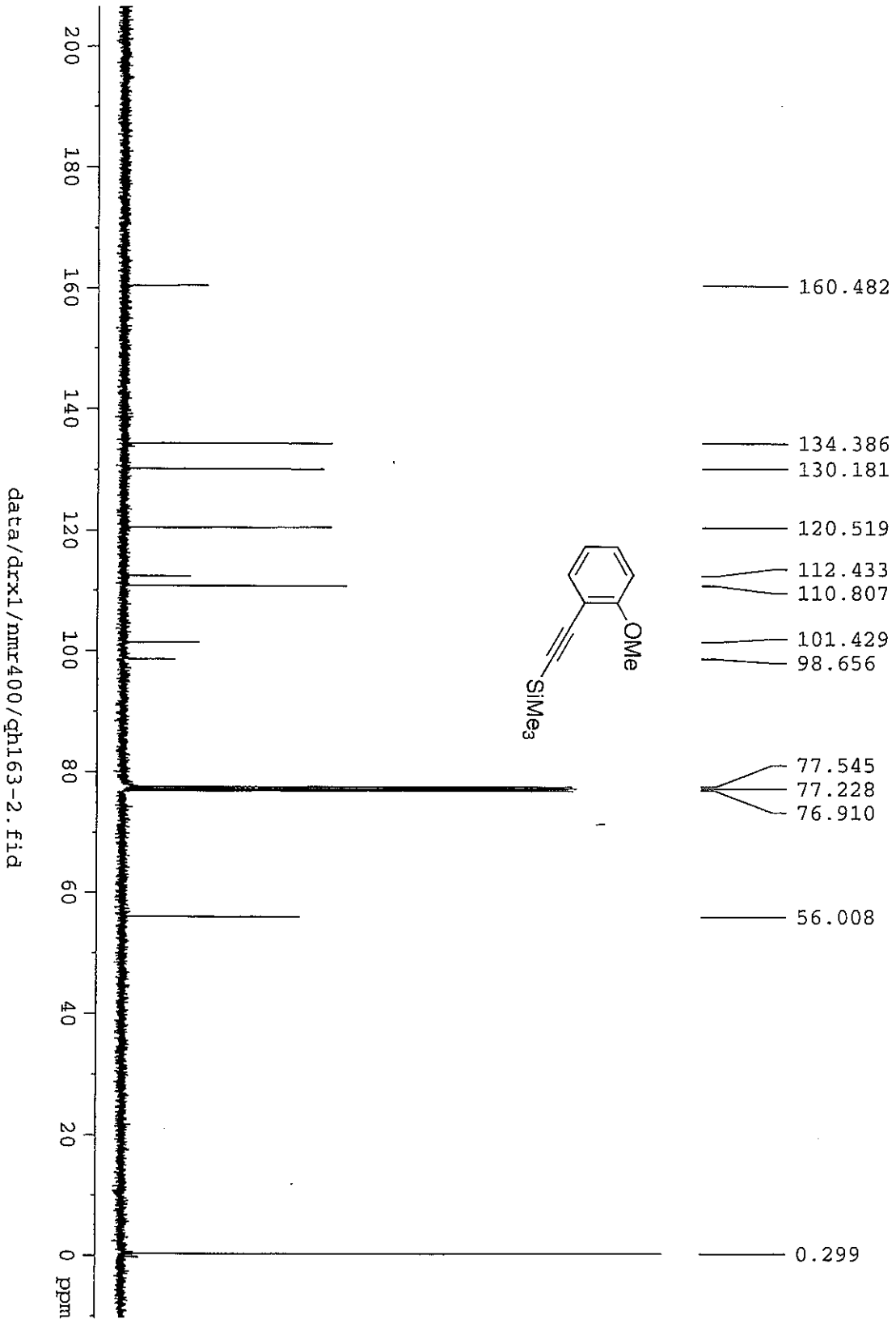

153.304
152.434
151.853
144.624
138.920
131.418
129.372
129.356
129.195
127.247
119.406
115.157
77.617
77.299
76.982
Compound 45, Table 2
N
N
Ph
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr400/qh037-2.fid

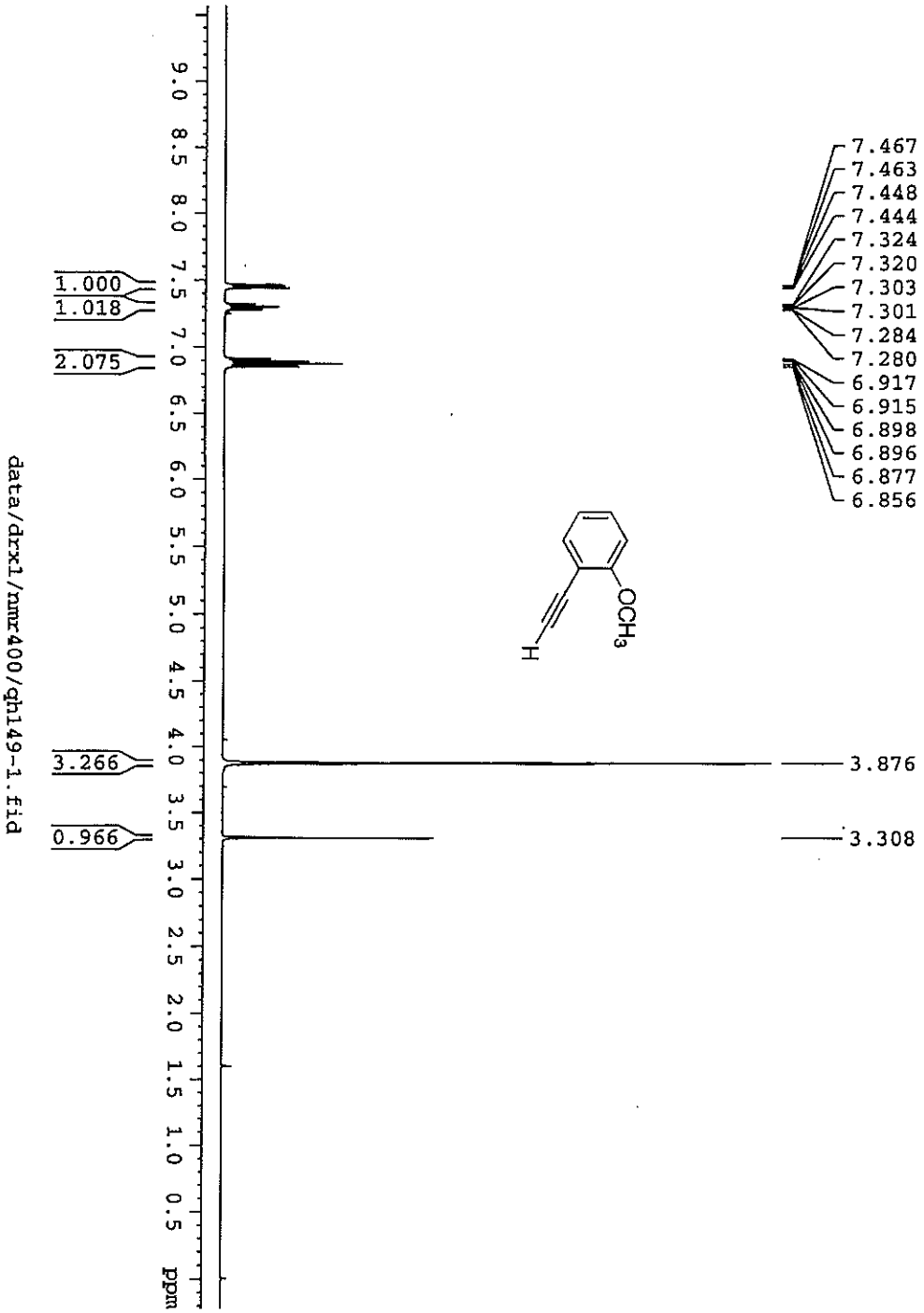

7.906
7.904
7.902
7.889
7.886
7.885
7.665
7.662
7.644
7.641
7.541
7.538
7.528
7.524
7.520
7.519
7.514
7.510
7.500
7.497
7.491
7.334
7.315
7.313
7.294
7.270
7.181
7.179
7.175
7.162
7.160
5.737
1.643
1.420
0.004
1.044
2.168
3.336
2.201
1.021
1.000
0.890
9.852
data/nmr/qh008-9.fid
Compound 3, Table 1
O
O
N
t-Bu
Ph
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

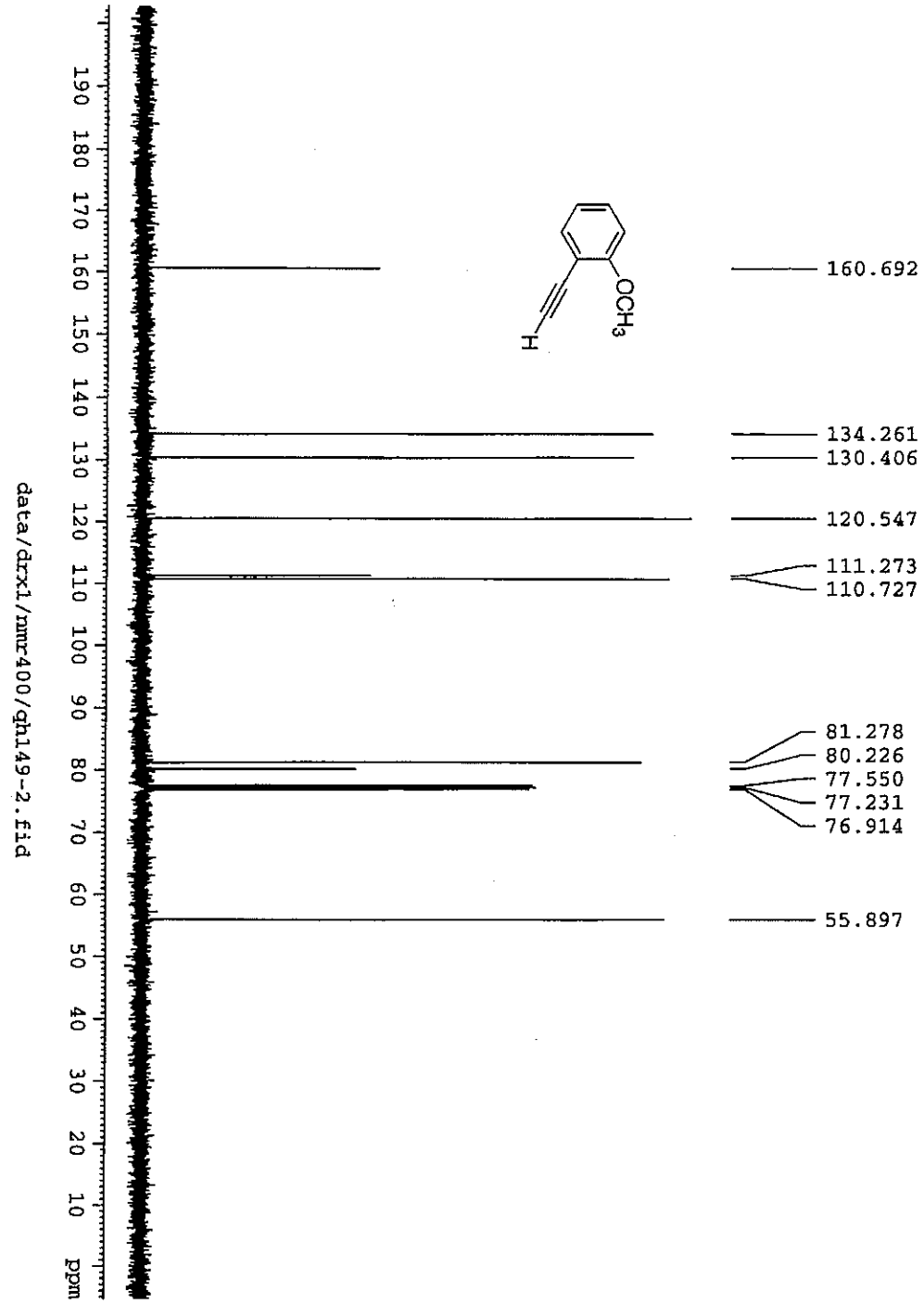

198.215
169.981
145.105
134.509
133.181
132.499
132.055
130.674
130.108
129.012
124.246
121.481
93.066
77.584
77.267
76.949
57.260
28.380
Compound 3, Table 1
Ph
N
t-Bu
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm
data/nmr/qh008-11.fid

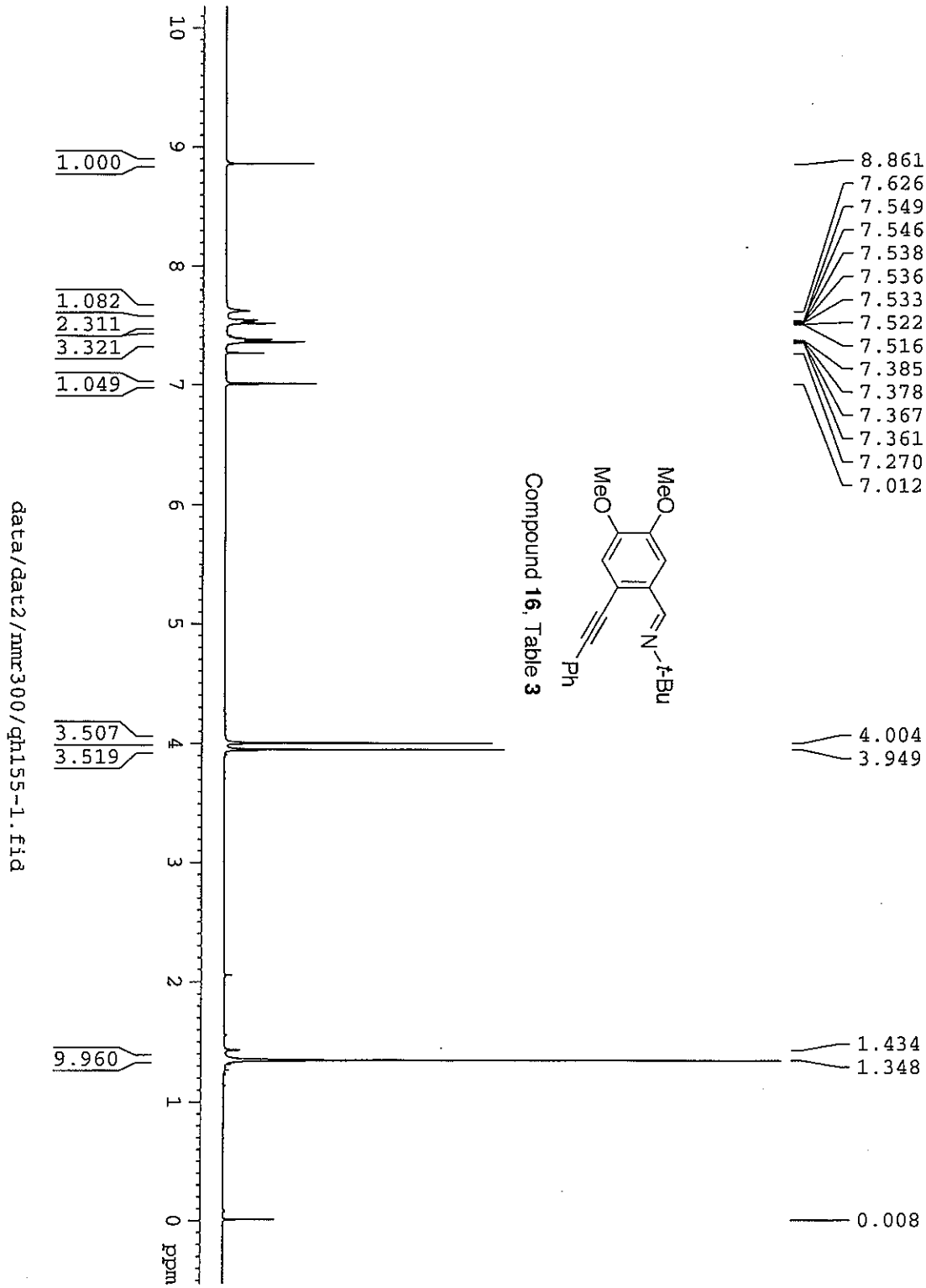
APPENDIX B. CHAPTER 2 ^{1}H AND ^{13}C NMR SPECTRA

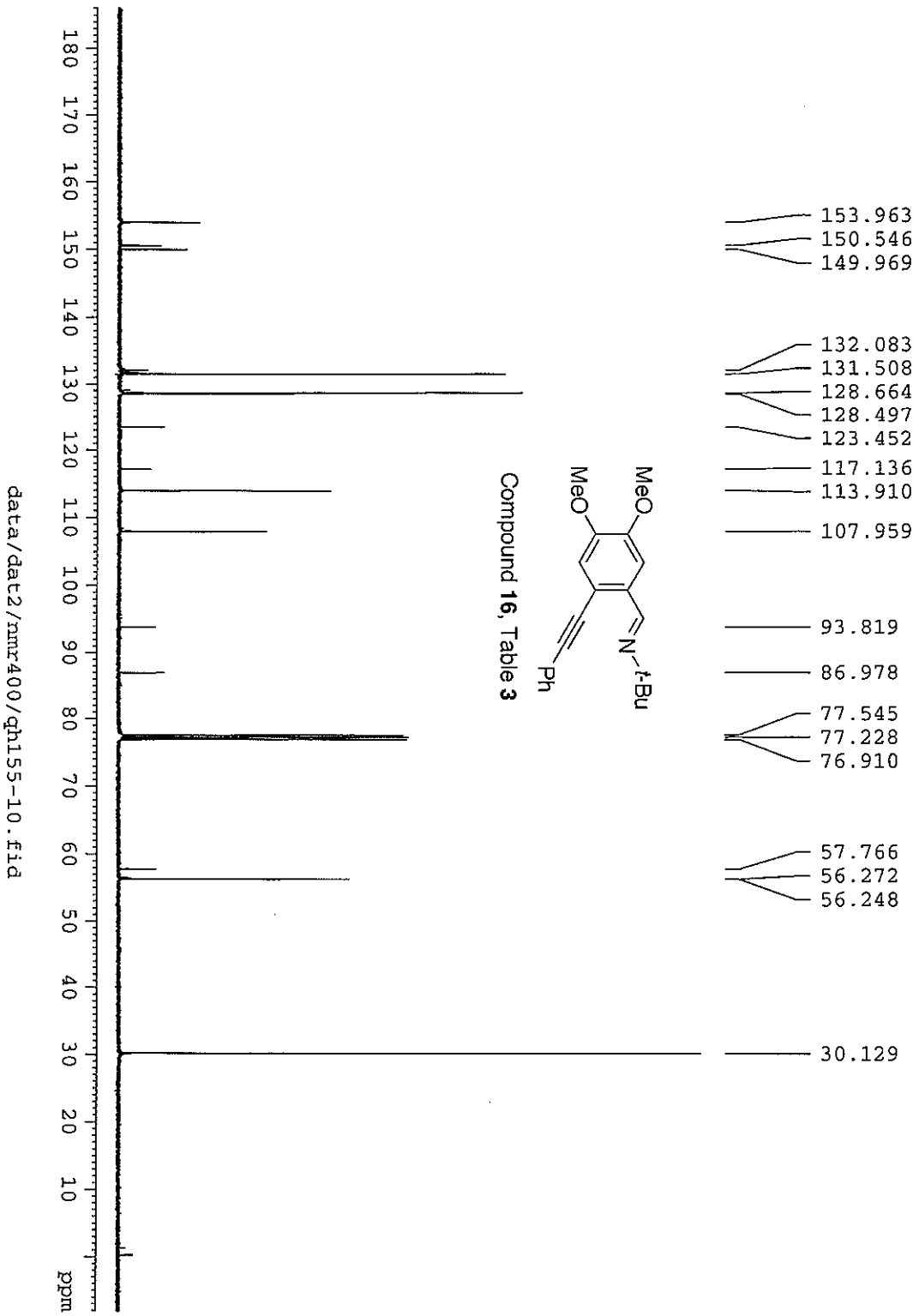

7.447
7.443
7.428
7.424
7.297
7.293
7.276
7.274
7.258
7.253
6.900
6.898
6.881
6.879
6.859
6.837
OMe
SiMe3
3.873
0.274
0.266
0.257
0.189
1.000
1.141
1.990
3.006
8.886
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/drxl/nmr400/qh163-1.fid

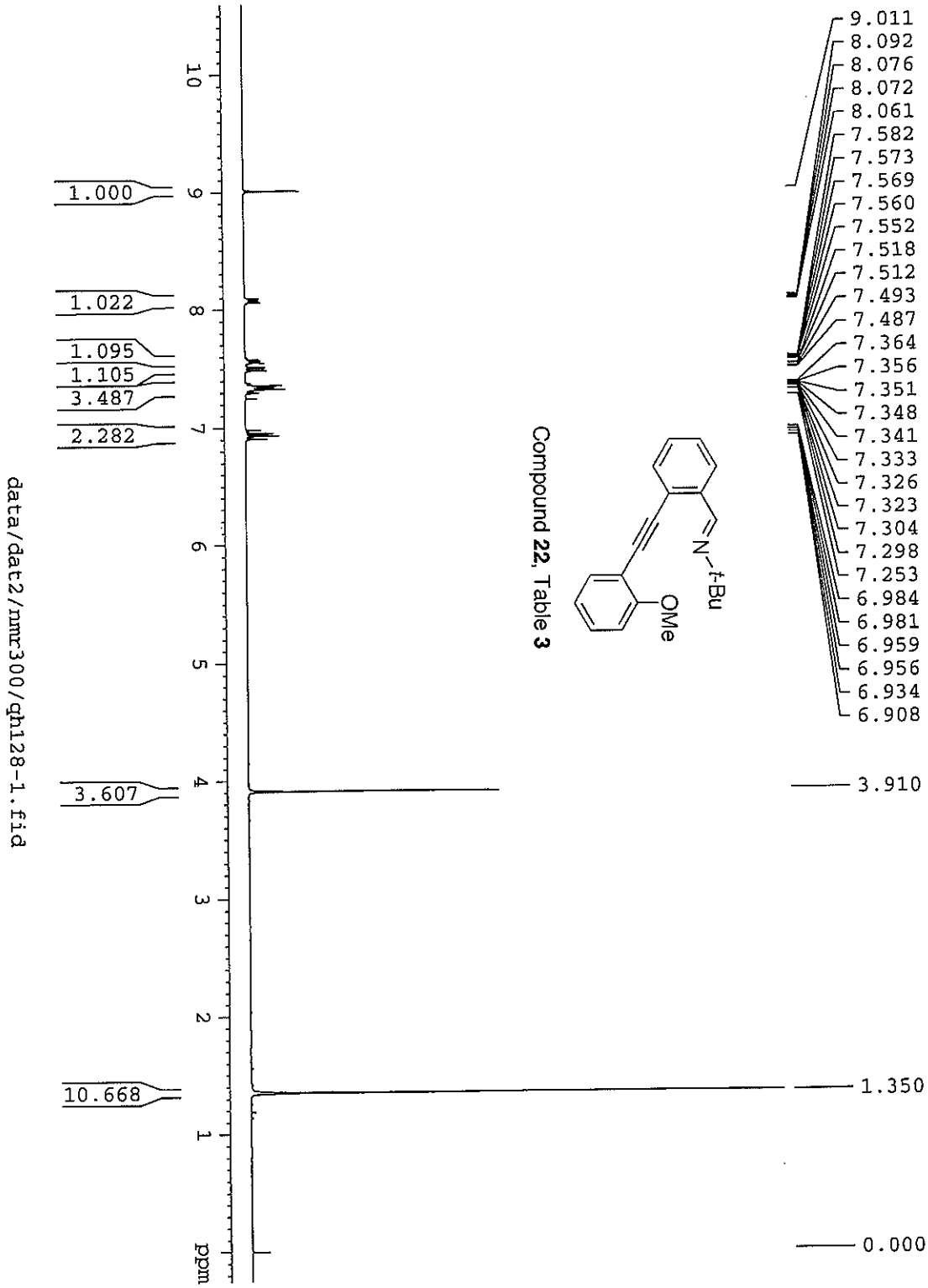

160.482
134.386
130.181
120.519
112.433
110.807
101.429
98.656
77.545
77.228
76.910
56.008
0.299
OMe
SiMe3
200
180
160
140
120
100
80
60
40
20
0
ppm
data/drx1/nmr400/qh163-2.fid

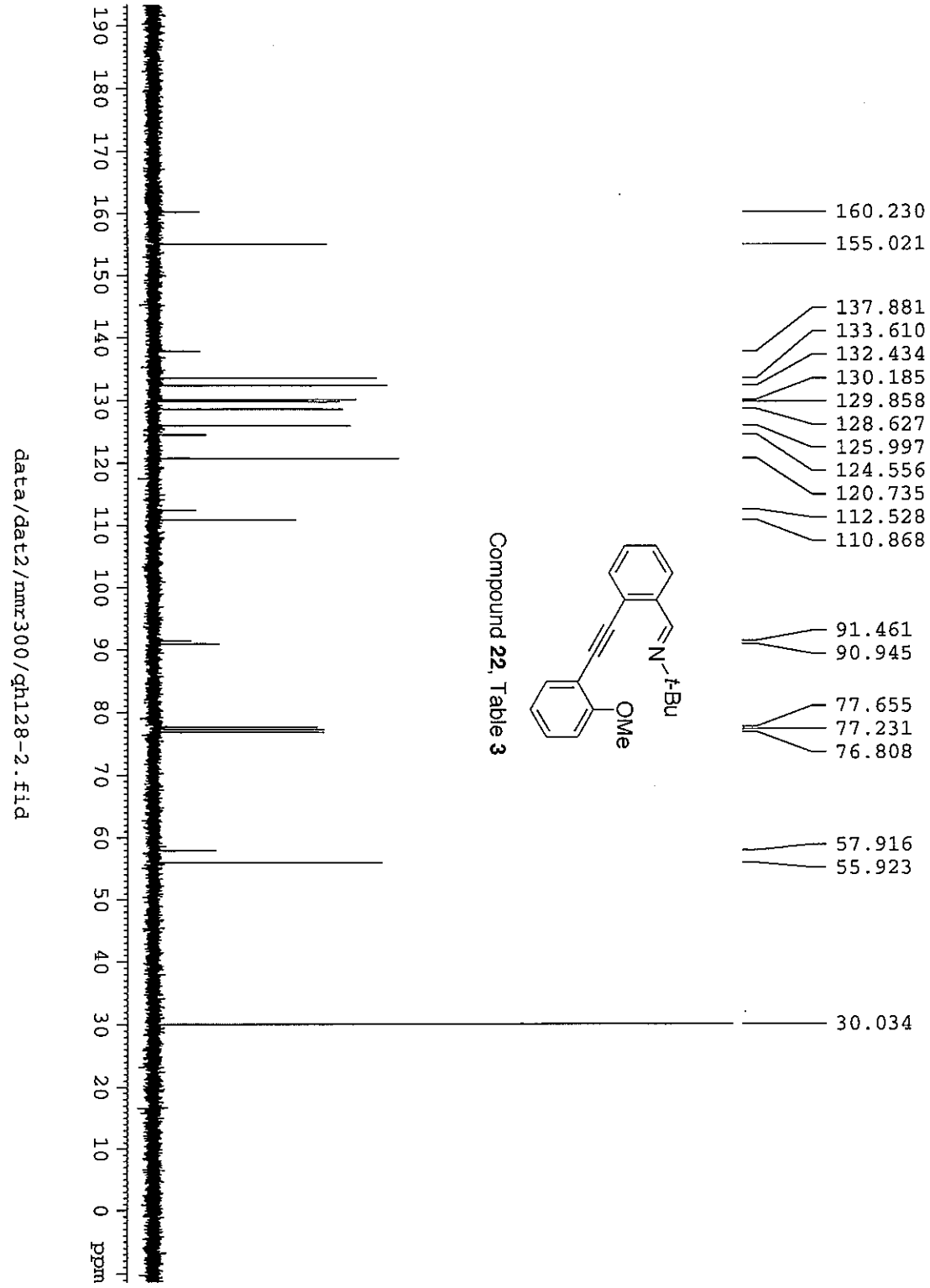

7.467
7.463
7.448
7.444
7.324
7.320
7.303
7.301
7.284
7.280
6.917
6.915
6.898
6.896
6.877
6.856
3.876
3.308
1.000
1.018
2.075
3.266
0.966
OCH3
H
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
data/drx1/nmr400/qh149-1.fid

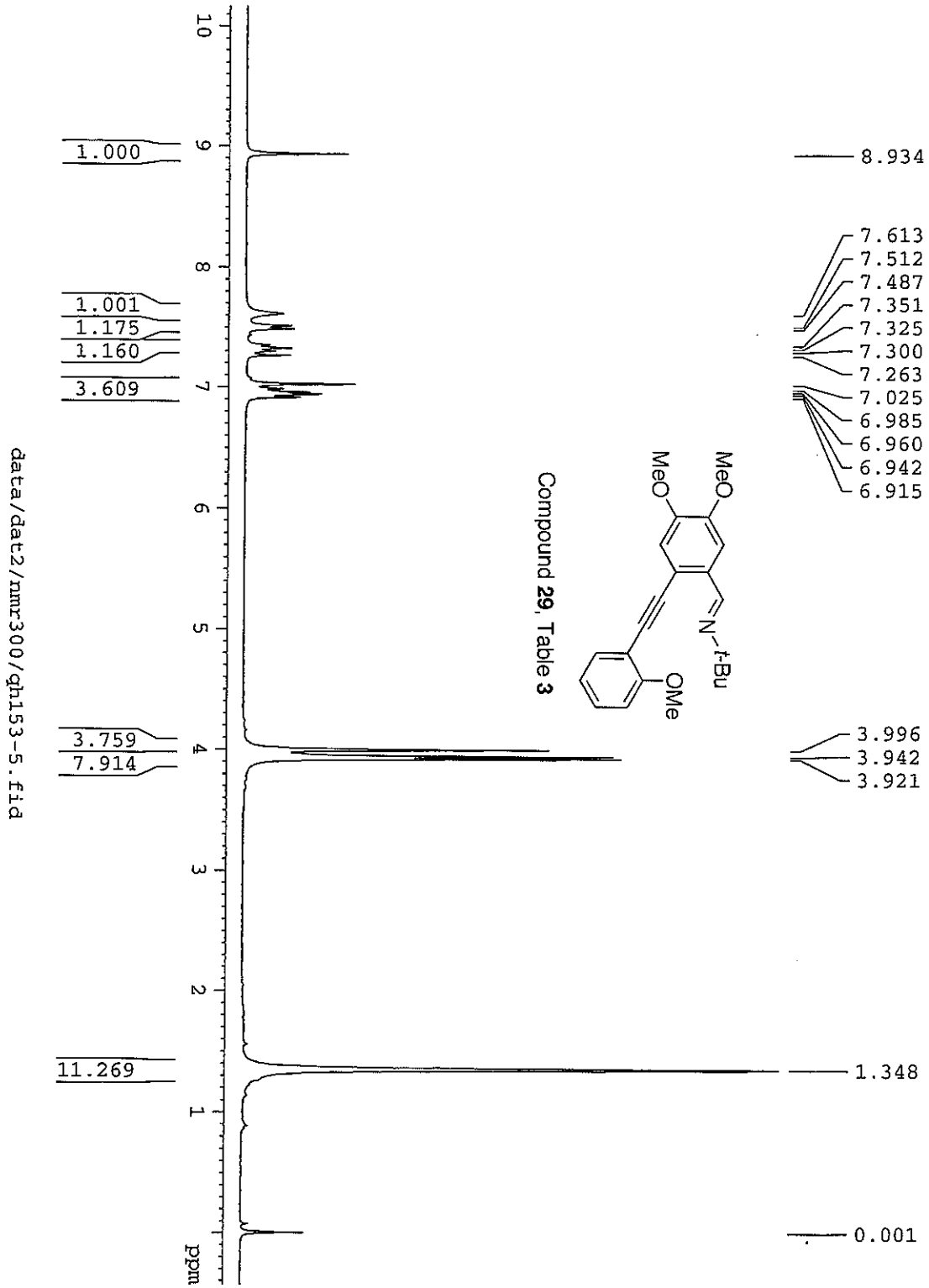

160.692
134.261
130.406
120.547
111.273
110.727
81.278
80.226
77.550
77.231
76.914
55.897
OCH3
H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh149-2.fid


8.861
7.626
7.549
7.546
7.538
7.536
7.533
7.522
7.516
7.385
7.378
7.367
7.361
7.270
7.012
4.004
3.949
1.434
1.348
0.008
1.000
1.082
2.311
3.321
1.049
3.507
3.519
9.960
MeO
MeO
N
t-Bu
Ph
Compound 16, Table 3
data/dat2/nmr300/qh155-1.fid
ppm


153.963
150.546
149.969
132.083
131.508
128.664
128.497
123.452
117.136
113.910
107.959
93.819
86.978
77.545
77.228
76.910
57.766
56.272
56.248
30.129
MeO
MeO
N
t-Bu
Ph
Compound 16, Table 3
data/dat2/nmr400/qh155-10.fid
ppm


9.011
8.092
8.076
8.072
8.061
7.582
7.573
7.569
7.560
7.552
7.518
7.512
7.493
7.487
7.364
7.356
7.351
7.348
7.341
7.333
7.326
7.323
7.304
7.298
7.253
6.984
6.981
6.959
6.956
6.934
6.908
3.910
1.350
0.000
1.000
1.022
1.095
1.105
3.487
2.282
3.607
10.668
ppm
Compound 22, Table 3
N-t-Bu
OMe
data/dat2/nmr300/qh128-1.fid


160.230
155.021
137.881
133.610
132.434
130.185
129.858
128.627
125.997
124.556
120.735
112.528
110.868
91.461
90.945
77.655
77.231
76.808
57.916
55.923
30.034
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
N
t-Bu
OMe
Compound 22, Table 3
data/dat2/nmr300/qh128-2.fid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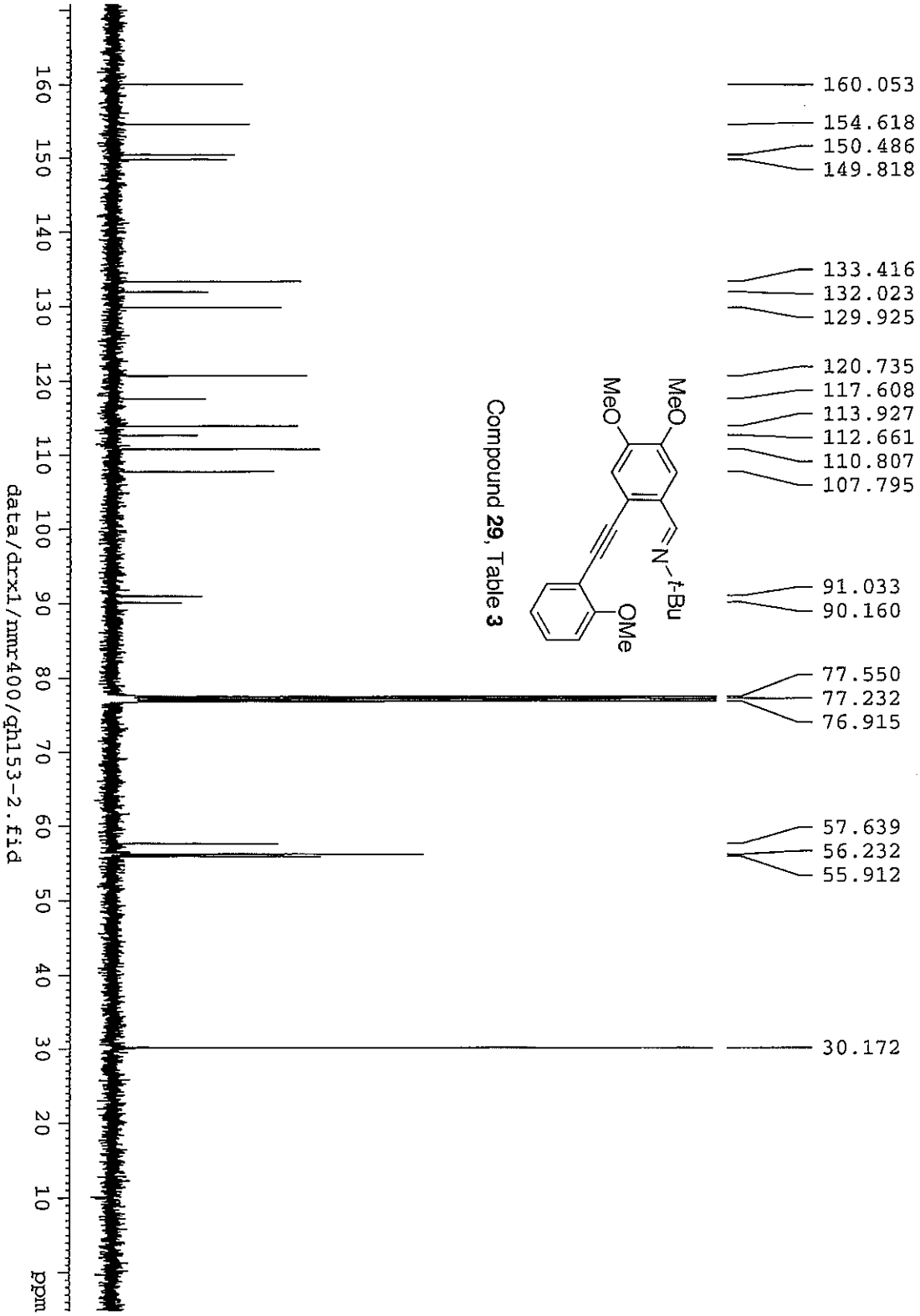
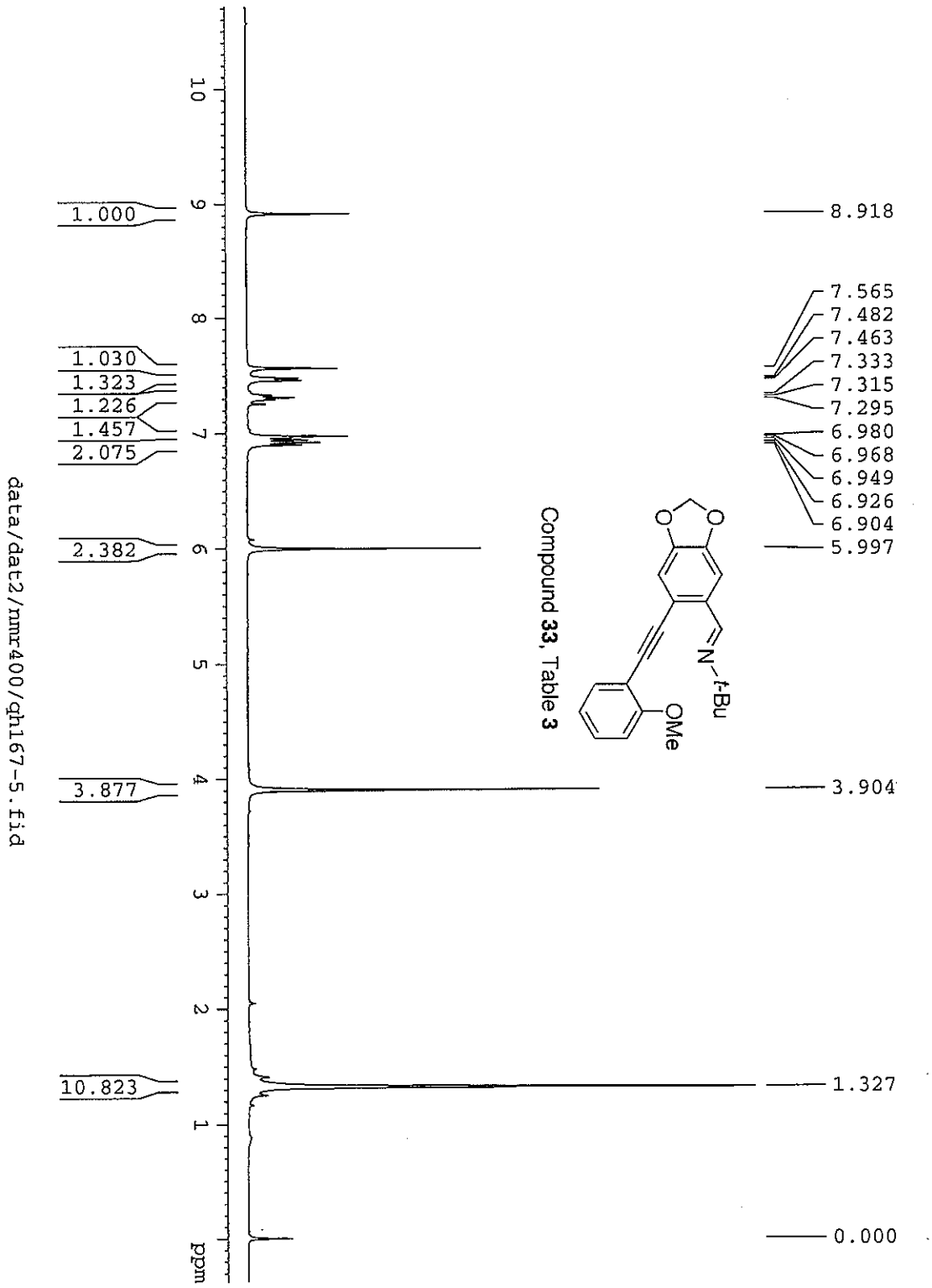
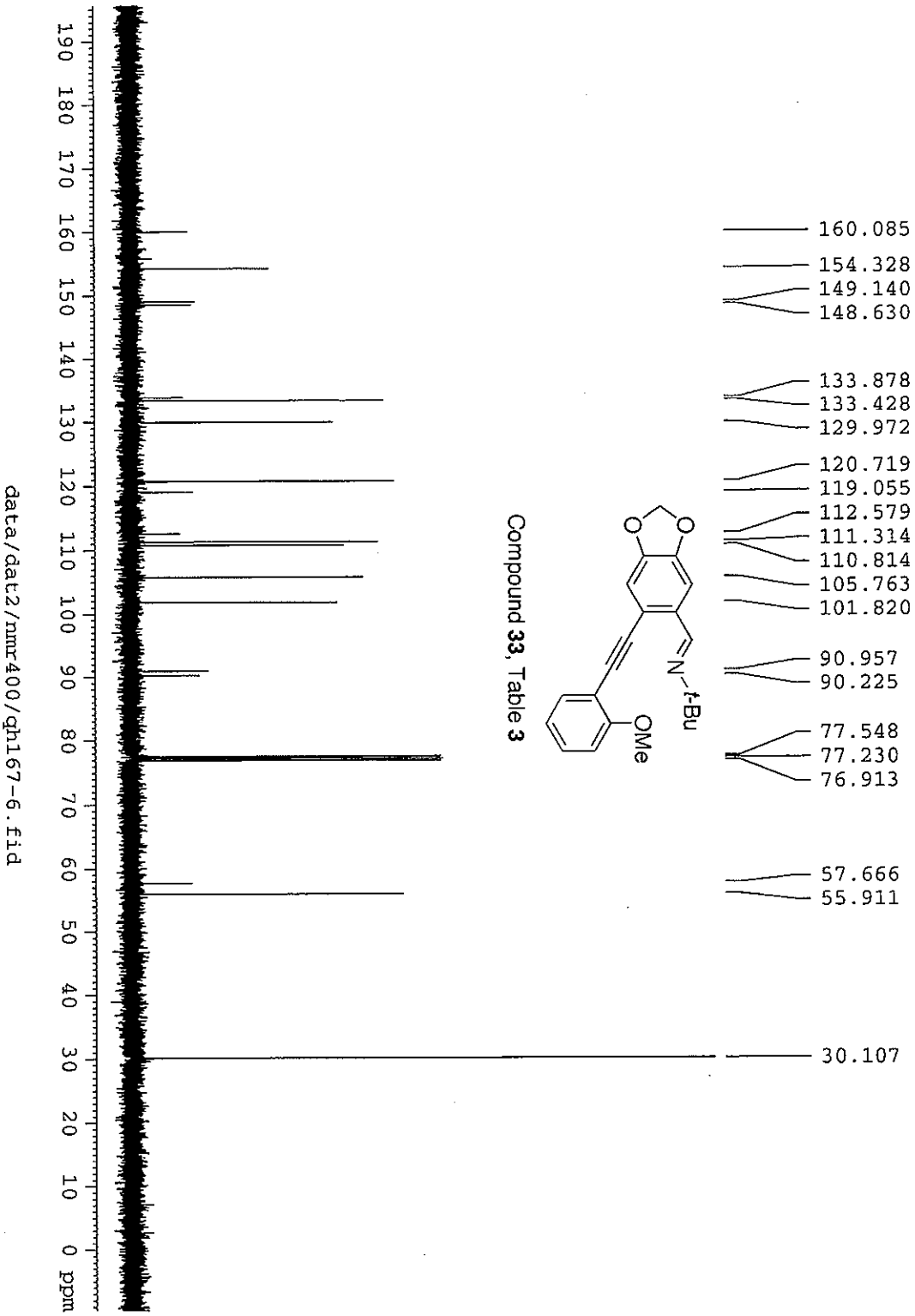
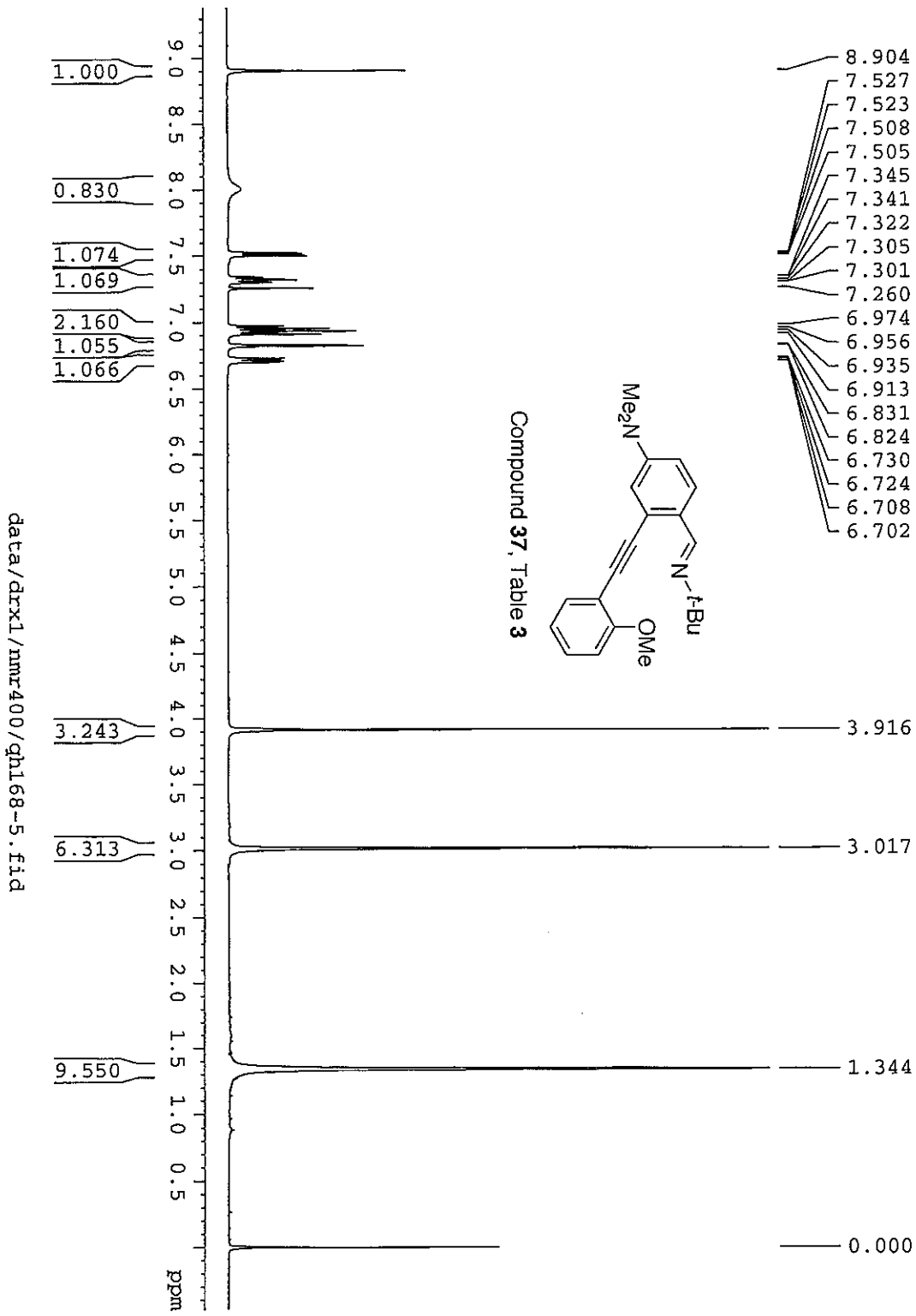
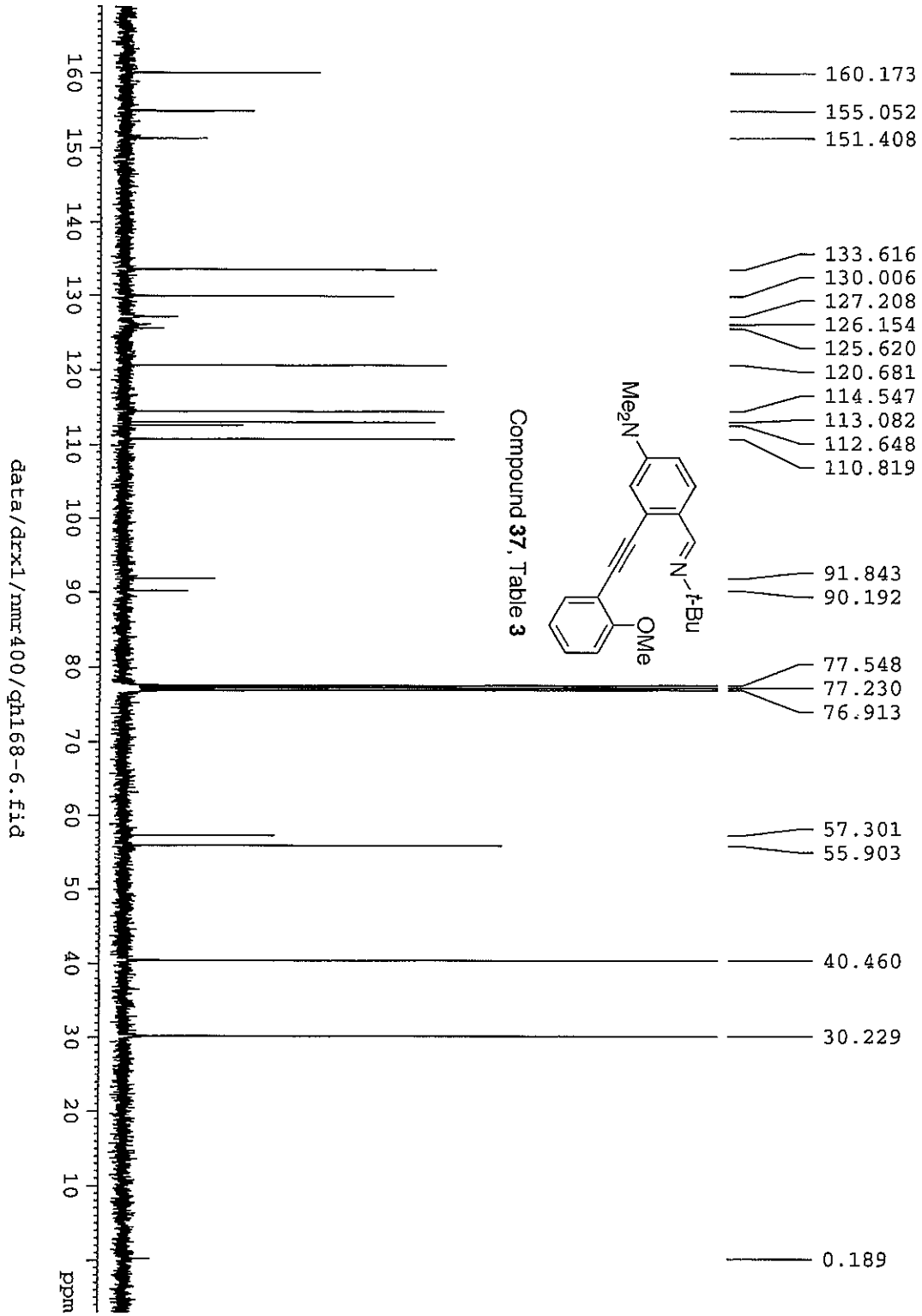
1.000
1.001
1.175
1.160
3.609
3.759
7.914
11.269
8.934
7.613
7.512
7.487
7.351
7.325
7.300
7.263
7.025
6.985
6.960
6.942
6.915
3.996
3.942
3.921
1.348
0.001
Compound 29, Table 3
MeO
MeO
N
t-Bu
OMe
ppm

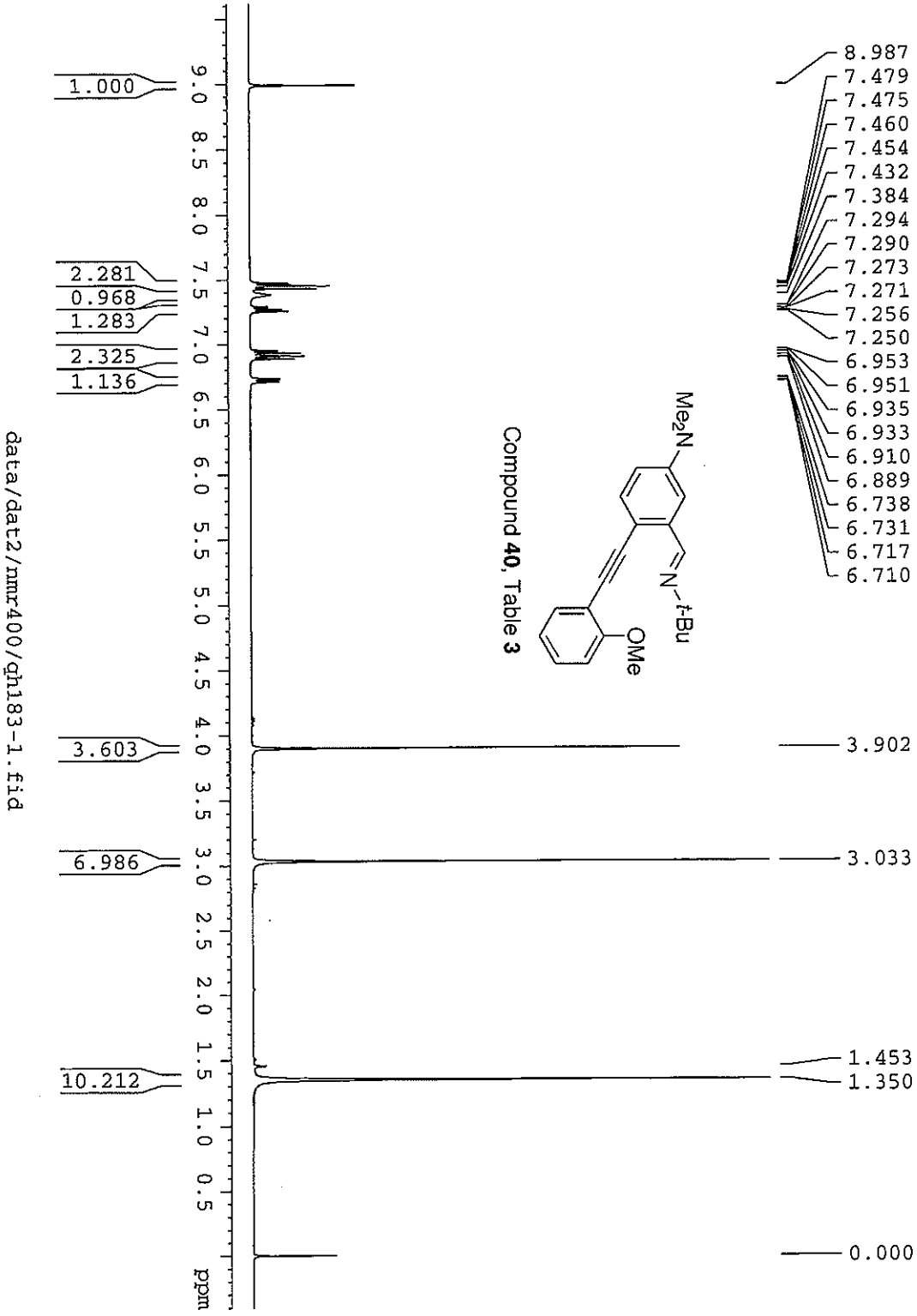

160.053
154.618
150.486
149.818
133.416
132.023
129.925
120.735
117.608
113.927
112.661
110.807
107.795
91.033
90.160
77.550
77.232
76.915
57.639
56.232
55.912
30.172
MeO
MeO
N
t-Bu
OMe
Compound 29, Table 3
data/drxl/nmr400/qh153-2.fid
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

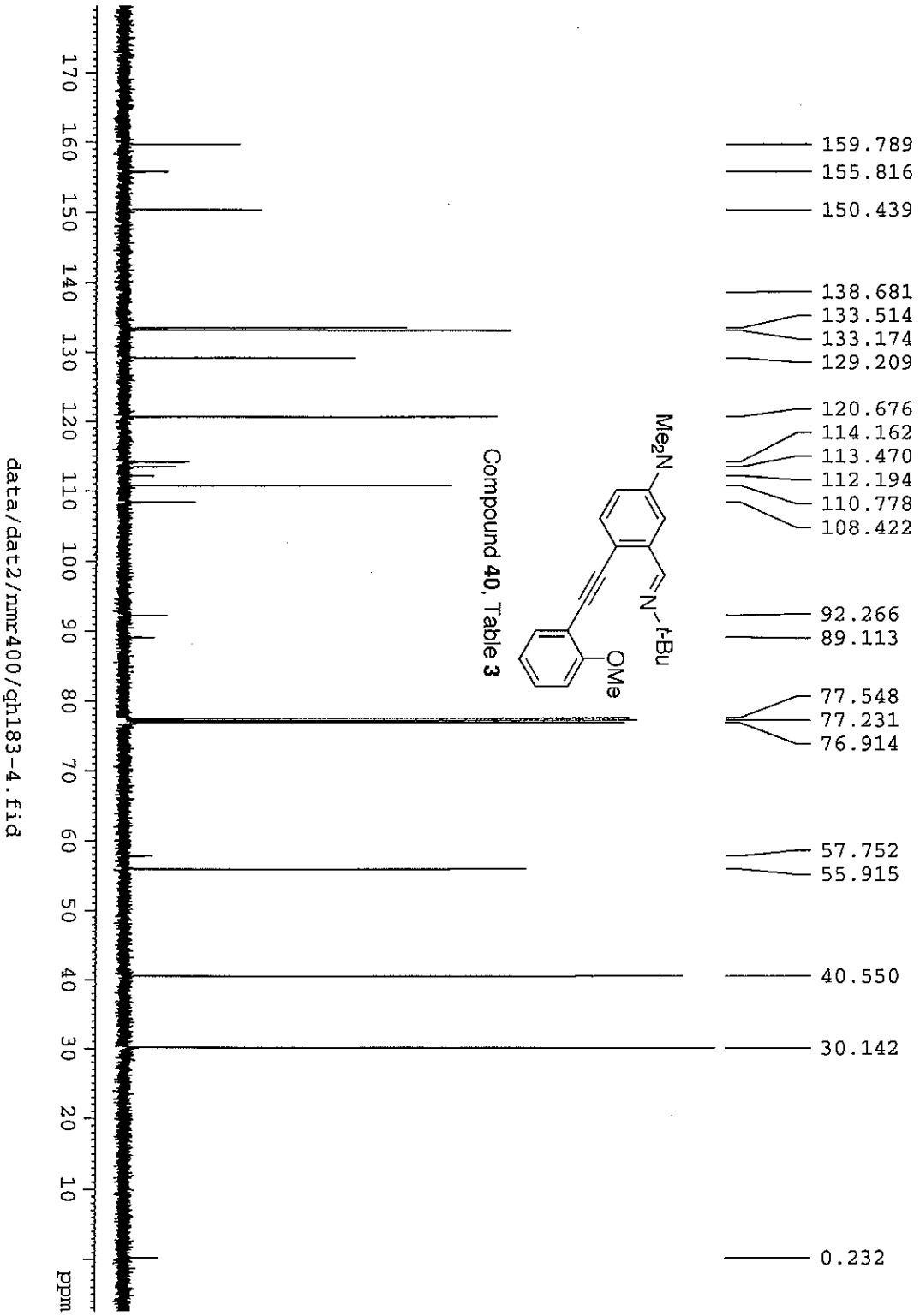

data/dat2/nmr400/qh167-5.fid
Compound 33, Table 3
N
t-Bu
OMe
1.000
1.030
1.323
1.226
1.457
2.075
2.382
3.877
10.823
8.918
7.565
7.482
7.463
7.333
7.315
7.295
6.980
6.968
6.949
6.926
6.904
5.997
3.904
1.327
0.000
ppm

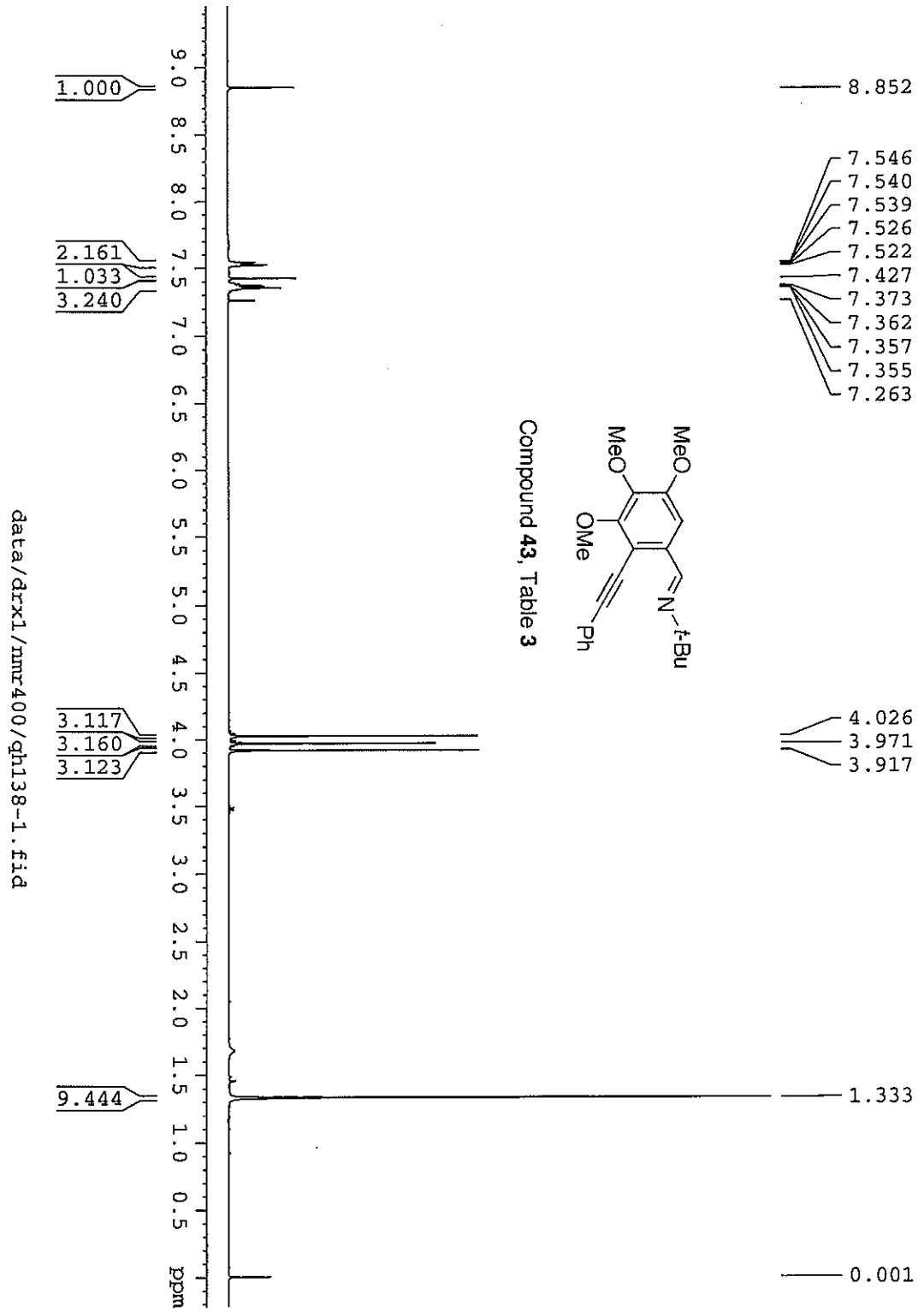

160.085
154.328
149.140
148.630
133.878
133.428
129.972
120.719
119.055
112.579
111.314
110.814
105.763
101.820
90.957
90.225
77.548
77.230
76.913
57.666
55.911
30.107
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh167-6.fid
Compound 33, Table 3
OMe
N
t-Bu

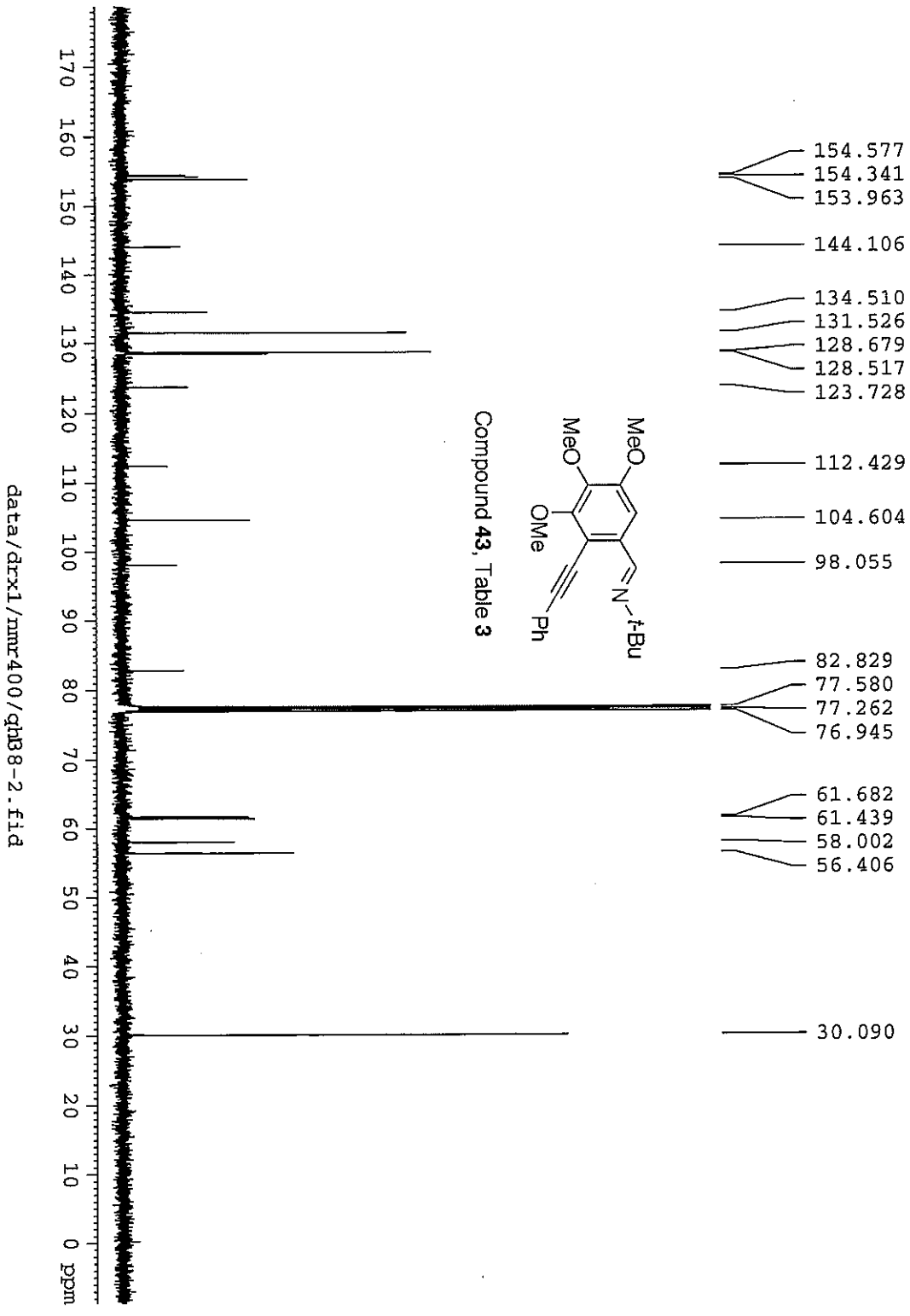

8.904
7.527
7.523
7.508
7.505
7.345
7.341
7.322
7.305
7.301
7.260
6.974
6.956
6.935
6.913
6.831
6.824
6.730
6.724
6.708
6.702
3.916
3.017
1.344
0.000
1.000
0.830
1.074
1.069
2.160
1.055
1.066
3.243
6.313
9.550
ppm
Compound 37, Table 3
Me2N
N-t-Bu
OMe
data/drx1/nmr400/qh168-5.fid

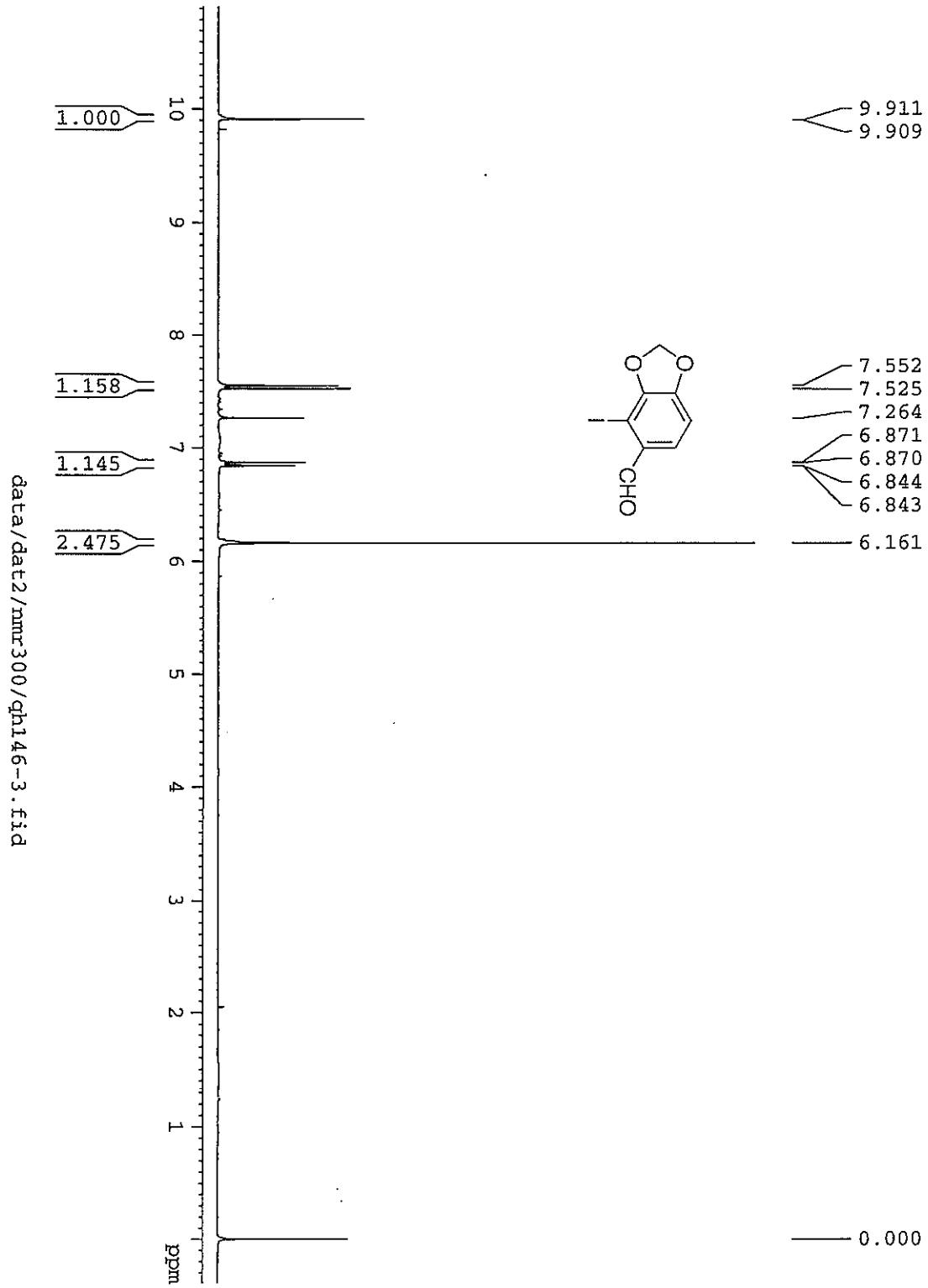

160.173
155.052
151.408
133.616
130.006
127.208
126.154
125.620
120.681
114.547
113.082
112.648
110.819
91.843
90.192
77.548
77.230
76.913
57.301
55.903
40.460
30.229
0.189
Me2N
N-t-Bu
OMe
Compound 37, Table 3
data/drx1/nmr400/qh168-6.fid
ppm

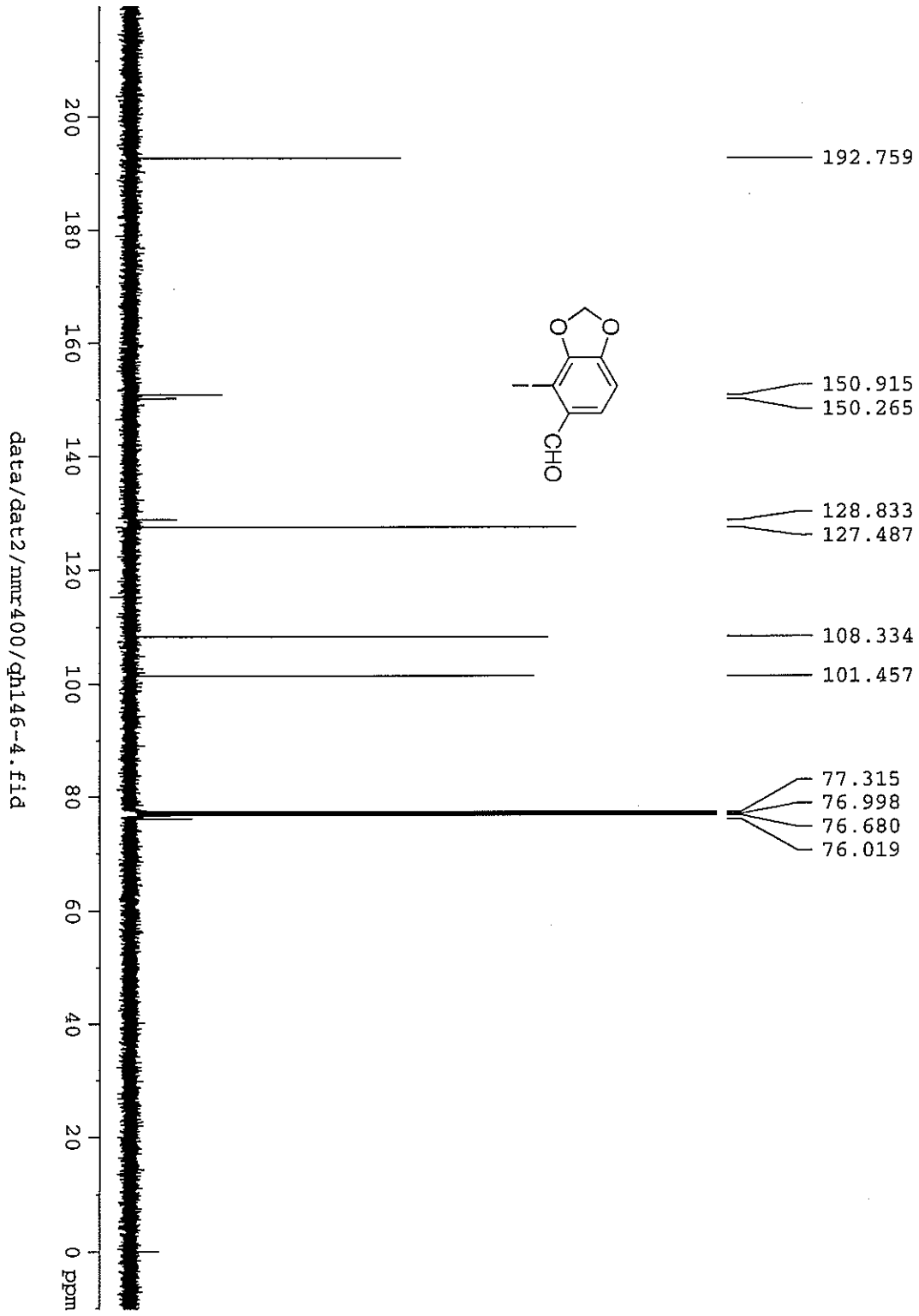

8.987
7.479
7.475
7.460
7.454
7.432
7.384
7.294
7.290
7.273
7.271
7.256
7.250
6.953
6.951
6.935
6.933
6.910
6.889
6.738
6.731
6.717
6.710
3.902
3.033
1.453
1.350
0.000
Me2N
N-t-Bu
OMe
Compound 40, Table 3
1.000
2.281
0.968
1.283
2.325
1.136
3.603
6.986
10.212
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
data/dat2/nmr400/qh183-1.fid

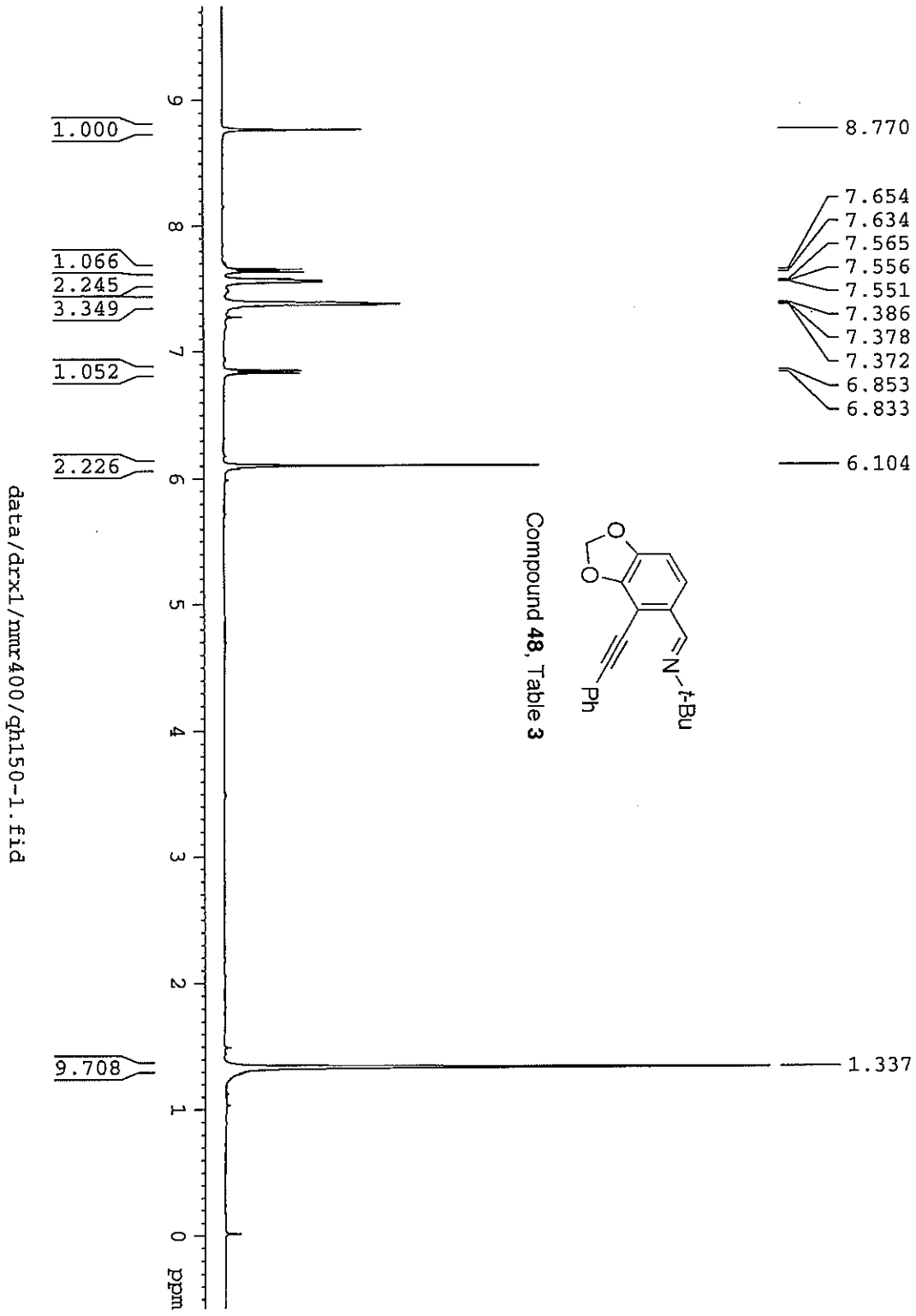

159.789
155.816
150.439
138.681
133.514
133.174
129.209
120.676
114.162
113.470
112.194
110.778
108.422
92.266
89.113
77.548
77.231
76.914
57.752
55.915
40.550
30.142
0.232
Me2N
N
t-Bu
OMe
Compound 40, Table 3
data/dat2/nmr400/qh183-4.fid
ppm

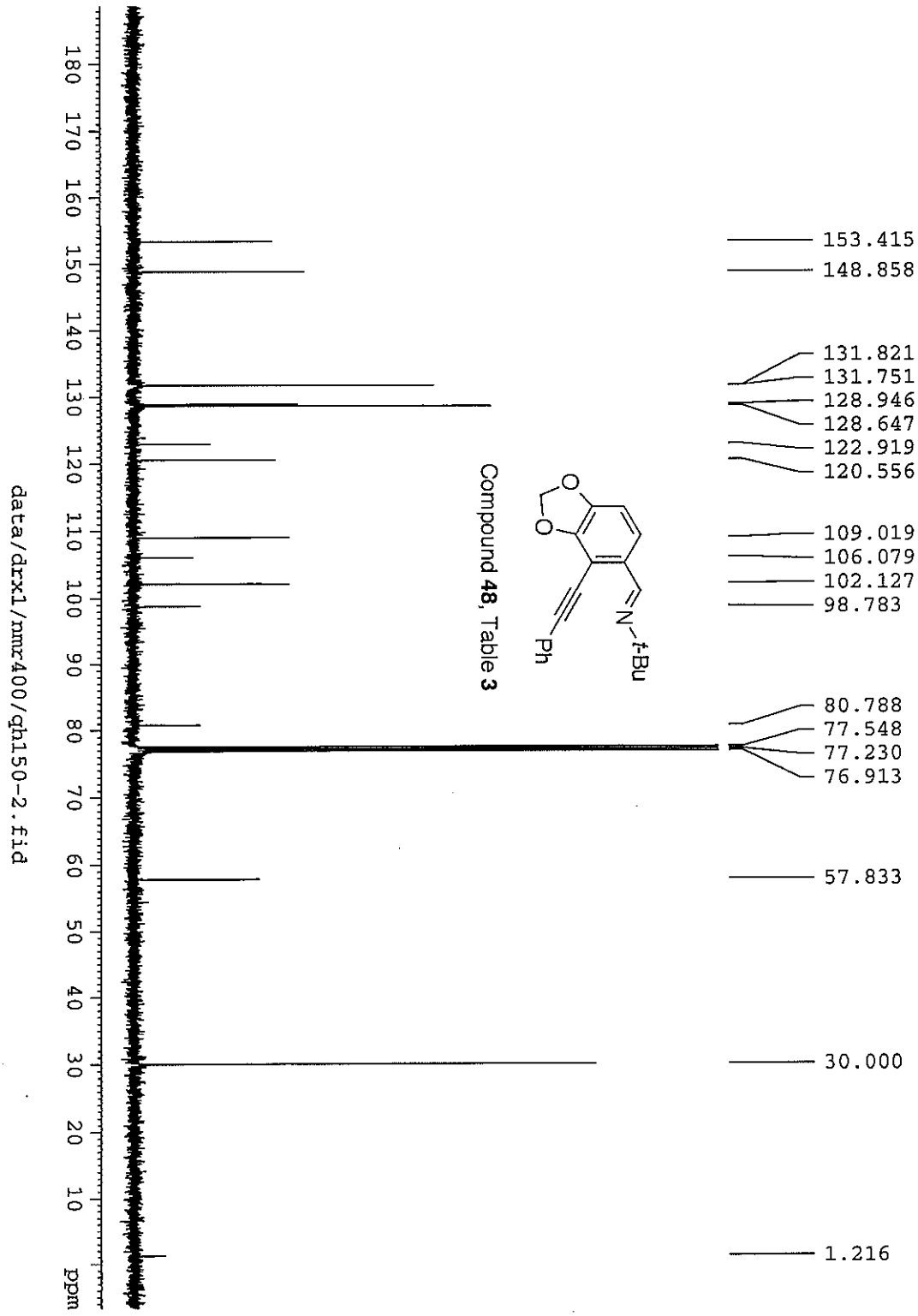

8.852
7.546
7.540
7.539
7.526
7.522
7.427
7.373
7.362
7.357
7.355
7.263
4.026
3.971
3.917
1.333
0.001
1.000
2.161
1.033
3.240
3.117
3.160
3.123
9.444
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
MeO
MeO
OMe
Ph
N
t-Bu
Compound 43, Table 3
data/drx1/nmr400/qh138-1.fid

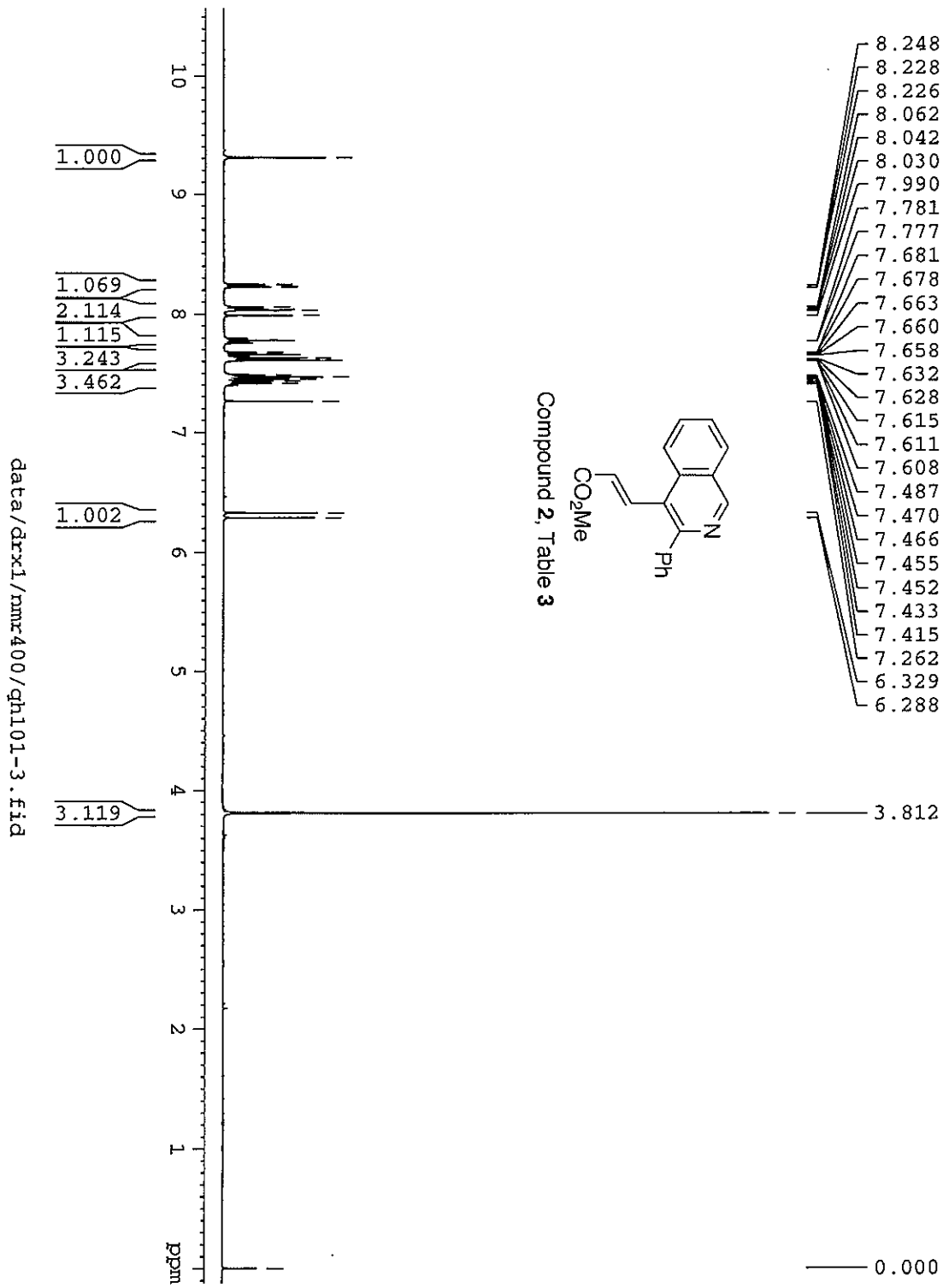

154.577
154.341
153.963
144.106
134.510
131.526
128.679
128.517
123.728
112.429
104.604
98.055
82.829
77.580
77.262
76.945
61.682
61.439
58.002
56.406
30.090
MeO
MeO
OMe
Ph
N
t-Bu
Compound 43, Table 3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/drx1/nmr400/qh38-2.fid

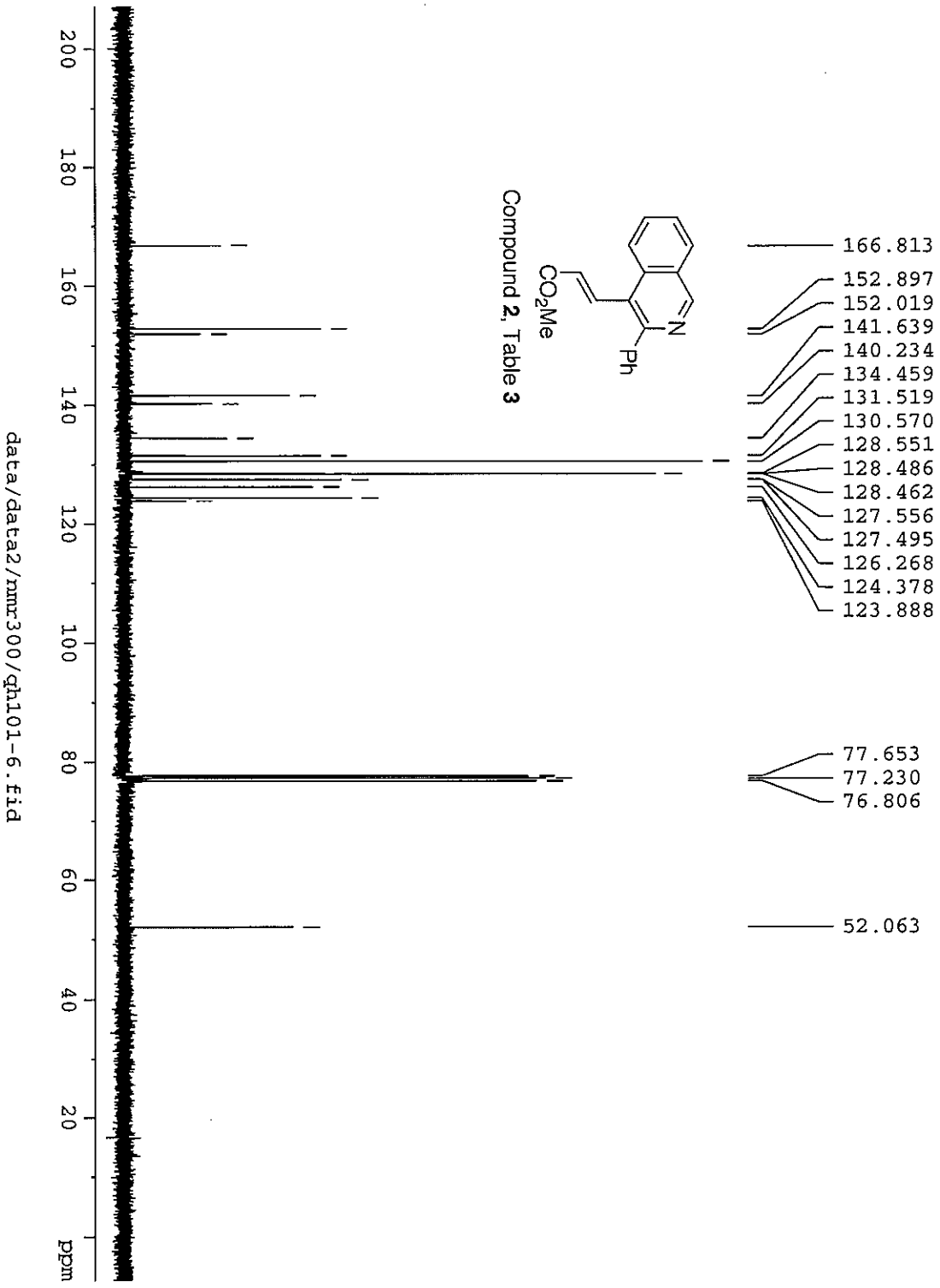

1.000
1.158
1.145
2.475
9.911
9.909
7.552
7.525
7.264
6.871
6.870
6.844
6.843
6.161
0.000
CHO
ppm
data/dat2/nmr300/qh146-3.fid

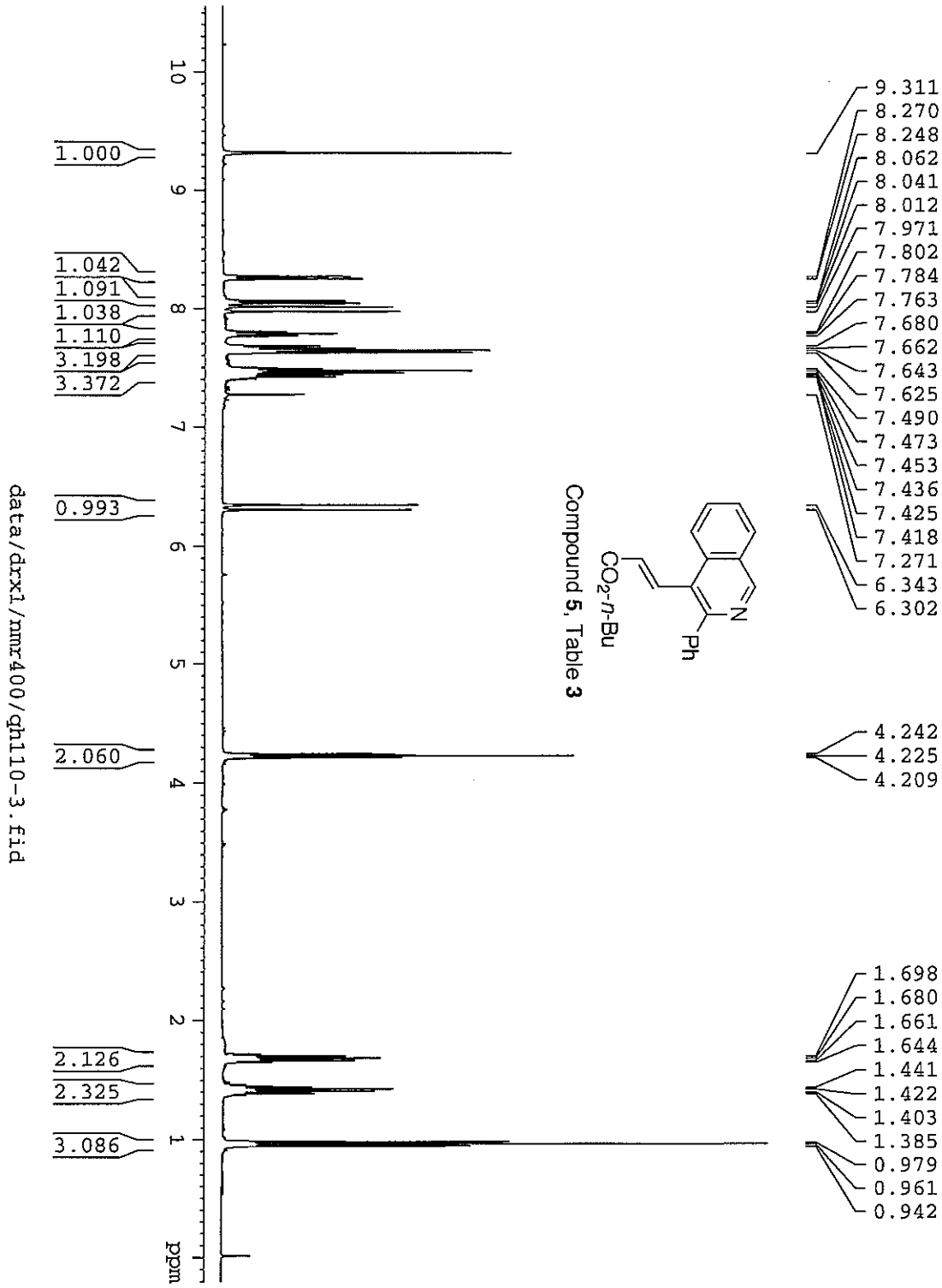

192.759
150.915
150.265
128.833
127.487
108.334
101.457
77.315
76.998
76.680
76.019
CHO
200
180
160
140
120
100
80
60
40
20
0 ppm
data/dat2/nmr400/qh146-4.fid

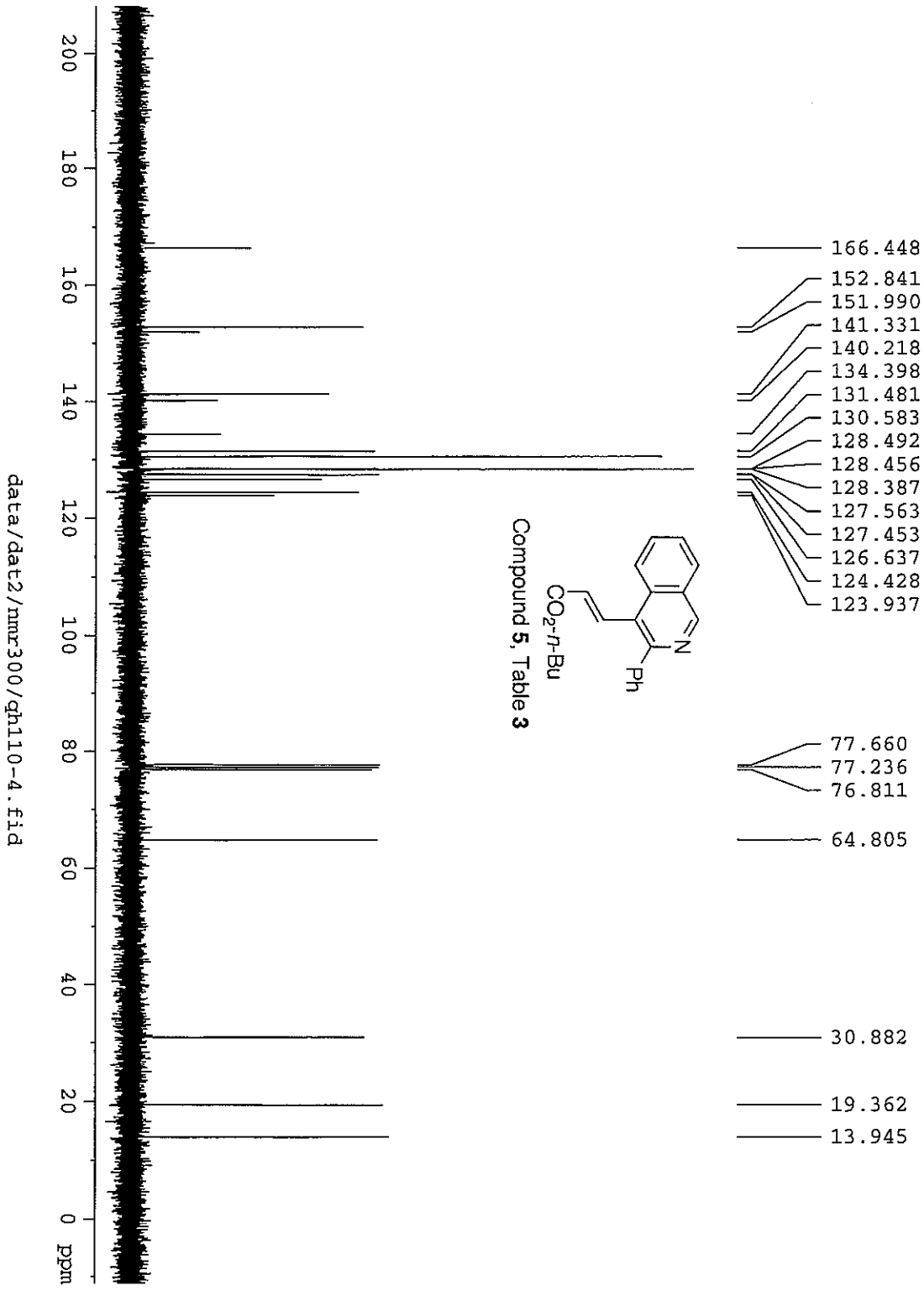

1.000
1.066
2.245
3.349
1.052
2.226
9.708
8.770
7.654
7.634
7.565
7.556
7.551
7.386
7.378
7.372
6.853
6.833
6.104
1.337
ppm
Compound 48, Table 3
Ph
N
t-Bu
data/drx1/nmr400/qh150-1.fid

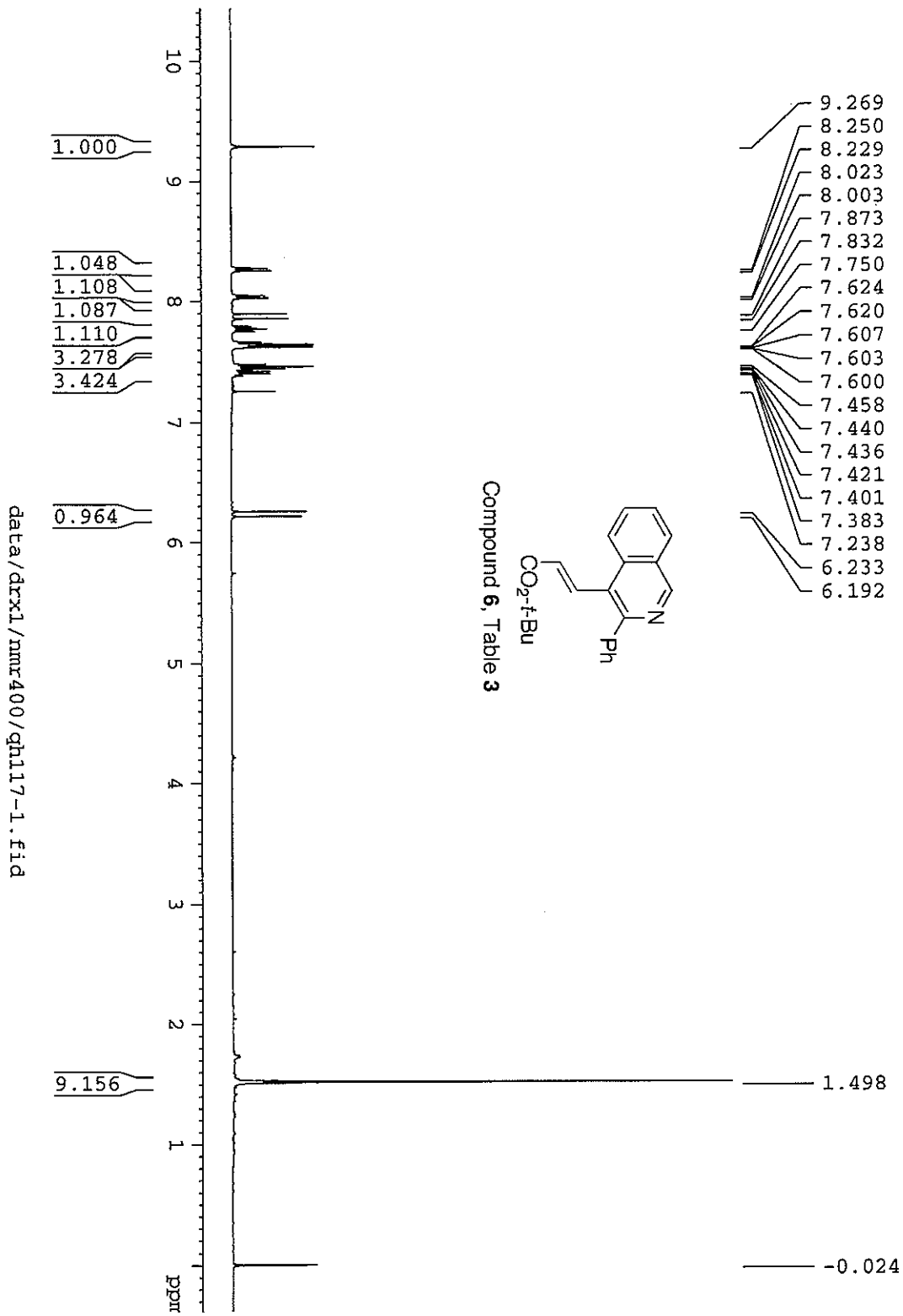

153.415
148.858
131.821
131.751
128.946
128.647
122.919
120.556
109.019
106.079
102.127
98.783
80.788
77.548
77.230
76.913
57.833
30.000
1.216
Compound 48, Table 3
Ph
N-t-Bu
O
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh150-2.fid

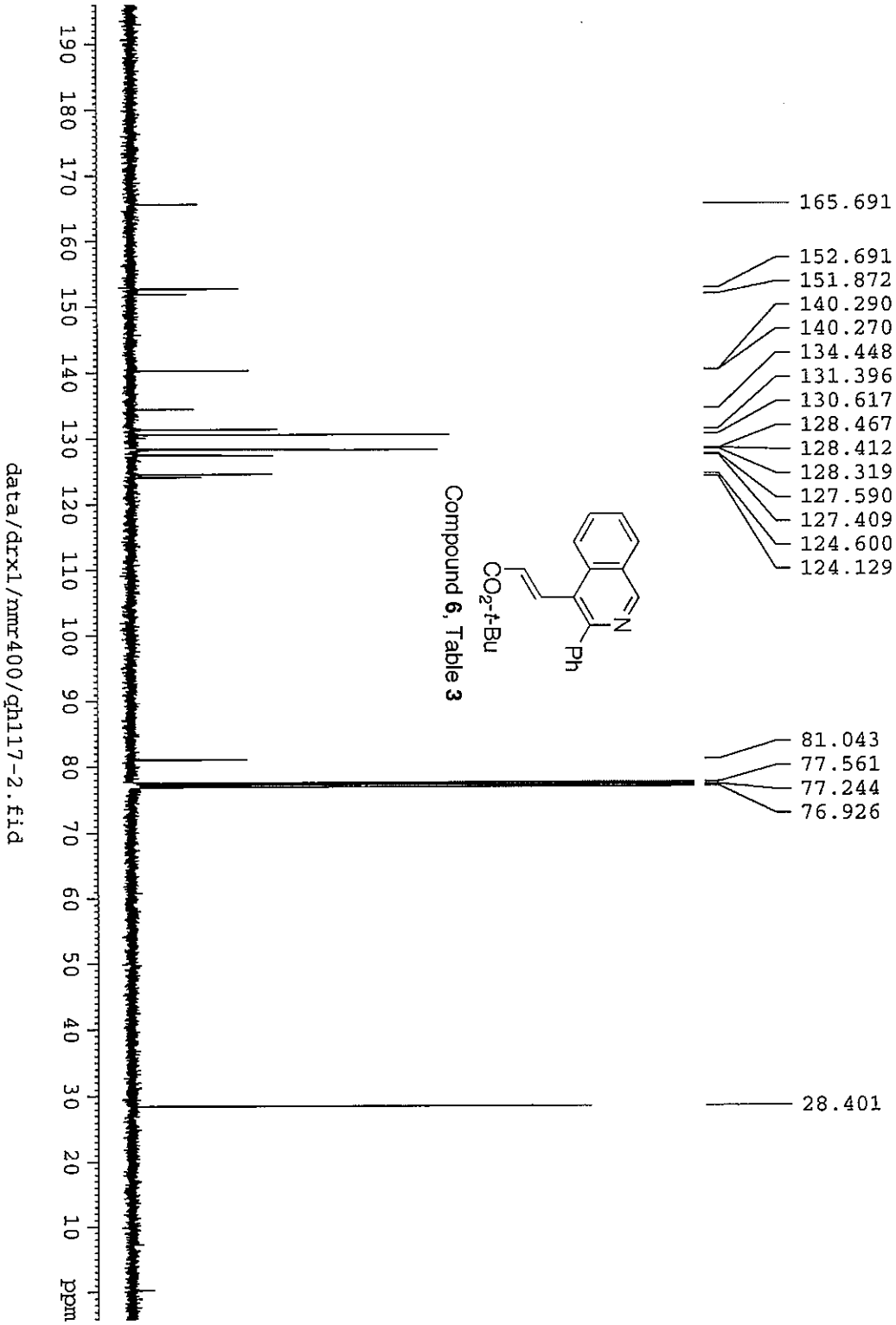

8.248
8.228
8.226
8.062
8.042
8.030
7.990
7.781
7.777
7.681
7.678
7.663
7.660
7.658
7.632
7.628
7.615
7.611
7.608
7.487
7.470
7.466
7.455
7.452
7.433
7.415
7.262
6.329
6.288
3.812
0.000
1.000
1.069
2.114
1.115
3.243
3.462
1.002
3.119
Compound 2, Table 3
CO2Me
Ph
N
ppm
data/drx1/nmr400/qh101-3.fid

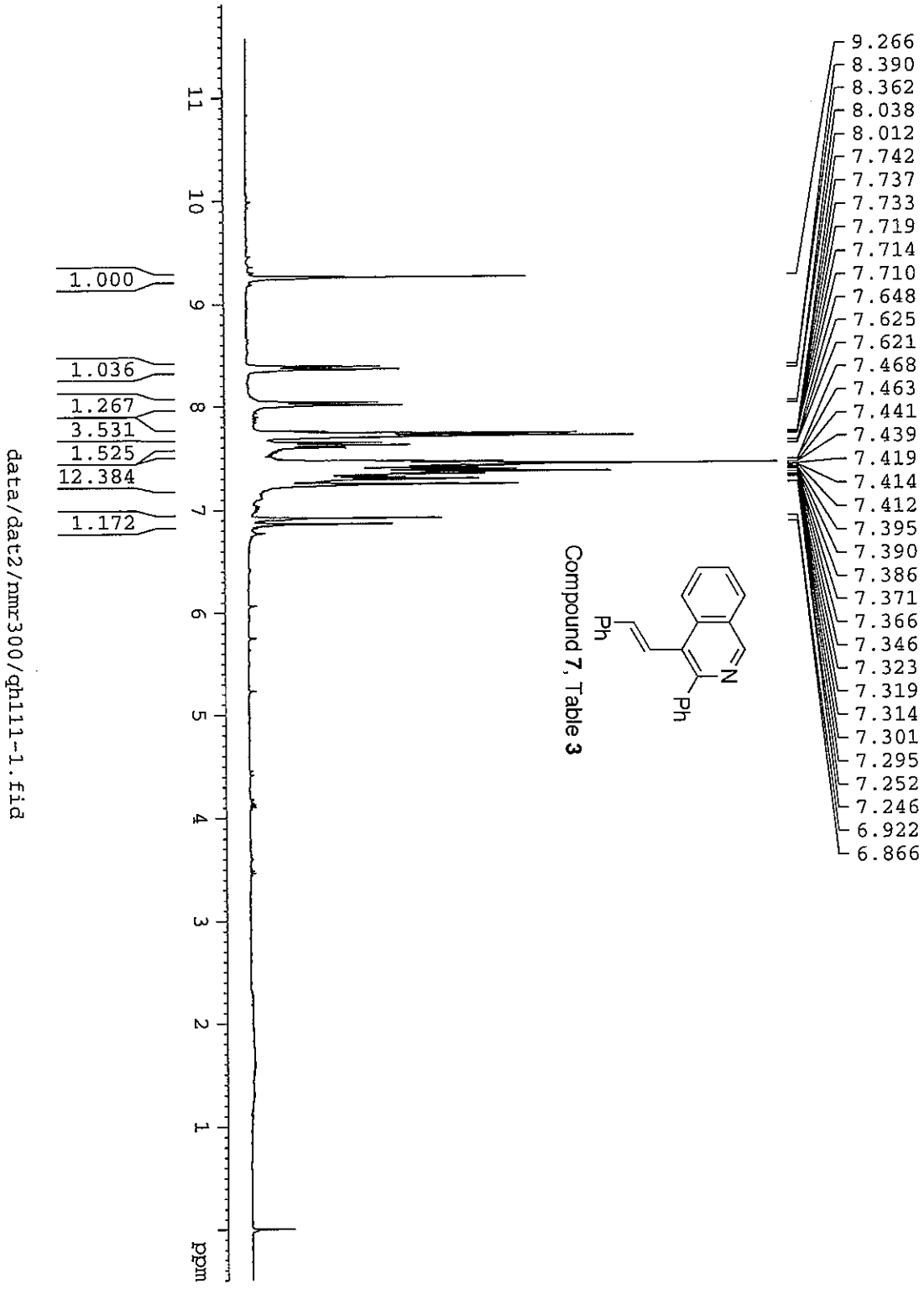

Compound 2, Table 3
CO2Me
N
Ph
166.813
152.897
152.019
141.639
140.234
134.459
131.519
130.570
128.551
128.486
128.462
127.556
127.495
126.268
124.378
123.888
77.653
77.230
76.806
52.063
200
180
160
140
120
100
80
60
40
20
ppm
data/data2/nmr300/qh101-6.fid

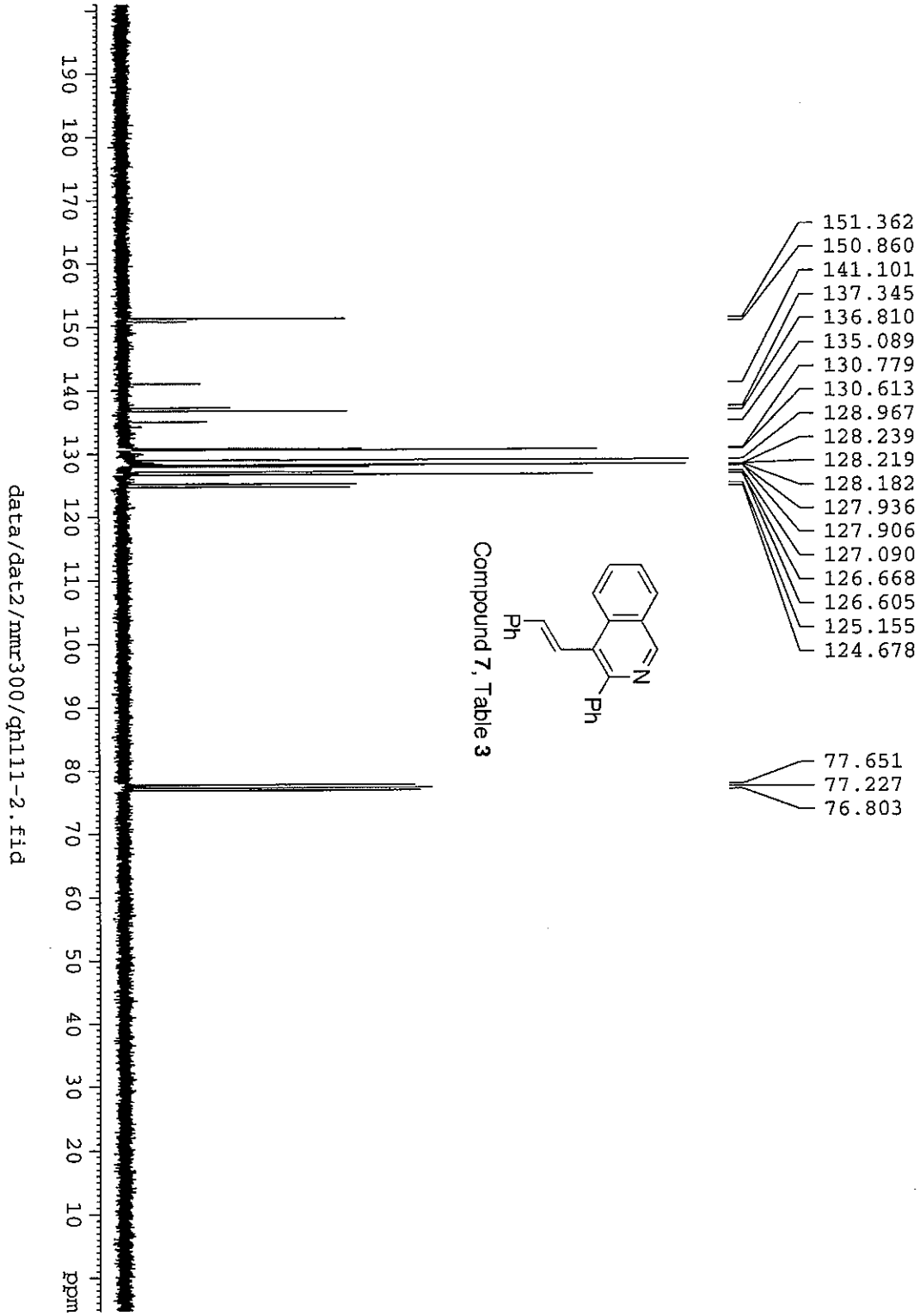

9.311
8.270
8.248
8.062
8.041
8.012
7.971
7.802
7.784
7.763
7.680
7.662
7.643
7.625
7.490
7.473
7.453
7.436
7.425
7.418
7.271
6.343
6.302
4.242
4.225
4.209
1.698
1.680
1.661
1.644
1.441
1.422
1.403
1.385
0.979
0.961
0.942
1.000
1.042
1.091
1.038
1.110
3.198
3.372
0.993
2.060
2.126
2.325
3.086
ppm
Compound 5, Table 3
CO2-n-Bu
Ph
N
data/drx1/nmr400/qh110-3.fid

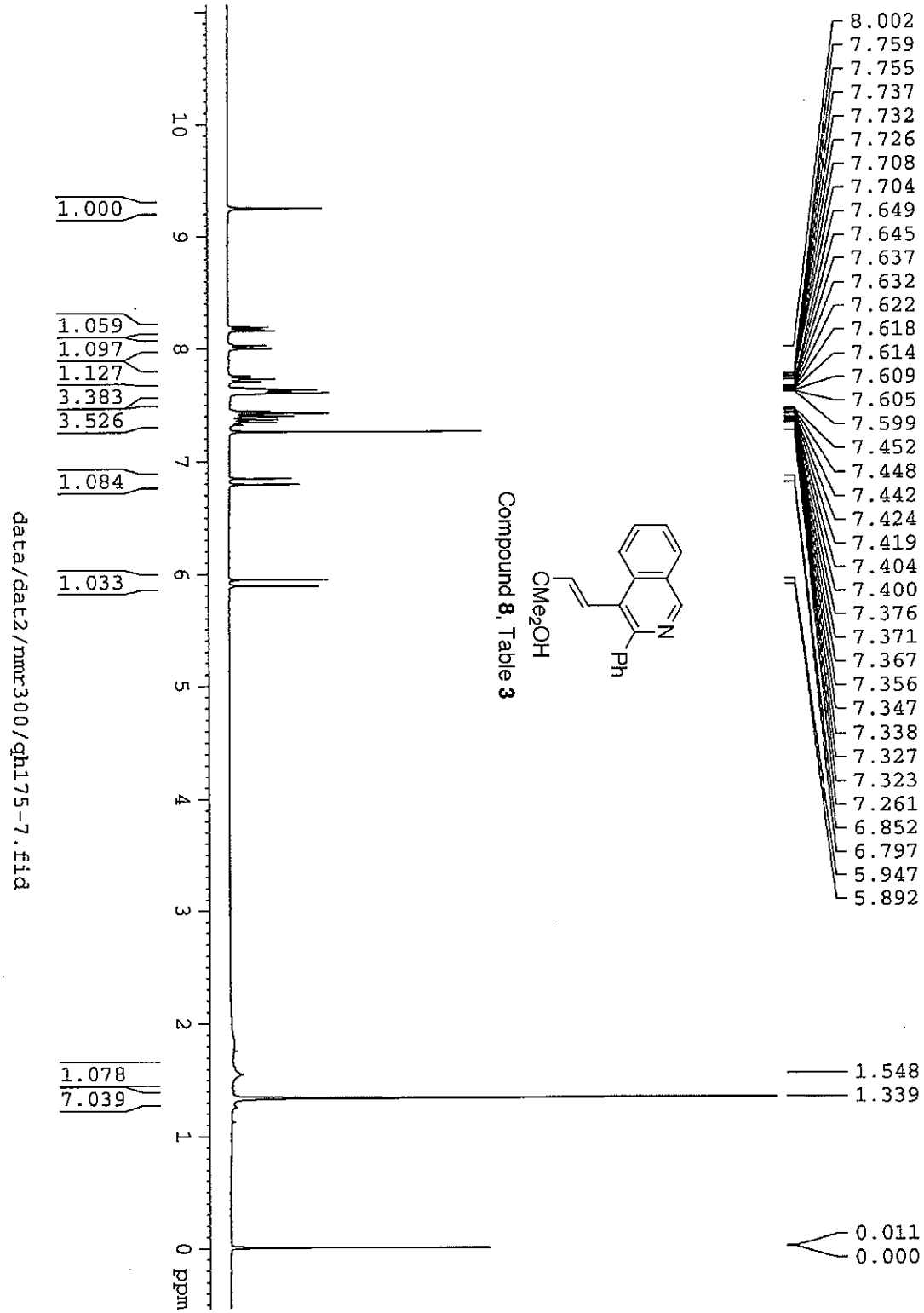

166.448
152.841
151.990
141.331
140.218
134.398
131.481
130.583
128.492
128.456
128.387
127.563
127.453
126.637
124.428
123.937
77.660
77.236
76.811
64.805
30.882
19.362
13.945
200
180
160
140
120
100
80
60
40
20
0 ppm
Compound 5, Table 3
CO2-n-Bu
Ph
N
data/dat2/nmr300/qh110-4.fid

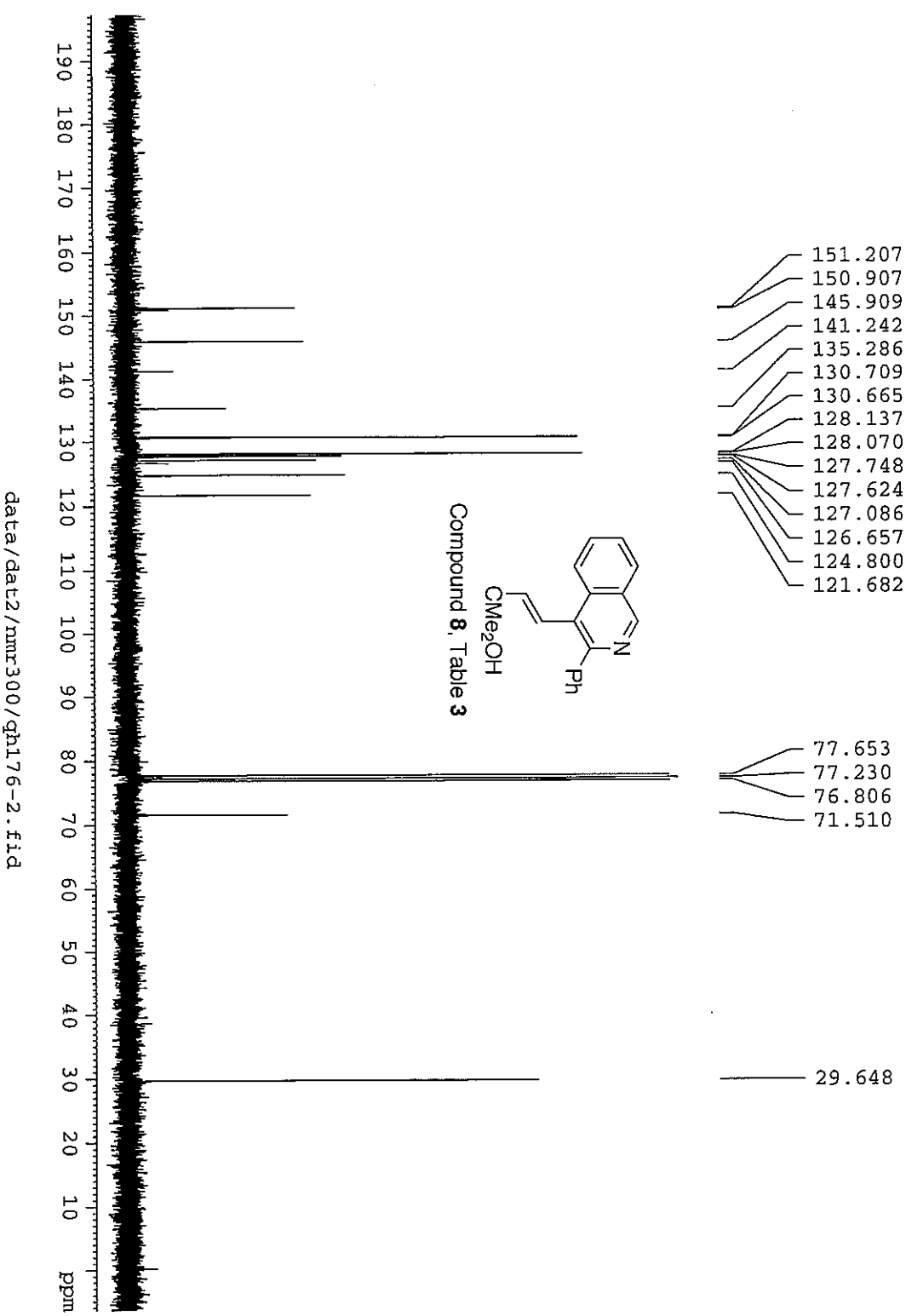

9.269
8.250
8.229
8.023
8.003
7.873
7.832
7.750
7.624
7.620
7.607
7.603
7.600
7.458
7.440
7.436
7.421
7.401
7.383
7.238
6.233
6.192
1.498
-0.024
1.000
1.048
1.108
1.087
1.110
3.278
3.424
0.964
9.156
10
9
8
7
6
5
4
3
2
1
ppm
N
Ph
CO2-t-Bu
Compound 6, Table 3
data/drx1/nmr400/qh117-1.fid

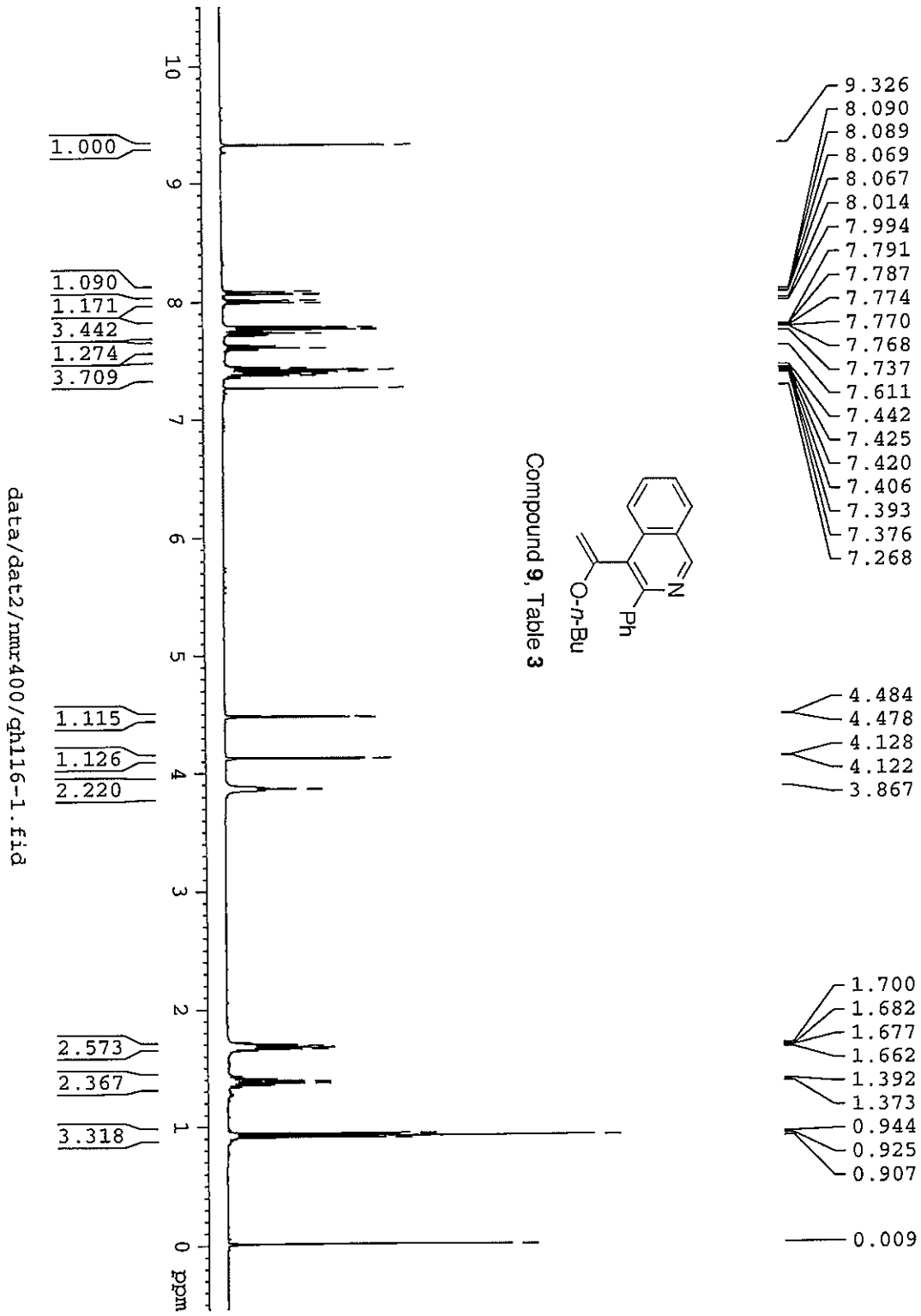

165.691
152.691
151.872
140.290
140.270
134.448
131.396
130.617
128.467
128.412
128.319
127.590
127.409
124.600
124.129
81.043
77.561
77.244
76.926
28.401
Compound 6, Table 3
CO2-t-Bu
N
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh117-2.fid


9.266
8.390
8.362
8.038
8.012
7.742
7.737
7.733
7.719
7.714
7.710
7.648
7.625
7.621
7.468
7.463
7.441
7.439
7.419
7.414
7.412
7.395
7.390
7.386
7.371
7.366
7.346
7.323
7.319
7.314
7.301
7.295
7.252
7.246
6.922
6.866
1.000
1.036
1.267
3.531
1.525
12.384
1.172
11
10
9
8
7
6
5
4
3
2
1
ppm
Ph
N
Ph
Compound 7, Table 3
data/dat2/nmr300/qh111-1.fid


151.362
150.860
141.101
137.345
136.810
135.089
130.779
130.613
128.967
128.239
128.219
128.182
127.936
127.906
127.090
126.668
126.605
125.155
124.678
77.651
77.227
76.803
Ph
N
Ph
Compound 7, Table 3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh111-2.fid


8.002
7.759
7.755
7.737
7.732
7.726
7.708
7.704
7.649
7.645
7.637
7.632
7.622
7.618
7.614
7.609
7.605
7.599
7.452
7.448
7.442
7.424
7.419
7.404
7.400
7.376
7.371
7.367
7.356
7.347
7.338
7.327
7.323
7.261
6.852
6.797
5.947
5.892
1.548
1.339
0.011
0.000
1.000
1.059
1.097
1.127
3.383
3.526
1.084
1.033
1.078
7.039
10
9
8
7
6
5
4
3
2
1
0 ppm
Compound 8, Table 3
CMe2OH
Ph
N
data/dat2/nmr300/qh175-7.fid


151.207
150.907
145.909
141.242
135.286
130.709
130.665
128.137
128.070
127.748
127.624
127.086
126.657
124.800
121.682
77.653
77.230
76.806
71.510
29.648
Compound 8, Table 3
CMe2OH
Ph
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh176-2.fid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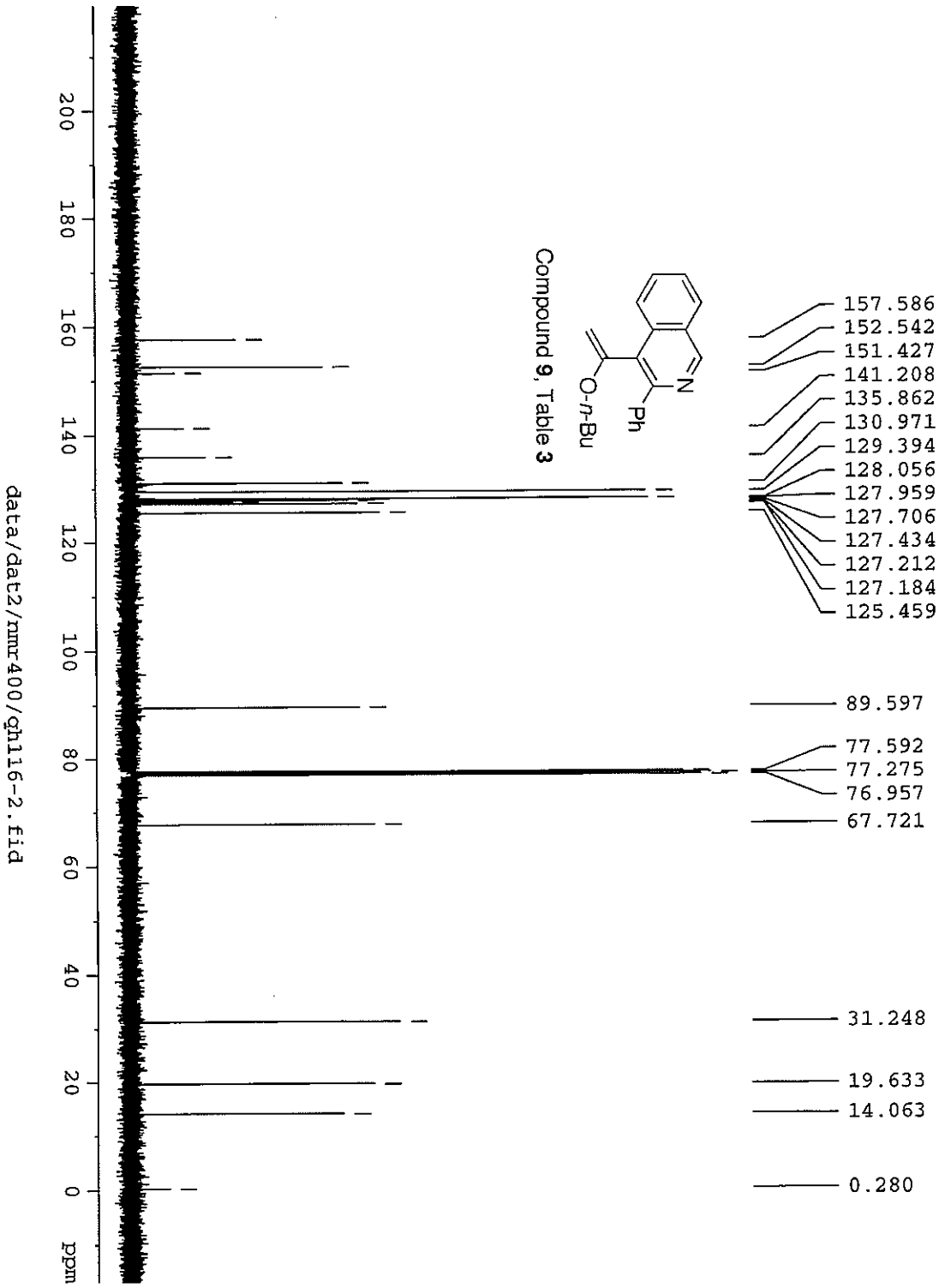
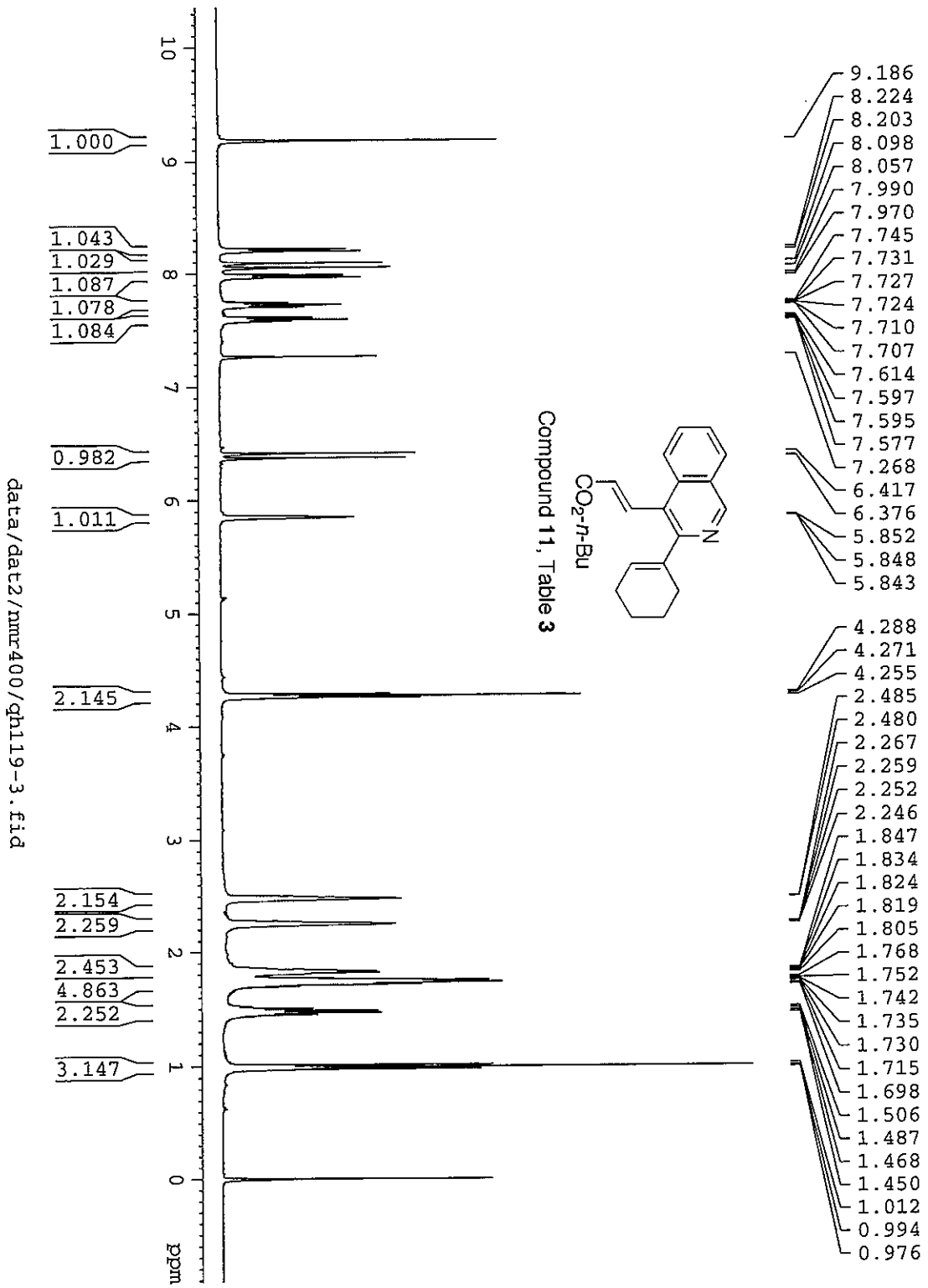
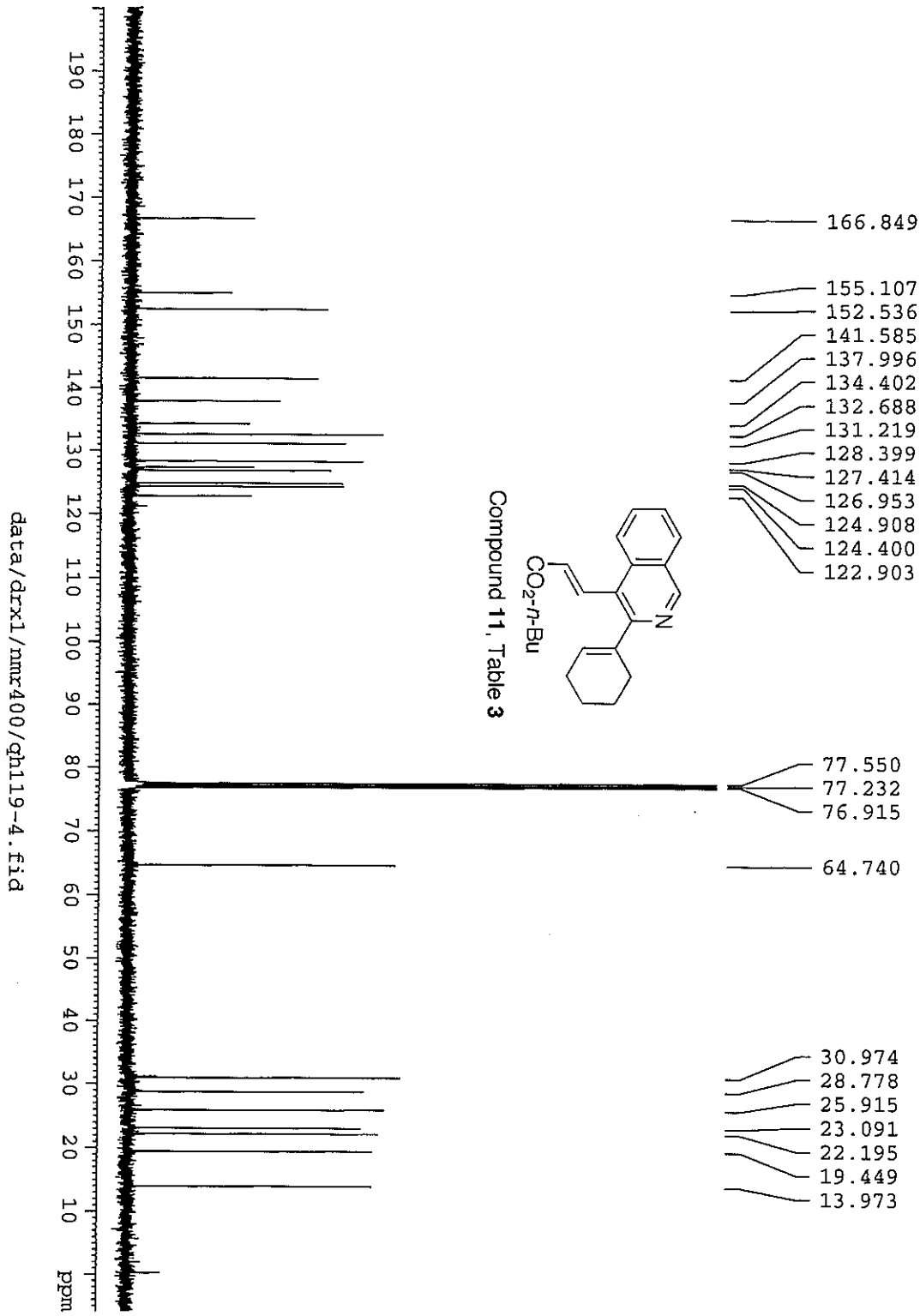
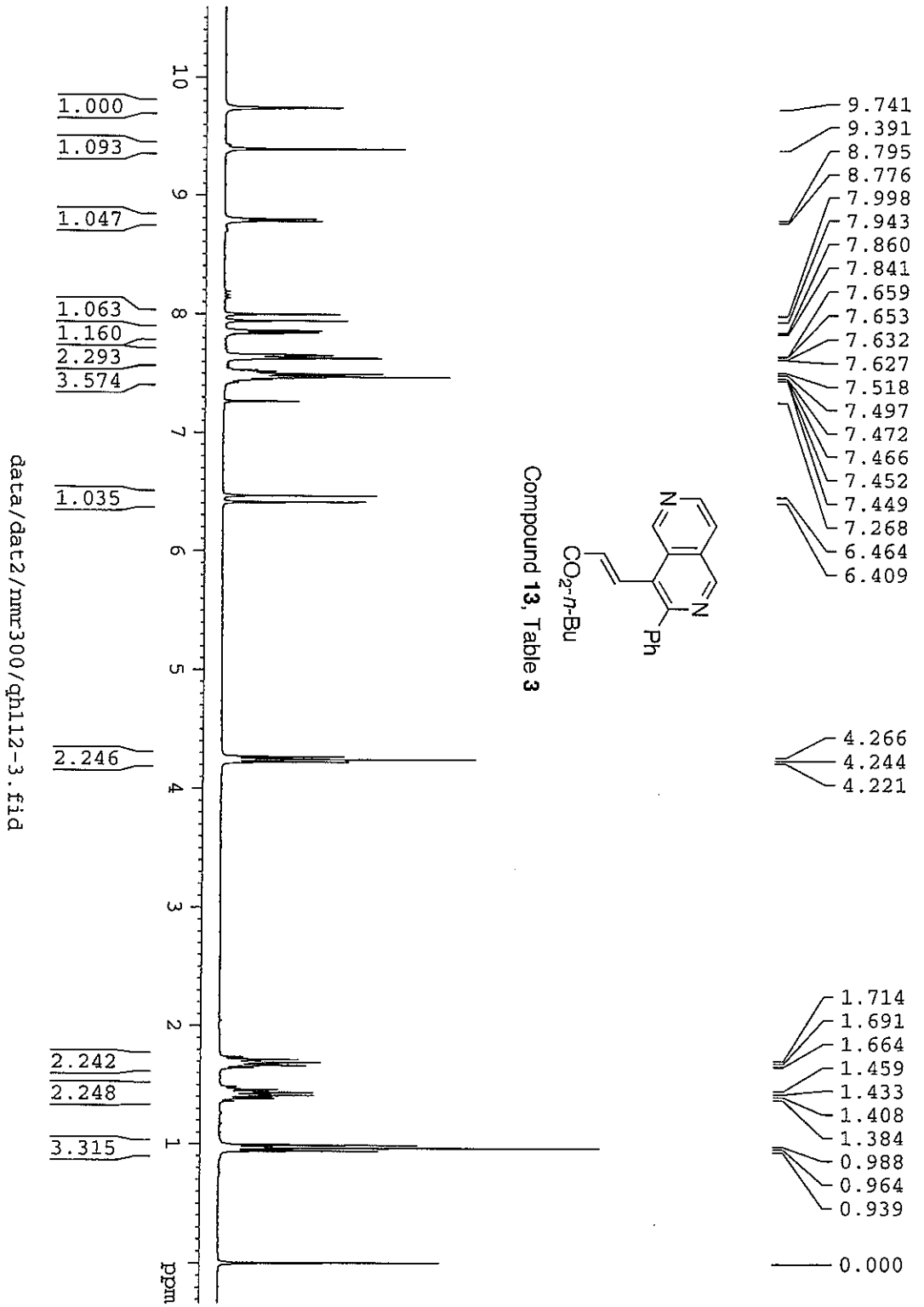
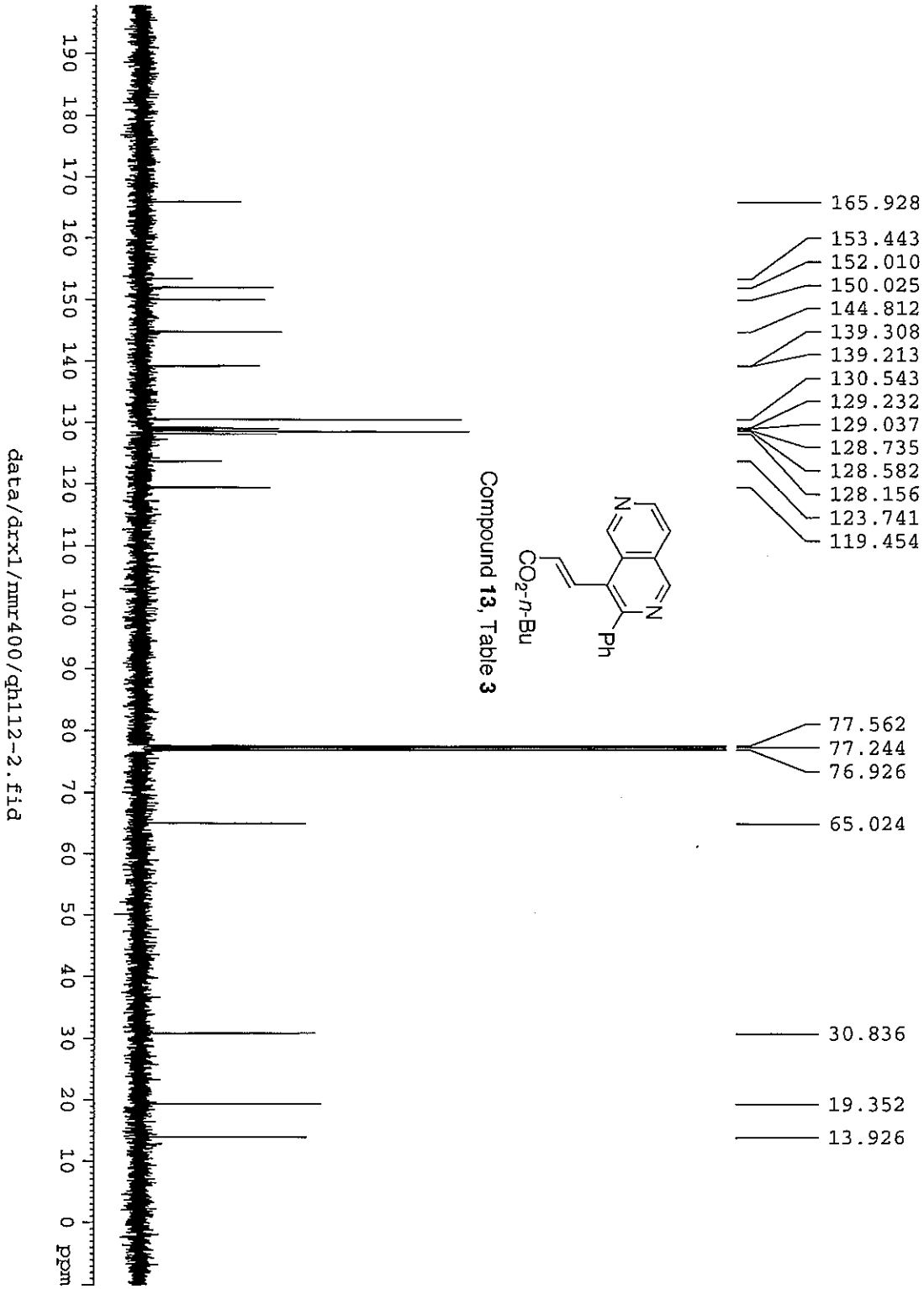
Compound 9, Table 3
O-n-Bu
Ph
N
9.326
8.090
8.089
8.069
8.067
8.014
7.994
7.791
7.787
7.774
7.770
7.768
7.737
7.611
7.442
7.425
7.420
7.406
7.393
7.376
7.268
4.484
4.478
4.128
4.122
3.867
1.700
1.682
1.677
1.662
1.392
1.373
0.944
0.925
0.907
0.009
1.000
1.090
1.171
3.442
1.274
3.709
1.115
1.126
2.220
2.573
2.367
3.318
10
9
8
7
6
5
4
3
2
1
0
ppm

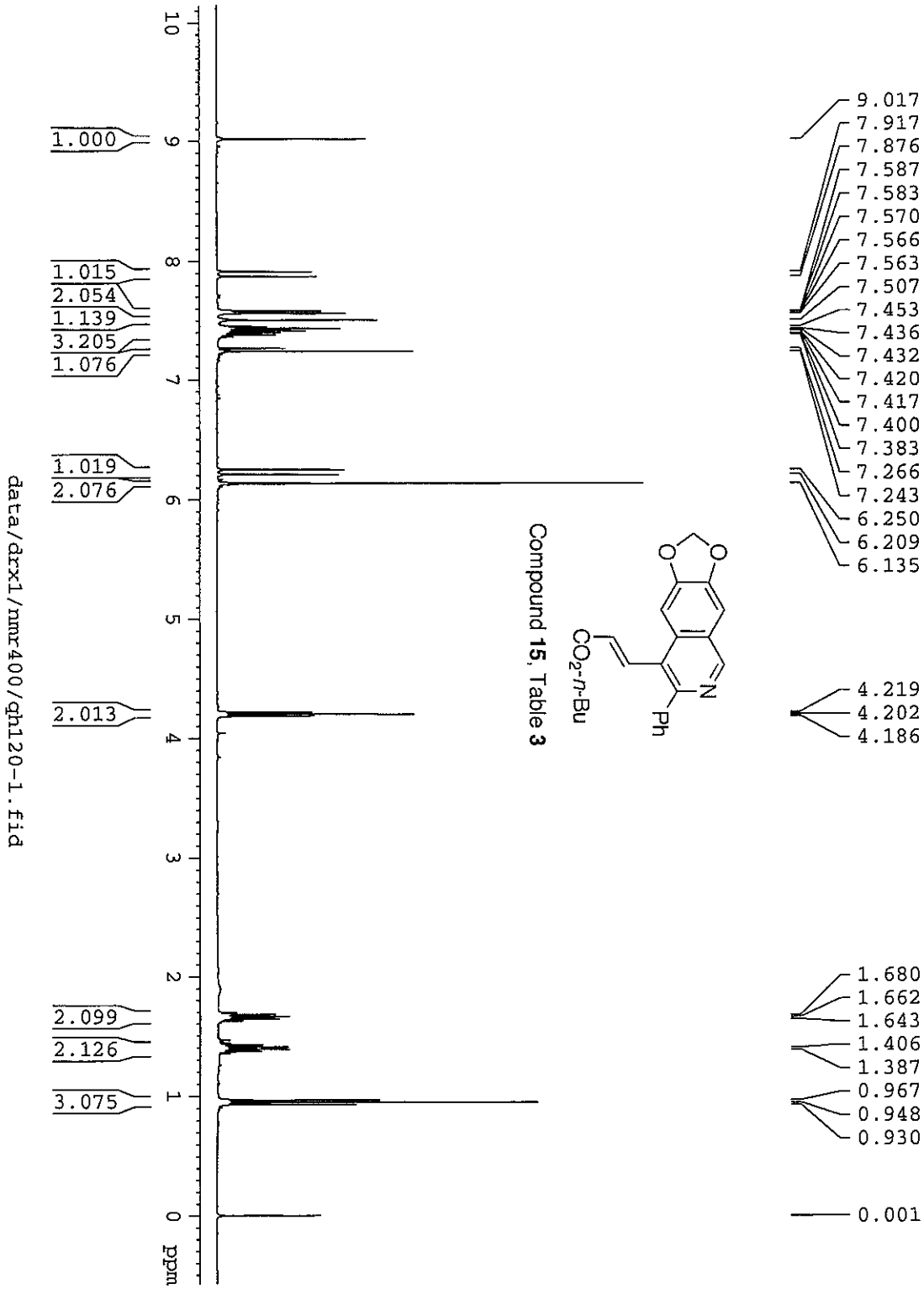

Compound 9, Table 3
O-n-Bu
Ph
N
157.586
152.542
151.427
141.208
135.862
130.971
129.394
128.056
127.959
127.706
127.434
127.212
127.184
125.459
89.597
77.592
77.275
76.957
67.721
31.248
19.633
14.063
0.280
200
180
160
140
120
100
80
60
40
20
0
ppm
data/dat2/nmr400/qh116-2.fid


data/dat2/nmr400/qh119-3.fid
Compound 11, Table 3
CO2-n-Bu
N
1.000
1.043
1.029
1.087
1.078
1.084
0.982
1.011
2.145
2.154
2.259
2.453
4.863
2.252
3.147
9.186
8.224
8.203
8.098
8.057
7.990
7.970
7.745
7.731
7.727
7.724
7.710
7.707
7.614
7.597
7.595
7.577
7.268
6.417
6.376
5.852
5.848
5.843
4.288
4.271
4.255
2.485
2.480
2.267
2.259
2.252
2.246
1.847
1.834
1.824
1.819
1.805
1.768
1.752
1.742
1.735
1.730
1.715
1.698
1.506
1.487
1.468
1.450
1.012
0.994
0.976
ppm


166.849
155.107
152.536
141.585
137.996
134.402
132.688
131.219
128.399
127.414
126.953
124.908
124.400
122.903
77.550
77.232
76.915
64.740
30.974
28.778
25.915
23.091
22.195
19.449
13.973
Compound 11, Table 3
CO2-n-Bu
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh119-4.fid


data/dat2/nmr300/qh112-3.fid
1.000
1.093
1.047
1.063
1.160
2.293
3.574
1.035
2.246
2.242
2.248
3.315
ppm
Compound 13, Table 3
CO2-n-Bu
Ph
9.741
9.391
8.795
8.776
7.998
7.943
7.860
7.841
7.659
7.653
7.632
7.627
7.518
7.497
7.472
7.466
7.452
7.449
7.268
6.464
6.409
4.266
4.244
4.221
1.714
1.691
1.664
1.459
1.433
1.408
1.384
0.988
0.964
0.939
0.000


165.928
153.443
152.010
150.025
144.812
139.308
139.213
130.543
129.232
129.037
128.735
128.582
128.156
123.741
119.454
77.562
77.244
76.926
65.024
30.836
19.352
13.926
Compound 13, Table 3
CO2-n-Bu
Ph
N
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/drx1/nmr400/qh112-2.fid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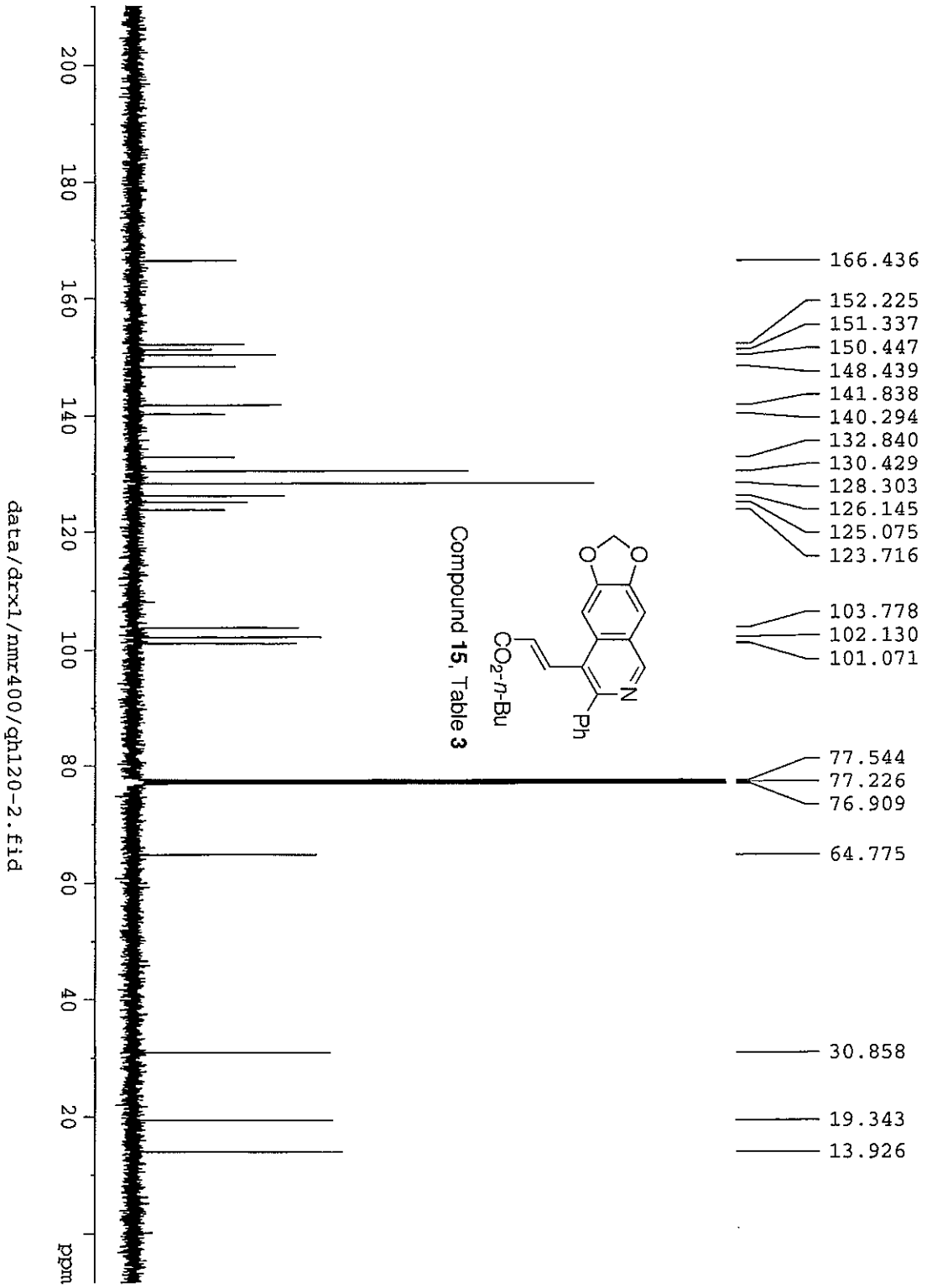
7.917
7.876
7.587
7.583
7.570
7.566
7.563
7.507
7.453
7.436
7.432
7.420
7.417
7.400
7.383
7.266
7.243
6.250
6.209
6.135
4.219
4.202
4.186
1.680
1.662
1.643
1.406
1.387
0.967
0.948
0.930
0.001
1.000
1.015
2.054
1.139
3.205
1.076
1.019
2.076
2.013
2.099
2.126
3.075
10
9
8
7
6
5
4
3
2
1
0
ppm
Compound 15, Table 3
CO2-n-Bu
Ph
N
O
O
O
data/drx1/nmr400/qh120-1.fid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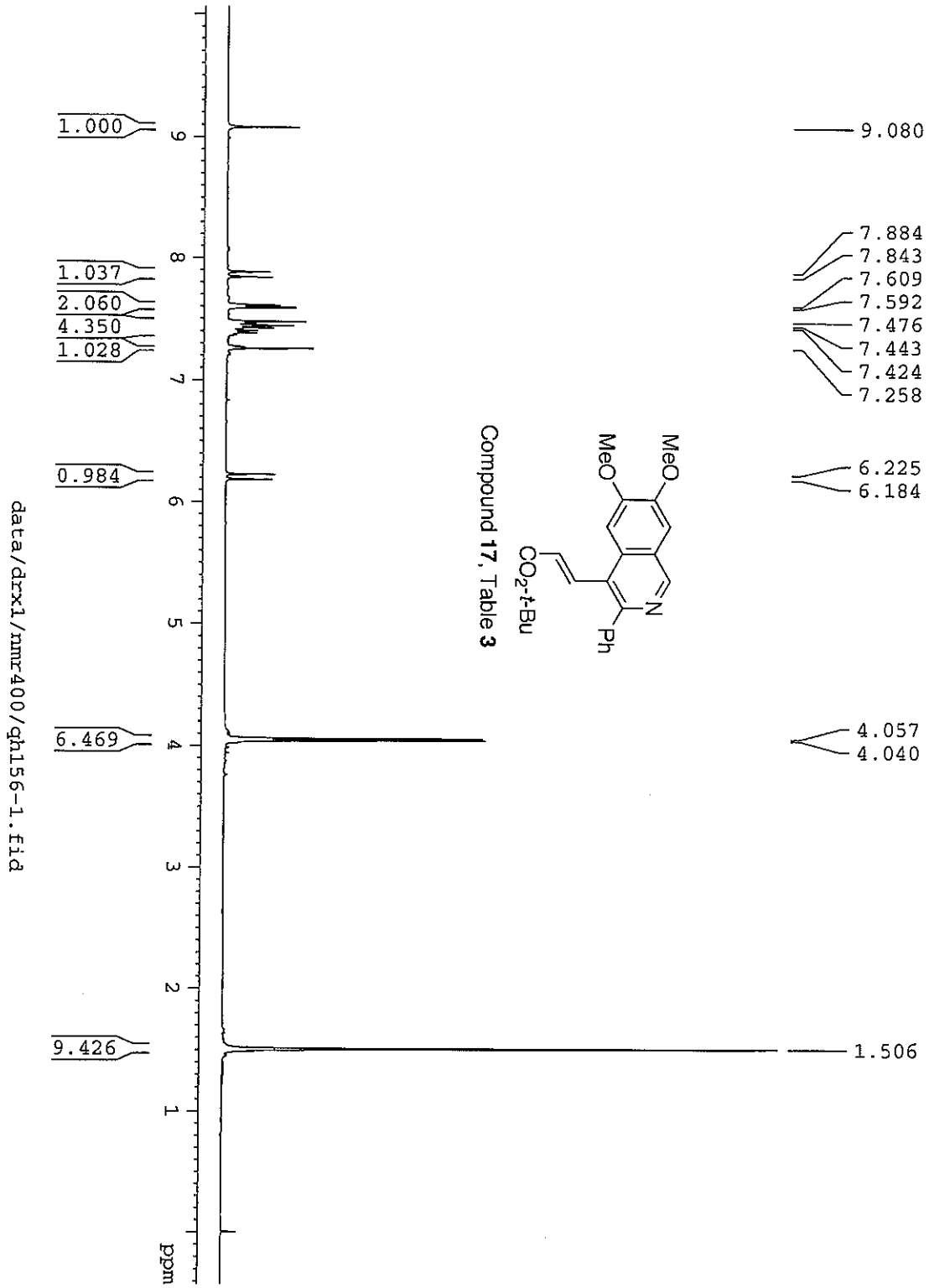
152.225
151.337
150.447
148.439
141.838
140.294
132.840
130.429
128.303
126.145
125.075
123.716
103.778
102.130
101.071
77.544
77.226
76.909
64.775
30.858
19.343
13.926
Compound 15, Table 3
CO2-n-Bu
Ph
N
O
O
200
180
160
140
120
100
80
60
40
20
ppm
data/drx1/nmr400/qh120-2.fid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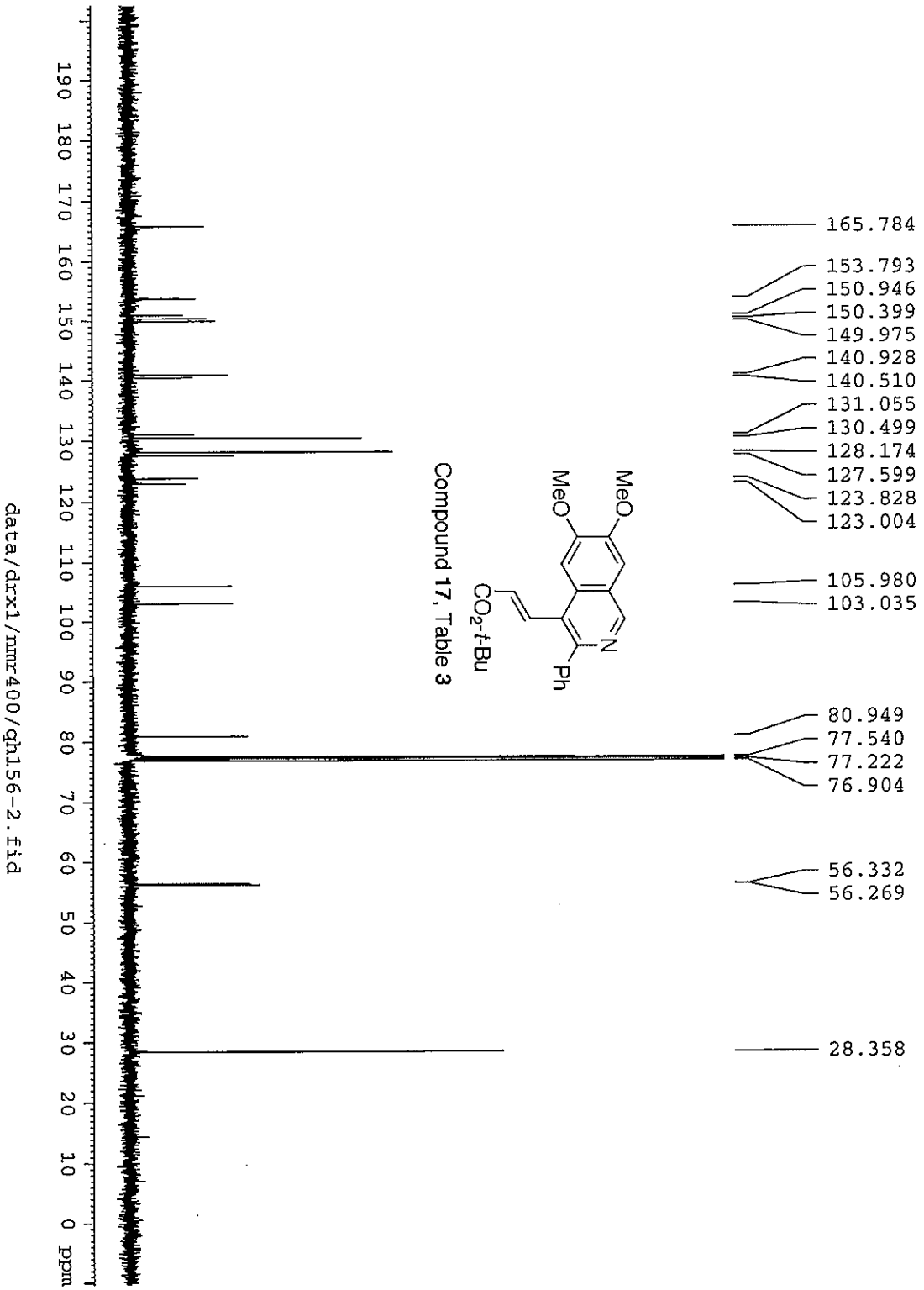
1.037
2.060
4.350
1.028
0.984
6.469
9.426
9.080
7.884
7.843
7.609
7.592
7.476
7.443
7.424
7.258
6.225
6.184
4.057
4.040
1.506
MeO
MeO
CO2-t-Bu
Ph
N
Compound 17, Table 3
data/drx1/nmr400/qh156-1.fid
ppm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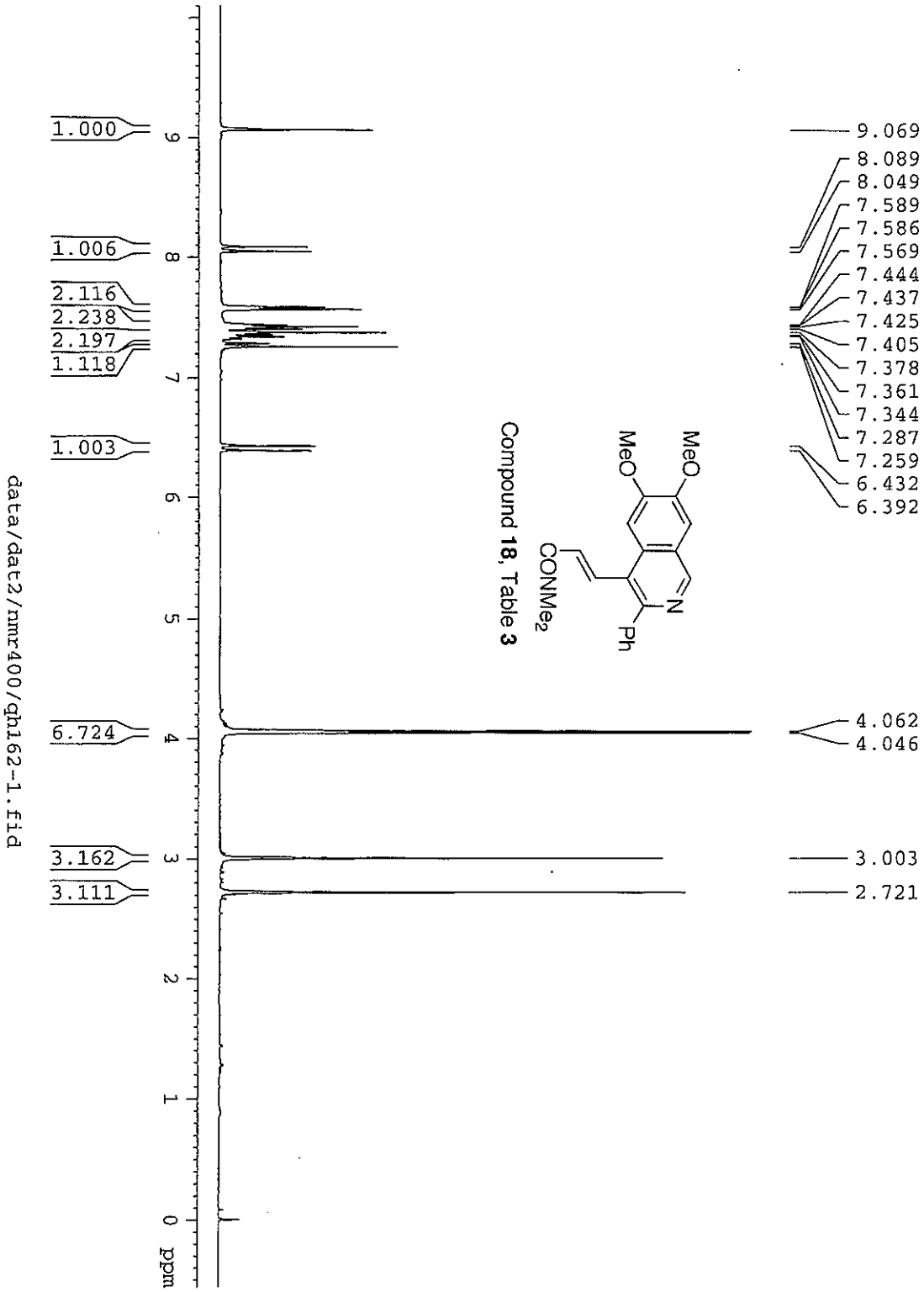
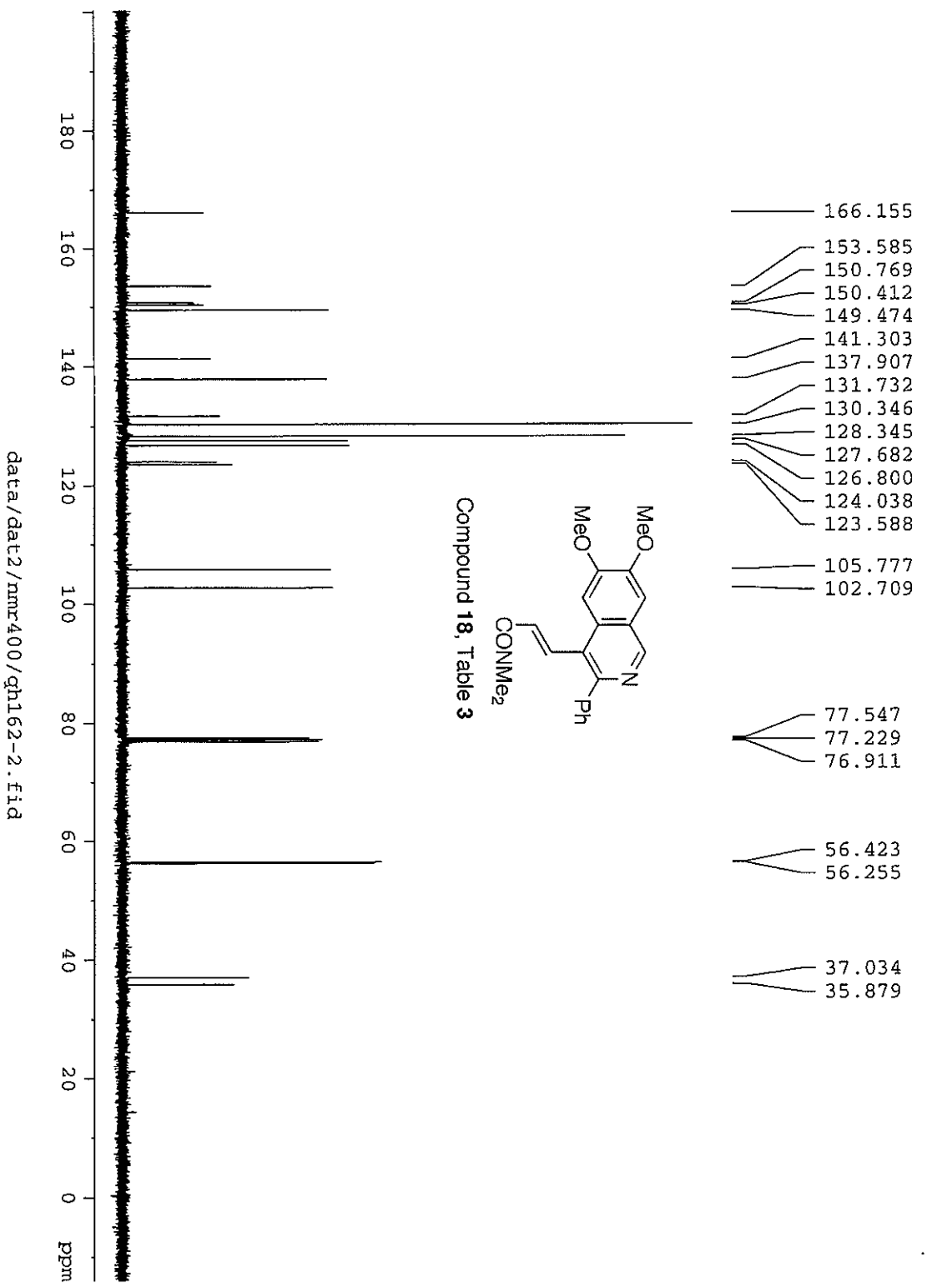
153.793
150.946
150.399
149.975
140.928
140.510
131.055
130.499
128.174
127.599
123.828
123.004
105.980
103.035
80.949
77.540
77.222
76.904
56.332
56.269
28.358
MeO
MeO
N
Ph
CO2-t-Bu
Compound 17, Table 3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/drx1/nmr400/qh156-2.fid


1.000
1.006
2.116
2.238
2.197
1.118
1.003
6.724
3.162
3.111
9 8 7 6 5 4 3 2 1 0 ppm
9.069
8.089
8.049
7.589
7.586
7.569
7.444
7.437
7.425
7.405
7.378
7.361
7.344
7.287
7.259
6.432
6.392
4.062
4.046
3.003
2.721
MeO
MeO
CONMe2
N
Ph
Compound 18, Table 3
data/dat2/nmr400/qh162-1.fid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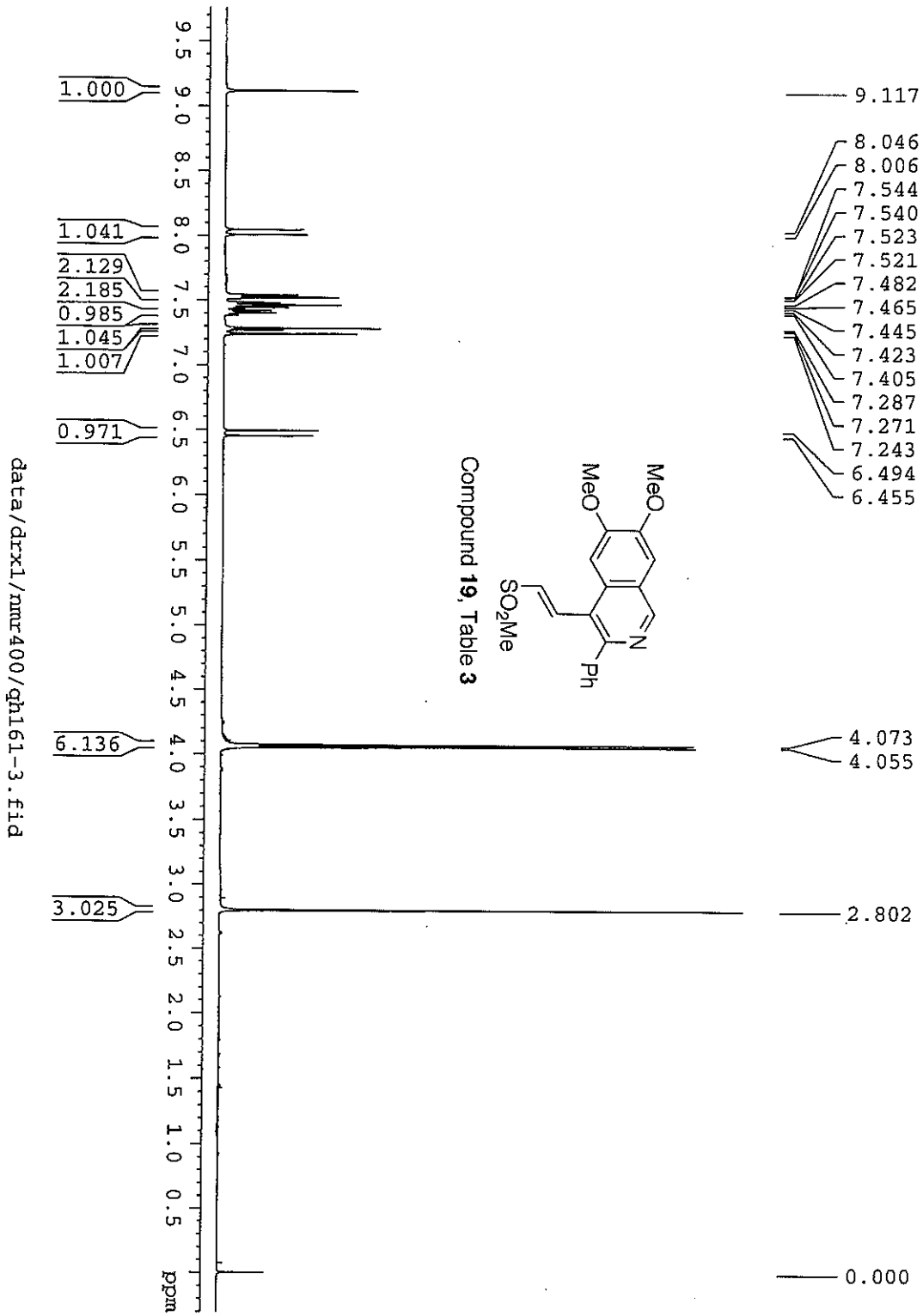
153.585
150.769
150.412
149.474
141.303
137.907
131.732
130.346
128.345
127.682
126.800
124.038
123.588
105.777
102.709
77.547
77.229
76.911
56.423
56.255
37.034
35.879
MeO
MeO
CONMe2
N
Ph
Compound 18, Table 3
180
160
140
120
100
80
60
40
20
0
ppm
data/dat2/nmr400/qh162-2.fid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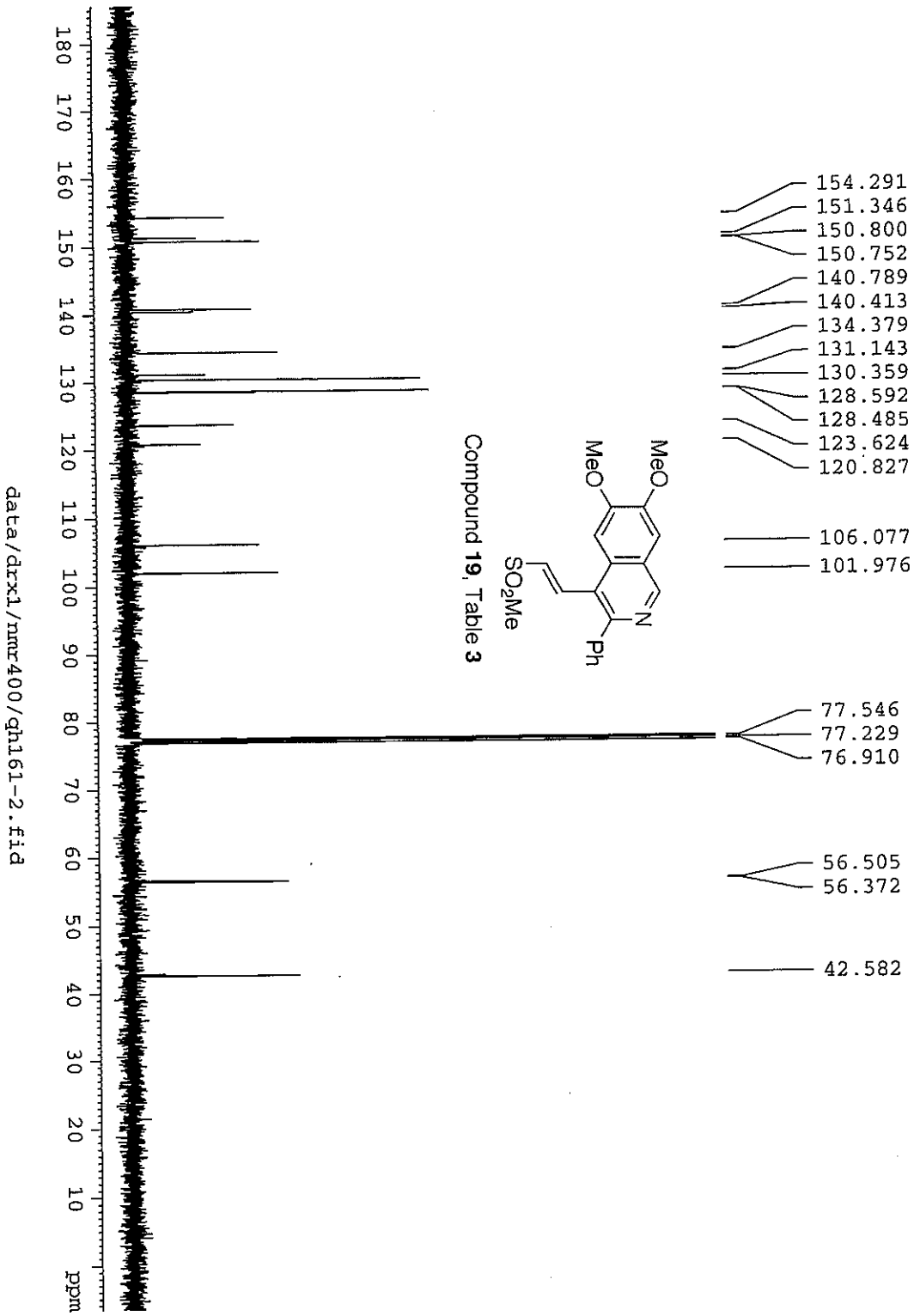
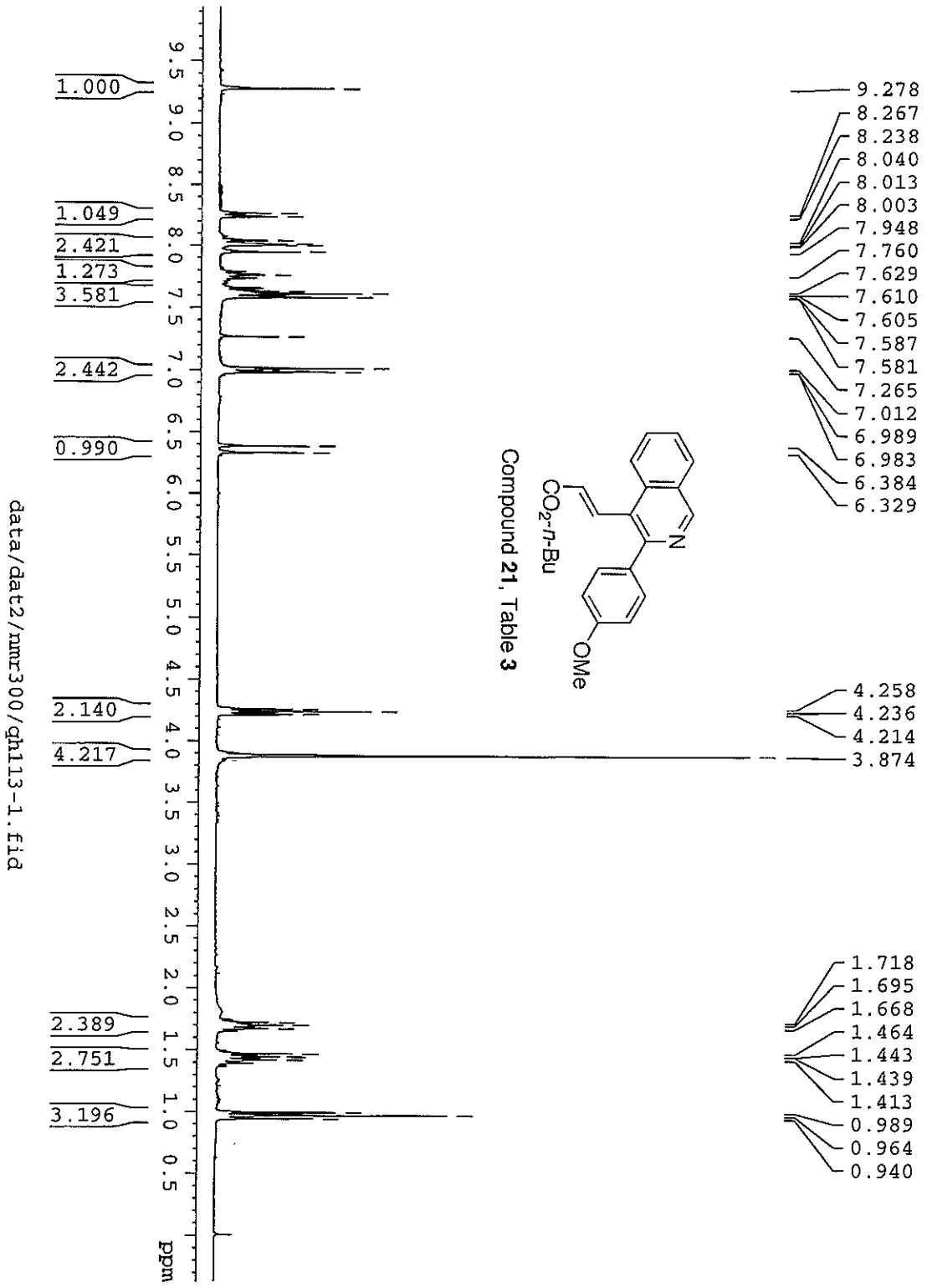
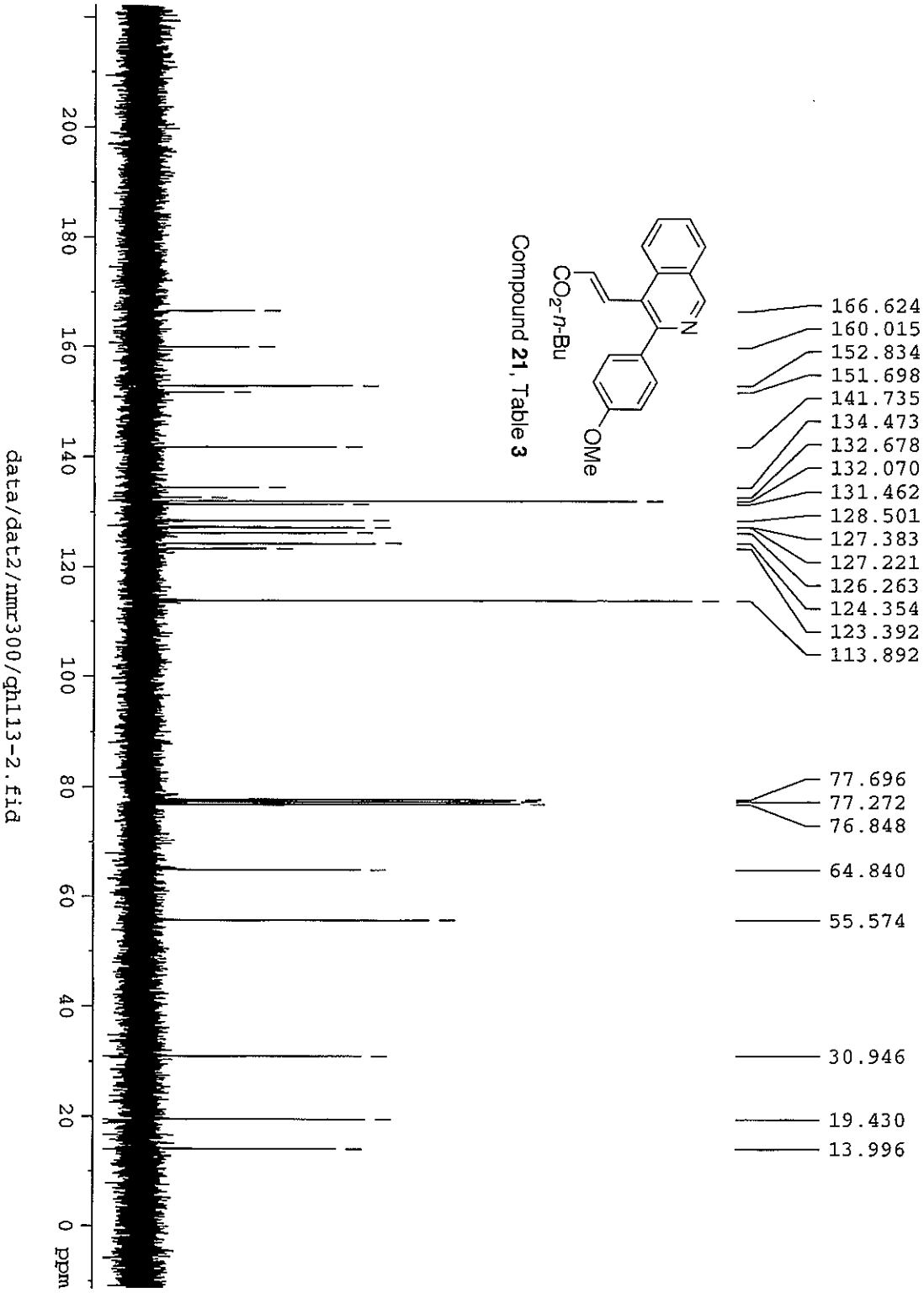
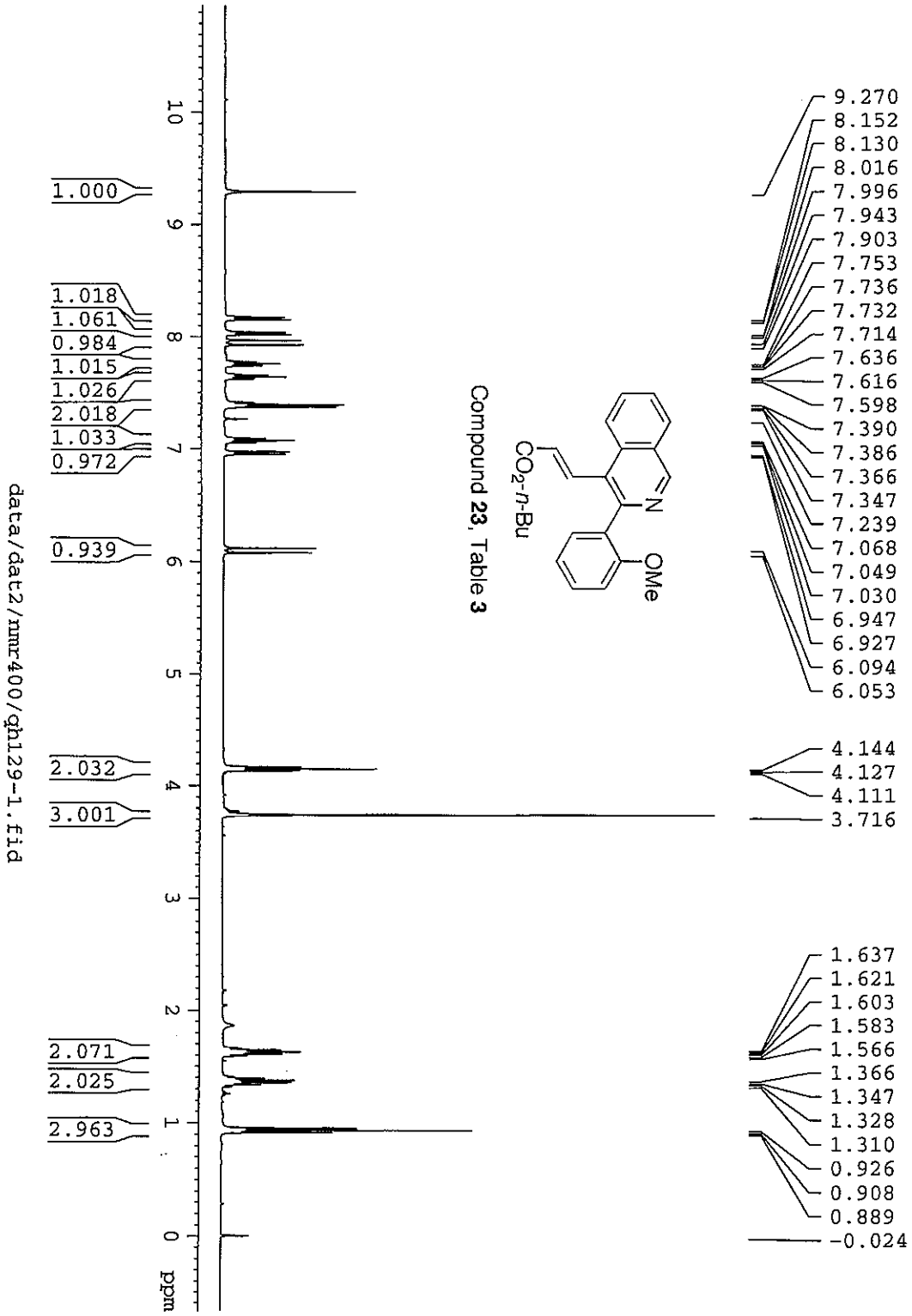
8.046
8.006
7.544
7.540
7.523
7.521
7.482
7.465
7.445
7.423
7.405
7.287
7.271
7.243
6.494
6.455
4.073
4.055
2.802
0.000
1.000
1.041
2.129
2.185
0.985
1.045
1.007
0.971
6.136
3.025
MeO
MeO
SO2Me
Ph
N
Compound 19, Table 3
ppm
data/drx1/nmr400/qh161-3.fid


154.291
151.346
150.800
150.752
140.789
140.413
134.379
131.143
130.359
128.592
128.485
123.624
120.827
106.077
101.976
77.546
77.229
76.910
56.505
56.372
42.582
MeO
MeO
N
Ph
SO2Me
Compound 19, Table 3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh161-2.fid


9.278
8.267
8.238
8.040
8.013
8.003
7.948
7.760
7.629
7.610
7.605
7.587
7.581
7.265
7.012
6.989
6.983
6.384
6.329
4.258
4.236
4.214
3.874
1.718
1.695
1.668
1.464
1.443
1.439
1.413
0.989
0.964
0.940
1.000
1.049
2.421
1.273
3.581
2.442
0.990
2.140
4.217
2.389
2.751
3.196
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
data/dat2/nmr300/qh113-1.fid
Compound 21, Table 3
CO2-n-Bu
OMe
N


Compound 21, Table 3
CO2-n-Bu
OMe
N
166.624
160.015
152.834
151.698
141.735
134.473
132.678
132.070
131.462
128.501
127.383
127.221
126.263
124.354
123.392
113.892
77.696
77.272
76.848
64.840
55.574
30.946
19.430
13.996
200
180
160
140
120
100
80
60
40
20
0 ppm
data/dat2/nmr300/qh113-2.fid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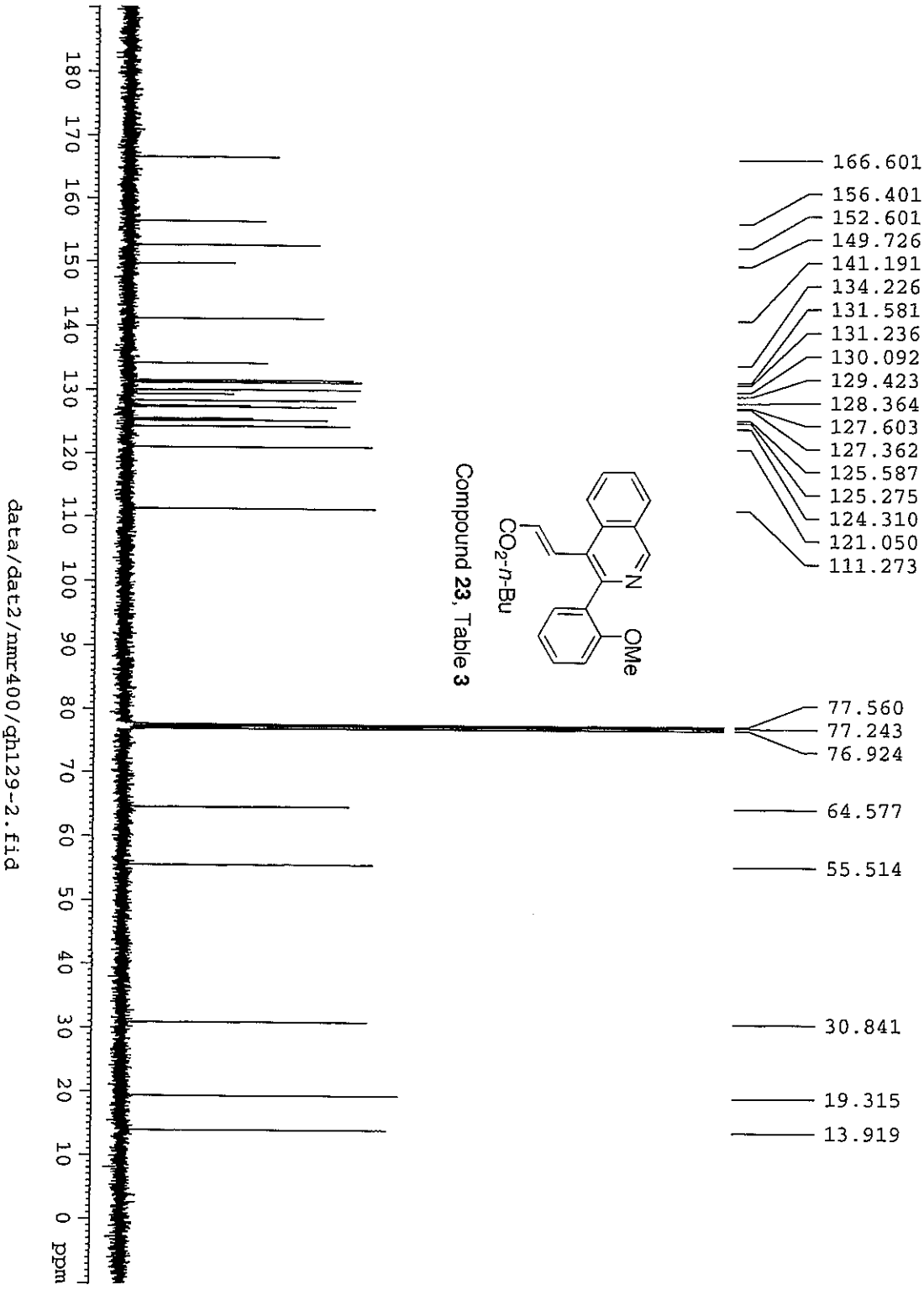
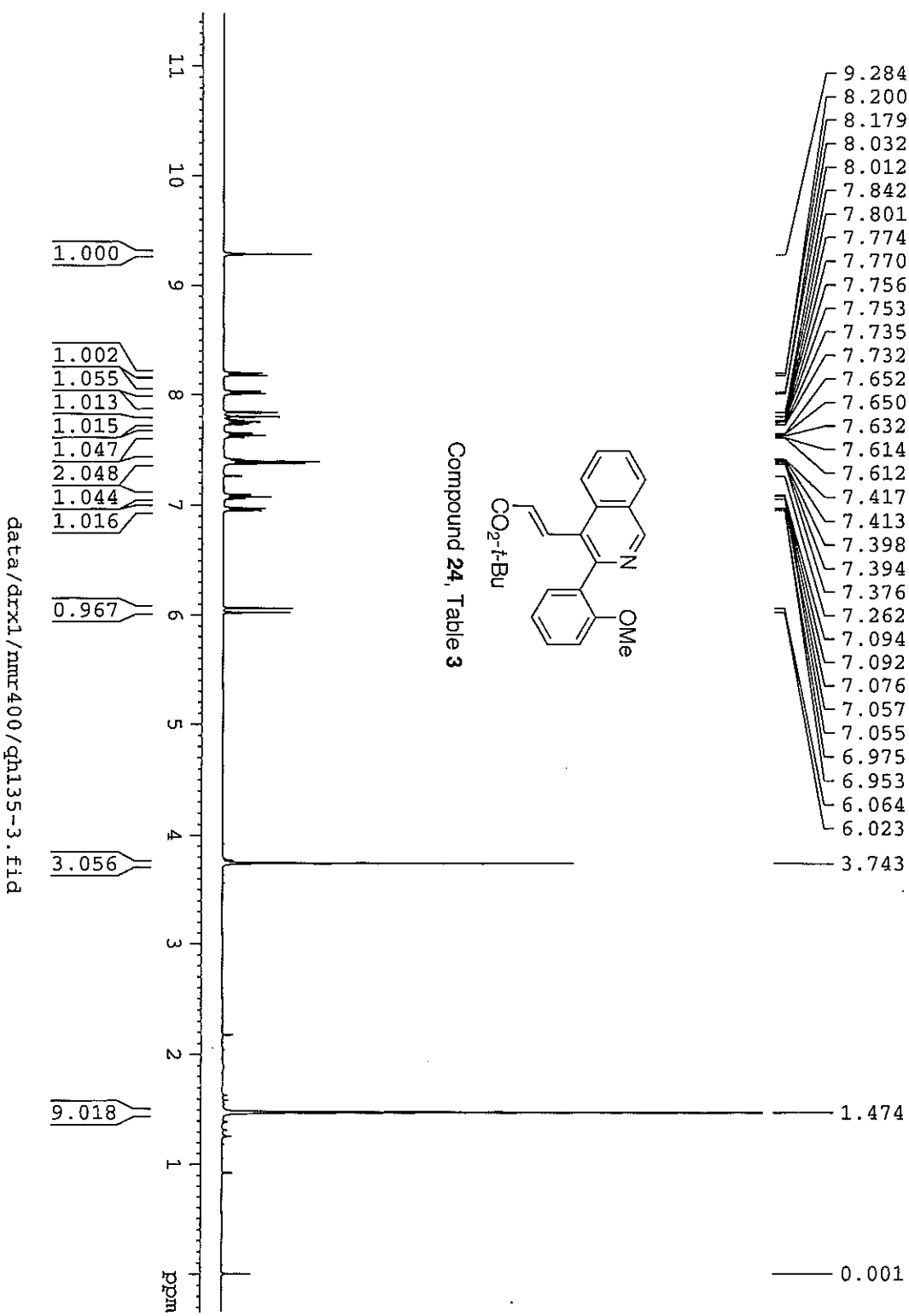
8.152
8.130
8.016
7.996
7.943
7.903
7.753
7.736
7.732
7.714
7.636
7.616
7.598
7.390
7.386
7.366
7.347
7.239
7.068
7.049
7.030
6.947
6.927
6.094
6.053
4.144
4.127
4.111
3.716
1.637
1.621
1.603
1.583
1.566
1.366
1.347
1.328
1.310
0.926
0.908
0.889
-0.024
1.000
1.018
1.061
0.984
1.015
1.026
2.018
1.033
0.972
0.939
2.032
3.001
2.071
2.025
2.963
ppm
Compound 23, Table 3
CO2-n-Bu
OMe
N
data/dat2/nmr400/qh129-1.fid


166.601
156.401
152.601
149.726
141.191
134.226
131.581
131.236
130.092
129.423
128.364
127.603
127.362
125.587
125.275
124.310
121.050
111.273
77.560
77.243
76.924
64.577
55.514
30.841
19.315
13.919
Compound 23, Table 3
CO2-n-Bu
N
OMe
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh129-2.fid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8.200
8.179
8.032
8.012
7.842
7.801
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7.770
7.756
7.753
7.735
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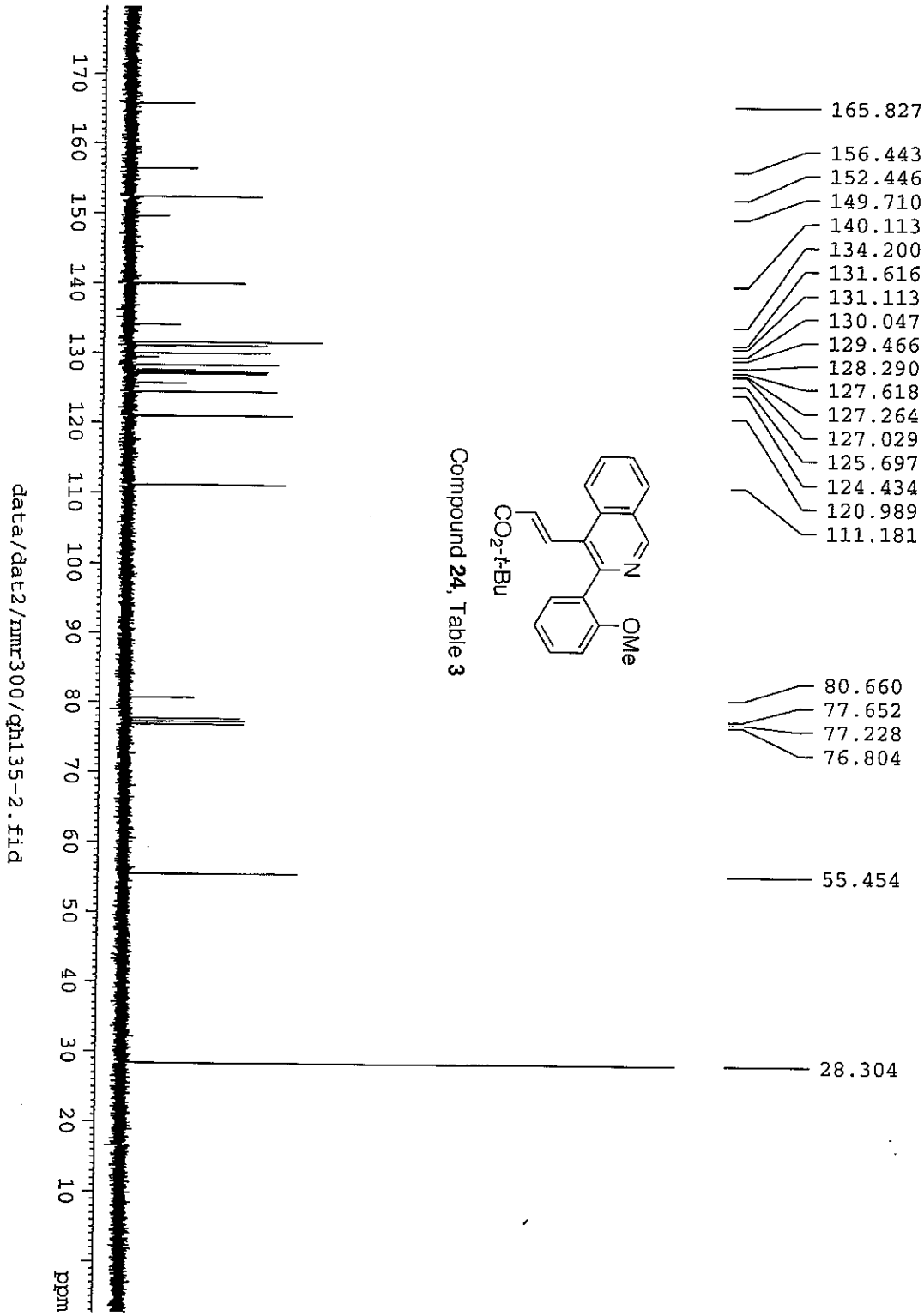
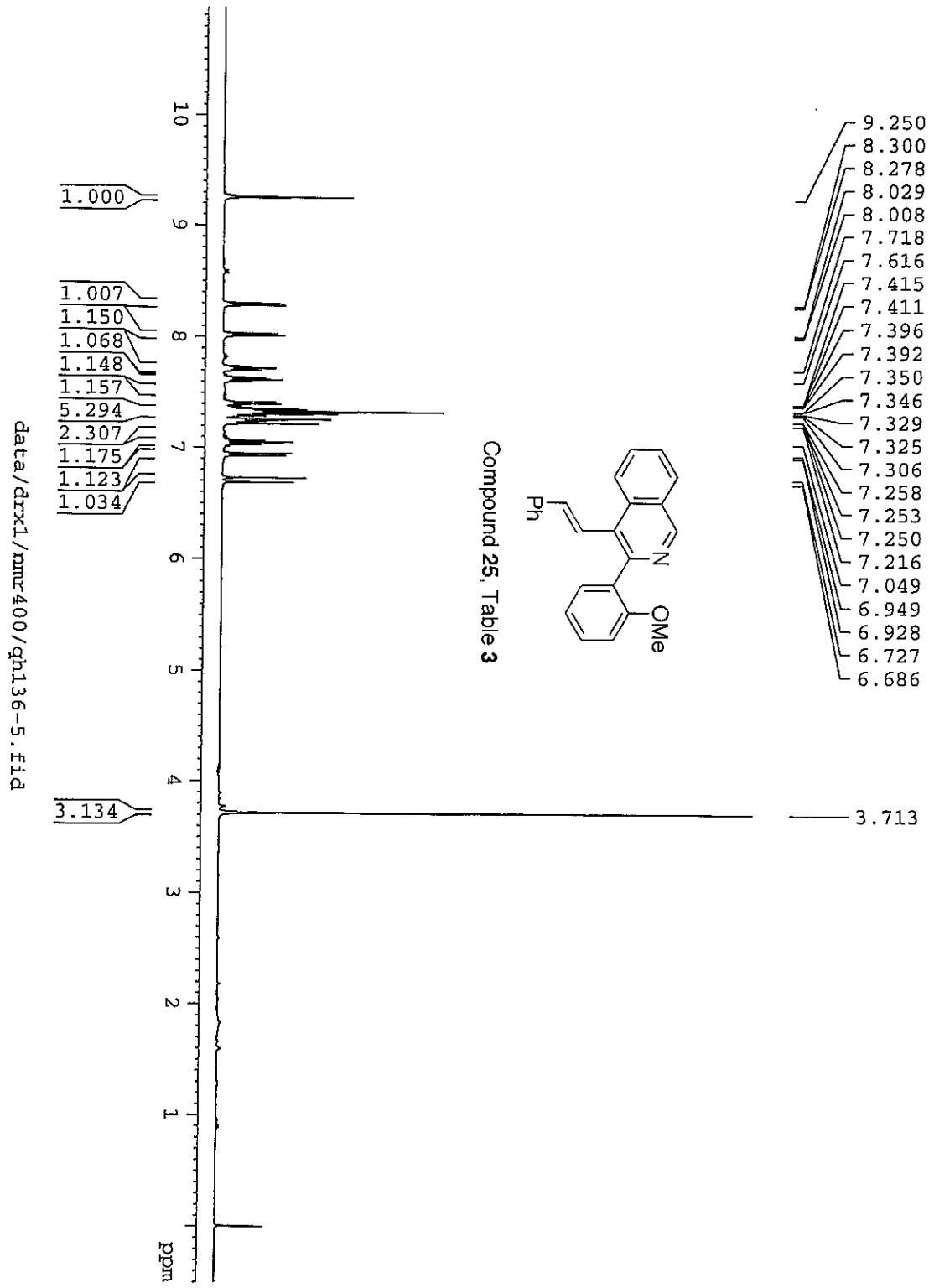
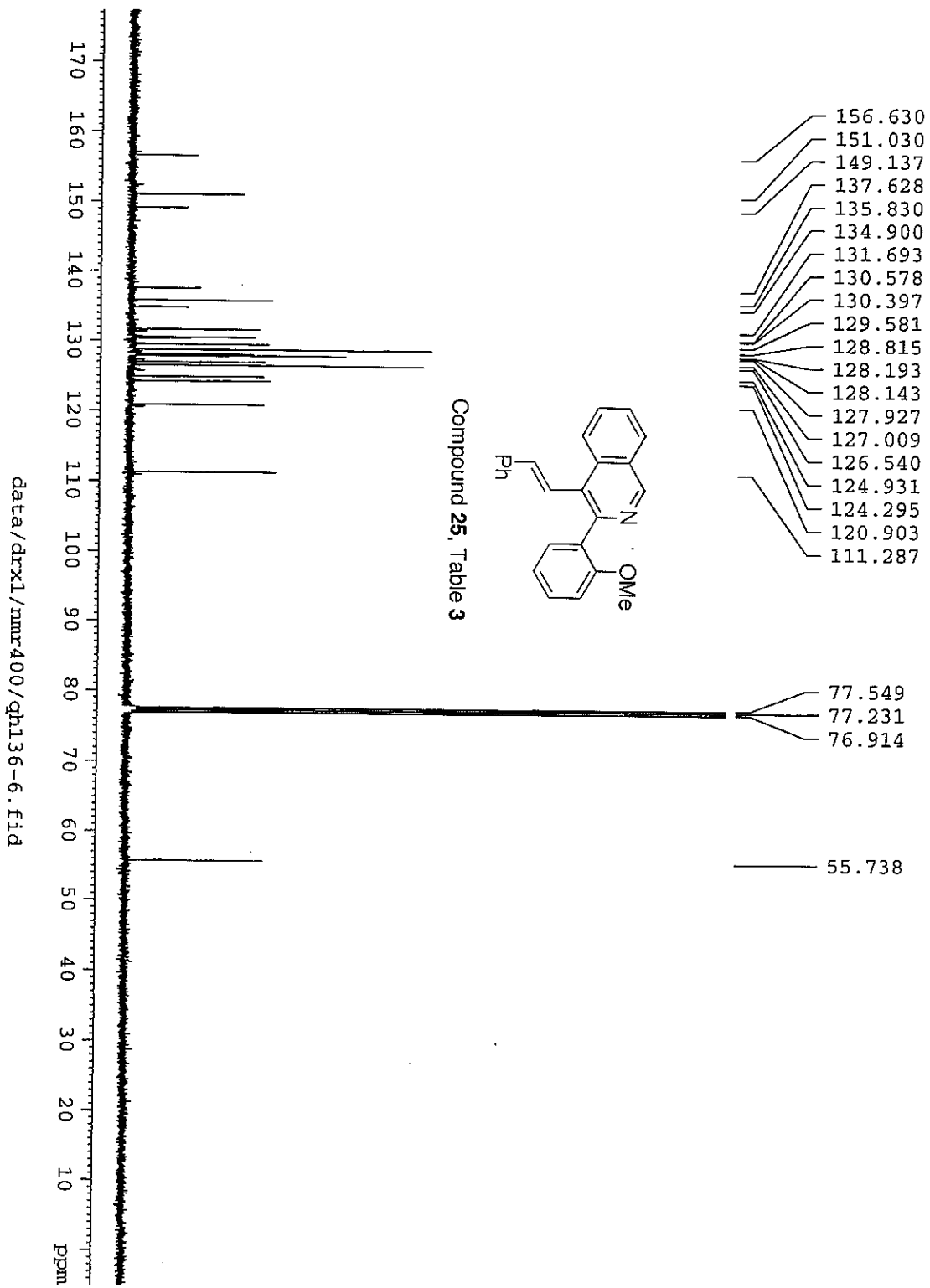
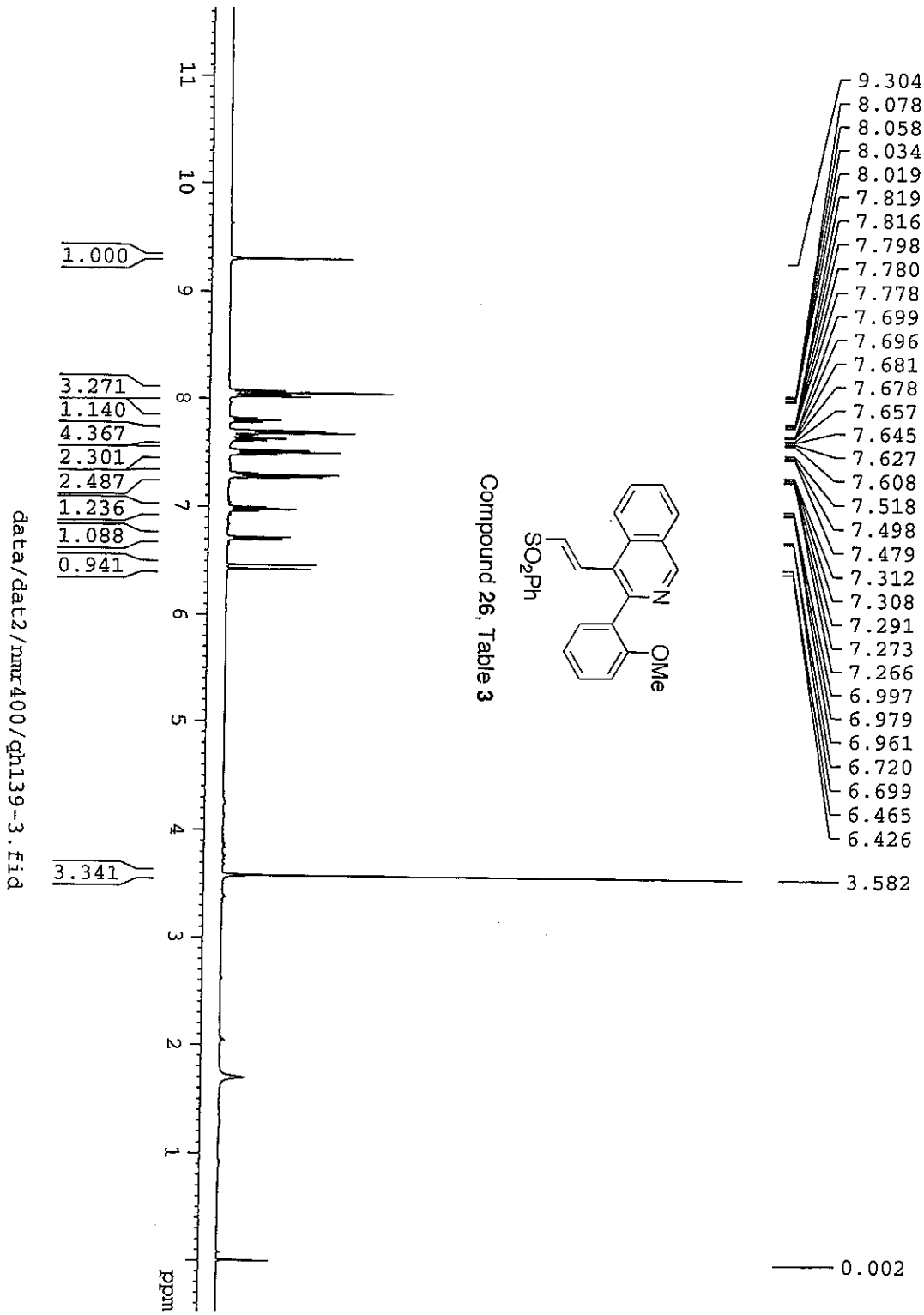
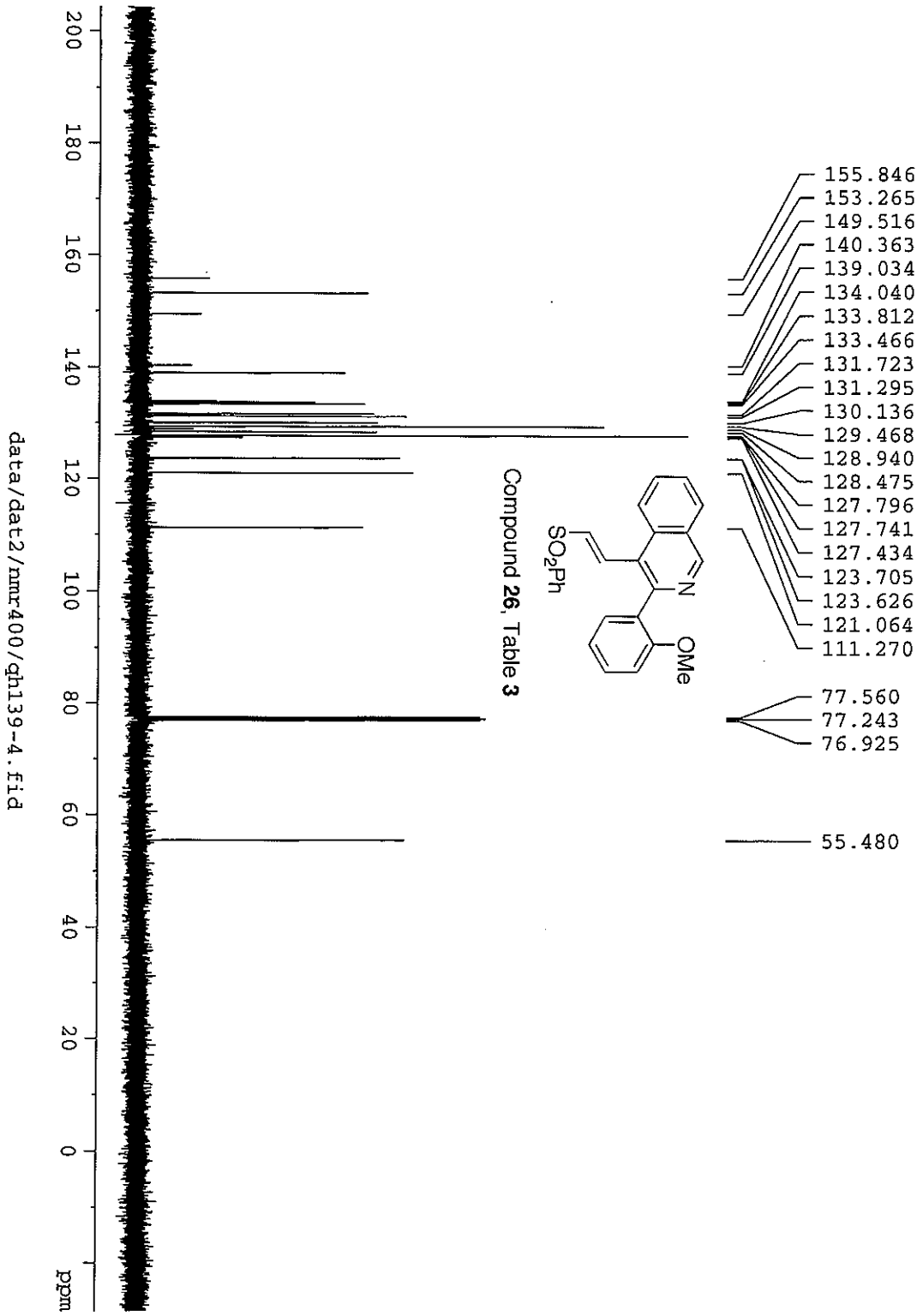
7.652
7.650
7.632
7.614
7.612
7.417
7.413
7.398
7.394
7.376
7.262
7.094
7.092
7.076
7.057
7.055
6.975
6.953
6.064
6.023
3.743
1.474
0.001
1.000
1.002
1.055
1.013
1.015
1.047
2.048
1.044
1.016
0.967
3.056
9.018
ppm
Compound 24, Table 3
CO2-t-Bu
N
OMe
data/drxl/nmr400/qh135-3.fid


165.827
156.443
152.446
149.710
140.113
134.200
131.616
131.113
130.047
129.466
128.290
127.618
127.264
127.029
125.697
124.434
120.989
111.181
80.660
77.652
77.228
76.804
55.454
28.304
N
OMe
CO2-t-Bu
Compound 24, Table 3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh135-2.fid

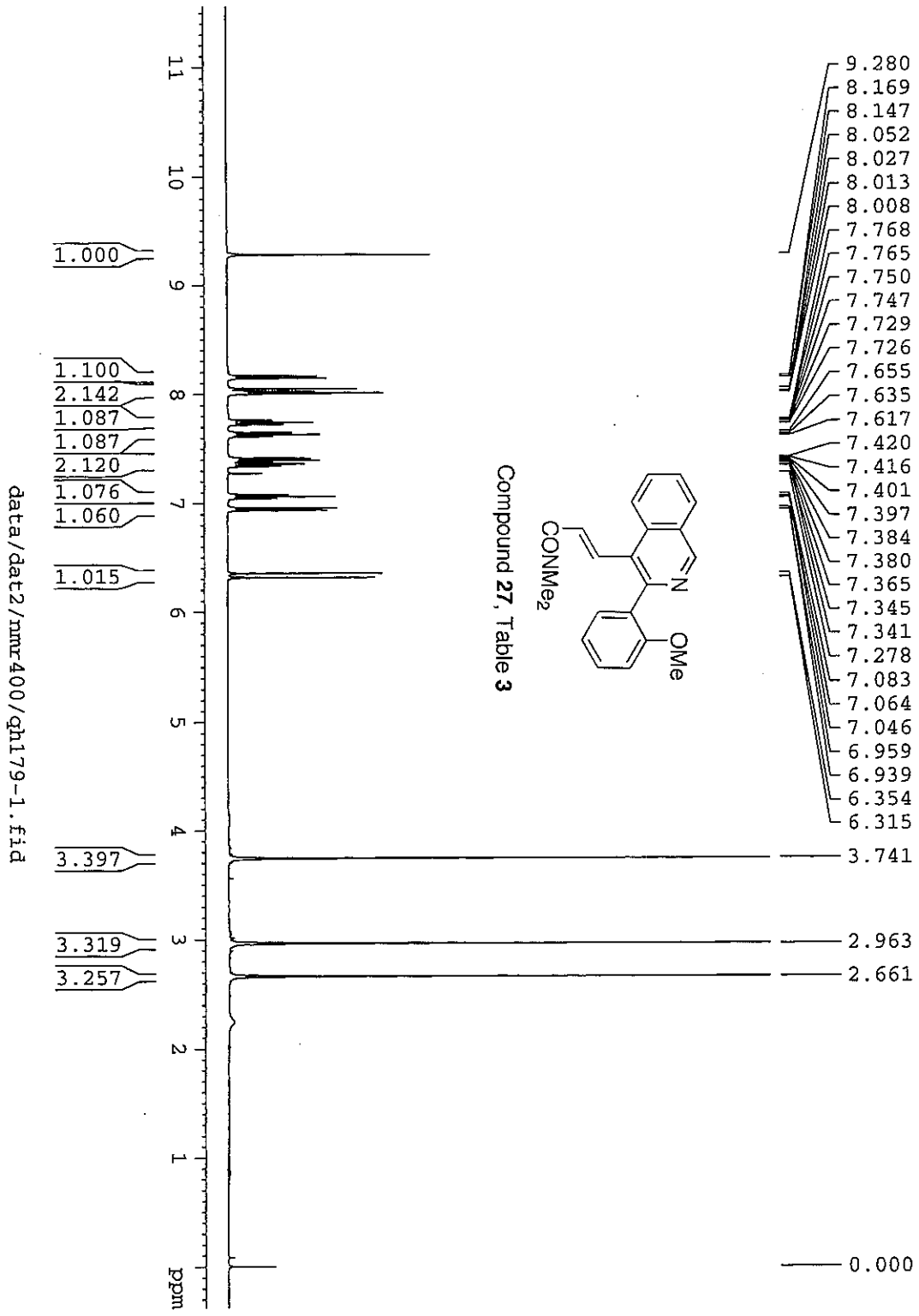

9.250
8.300
8.278
8.029
8.008
7.718
7.616
7.415
7.411
7.396
7.392
7.350
7.346
7.329
7.325
7.306
7.258
7.253
7.250
7.216
7.049
6.949
6.928
6.727
6.686
3.713
1.000
1.007
1.150
1.068
1.148
1.157
5.294
2.307
1.175
1.123
1.034
3.134
ppm
Ph
N
OMe
Compound 25, Table 3
data/drx1/nmr400/qh136-5.fid

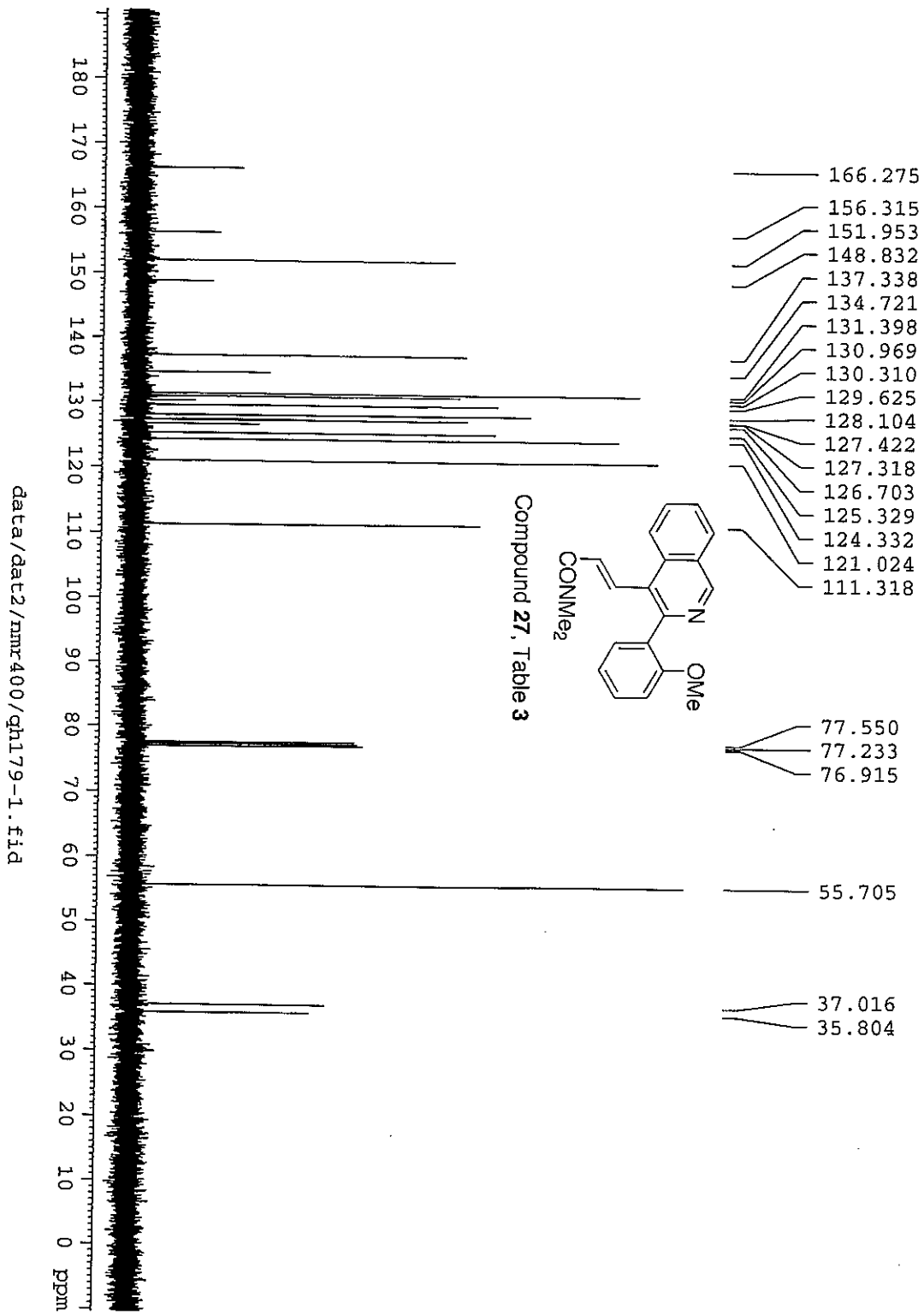

156.630
151.030
149.137
137.628
135.830
134.900
131.693
130.578
130.397
129.581
128.815
128.193
128.143
127.927
127.009
126.540
124.931
124.295
120.903
111.287
77.549
77.231
76.914
55.738
Ph
N
OMe
Compound 25, Table 3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh136-6.fid

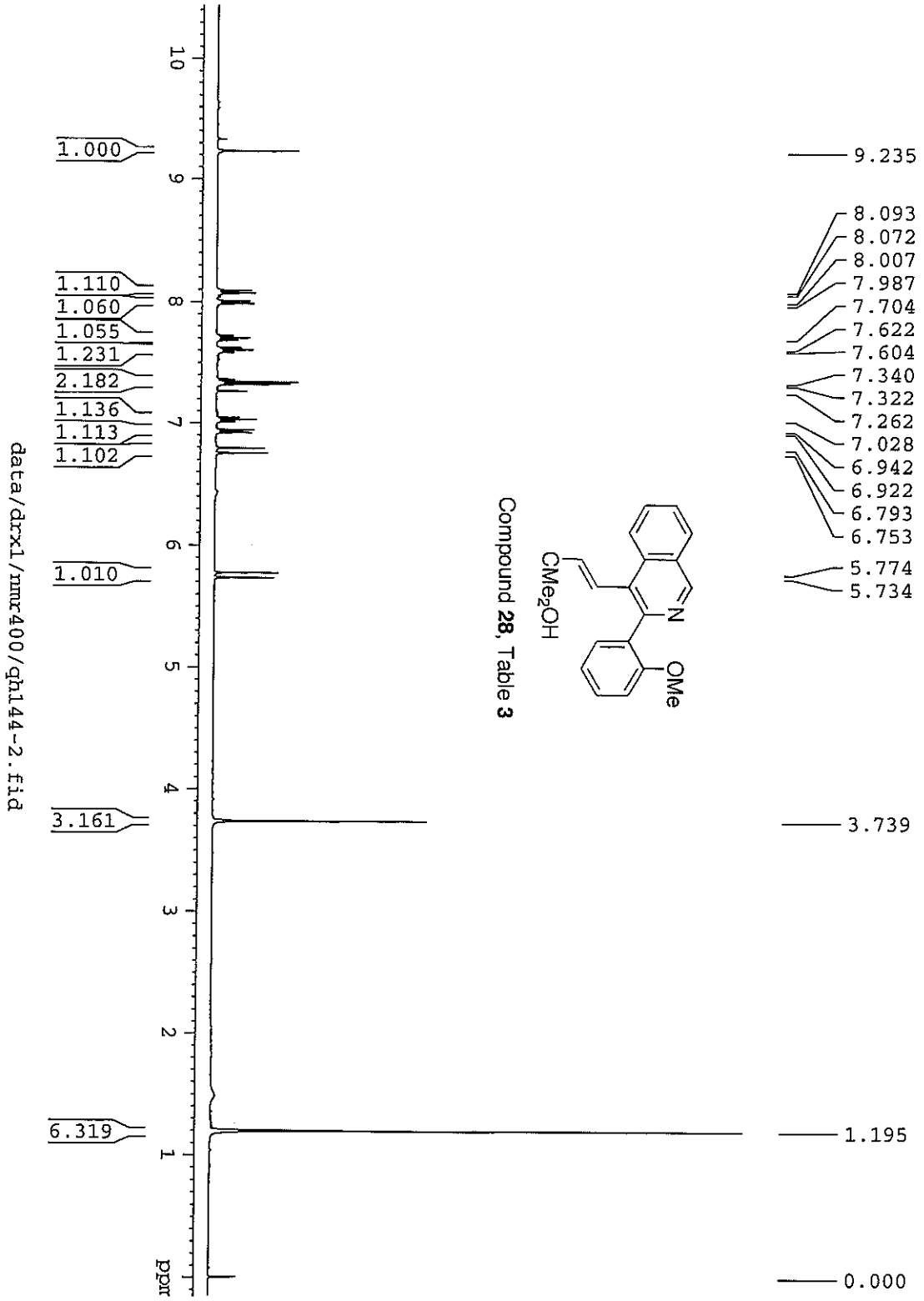

9.304
8.078
8.058
8.034
8.019
7.819
7.816
7.798
7.780
7.778
7.699
7.696
7.681
7.678
7.657
7.645
7.627
7.608
7.518
7.498
7.479
7.312
7.308
7.291
7.273
7.266
6.997
6.979
6.961
6.720
6.699
6.465
6.426
3.582
0.002
1.000
3.271
1.140
4.367
2.301
2.487
1.236
1.088
0.941
3.341
ppm
Compound 26, Table 3
SO2Ph
N
OMe
data/dat2/nmr400/qh139-3.fid

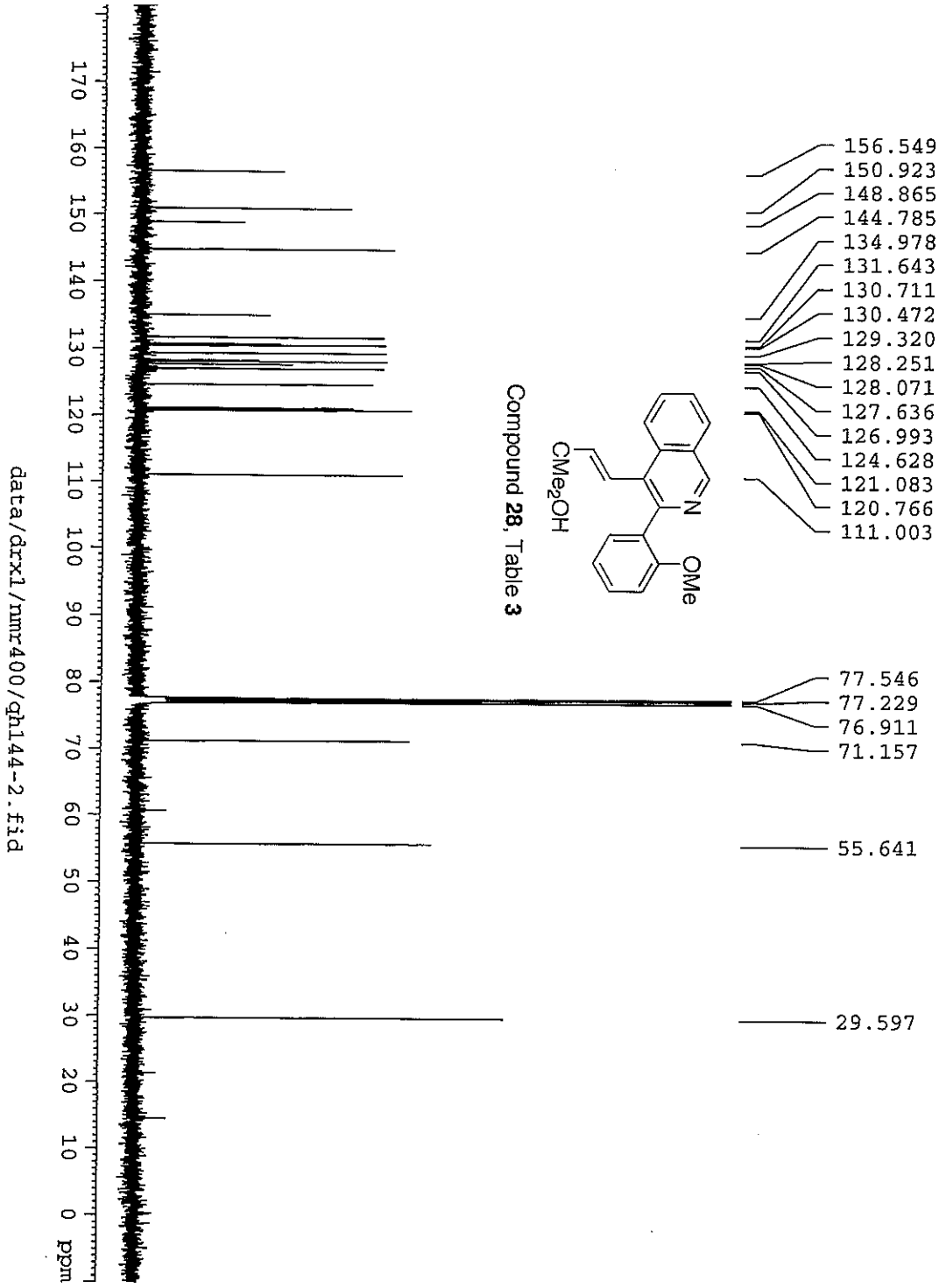


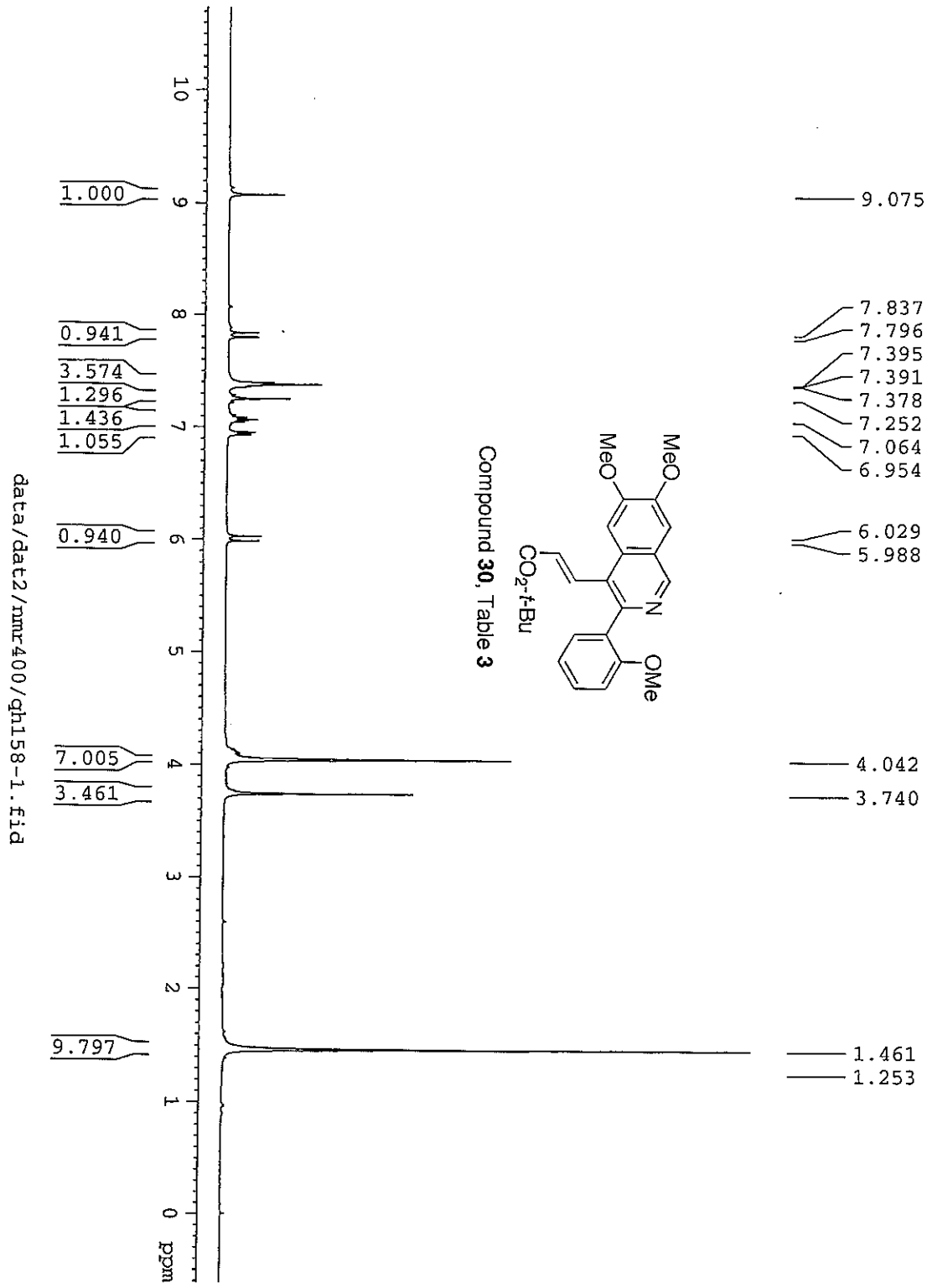
Compound **26**, Table **3**

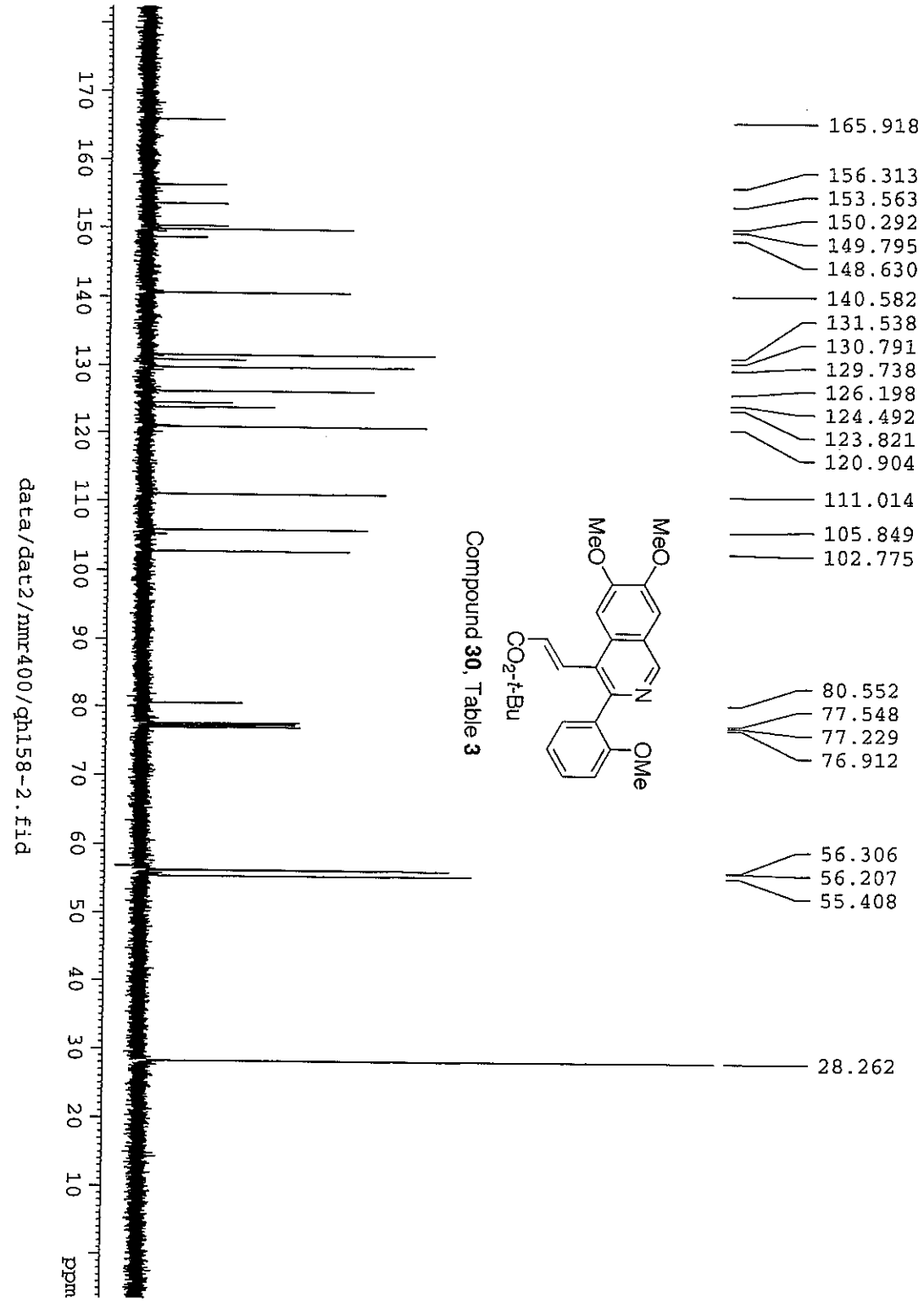

9.280
8.169
8.147
8.052
8.027
8.013
8.008
7.768
7.765
7.750
7.747
7.729
7.726
7.655
7.635
7.617
7.420
7.416
7.401
7.397
7.384
7.380
7.365
7.345
7.341
7.278
7.083
7.064
7.046
6.959
6.939
6.354
6.315
3.741
2.963
2.661
0.000
1.000
1.100
2.142
1.087
1.087
2.120
1.076
1.060
1.015
3.397
3.319
3.257
11
10
9
8
7
6
5
4
3
2
1
ppm
CONMe2
N
OMe
Compound 27, Table 3
data/dat2/nmr400/qh179-1.fid

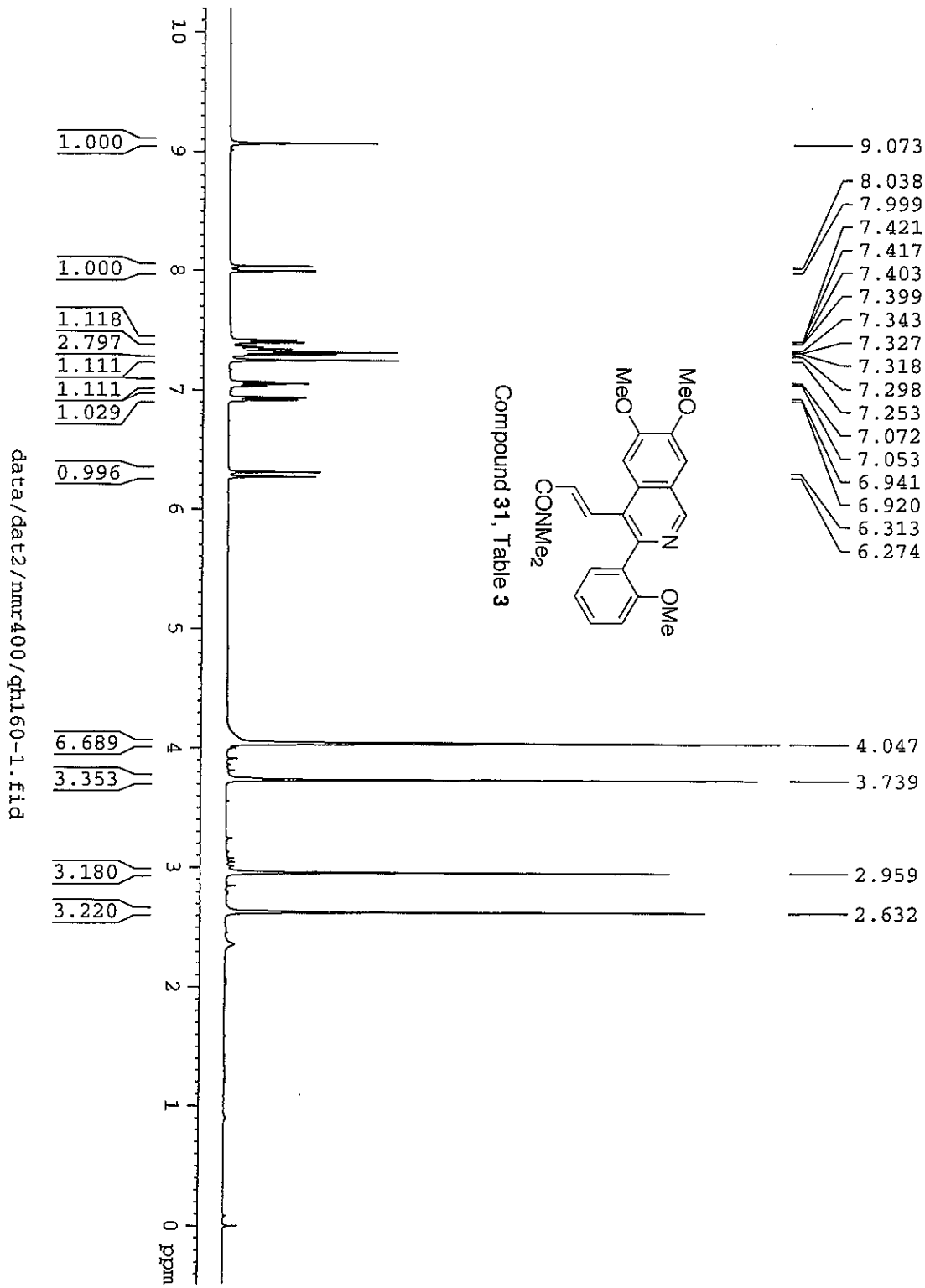

166.275
156.315
151.953
148.832
137.338
134.721
131.398
130.969
130.310
129.625
128.104
127.422
127.318
126.703
125.329
124.332
121.024
111.318
77.550
77.233
76.915
55.705
37.016
35.804
Compound 27, Table 3
CONMe2
N
OMe
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/gh179-1.fid

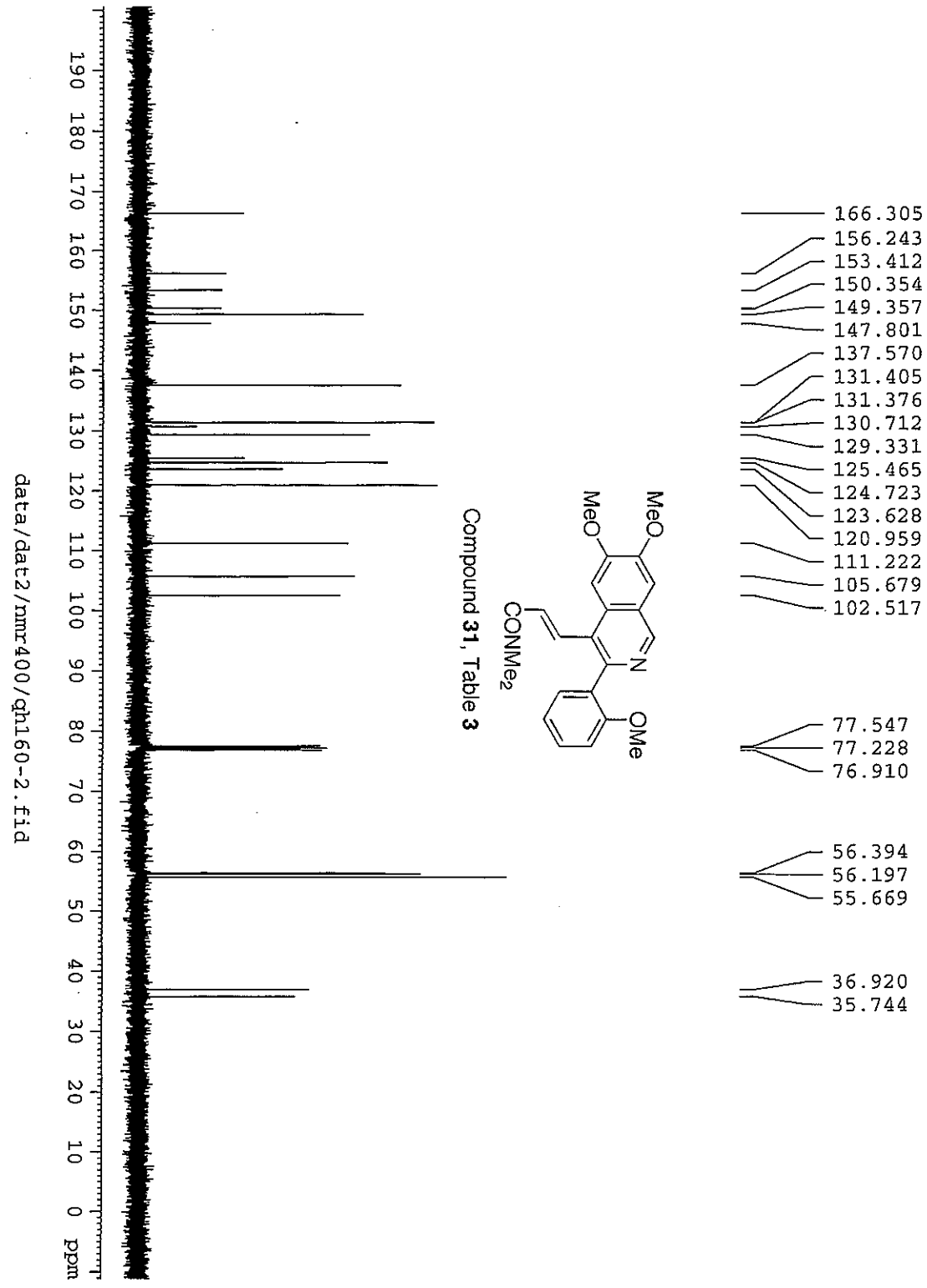

data/drx1/nmr400/qh144-2.fid
Compound 28, Table 3
CMe2OH
OMe
N
1.000
1.110
1.060
1.055
1.231
2.182
1.136
1.113
1.102
1.010
3.161
6.319
9.235
8.093
8.072
8.007
7.987
7.704
7.622
7.604
7.340
7.322
7.262
7.028
6.942
6.922
6.793
6.753
5.774
5.734
3.739
1.195
0.000
ppm

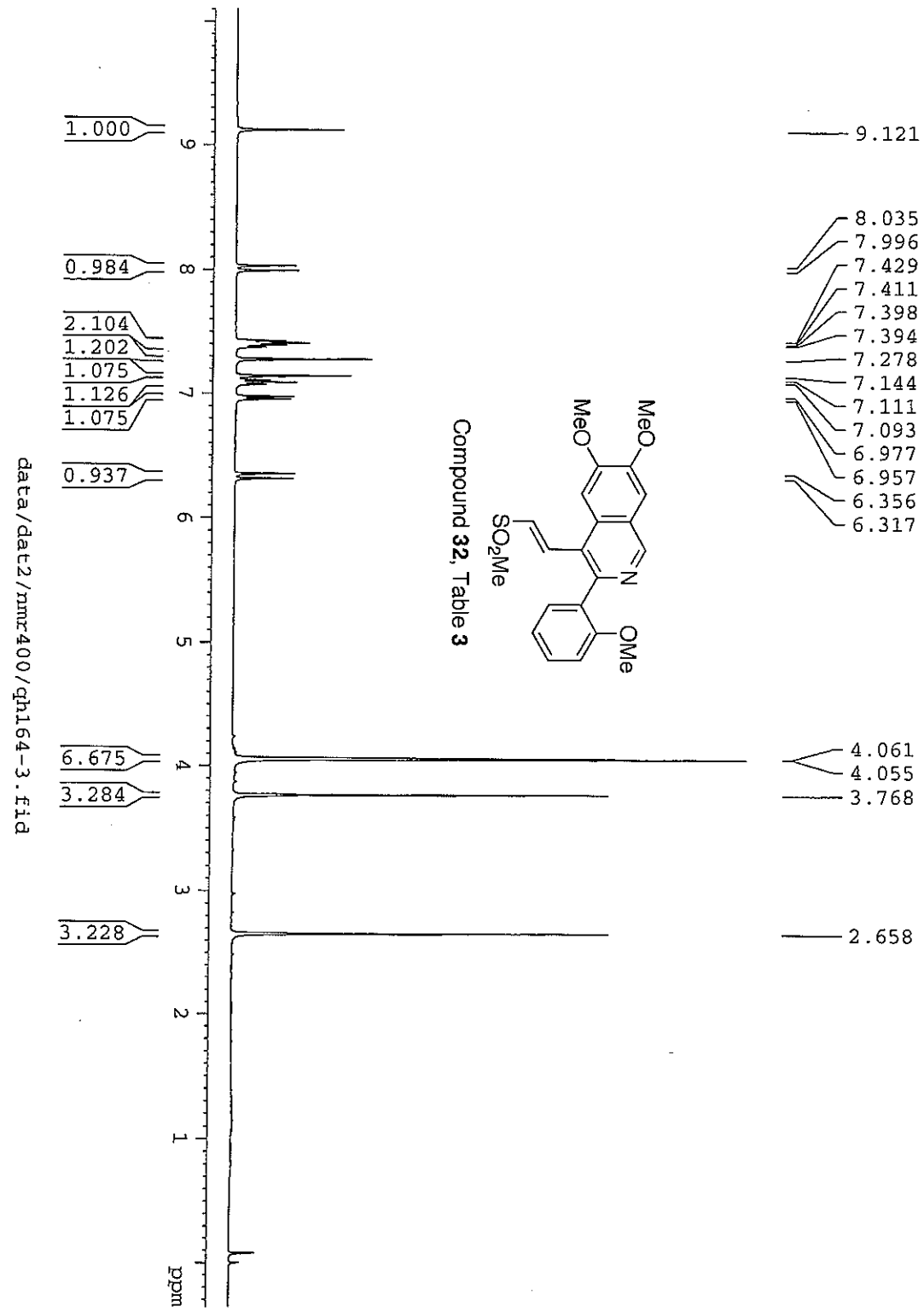

156.549
150.923
148.865
144.785
134.978
131.643
130.711
130.472
129.320
128.251
128.071
127.636
126.993
124.628
121.083
120.766
111.003
77.546
77.229
76.911
71.157
55.641
29.597
CMe2OH
N
OMe
Compound 28, Table 3
data/drx1/nmr400/qh144-2.fid
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

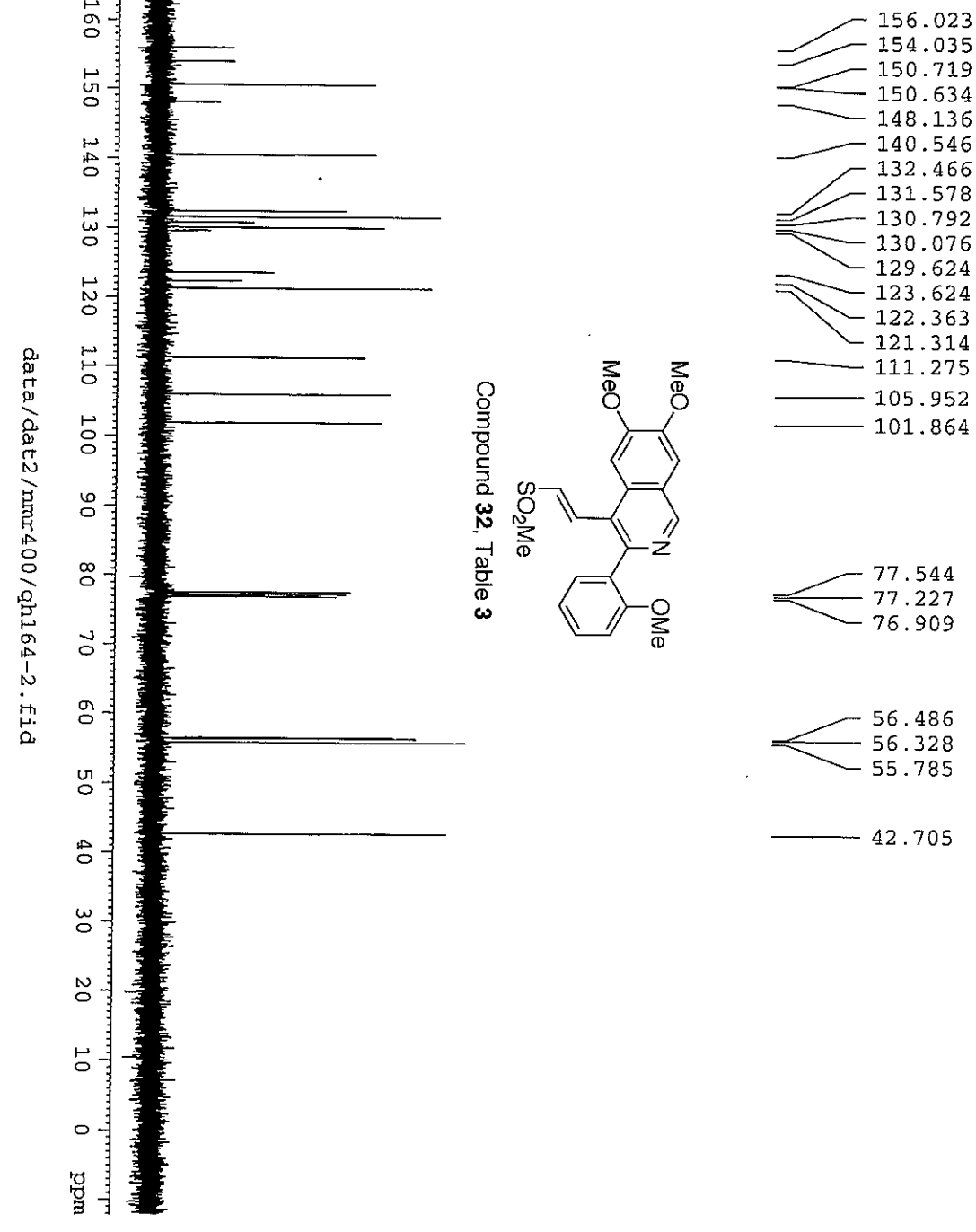

data/dat2/nmr400/qh158-1.fid
1.000
0.941
3.574
1.296
1.436
1.055
0.940
7.005
3.461
9.797
10
9
8
7
6
5
4
3
2
1
0
ppm
Compound 30, Table 3
MeO
MeO
N
OMe
CO2-t-Bu
9.075
7.837
7.796
7.395
7.391
7.378
7.252
7.064
6.954
6.029
5.988
4.042
3.740
1.461
1.253

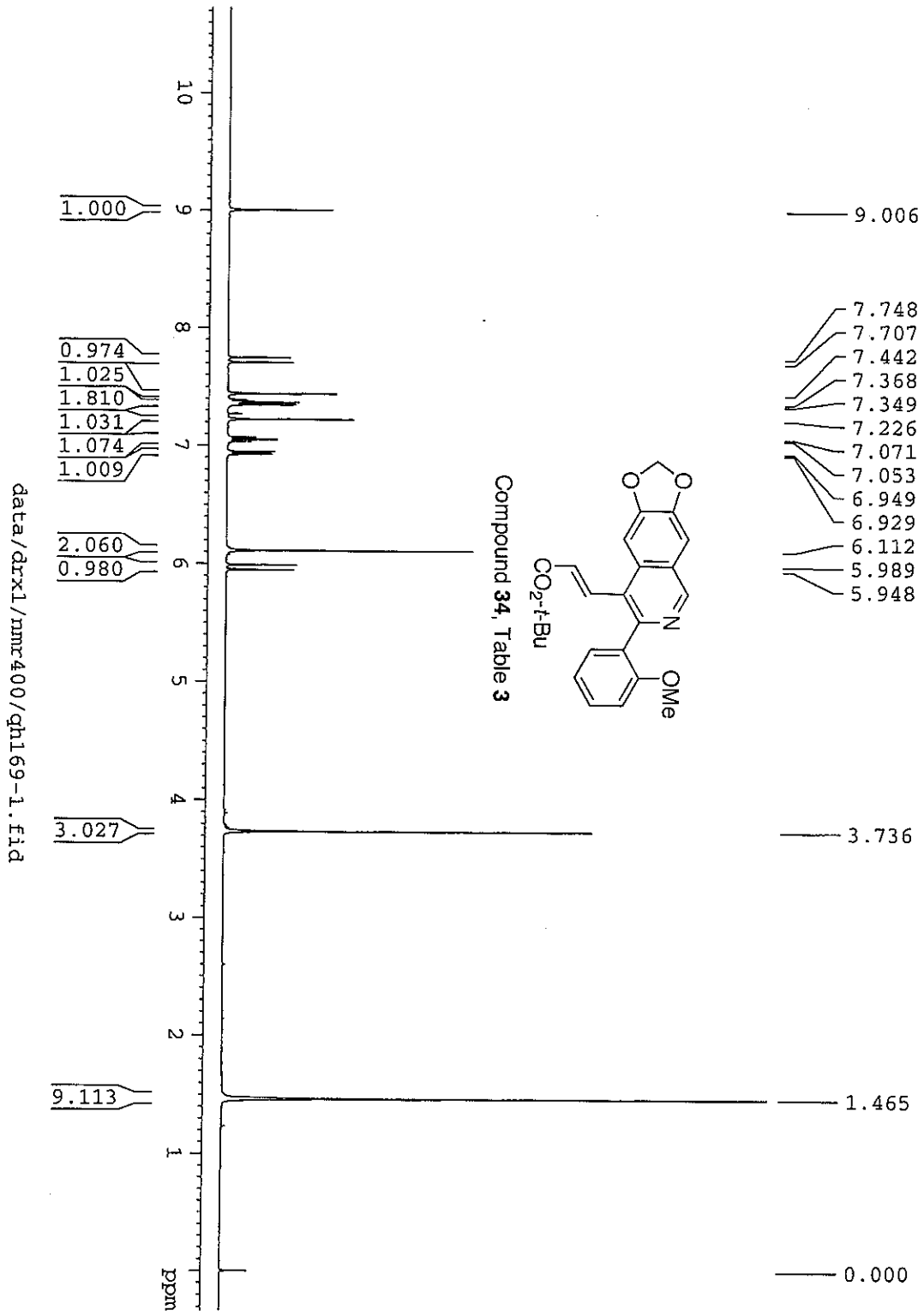

165.918
156.313
153.563
150.292
149.795
148.630
140.582
131.538
130.791
129.738
126.198
124.492
123.821
120.904
111.014
105.849
102.775
80.552
77.548
77.229
76.912
56.306
56.207
55.408
28.262
MeO
MeO
OMe
N
CO2-t-Bu
Compound 30, Table 3
data/dat2/nmr400/qh158-2.fid
ppm

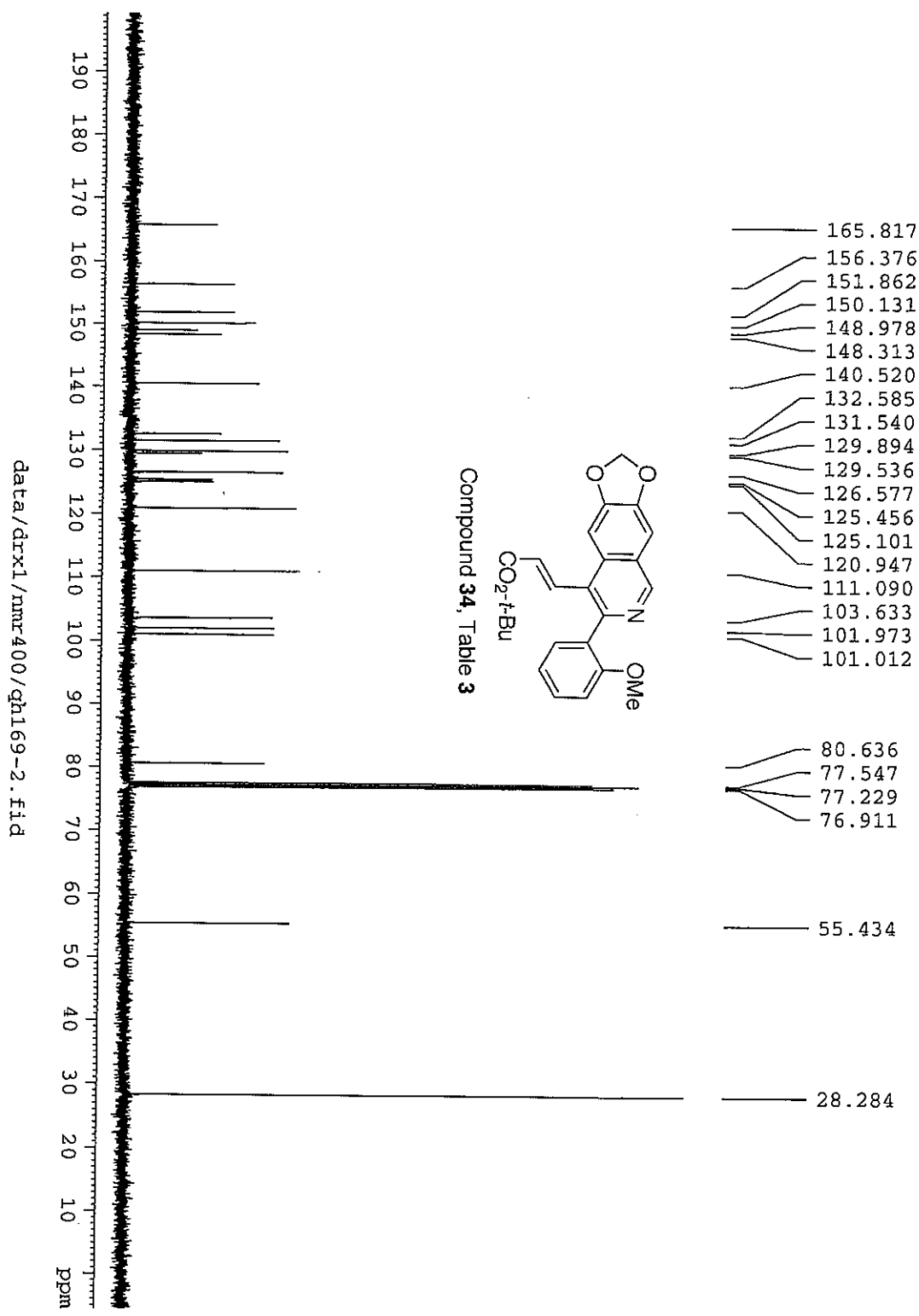

9.073
8.038
7.999
7.421
7.417
7.403
7.399
7.343
7.327
7.318
7.298
7.253
7.072
7.053
6.941
6.920
6.313
6.274
4.047
3.739
2.959
2.632
1.000
1.000
1.118
2.797
1.111
1.111
1.029
0.996
6.689
3.353
3.180
3.220
MeO
MeO
OMe
N
CONMe2
Compound 31, Table 3
data/dat2/nmr400/qh160-1.fid
10
9
8
7
6
5
4
3
2
1
0 ppm

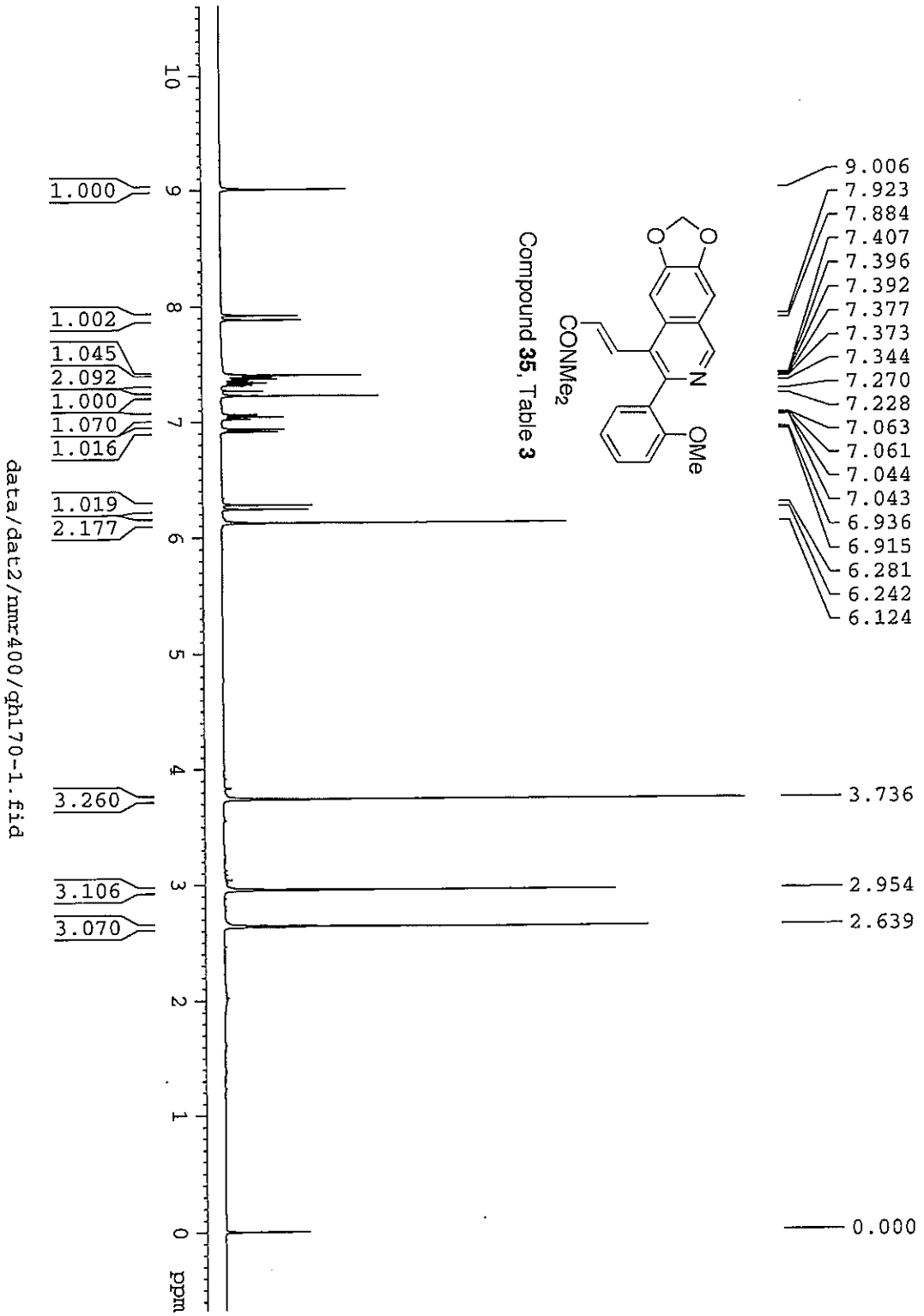

166.305
156.243
153.412
150.354
149.357
147.801
137.570
131.405
131.376
130.712
129.331
125.465
124.723
123.628
120.959
111.222
105.679
102.517
77.547
77.228
76.910
56.394
56.197
55.669
36.920
35.744
MeO
MeO
CONMe2
N
OMe
Compound 31, Table 3
data/dat2/nmr400/qh160-2.fid
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

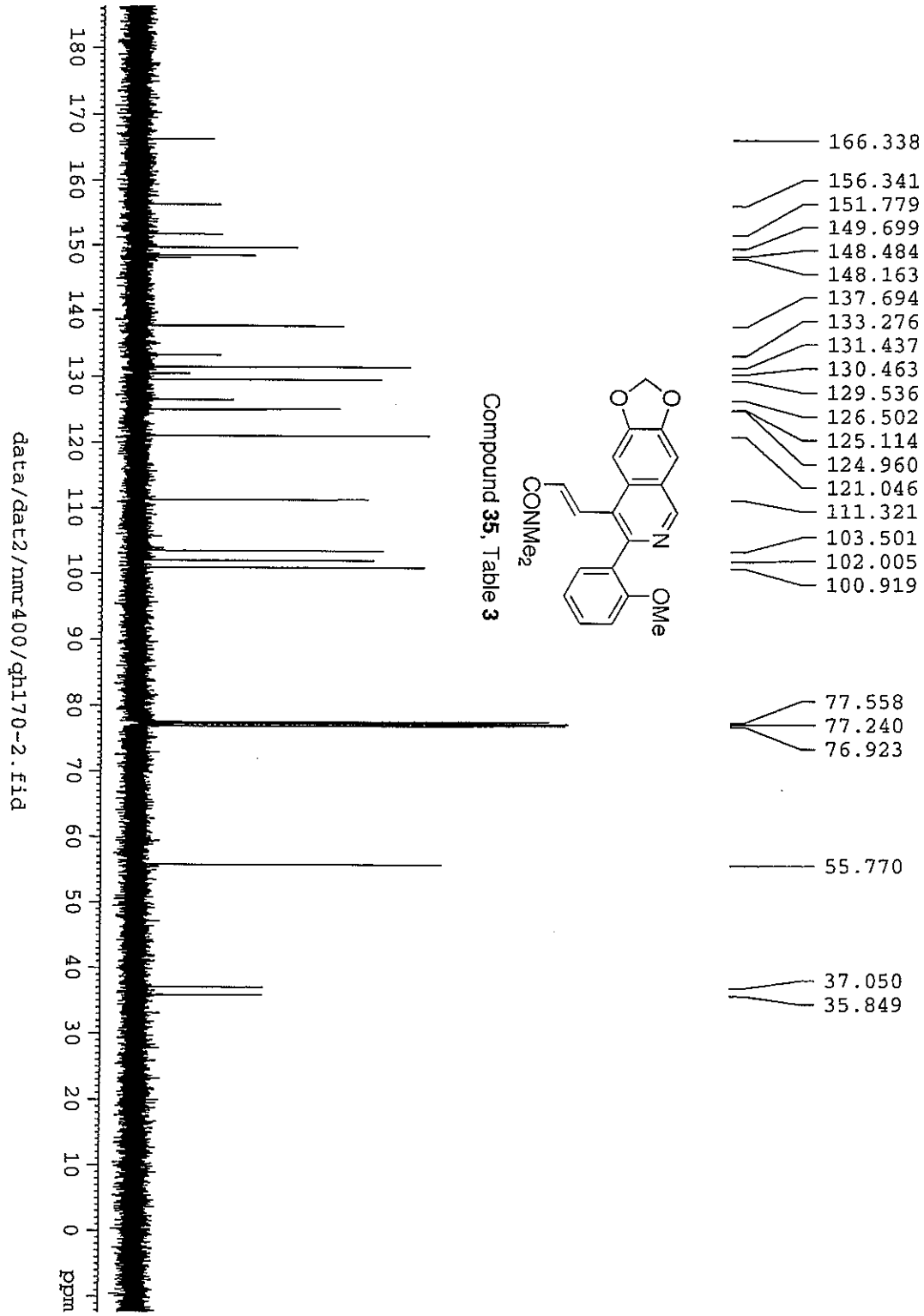

1.000
0.984
2.104
1.202
1.075
1.126
1.075
0.937
6.675
3.284
3.228
9.121
8.035
7.996
7.429
7.411
7.398
7.394
7.278
7.144
7.111
7.093
6.977
6.957
6.356
6.317
4.061
4.055
3.768
2.658
MeO
MeO
SO2Me
N
OMe
Compound 32, Table 3
data/dat2/nmr400/qh164-3.fid
ppm

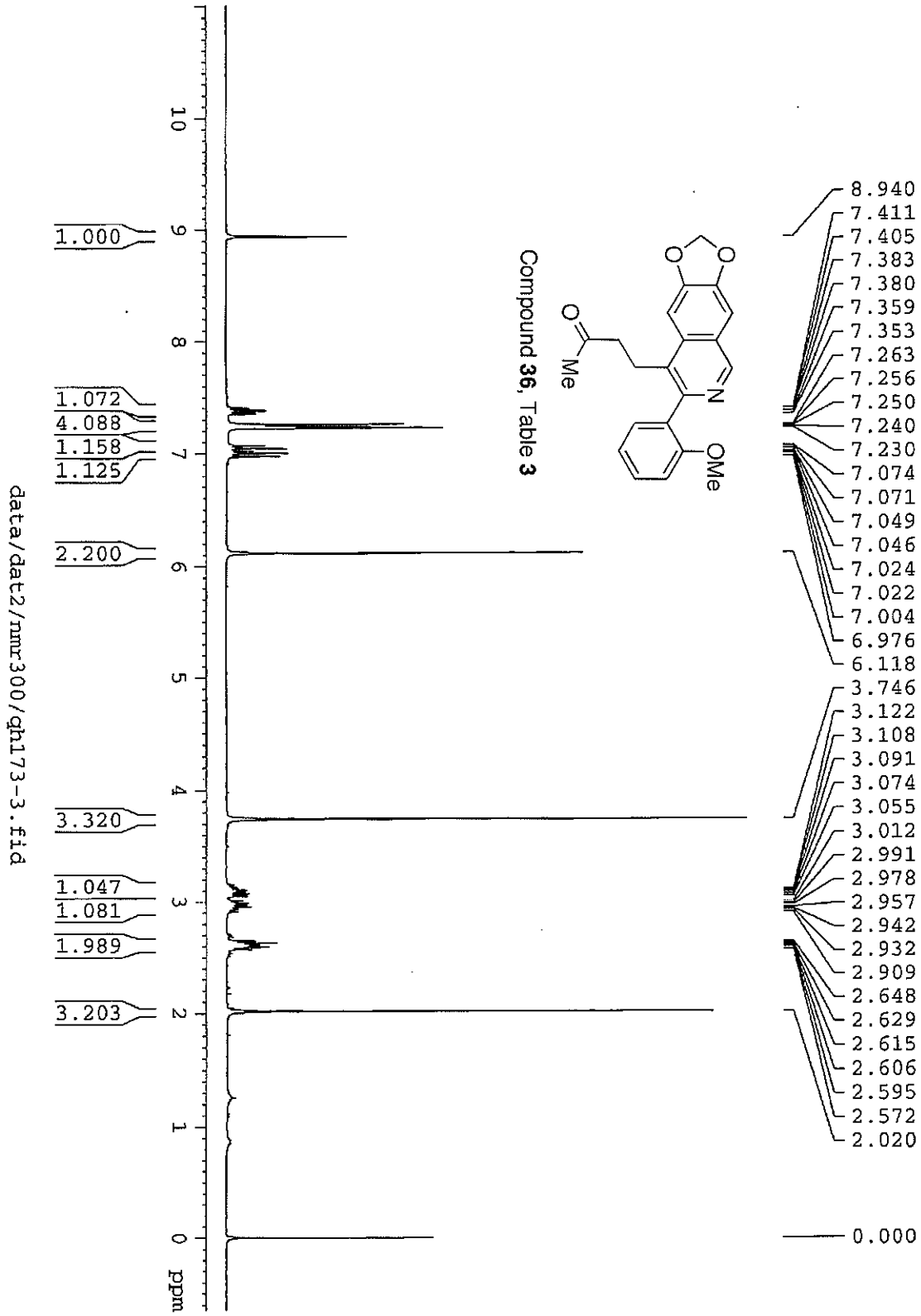

156.023
154.035
150.719
150.634
148.136
140.546
132.466
131.578
130.792
130.076
129.624
123.624
122.363
121.314
111.275
105.952
101.864
77.544
77.227
76.909
56.486
56.328
55.785
42.705
MeO
MeO
OMe
N
SO2Me
Compound 32, Table 3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh164-2.fid

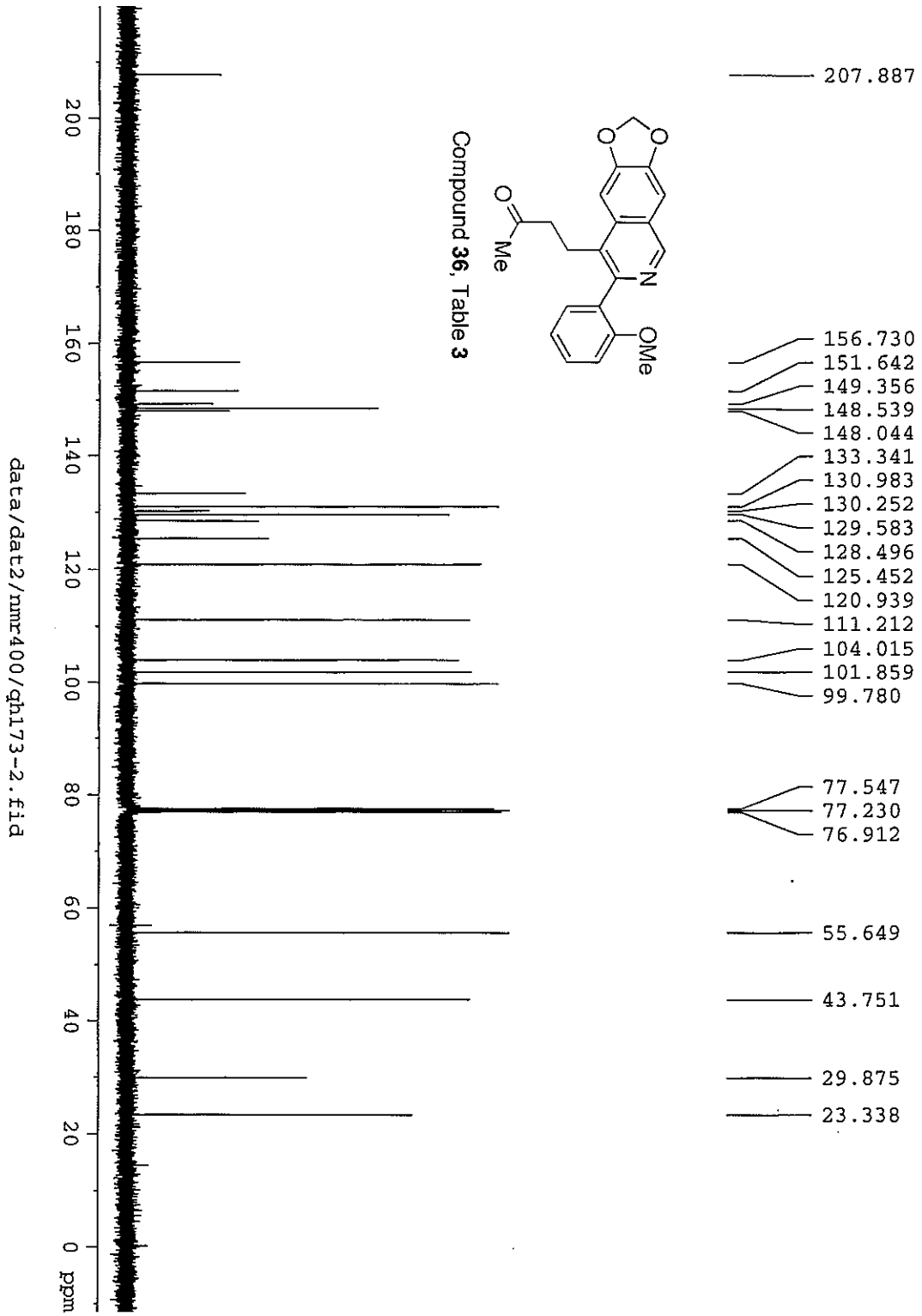

data/drx1/nmr400/qh169-1.fid
1.000
0.974
1.025
1.810
1.031
1.074
1.009
2.060
0.980
3.027
9.113
9.006
7.748
7.707
7.442
7.368
7.349
7.226
7.071
7.053
6.949
6.929
6.112
5.989
5.948
3.736
1.465
0.000
ppm
Compound 34, Table 3
CO2-t-Bu
OMe
N

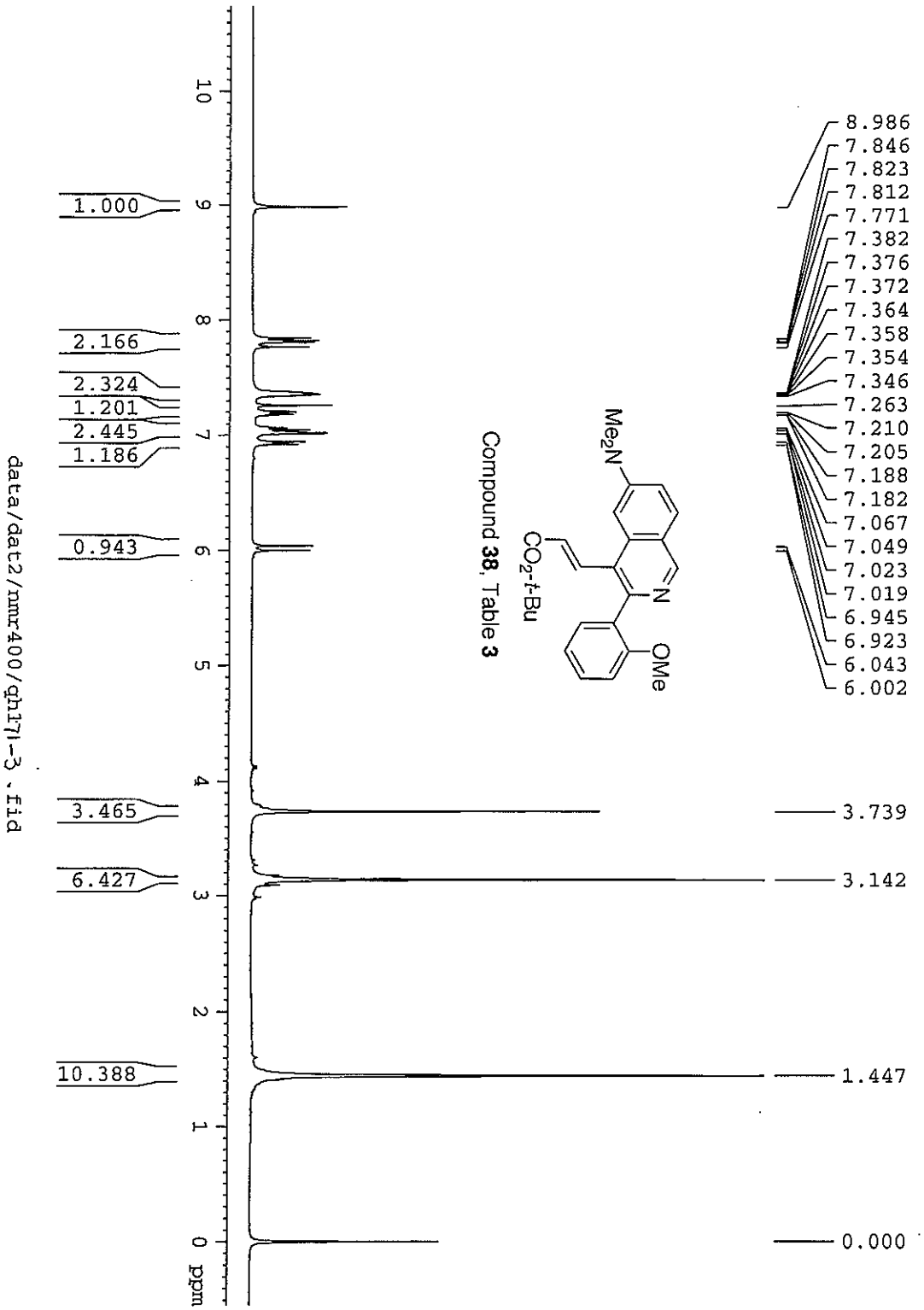

165.817
156.376
151.862
150.131
148.978
148.313
140.520
132.585
131.540
129.894
129.536
126.577
125.456
125.101
120.947
111.090
103.633
101.973
101.012
80.636
77.547
77.229
76.911
55.434
28.284
Compound 34, Table 3
CO2-t-Bu
OMe
N
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh169-2.fid

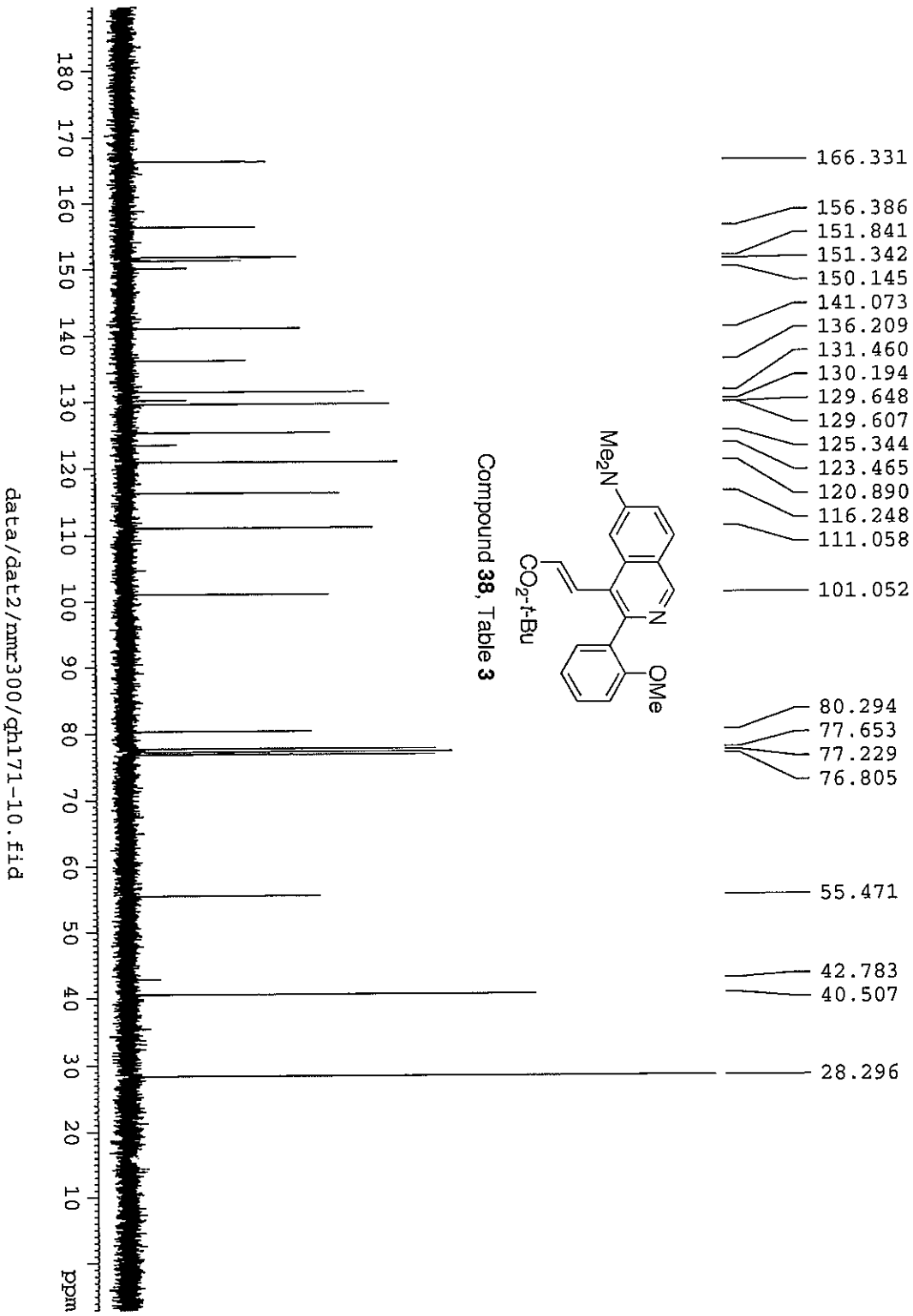

data/dat2/nmr400/qh170-1.fid
Compound 35, Table 3
CONMe2
OMe
N
1.000
1.002
1.045
2.092
1.000
1.070
1.016
1.019
2.177
3.260
3.106
3.070
9.006
7.923
7.884
7.407
7.396
7.392
7.377
7.373
7.344
7.270
7.228
7.063
7.061
7.044
7.043
6.936
6.915
6.281
6.242
6.124
3.736
2.954
2.639
0.000
ppm

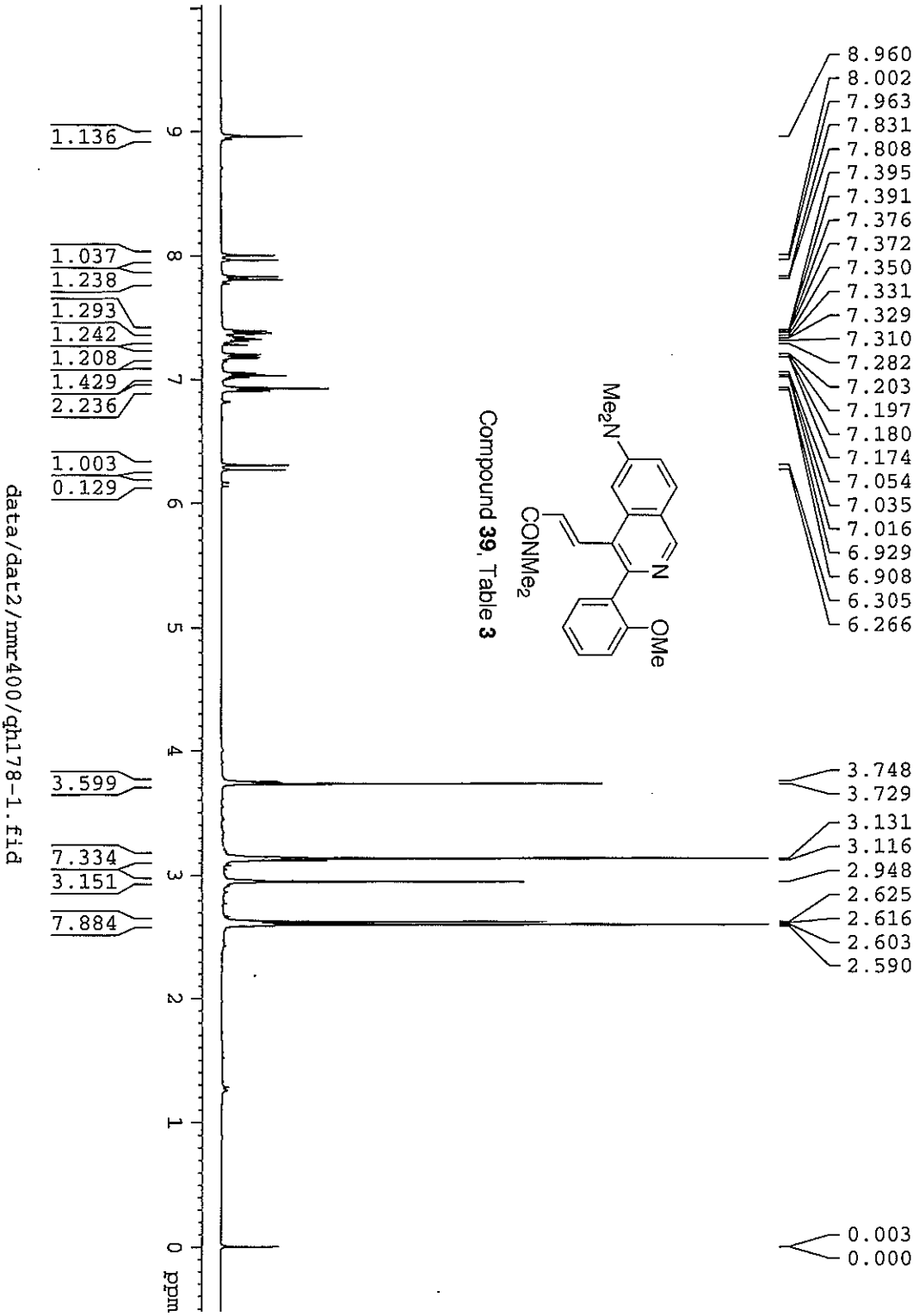

166.338
156.341
151.779
149.699
148.484
148.163
137.694
133.276
131.437
130.463
129.536
126.502
125.114
124.960
121.046
111.321
103.501
102.005
100.919
77.558
77.240
76.923
55.770
37.050
35.849
CONMe2
OMe
N
O
O
Compound 35, Table 3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh170-2.fid

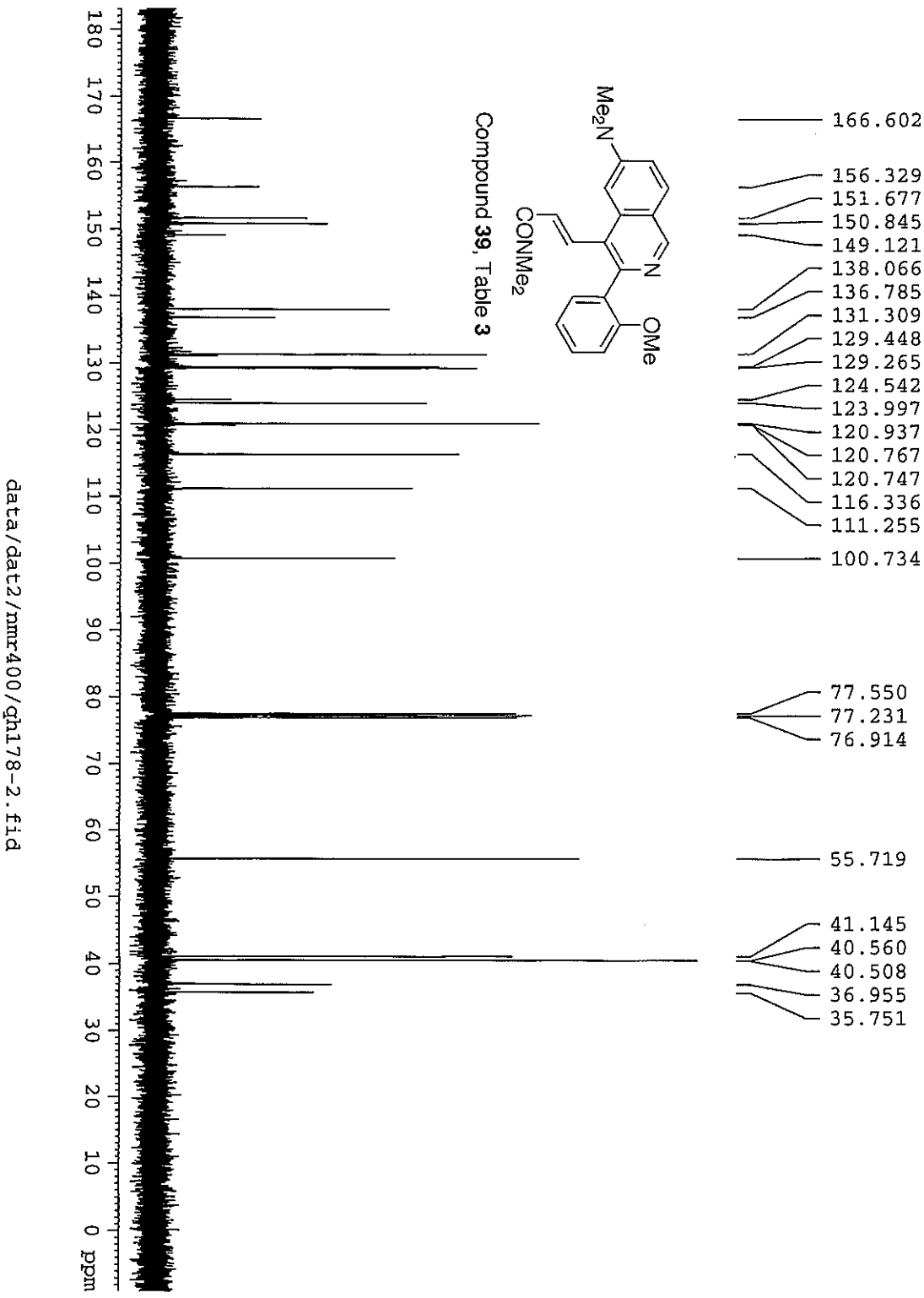

Compound 36, Table 3
Me
O
O
O
N
OMe
1.000
1.072
4.088
1.158
1.125
2.200
3.320
1.047
1.081
1.989
3.203
8.940
7.411
7.405
7.383
7.380
7.359
7.353
7.263
7.256
7.250
7.240
7.230
7.074
7.071
7.049
7.046
7.024
7.022
7.004
6.976
6.118
3.746
3.122
3.108
3.091
3.074
3.055
3.012
2.991
2.978
2.957
2.942
2.932
2.909
2.648
2.629
2.615
2.606
2.595
2.572
2.020
0.000
10
9
8
7
6
5
4
3
2
1
0
ppm
data/dat2/nmr300/qh173-3.fid

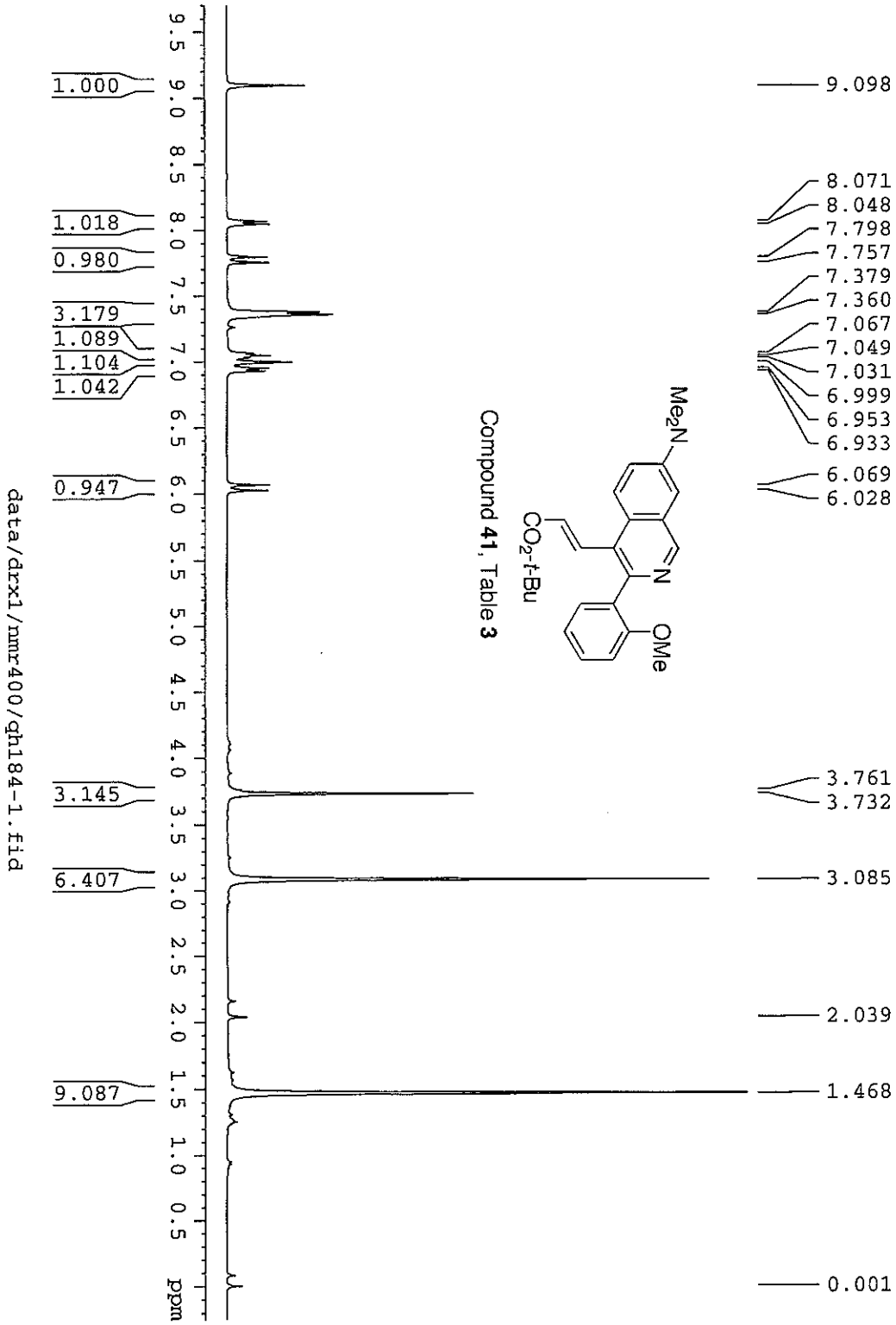

Compound 36, Table 3
Me
O
N
OMe
207.887
156.730
151.642
149.356
148.539
148.044
133.341
130.983
130.252
129.583
128.496
125.452
120.939
111.212
104.015
101.859
99.780
77.547
77.230
76.912
55.649
43.751
29.875
23.338
200
180
160
140
120
100
80
60
40
20
0
ppm
data/dat2/nmr400/qh173-2.fid

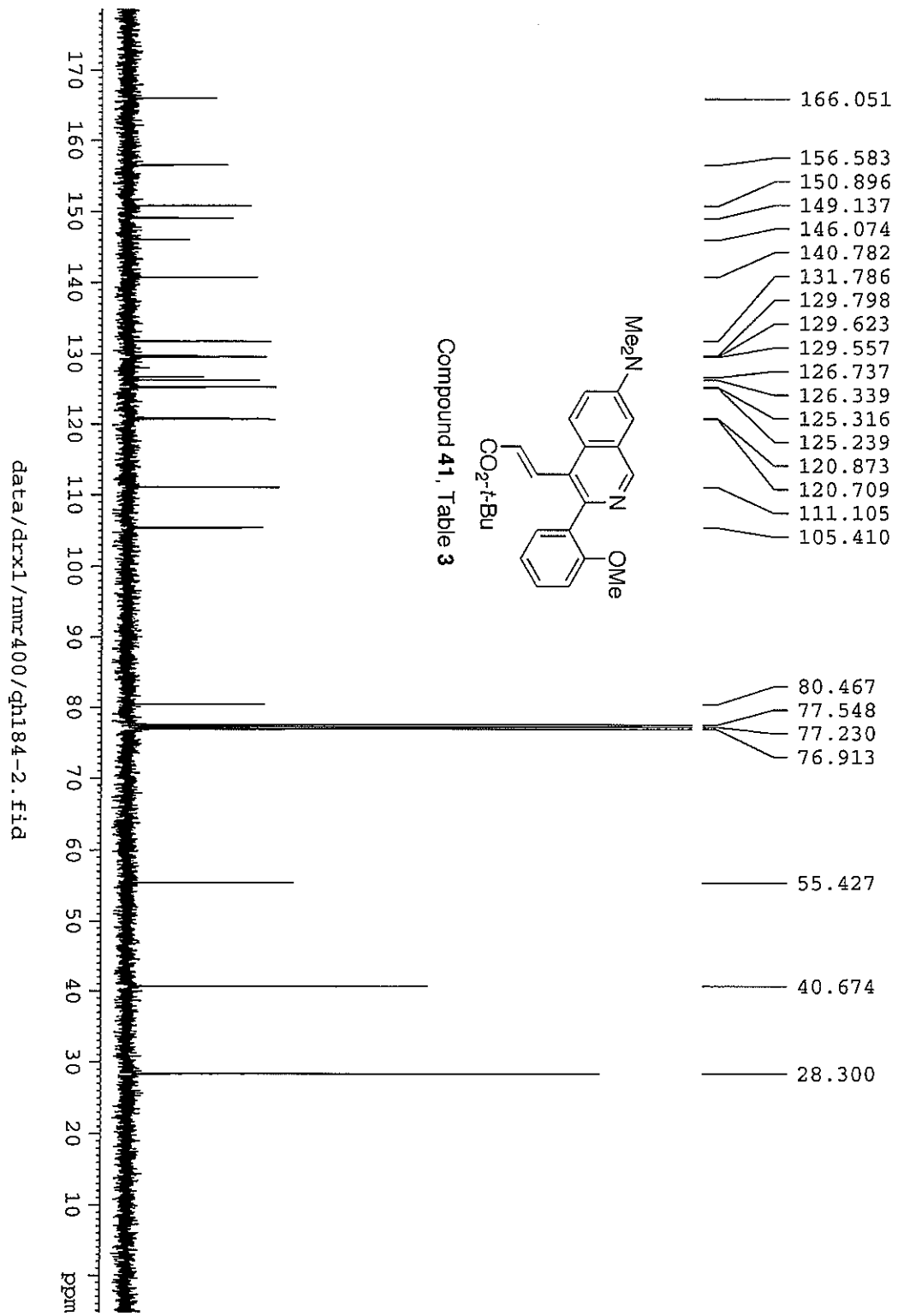

data/dat2/nmr400/qh171-3.fid
1.000
2.166
2.324
1.201
2.445
1.186
0.943
3.465
6.427
10.388
Compound 38, Table 3
Me2N
CO2-t-Bu
N
OMe
8.986
7.846
7.823
7.812
7.771
7.382
7.376
7.372
7.364
7.358
7.354
7.346
7.263
7.210
7.205
7.188
7.182
7.067
7.049
7.023
7.019
6.945
6.923
6.043
6.002
3.739
3.142
1.447
0.000
ppm

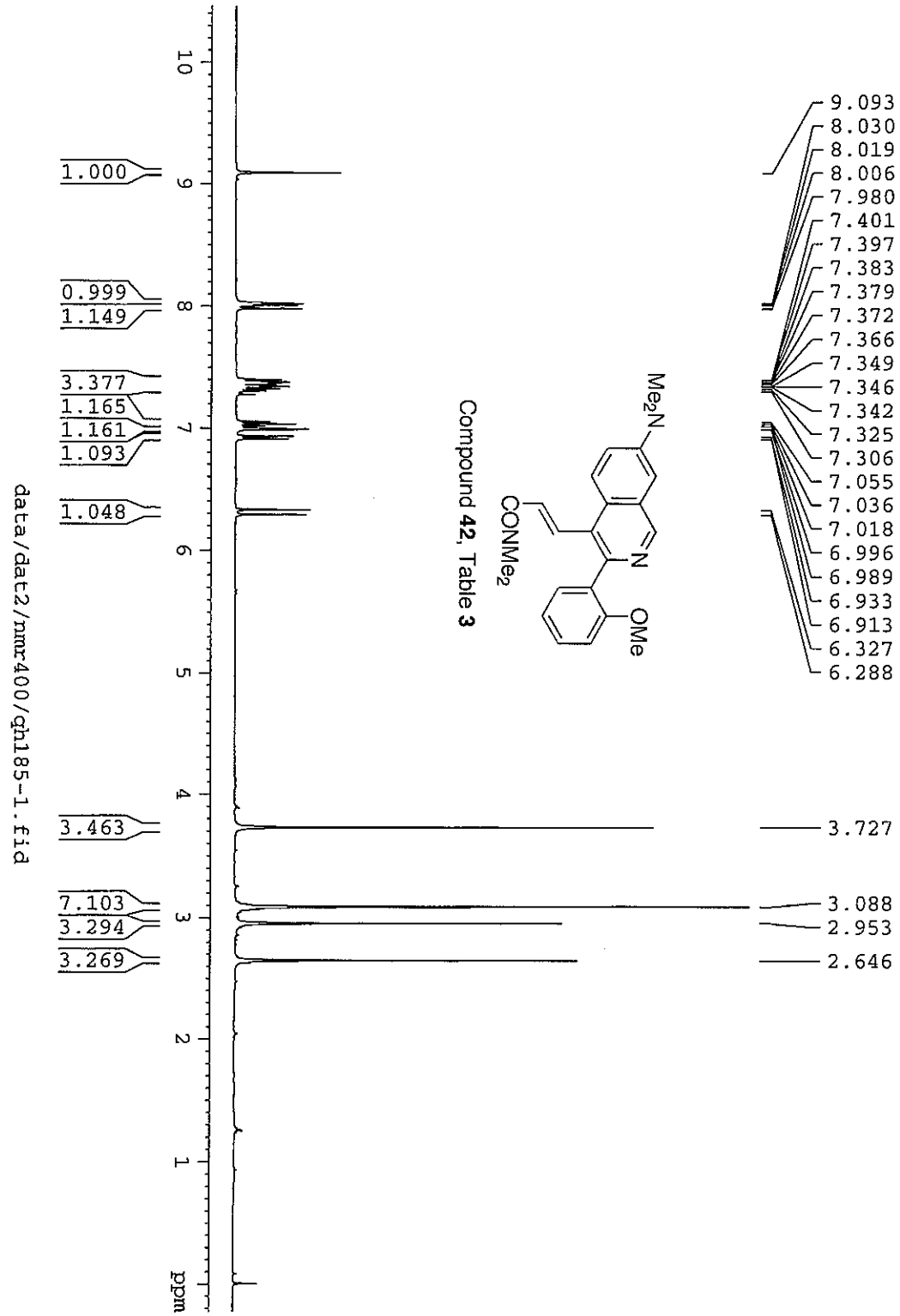

166.331
156.386
151.841
151.342
150.145
141.073
136.209
131.460
130.194
129.648
129.607
125.344
123.465
120.890
116.248
111.058
101.052
80.294
77.653
77.229
76.805
55.471
42.783
40.507
28.296
Me2N
CO2-t-Bu
N
OMe
Compound 38, Table 3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/dat2/nmr300/qh171-10.fid

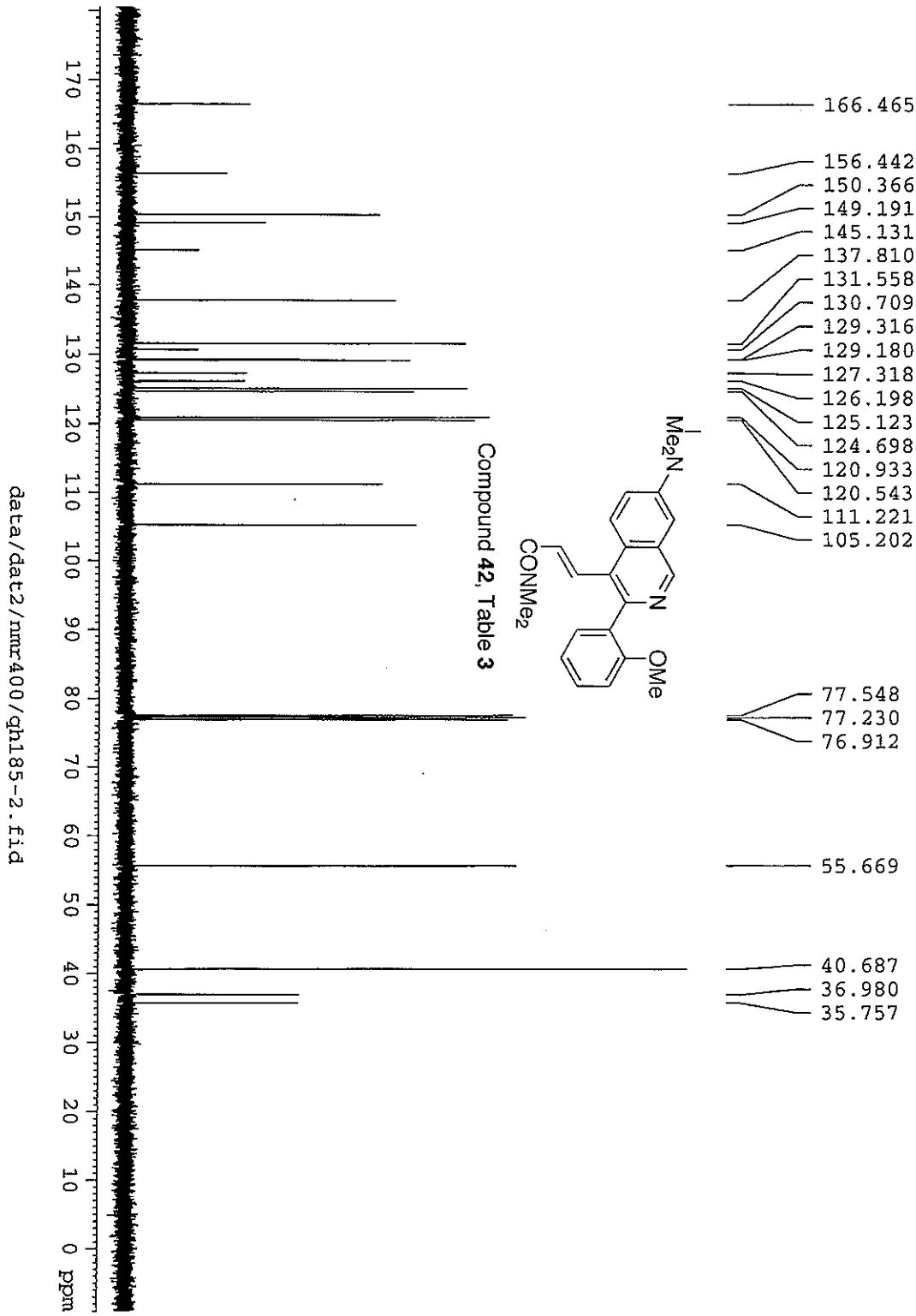

data/dat2/nmr400/qh178-1.fid
Compound 39, Table 3
Me2N
CONMe2
N
OMe
1.136
1.037
1.238
1.293
1.242
1.208
1.429
2.236
1.003
0.129
3.599
7.334
3.151
7.884
8.960
8.002
7.963
7.831
7.808
7.395
7.391
7.376
7.372
7.350
7.331
7.329
7.310
7.282
7.203
7.197
7.180
7.174
7.054
7.035
7.016
6.929
6.908
6.305
6.266
3.748
3.729
3.131
3.116
2.948
2.625
2.616
2.603
2.590
0.003
0.000
ppm

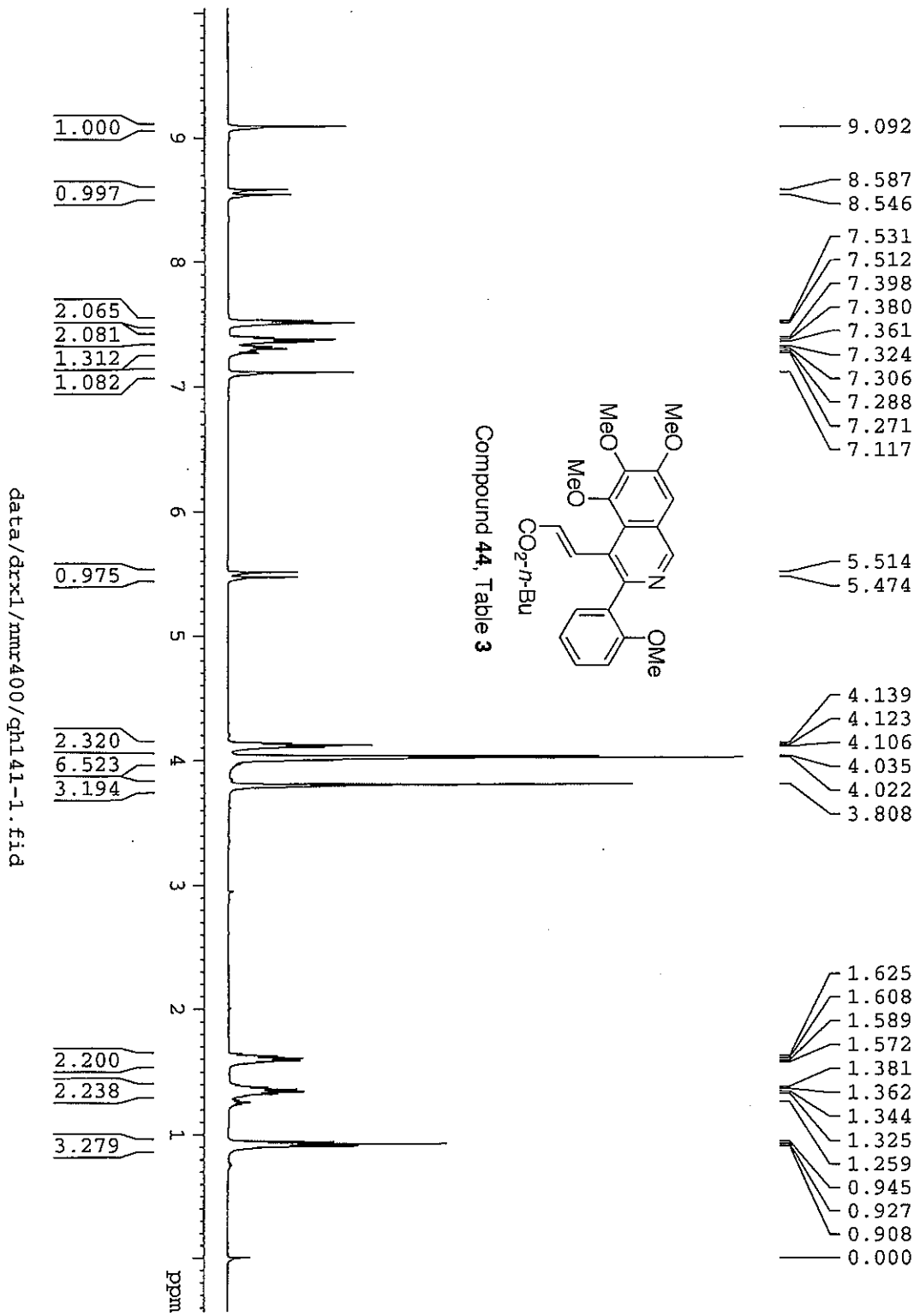

Compound 39, Table 3
Me2N
CONMe2
N
OMe
166.602
156.329
151.677
150.845
149.121
138.066
136.785
131.309
129.448
129.265
124.542
123.997
120.937
120.767
120.747
116.336
111.255
100.734
77.550
77.231
76.914
55.719
41.145
40.560
40.508
36.955
35.751
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh178-2.fid

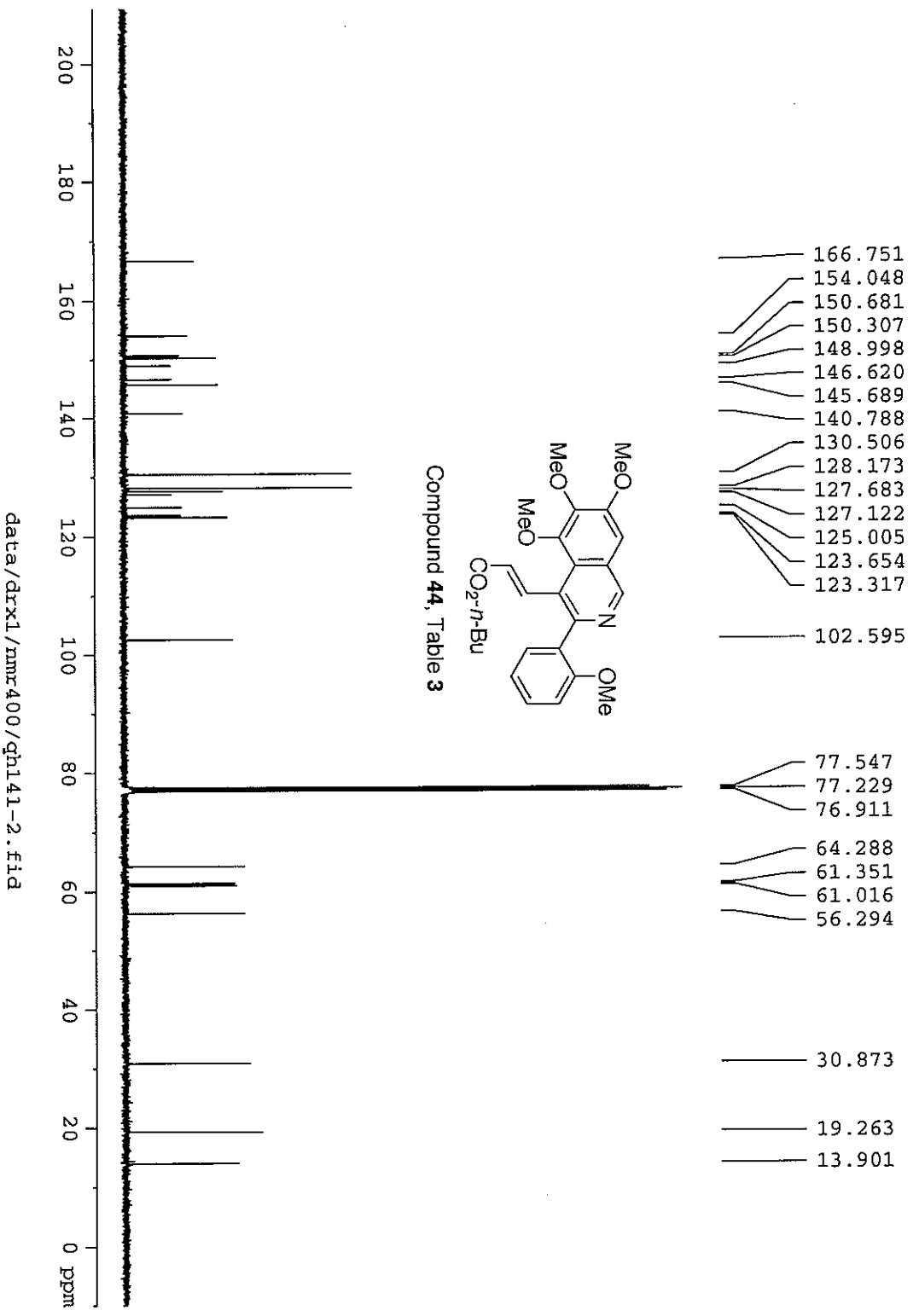

1.000
1.018
0.980
3.179
1.089
1.104
1.042
0.947
3.145
6.407
9.087
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
9.098
8.071
8.048
7.798
7.757
7.379
7.360
7.067
7.049
7.031
6.999
6.953
6.933
6.069
6.028
3.761
3.732
3.085
2.039
1.468
0.001
Me2N
CO2-t-Bu
N
OMe
Compound 41, Table 3
data/drx1/nmr400/qh184-1.fid

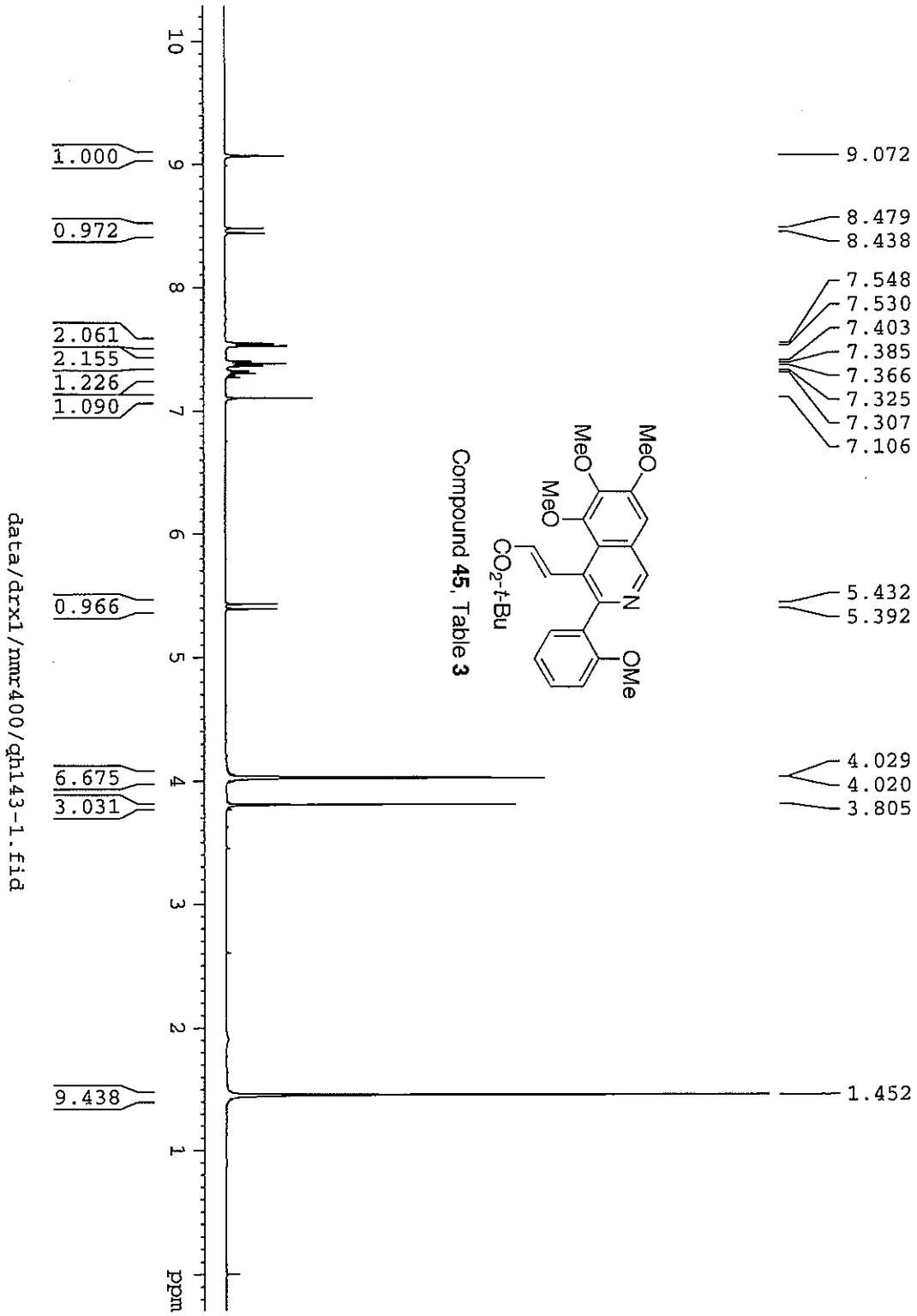

166.051
156.583
150.896
149.137
146.074
140.782
131.786
129.798
129.623
129.557
126.737
126.339
125.316
125.239
120.873
120.709
111.105
105.410
80.467
77.548
77.230
76.913
55.427
40.674
28.300
Me2N
N
OMe
CO2-t-Bu
Compound 41, Table 3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh184-2.fid

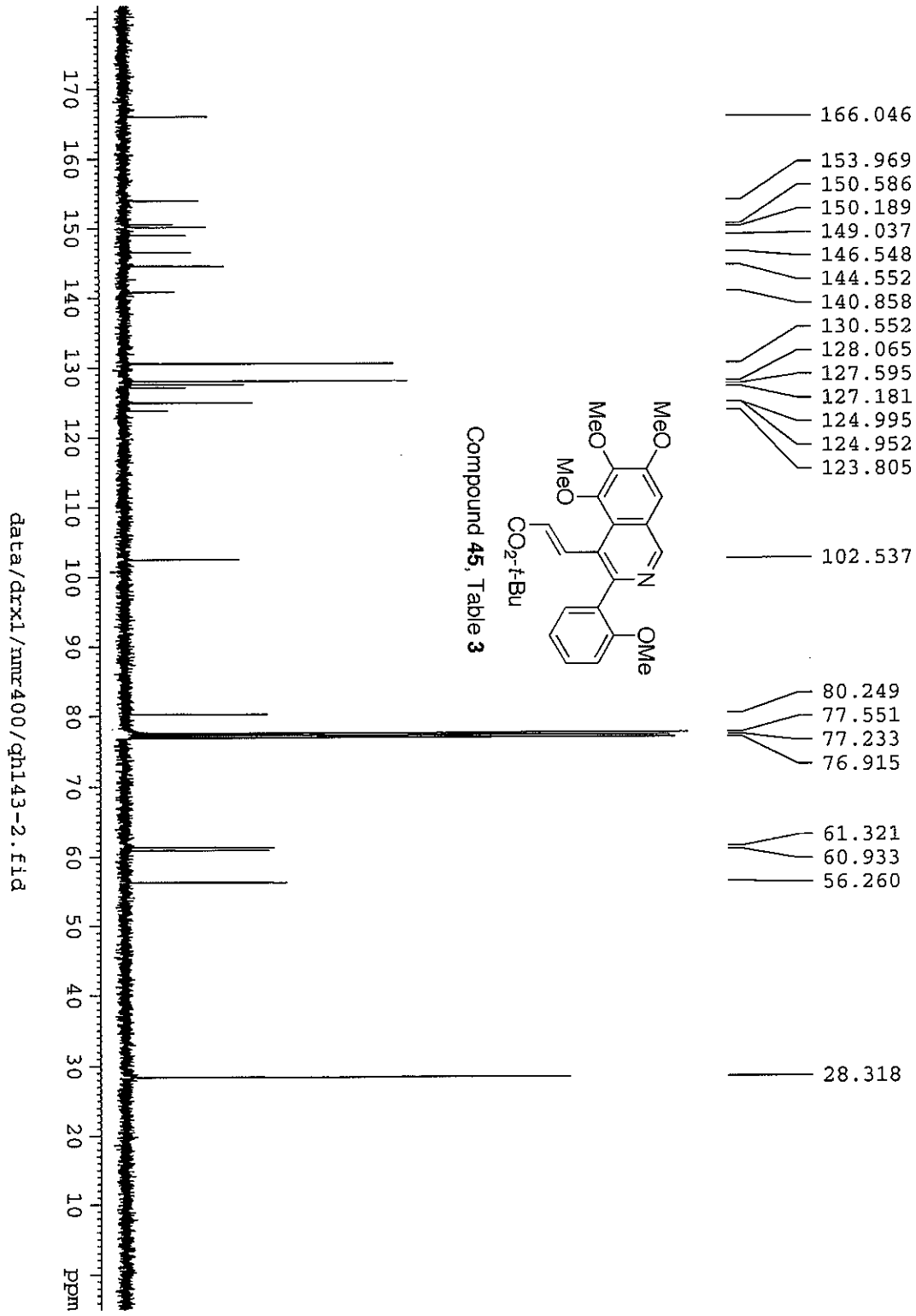

9.093
8.030
8.019
8.006
7.980
7.401
7.397
7.383
7.379
7.372
7.366
7.349
7.346
7.342
7.325
7.306
7.055
7.036
7.018
6.996
6.989
6.933
6.913
6.327
6.288
3.727
3.088
2.953
2.646
1.000
0.999
1.149
3.377
1.165
1.161
1.093
1.048
3.463
7.103
3.294
3.269
Me2N
CONMe2
N
OMe
Compound 42, Table 3
data/dat2/nmr400/qh185-1.fid
ppm

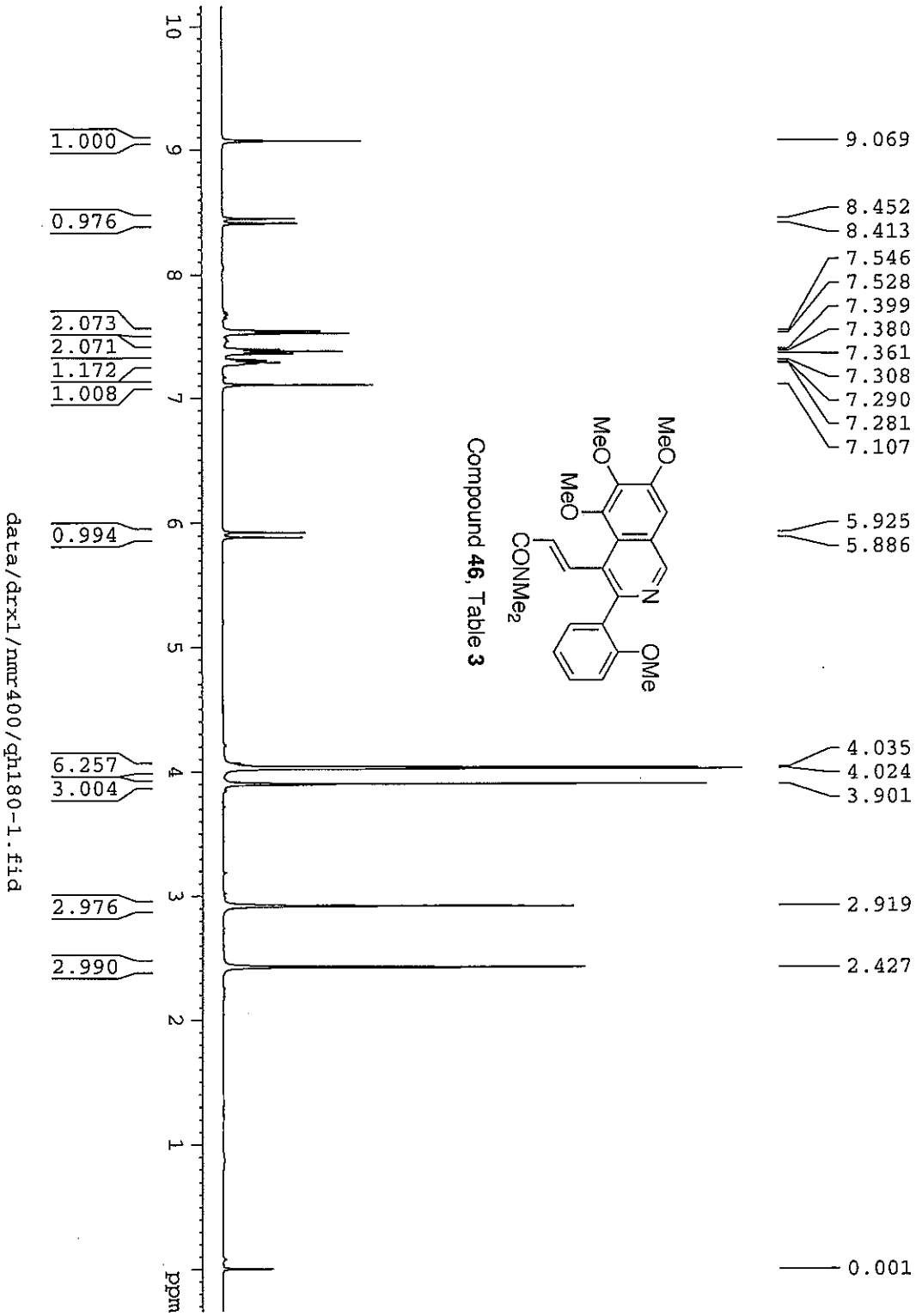

166.465
156.442
150.366
149.191
145.131
137.810
131.558
130.709
129.316
129.180
127.318
126.198
125.123
124.698
120.933
120.543
111.221
105.202
77.548
77.230
76.912
55.669
40.687
36.980
35.757
Me2N
CONMe2
N
OMe
Compound 42, Table 3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
data/dat2/nmr400/qh185-2.fid

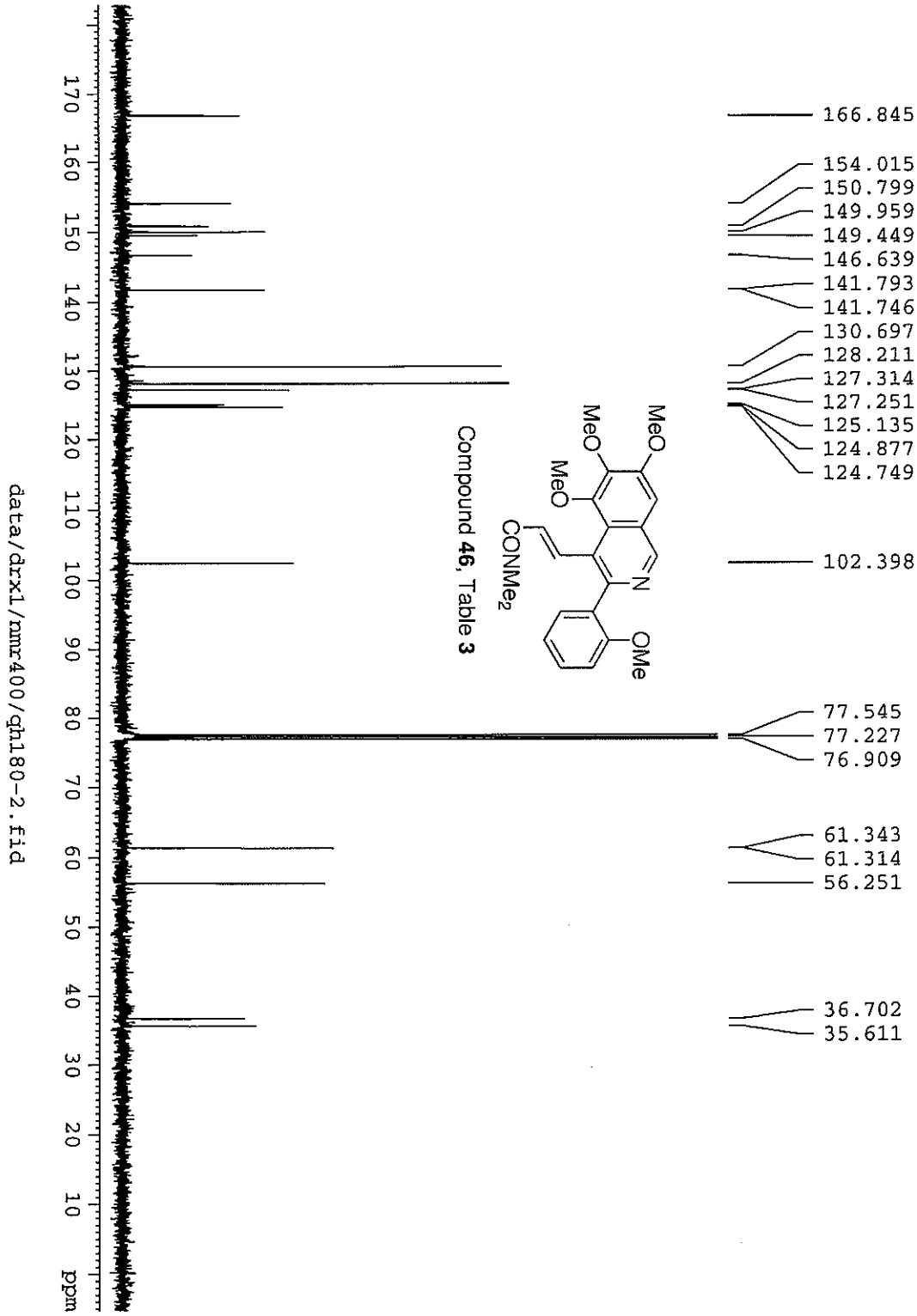

data/drx1/nmr400/qh141-1.fid
1.000
0.997
2.065
2.081
1.312
1.082
0.975
2.320
6.523
3.194
2.200
2.238
3.279
ppm
Compound 44, Table 3
MeO
MeO
MeO
CO2-n-Bu
N
OMe
9.092
8.587
8.546
7.531
7.512
7.398
7.380
7.361
7.324
7.306
7.288
7.271
7.117
5.514
5.474
4.139
4.123
4.106
4.035
4.022
3.808
1.625
1.608
1.589
1.572
1.381
1.362
1.344
1.325
1.259
0.945
0.927
0.908
0.000

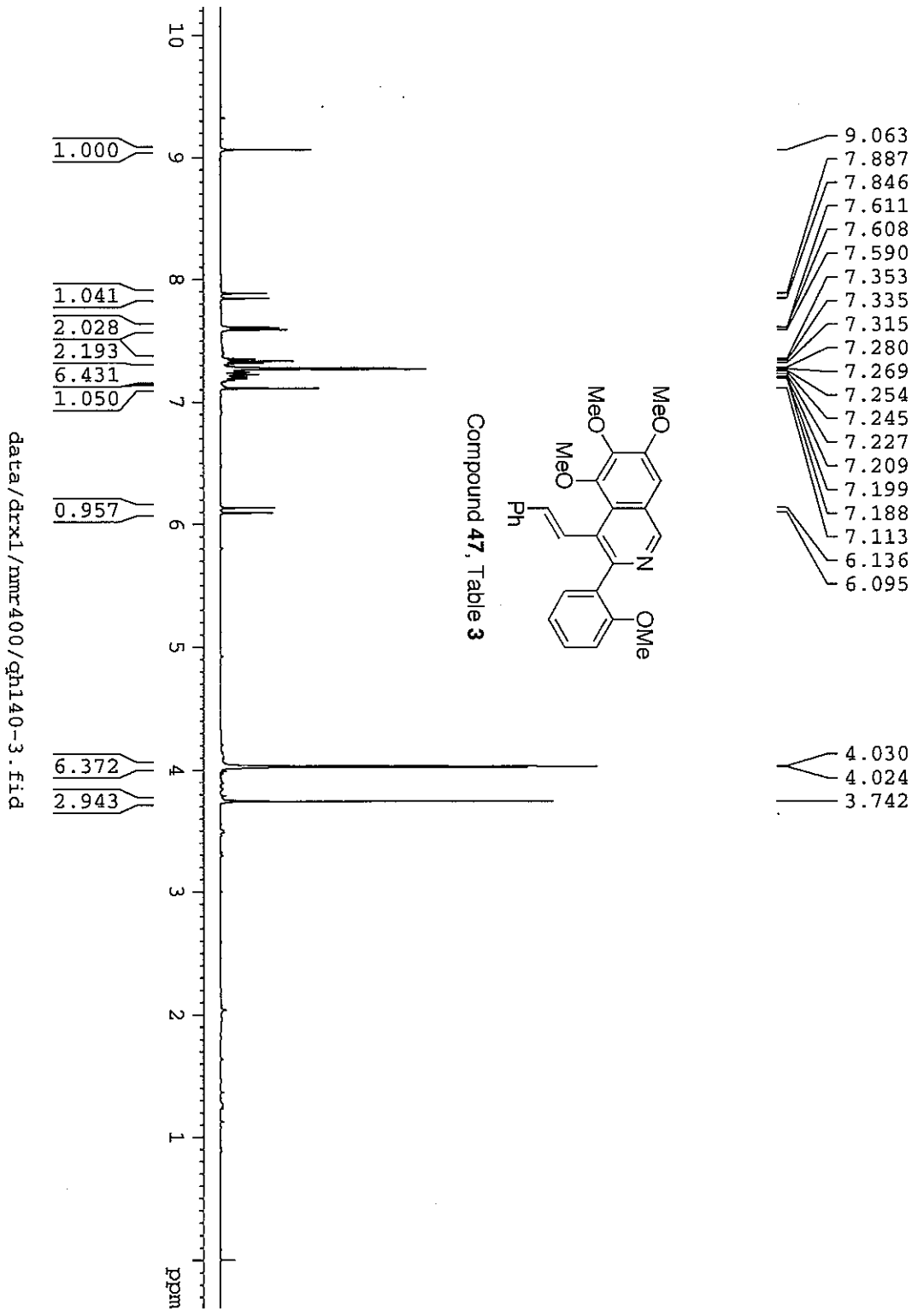

166.751
154.048
150.681
150.307
148.998
146.620
145.689
140.788
130.506
128.173
127.683
127.122
125.005
123.654
123.317
102.595
77.547
77.229
76.911
64.288
61.351
61.016
56.294
30.873
19.263
13.901
MeO
MeO
MeO
N
OMe
CO2-n-Bu
Compound 44, Table 3
200
180
160
140
120
100
80
60
40
20
0 ppm
data/drx1/nmr400/qh141-2.fid

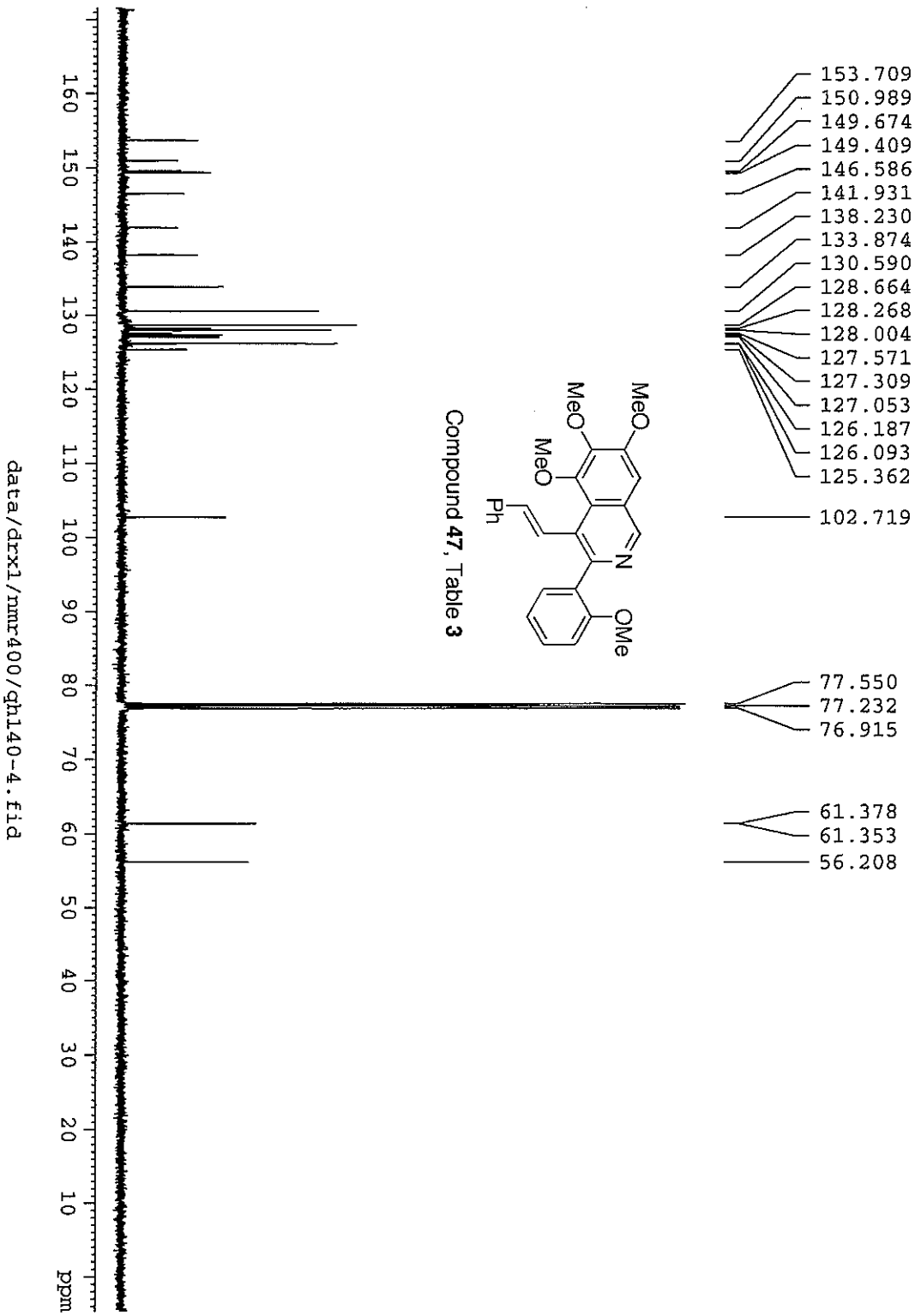

9.072
8.479
8.438
7.548
7.530
7.403
7.385
7.366
7.325
7.307
7.106
5.432
5.392
4.029
4.020
3.805
1.452
1.000
0.972
2.061
2.155
1.226
1.090
0.966
6.675
3.031
9.438
MeO
MeO
MeO
N
OMe
CO2-t-Bu
Compound 45, Table 3
data/drx1/nmr400/qh143-1.fid
ppm

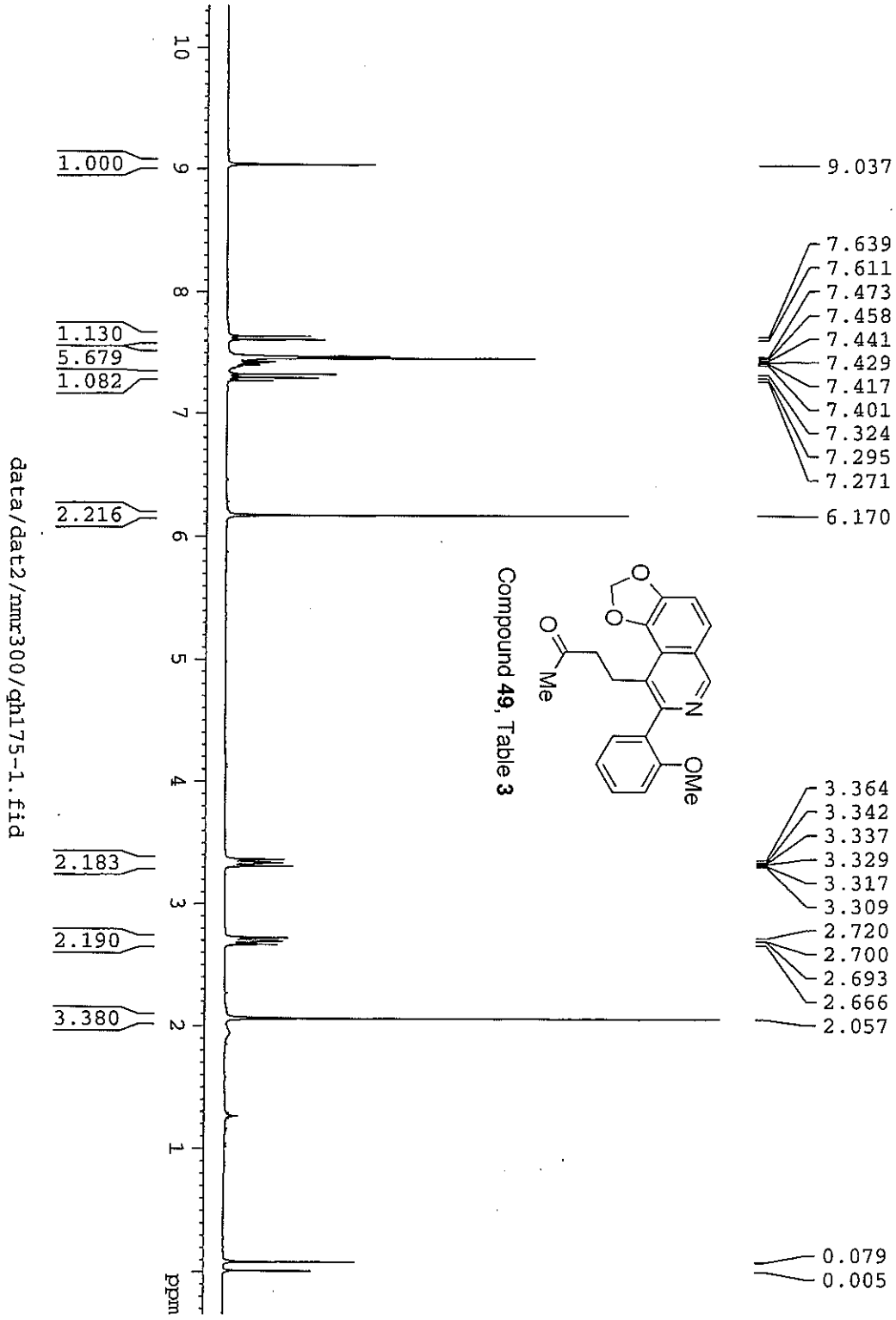

166.046
153.969
150.586
150.189
149.037
146.548
144.552
140.858
130.552
128.065
127.595
127.181
124.995
124.952
123.805
102.537
80.249
77.551
77.233
76.915
61.321
60.933
56.260
28.318
MeO
MeO
MeO
CO2-t-Bu
N
OMe
Compound 45, Table 3
data/drx1/nmr400/qh143-2.fid
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

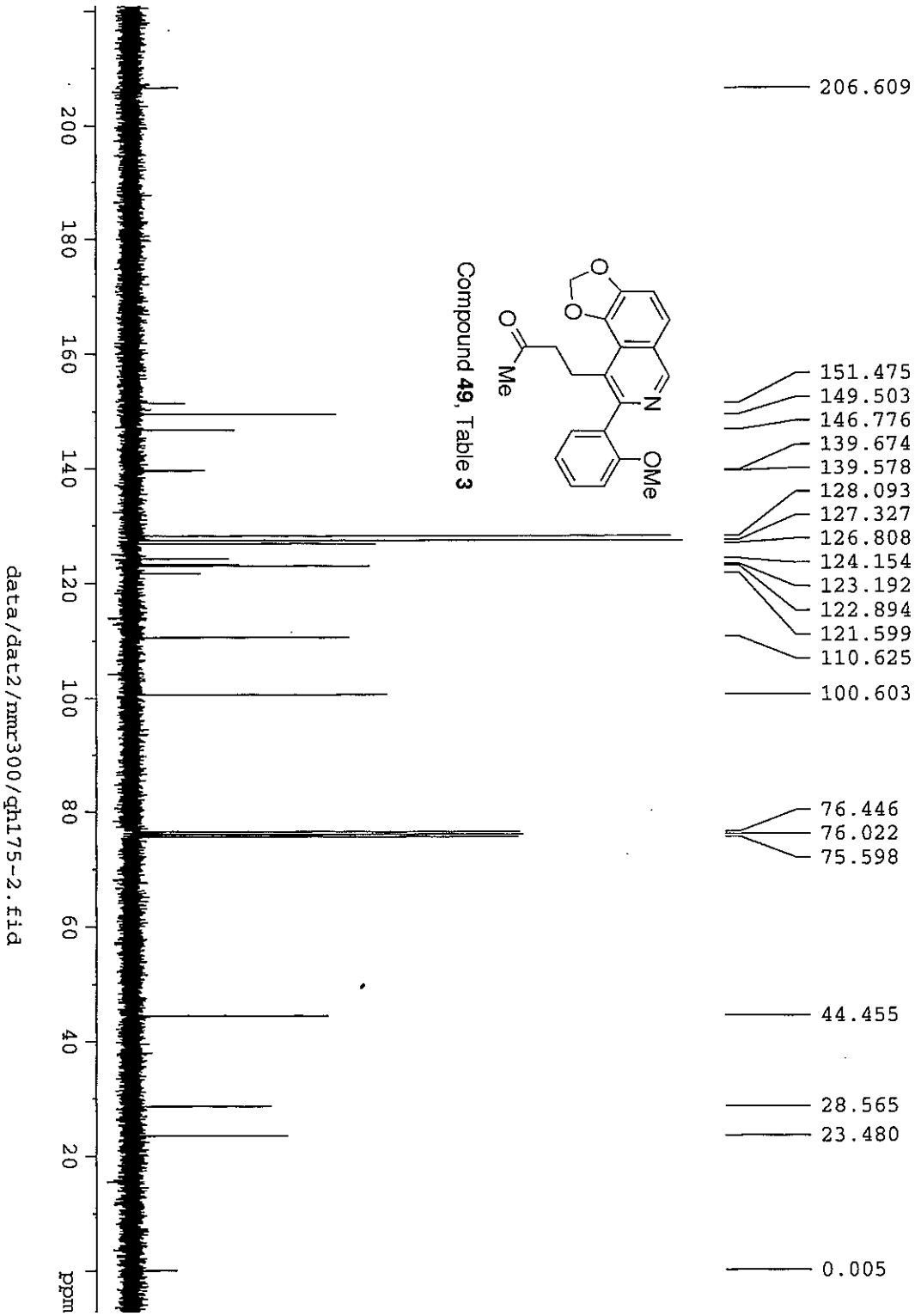

9.069
8.452
8.413
7.546
7.528
7.399
7.380
7.361
7.308
7.290
7.281
7.107
5.925
5.886
4.035
4.024
3.901
2.919
2.427
0.001
1.000
0.976
2.073
2.071
1.172
1.008
0.994
6.257
3.004
2.976
2.990
ppm
MeO
MeO
MeO
CONMe2
N
OMe
Compound 46, Table 3
data/drxl/nmr400/qh180-1.fid

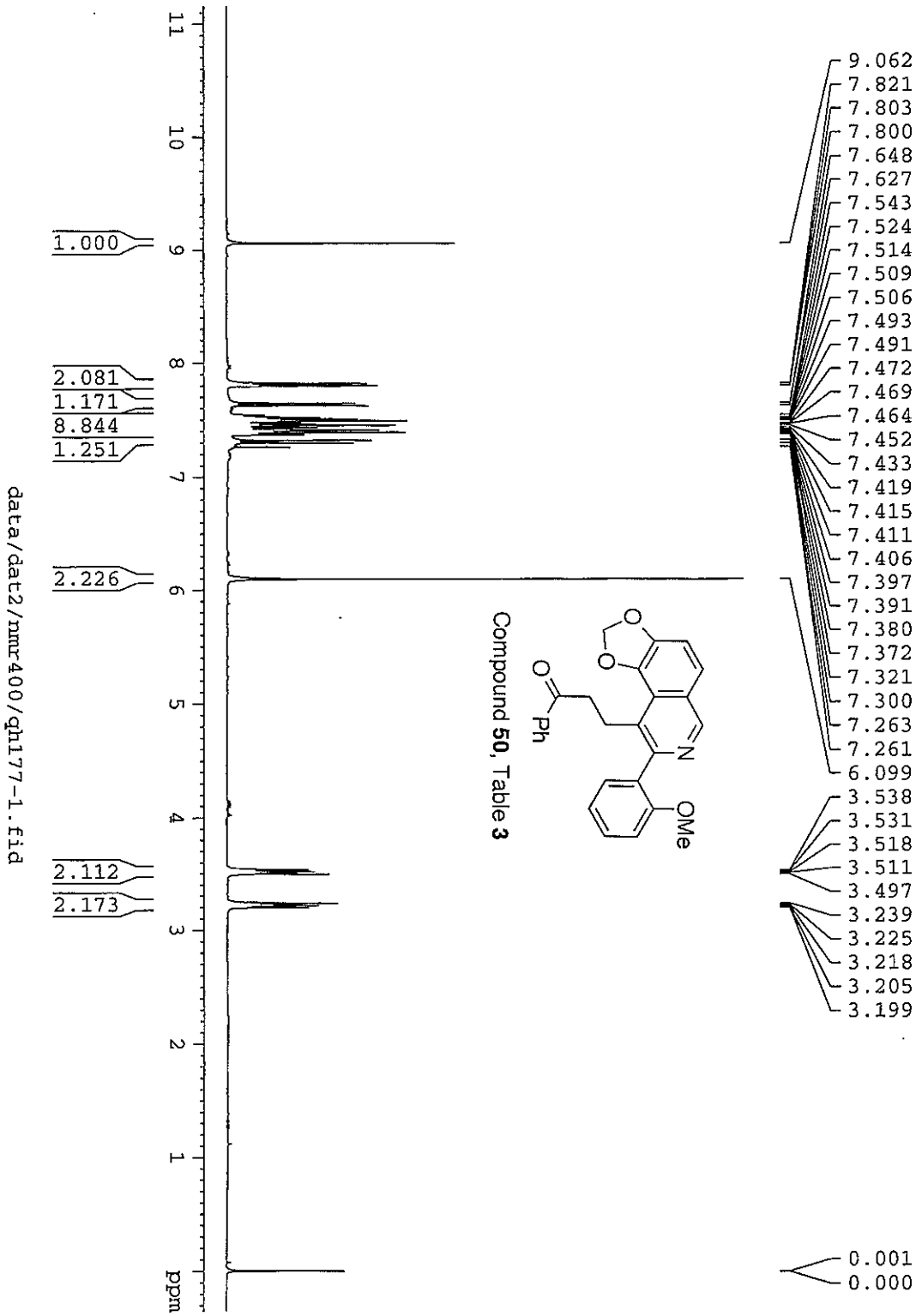

166.845
154.015
150.799
149.959
149.449
146.639
141.793
141.746
130.697
128.211
127.314
127.251
125.135
124.877
124.749
102.398
77.545
77.227
76.909
61.343
61.314
56.251
36.702
35.611
MeO
MeO
MeO
CONMe2
N
OMe
Compound 46, Table 3
data/drx1/nmr400/qh180-2.fid
ppm

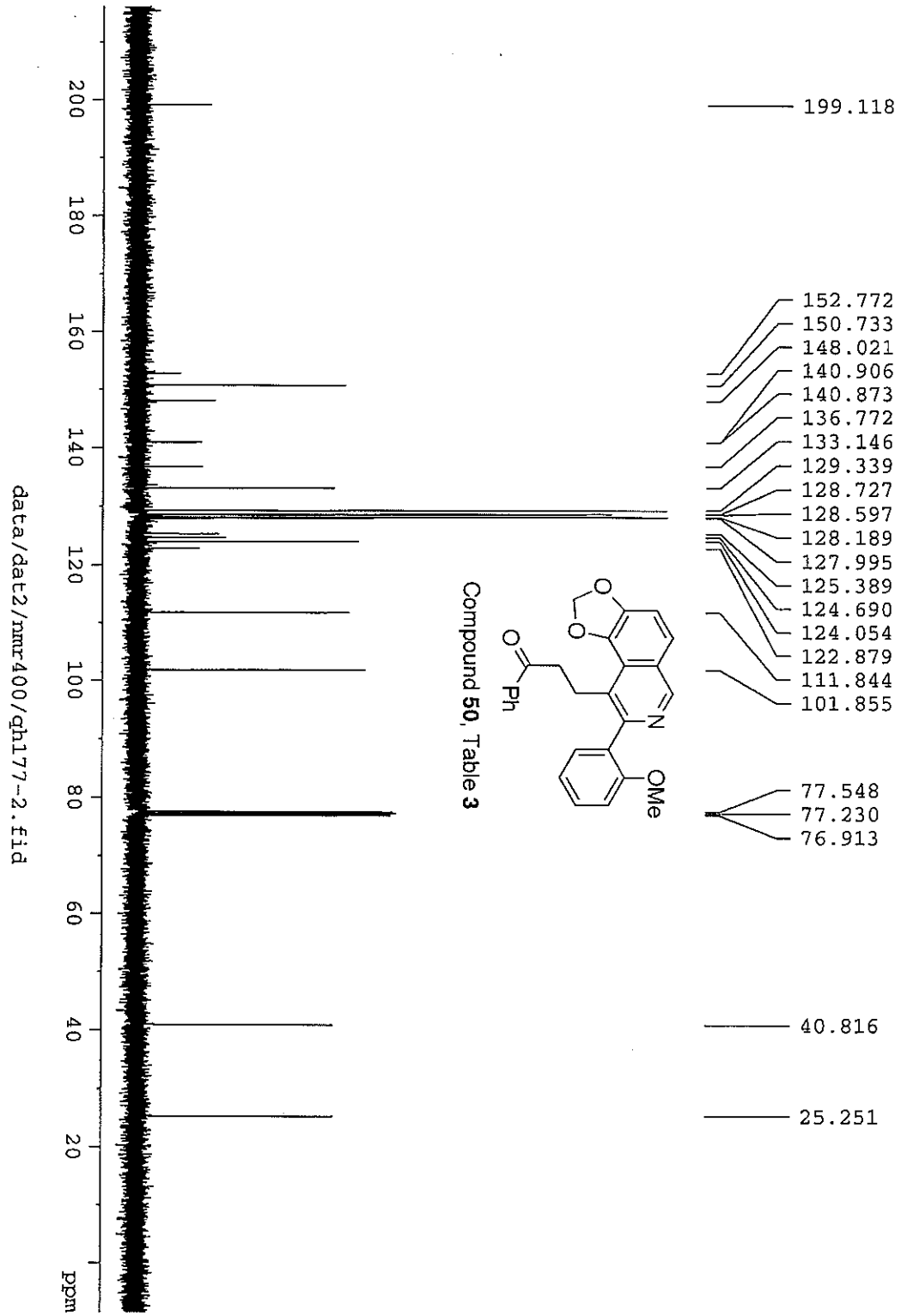

9.063
7.887
7.846
7.611
7.608
7.590
7.353
7.335
7.315
7.280
7.269
7.254
7.245
7.227
7.209
7.199
7.188
7.113
6.136
6.095
4.030
4.024
3.742
1.000
1.041
2.028
2.193
6.431
1.050
0.957
6.372
2.943
MeO
MeO
MeO
Ph
N
OMe
Compound 47, Table 3
data/drx1/nmr400/qh140-3.fid
ppm

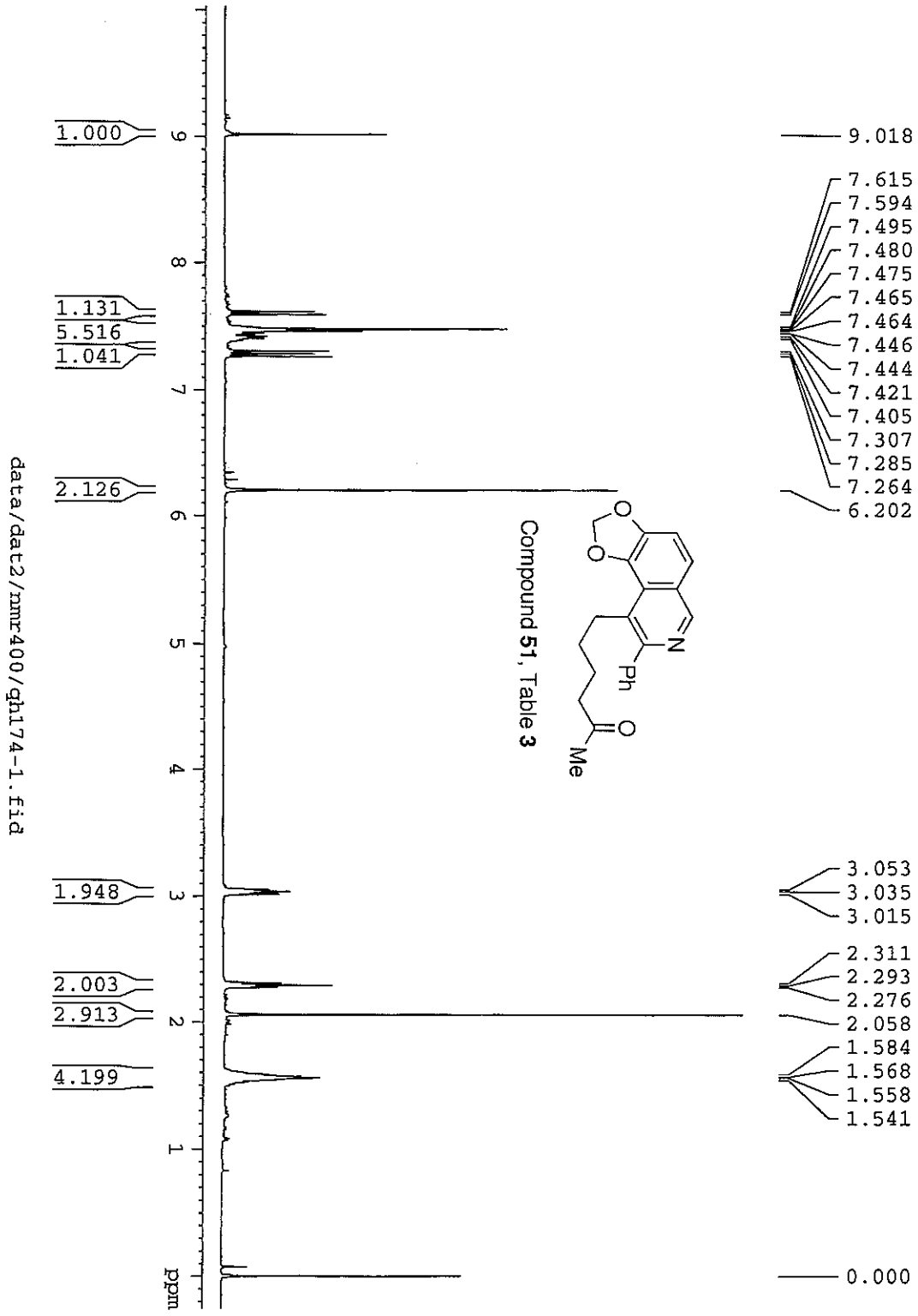

153.709
150.989
149.674
149.409
146.586
141.931
138.230
133.874
130.590
128.664
128.268
128.004
127.571
127.309
127.053
126.187
126.093
125.362
102.719
77.550
77.232
76.915
61.378
61.353
56.208
MeO
MeO
MeO
Ph
N
OMe
Compound 47, Table 3
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
data/drx1/nmr400/qh140-4.fid

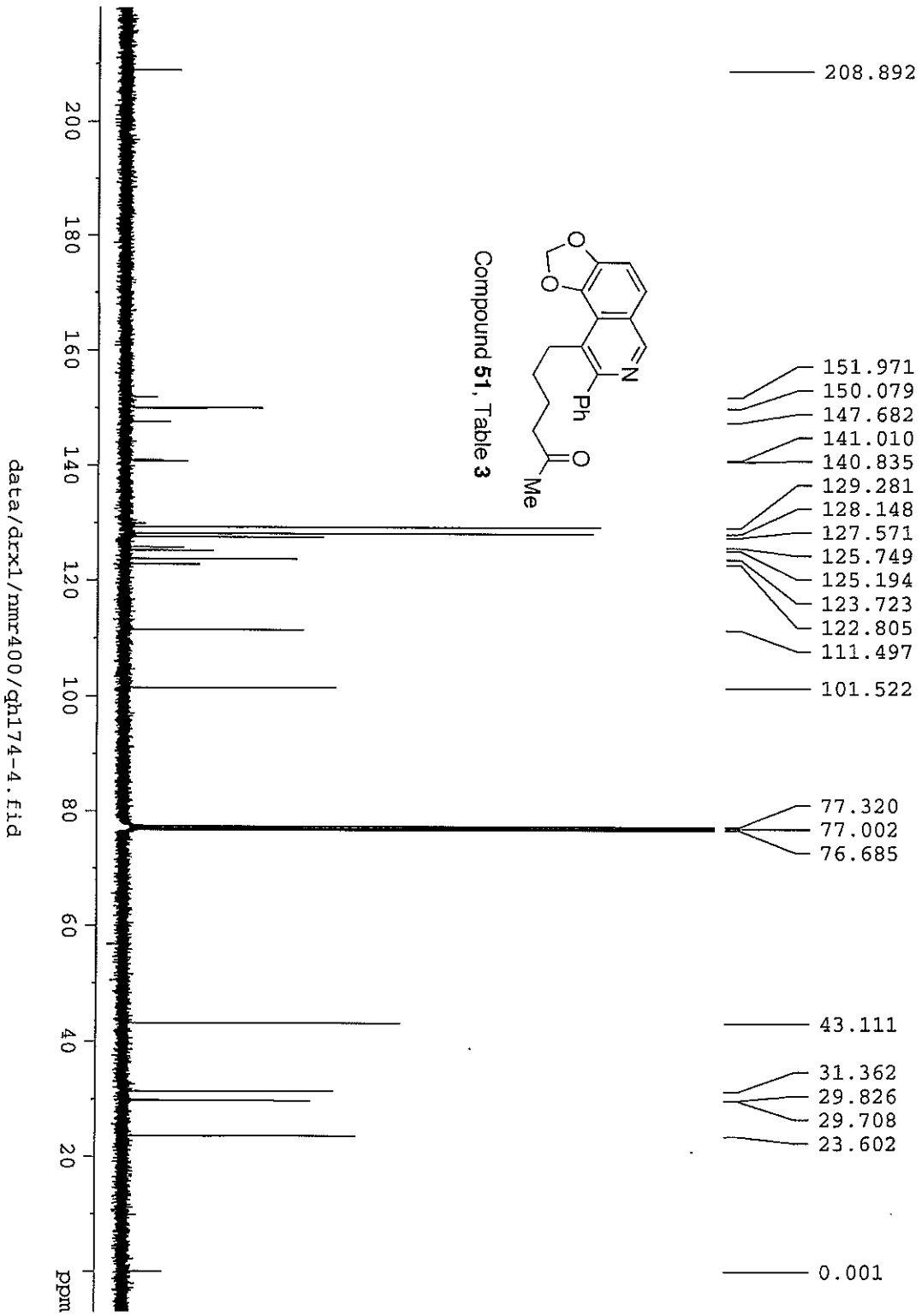

9.037
7.639
7.611
7.473
7.458
7.441
7.429
7.417
7.401
7.324
7.295
7.271
6.170
3.364
3.342
3.337
3.329
3.317
3.309
2.720
2.700
2.693
2.666
2.057
0.079
0.005
1.000
1.130
5.679
1.082
2.216
2.183
2.190
3.380
ppm
Compound 49, Table 3
Me
O
N
OMe
data/dat2/nmr300/qh175-1.fid


206.609
151.475
149.503
146.776
139.674
139.578
128.093
127.327
126.808
124.154
123.192
122.894
121.599
110.625
100.603
76.446
76.022
75.598
44.455
28.565
23.480
0.005
Compound 49, Table 3
O
O
O
Me
N
OMe
200
180
160
140
120
100
80
60
40
20
ppm
data/dat2/nmr300/qh175-2.fid


9.062
7.821
7.803
7.800
7.648
7.627
7.543
7.524
7.514
7.509
7.506
7.493
7.491
7.472
7.469
7.464
7.452
7.433
7.419
7.415
7.411
7.406
7.397
7.391
7.380
7.372
7.321
7.300
7.263
7.261
6.099
3.538
3.531
3.518
3.511
3.497
3.239
3.225
3.218
3.205
3.199
0.001
0.000
1.000
2.081
1.171
8.844
1.251
2.226
2.112
2.173
ppm
Compound 50, Table 3
Ph
OMe
data/dat2/nmr400/qh177-1.fid


199.118
152.772
150.733
148.021
140.906
140.873
136.772
133.146
129.339
128.727
128.597
128.189
127.995
125.389
124.690
124.054
122.879
111.844
101.855
77.548
77.230
76.913
40.816
25.251
200
180
160
140
120
100
80
60
40
20
ppm
data/dat2/nmr400/qh177-2.fid
Compound 50, Table 3
O
O
O
Ph
N
OMe


data/dat2/nmr400/qh174-1.fid
1.000
1.131
5.516
1.041
2.126
1.948
2.003
2.913
4.199
9
8
7
6
5
4
3
2
1
ppm
9.018
7.615
7.594
7.495
7.480
7.475
7.465
7.464
7.446
7.444
7.421
7.405
7.307
7.285
7.264
6.202
3.053
3.035
3.015
2.311
2.293
2.276
2.058
1.584
1.568
1.558
1.541
0.000
Compound 51, Table 3
O
O
N
Ph
O
Me


208.892
151.971
150.079
147.682
141.010
140.835
129.281
128.148
127.571
125.749
125.194
123.723
122.805
111.497
101.522
77.320
77.002
76.685
43.111
31.362
29.826
29.708
23.602
0.001
Compound 51, Table 3
Ph
Me
O
N
200
180
160
140
120
100
80
60
40
20
ppm
data/drx1/nmr400/qh174-4.fid