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Nuclear Medicine Progress Report for Quarter Ending September 30, 1985

F. F. Knapp, Jr.
K. R. Ambrose
M. M. Goodman
P. C. Srivastava

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Work sponsored by
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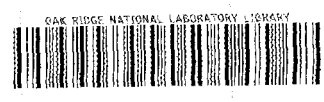

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ORNL/TM-7223
ORNL/TM-7411
ORNL/TM-7482
ORNL/TM-7605
ORNL/TM-7685
ORNL/TM-7775
ORNL/TM-7918
ORNL/TM-8123
ORNL/TM-8186
ORNL/TM-8363
ORNL/TM-8428
ORNL/TM-8533
ORNL/TM-8619
ORNL/TM-8746
ORNL/TM-8827
ORNL/TM-8966
ORNL/TM-9037
ORNL/TM-9124
ORNL/TM-9343
ORNL/TM-9394
ORNL/TM-9480
ORNL/TM-9609
ORNL/TM-9707

CONTENTS

SUMMARY

A new dimethyl-branched fatty acid analogue has been developed with radioiodide stabilized as an iodovinyl moiety at the terminus of the fatty acid chain. The model agent, 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN), was prepared by a 15-step sequence of reactions. Introduction of acyl substituents into the 2- and 5-positions of a thiophene ring followed by sulfur extrusion of the resulting 2,5-dialkyl thiophene derivative provided a key intermediate, 17-iodo-3,3-dimethylheptadecanoic acid. The model agent (DMIVN) was prepared by reaction of the iodoalkyl intermediate with an ethylenediamine complex of lithium acetylide, followed by hydrostannylation and treatment with iodine. The new radioiodinated terminal iodovinyl-3,3-dimethyl-branched fatty acid showed higher myocardial uptake (4.56% dose/gm at 2 min), longer myocardial retention (4.10% dose/gm at 60 min), lower blood levels (0.71% dose/gm at 60 min), and higher heart:blood ratios (5.8:1 at 60 min) in fasted Fischer rats than observed with the corresponding monomethyl analogue (BMIVN). This fatty acid represents a new candidate for the study of heart disease associated with regional alterations in normal myocardial fatty acid metabolism.

In this report subcellular distribution and lipid analysis studies of a series of iodovinyl fatty acids which include the straight chain parent, 19-iodo-18-nonadecenoic acid (IVN), monomethyl-branched analogue, 19-iodo-3-(R,S)-methyl-18-nonadecenoic acid (BMIVN), and the dimethyl-branched analogue, 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN), are described. Because of the observed differences within the iodophenyl series of the distribution of myocardial radioactivity in subcellular profiles and within various lipid pools extracted from cell components, an evaluation of the iodovinyl series was performed. Lipid analyses of the dimethyl-branched analogue (DMIVN) showed the greatest predominance of radioactivity to be associated with the free fatty acid pool indicating that this analogue was not oxidized by the myocardium. The straight chain (IVN) and monomethyl-branched (BMIVN) agents appeared to undergo oxidation

within the myocardium with BMIVN undergoing a slower rate of oxidation than IVN. Similar effects of methyl-branching have been previously observed in studies on the iodophenyl series. However, in contrast to the iodophenyl series, a significant increase of activity within the polar lipid pool was observed. The dimethyl (DMIVN) analogue showed the longest retention and highest association with the mitochondrial and microsomal fractions.

A new radioiodinated 1,4-disubstituted-1,4-dihydropyridine derivative was prepared to evaluate the effects of ring substitution and substituent chain length on the uptake and brain retention of dihydropyridines. A model agent, iodine-125-labeled 1-(E-1-iodo-1-penten-5-yl)-4-(2-N-acetyl-aminoethyl)-1,4-dihydropyridine, showed moderate initial brain uptake (0.49% dose/gm at 5 min) in rats, but rapid washout (0.12% dose/gm at 60 min).

Eight samples of ^{191}Os-potassium osmate, and three samples of ^{195m}Pt-cis-dichlorodiammineplatinum(II) (cis-DDP), and one sample of ^{64}Cu were supplied to collaborators through Medical Cooperative Programs during this period.

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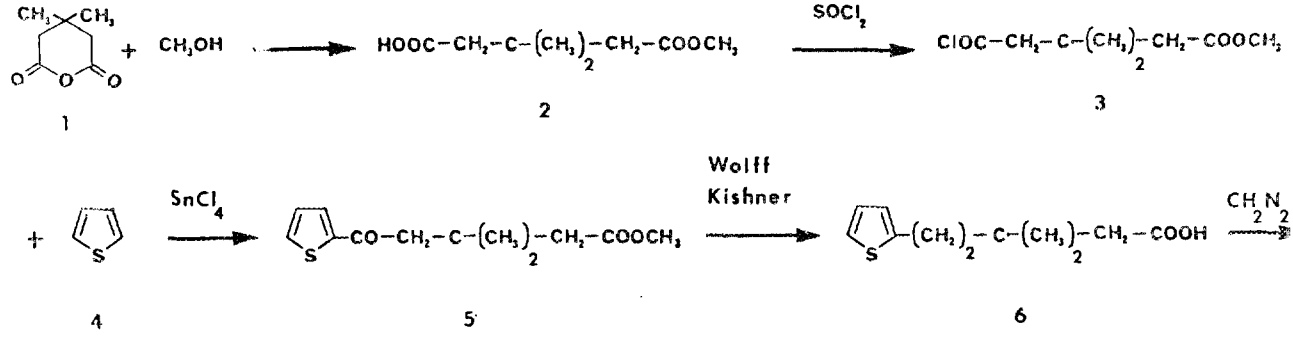
RADIOIODINATED LONG-CHAIN FATTY ACIDS — AGENTS TO EVALUATE MYOCARDIAL FUNCTION

A variety of methyl-branched fatty acids have been designed to show rapid high myocardial extraction with prolonged myocardial retention (ORNL/TM-9343). These agents were shown to localize within the myocardium similar to natural fatty acids but were not readily metabolized by the normal β-oxidative pathway as a result of methyl-branching at the 3-position of the alkanoic chain. Our initial strategy for the preparation of structurally-modified methyl-branched fatty acids involved the stabilization of radioiodide as a p-iodophenyl and a (E)-iodovinyl moiety. The effect of monomethyl-branching at the 3-position on myocardial retention in rats was assessed by a comparison of the myocardial uptake and retention of two model agents, 15-(p-iodophenyl)-3(R,S)-methylpentadecanoic acid (BMIPP) and 19-E-(iodovinyl)-3-(R,S)-methylnona-18-decenoic acid (BMIVN) with that of their corresponding straight chain analogues. The monomethyl agents, BMIPP and BMIVN showed longer myocardial retention in fasted rats ($t_{1/2}$ 45 min and $t_{1/2}$ 60 min, respectively) than the corresponding terminal iodophenyl and iodovinyl unbranched analogues ($t_{1/2}$ 10-15 min and $t_{1/2}$ 10-15 min, respectively). Although increased myocardial retention of radioactivity was achieved following i.v. administration of the monomethyl-branched agents in comparison with their straight-chain analogues, these agents however, did not demonstrate complete retention indicating catabolism was being impaired but not prevented.

More recently we have investigated the effects of dimethyl-branching in the 3-position of 15-(p-iodophenyl)pentadecanoic acid (ORNL/TM-9609). The model agent, 15-(p-iodophenyl)-3,3-dimethylpentadecanoic acid (DMIPP) exhibited rapid and pronounced myocardial uptake with irreversible retention after 60 min. The introduction of dimethyl-branching within the alkyl chain of 15-(p-iodophenyl)pentadecanoic acid gave greater mean heart to blood ratios for DMIPP (10:1 at 15 min) than observed with BMIPP (3.5:1 at 15 min). Since our studies with the model iodovinyl fatty acid DMIVN showed greater myocardial retention with higher heart to blood ratios 4.5:1 at 30 min than observed with BMIPP, we have now evaluated the effects of β-dimethyl-branching in a model agent in which radioiodide has

been stabilized as a terminal trans (E-) vinyl iodide. The goals of this investigation were to develop a synthesis for 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN) and to study the myocardial uptake and clearance of this agent in rats in comparison with the corresponding monomethyl and straight chain analogues.

The synthetic route chosen for the preparation of 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN) involved an adaption developed earlier for the monomethyl analogue BMIVN. This involved introduction of substituents into the 2- (Scheme I) and 5- positions of a thiophene ring followed by sulfur extrusion of an 2,5-dialkyl thiophene derivative to provide the desired 3-methyl-branched fatty acid. The key substrate 17-iodo-3,3-dimethylheptadecanoic acid (14) was prepared as described in Scheme II. Methyl-branching was introduced into the 2-position of the

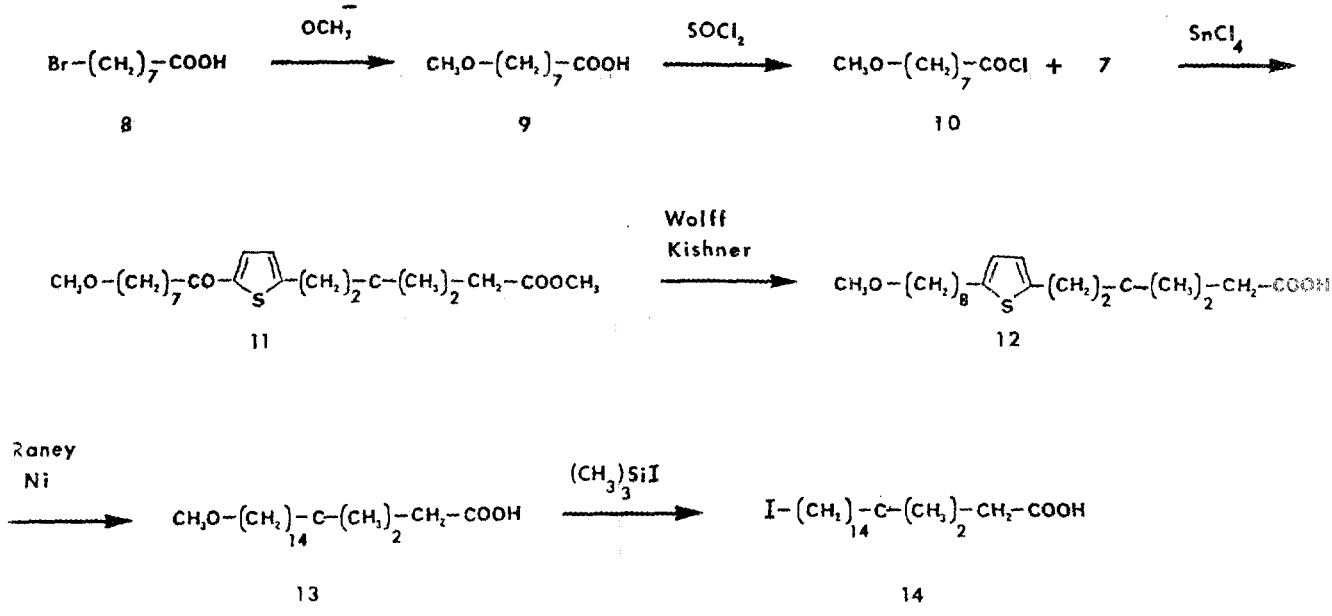


1 2 3 4 5 6 7

Scheme I

thiophene ring by acylation of the half ester acid chloride 3,3-dimethyl-4-carbomethoxybutanoyl chloride (3) (Scheme I) which was prepared from commercially available 3,3-dimethylglutaric anhydride (1) by treatment with methanol followed by thionyl chloride. Friedel-Crafts acylation of 3 using $SnCl_4$ gave the thienyl ketone 5. Wolff-Kishner reduction of 5 followed by treatment with CH_2N_2 afforded the methyl-branched 2-substituted thiophene 7. 8-Methoxyoctanoyl chloride 10 was used for introduction into the 5-position of the thiophene ring.

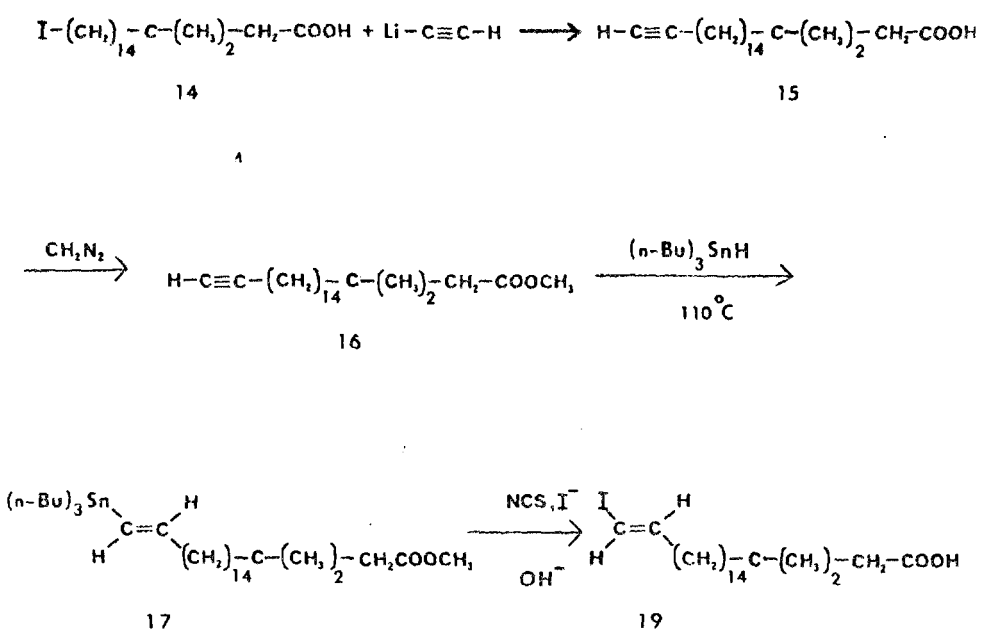
Functionalization of the terminal methylene group with a methoxy function allowed subsequent displacement with iodide (Scheme II). The



Scheme II

acyl chloride 10 was prepared by treatment of 8-bromooctanoic acid (8) with sodium methoxide followed by thionyl chloride. The methyl ester 7 was subjected to Friedel-Crafts condensation with the acyl chloride 10 to afford 2-[3,3-dimethyl-5-methoxypentanoyl]-5-(8-methoxy-1-oxooctyl)-thiophene (11). Wolff-Kishner (Huang-Minlon) reduction of the keto ester 11 gave 2-[3,3-dimethyl-5-hydroxypentanoyl]-5-(8-methoxyoctyl)-thiophene (12). Raney nickel was used for ring opening and desulfurization of 12. The sulfur from the thiophene ring was readily extruded by treatment with Raney nickel and the desired terminal methoxy methyl-branched acid 13 was obtained. Treatment of 13 with $(CH_3)_3SiI$ gave the terminal iodinated 3,3-dimethyl-branched fatty acid 17-iodo-3,3-dimethylheptadecanoic acid (14).

The (E)-vinyl iodide was introduced into the terminal position of the methyl-branched acid via the iododestannylation of the tri-n-butylstannyl derivative 17, prepared from 14 by a four-step sequence of reactions (Scheme III).



Scheme III

The pivotal step in the synthesis of the (E)-iodovinyl acid 19 involved hydrostannylation of the terminal ethynyl substrate 16 with $(n\text{-}Bu)_3SnH$ to give the key intermediate 17. The 3,3-dimethyl-18-nonadecyanoic acid 15 was prepared by treatment of the 17-iodo-3,3-dimethyl-branched acid 14 with lithium acetylide-ethylenediamine (LAEDA). The corresponding methyl ester 16 was prepared by treatment of the terminal ethynyl acid 15 with diazomethane. Iododestannylation of 17 by treatment with either I_2 or I^+ formed by in situ oxidation of I^- with N-chlorosuccinimide (NCS) followed by basic hydrolysis gave 19.

Tissue distribution studies where ^{125}I-DMIVN (19) was administered to groups of fasted rats are shown in Table 1 and Fig. 1. The animals were sacrificed at time periods varying from 2 min and 2 h. Fasting

conditions were chosen because fasting is the recommended protocol for clinical studies since all patients will be evaluated in a similar dietary state. In addition, previous dual-labeled studies in fasted

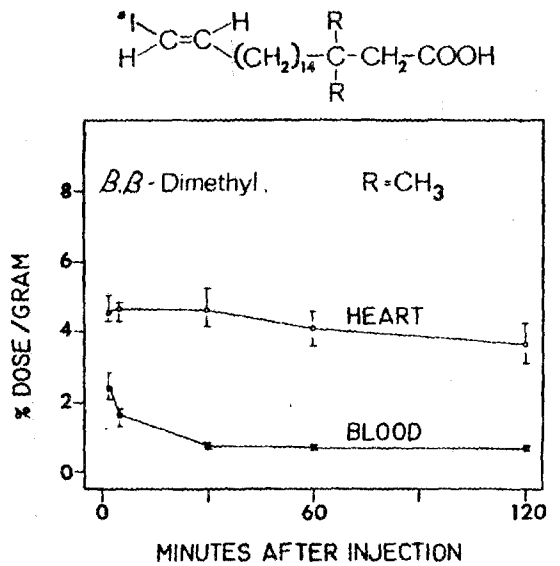


Fig. 1

rats of the terminal iodovinyl 3-methyl-branched and straight chain analogues dramatically delineated differences in myocardial clearance rates with the methyl-branched agent showing considerably longer retention. The new terminal iodovinyl-3,3-dimethyl-branched fatty acid showed higher myocardial uptake, longer myocardial retention, lower blood levels and higher heart:blood ratios than observed with the monomethyl-branched analogue. Iodine-125 DMIVN showed 90% retention of the initial myocardial uptake (4.56% dose/gm, at 2 min) after 60 min, while BMIVN showed 50% retention of the initial heart uptake (4.89% dose/gm at 5 min). In contrast to the prolonged myocardial retention observed with DMIVN, the activity in the blood rapidly cleared diminishing from 2.44% dose/gm at 2 min to 0.74% dose/gm at 30 min, resulting in a high mean heart:blood ratio of 6.2:1 at 30 min. These

Table 1. Distribution of Radioactivity (% Injected Dose/Gram of Tissue) in Fasted Rats at Various Times after Intravenous Administration of 19-[^{125}I]iodo-3,3-dimethyl-18-nonadecenoic Acid.[a]

Tissue	Time after injection; percent injected dose/gram (range)				
	2 min	5 min	30 min	1 h	2 h
Heart	4.56 (4.30-5.05)	4.66 (4.29-4.83)	4.60 (4.14-5.26)	4.10 (3.62-4.58)	3.66 (3.12-4.28)
Blood	2.44 (2.09-2.84)	1.62 (1.41-1.84)	0.74 (0.66-0.80)	0.71 (0.65-0.74)	0.70 (0.67-0.72)
Lungs	2.17 (1.96-2.35)	2.09 (1.90-2.26)	1.42 (1.27-1.57)	1.22 (1.14-1.33)	1.05 (1.01-1.08)
Liver	7.27 (6.92-8.04)	7.27 (7.18-7.46)	5.88 (4.69-6.72)	4.93 (4.67-5.39)	3.89 (3.71-4.17)
Kidneys	1.38 (1.17-1.53)	1.46 (1.31-1.61)	1.49 (1.37-1.63)	1.46 (1.35-1.56)	1.29 (1.23-1.37)
Thyroid	24.21 (21.42-25.72)	23.53 (20.60-26.37)	40.62 (33.82-44.14)	83.10 (62.11-117.75)	157.04 (122.63-209.34)
Mean Heart:Blood	1.9:1	2.9:1	6.2:1	5.8:1	5.3:1

[a]Mean and range value for five female Fischer rats.

results have also been observed in similar studies with 15-(p-iodophenyl)-3,3-dimethylpentadecanoic acid (DMIPP) and demonstrates that the unique biological behavior observed with the dimethyl structural modification is reproducible with a terminal iodovinyl substituted fatty acid. These data suggest that terminal iodovinyl 3,3-dimethyl-branched fatty acids are promising candidates for evaluating regional differences delineated by mapping myocardial uptake and retention of the radiolabel in diseased myocardium. The biochemical fate of ^{125}I-DMIVN in heart tissue is currently being evaluated in detail. Lipid analysis studies have been performed and will be discussed in the following section of this report.

The availability of 17-iodo-3,3-dimethylheptadecanoic acid (14) prepared as a synthetic intermediate (Scheme II) allowed for the further study of the extent and mechanism of iodide loss in the absence of β-oxidation. Iodine-125-17-iodo-3,3-dimethylheptadecanoic acid (14) was prepared by isotopic exchange in refluxing 2-butanone. Tissue distribution studies of ^{123}I-labeled 14 in fed rats (Table 2) demonstrated rapid myocardial washout and pronounced in vivo deiodination, indicating significant carbon-iodine cleavage in the apparent absence of β-oxidation. These results are similar to our earlier studies using 17-iodo-3-(R,S)-methyl heptadecanoic acid (ORNL/TM-9124) and 17-[^{131}I]iodo-9-telluraheptadecanoic acid (ORNL/TM-7775) which exhibited initial high heart uptake in rats but showed rapid myocardial washout and significant in vivo deiodination resulting in high thyroid uptake. In addition, the significant difference in myocardial extraction and retention of the iodovinyl agent compared with the iodoalkyl derivative dramatically illustrate the enhanced stability of iodide attached to a iodovinyl moiety in comparison to a sp^3 hydridized carbon. Iodine-125-labeled DMIVN is currently being studied in salt sensitive hypertensive rats by quantitative dual tracer autoradiography as a candidate for the clinical evaluation of hypertensive heart disease by collaborators (P. Som, A. B. Brill et al) at Brookhaven National Laboratory.

Table 2. Distribution of Radioactivity (% Injected Dose/Gram of Tissue) in Nonfasted Rats at Various Times after Intravenous Administration of 17-[^{125}I]iodo-3,3-dimethyl-heptadecanoic Acid.[a]

Tissue	Time after injection; percent injected dose/gram (range)				
	2 min	5 min	15 min	30 min	1 h
Heart	2.84 (2.50-3.27)	2.06 (1.91-2.31)	1.22 (1.12-1.42)	0.84 (0.73-0.90)	0.68 (0.54-0.84)
Blood	2.59 (2.14-2.98)	1.87 (1.75-2.01)	1.36 (1.29-1.43)	1.04 (1.00-1.09)	0.83 (0.74-0.96)
Lungs	2.19 (1.98-2.38)	1.96 (1.83-2.13)	1.40 (1.34-1.44)	0.98 (0.96-1.02)	0.64 (0.07-0.82)
Liver	5.26 (4.81-5.55)	3.99 (3.66-4.35)	2.34 (2.09-2.61)	1.44 (1.41-1.50)	1.07 (0.88-1.27)
Kidneys	1.38 (1.31-1.50)	1.48 (1.45-1.54)	1.33 (1.24-1.43)	0.97 (0.93-1.03)	0.74 (0.63-0.86)
Thyroid	15.93 (13.49-20.02)	16.83 (13.55-19.04)	42.89 (29.88-57.48)	78.40 (66.29-92.69)	148.83 (130.32-188.72)
Mean Heart:Blood	1.1:1	1.1:1	0.9:1	0.8:1	0.8:1

[a]Mean and range value for five female Fischer rats.

EFFECTS OF 3-METHYL-BRANCHING ON INCORPORATION OF IODOVINYL FATTY ACIDS INTO LIPIDS AND SUBCELLULAR FRACTIONS FROM RAT HEARTS

In the continuing investigation of the metabolism of radiolabeled methyl-branched fatty acids within rat hearts, we have now initiated studies on the subcellular distribution and lipid analysis of the iodovinyl series of fatty acids. The analogues tested include the straight chain 19-iodo-18-nonadecenoic acid (IVN), the monomethyl-branched 19-iodo-3-(R,S)-methyl-18-nonadecenoic acid (BMIVN) and the dimethyl-branched 19-iodo-3,3-dimethyl-18-nonadecenoic acid (DMIVN). Subcellular distribution studies which involve differential centrifugation to isolate the mitochondrial, microsomal and cytoplasmic fractions have thus far been performed with the monomethyl-branched BMIVN analogue and the straight chain IVN analogue. Rats either fasted (24 h) or non-fasted were injected intravenously with the ^{125}I-labeled analogues and the hearts removed for subcellular fractionation 30 min later. Comparison of the subcellular profiles of radioactivity show no statistically significant difference (Wilcoxon test) between IVN and BMIVN in non-fasted animals (Fig. 2). In fasted rats however, there were statistically significant differences ($p=0.002$) between the profiles of the IVN versus the BMIVN injected animals. The dietary status of the animals injected with IVN resulted in significant differences ($p=0.001$) in the percentage of radioactivity in the mitochondrial and cytoplasmic fractions with smaller differences in the microsomal fraction ($p=0.025$). With BMIVN the effects of fasting were seen primarily in the differences in the cytoplasmic fractions ($p=0.001$), whereas, the mitochondrial fractions showed only a slight difference ($p=0.05$) and there was no significant difference in the percentage of activity in the microsomal fractions of hearts from fasted versus non-fasted rats. Similar effects of methyl-branching of the analogue and of the dietary status of the animals on the subcellular distribution profiles have previously been observed in studies on the iodophenyl series of fatty acids (ORNL/TM-9707). These studies also confirmed the correlation of prolonged heart retention by methyl-branched fatty acids with relatively higher association of activity with the

mitochondrial versus the cytoplasmic fraction. Future work with this iodovinyl series of fatty acids will include subcellular distribution studies on the dimethyl-branched analogue in comparison with the straight chain analogue.

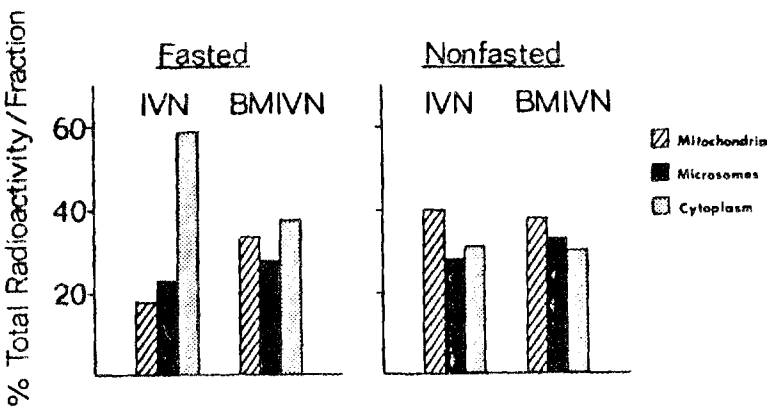


Fig. 2

During this quarter we have also evaluated the distribution of radioactivity in the lipid pools of whole hearts of fasted rats up to 1 h after the administration of the ^{125}I-labeled dimethyl DMIVN analogue. Tissue distribution studies of the compound have shown high myocardial extraction with significant retention over the 2 h assay period. Lipid analyses showed that the initial predominance of radioactivity in the free fatty acid pool was replaced after 10 min by an increase of activity in the triglyceride fraction (Fig. 3). The rate of this "conversion" is very similar to that observed with the dimethyl-branched iodophenyl compound, DMIPP (ORNL/TM-9707). As with DMIPP, no activity was observed in the diglyceride fraction following DMIVN injection; however, there was a significant increase in the activity within the polar lipid pool. In future studies both the straight chain IVN and the monomethyl-branched BMIVN analogues will be examined as to their distribution into lipid pools of rat hearts.

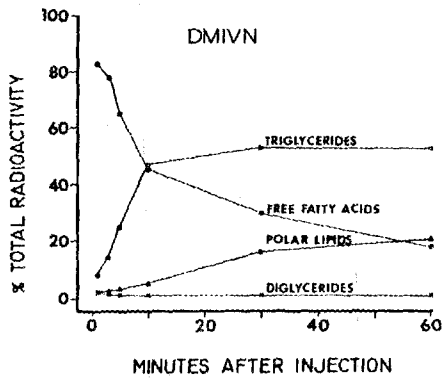


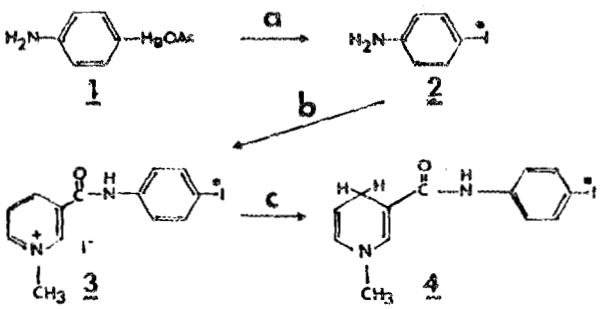
Fig. 3

RADIOIODINATED BRAIN IMAGING AGENTS: TISSUE DISTRIBUTION PROPERTIES OF A RADIOIODINATED 1,4-DISUBSTITUTED REDUCED PYRIDINE IN LABORATORY ANIMALS

Many radiolabeled lypophilic agents cross the intact blood brain barrier and distribute in the brain as a function of regional cerebral blood flow. If such agents are modified and appropriately radiolabeled to show high brain uptake, high brain:blood ratios and prolonged retention with minimal redistribution in the brain, they can potentially be used for single photon emission computerized tomographic (SPECT) imaging studies.

Recently a new approach for the delivery of radiolabeled agents to the brain for high brain uptake and prolonged retenion has been reported from this laboratory. The report (ORNL/TM-9394), for example, takes into account the synthesis of a radiolabeled agent (a) coupled to a dihydropyridine moiety (4) (b → c) which apparently helps carry the radiolabeled agent to the brain (Scheme IV). The radiolabeled agent 4, in the brain, is considered to undergo oxidation of the dihydropyridine moiety and cleavage of the carboxamide (-CONH-) bond to generate non-lypophilic 3 and/or 2 respectively, which are retained in the brain.

The present study was directed toward evaluating the retention properties of dihydropyridine moieties which can undergo oxidation in the brain.



Scheme IV

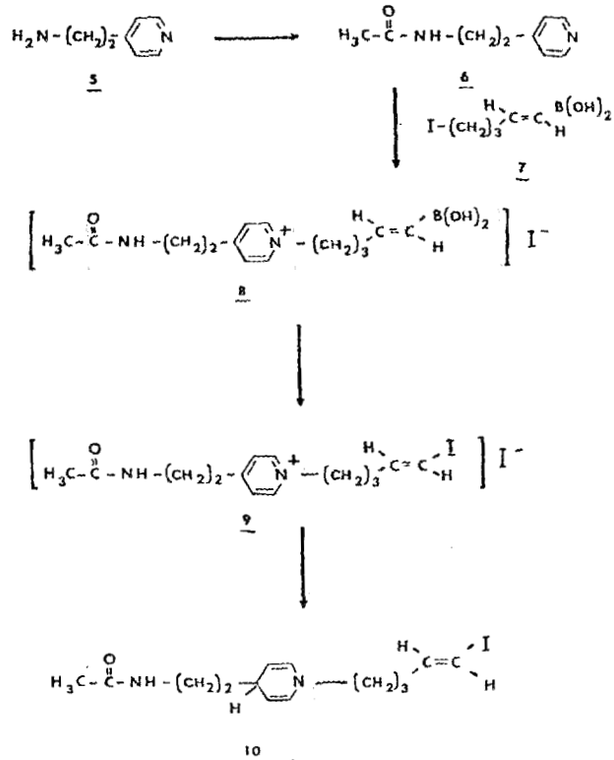
The synthesis of the target compound was as follows. The precursor, 4-(2-aminoethyl)pyridine (5) was first acetylated with acetic anhydride to give 4-(2-N-acetylaminoethyl)pyridine (6). Condensation of 6 with E-1-borono-5-iodo-1-pentene (7) in dimethylformamide gave 1-(E-1-borono-1-penten-5-yl)-4-(2-N-acetylaminoethyl)pyridinium iodide (8). Iodination of 8 in the presence of chloroamine-T and sodium iodide gave 1-(E-1-iodo-1-penten-5-yl)-4-(2-N-acetylaminoethyl)pyridinium iodide (9). The 1,4-disubstituted pyridinium compound 9 was found resistent to sodium dithionite reduction as compared to 1,3-disubstituted pyridinium compounds. The sodium borohydride reduction of 9, however, gave the reduced compound, presumably the desired product, 1-(E-1-iodo-1-penten-5-yl)-4-(2-N-acetylaminoethyl)-1,4-dihydropyridine (10). The radioiodinated compounds 9 and 10 were synthesized similarly using Na[^{125}I] instead of NaI during iodination.

The data from Table 3 shows moderate (0.49% dose/gm after 5 min) brain uptake of [^{125}I]10 which gradually washes out. This may indicate the inability of 1,4-disubstituted dihydro pyridines to undergo facile oxidation in the brain. In the absence of such oxidation mechanism (or in a slow oxidation process), [^{125}I]10 will not be converted to the active quaternary species (such as 9) resulting in washout of 10 from the brain (Scheme V).

Table 3. Distribution of radioactivity in tissues of Fisher-144 rats following intravenous administration of 1-(E-[^{125}I]iodopenten-5-yl)-4-(2-N-acetylaminoehtyl)-1,4-dihydropyridine ([^{125}I]10).[a]

Time After Injection	Mean percent injection dose/gm (range) Tissue					
	Brain	Blood	Liver	Kidneys	Heart	Lungs
5 min	0.49 (0.42-0.58)	0.38 (0.34-0.42)	2.95 (2.31-3.50)	5.45 (4.19-6.53)	0.88 (0.84-0.92)	1.80 (1.52-2.02)
30 min	0.20 (0.16-0.23)	0.46 (0.42-0.50)	2.17 (1.95-2.32)	2.37 (2.04-2.85)	0.52 (0.43-0.59)	1.21 (1.05-1.29)
60 min	0.12 (0.10-0.13)	0.44 (0.39-0.48)	1.72 (1.62-1.84)	1.48 (1.35-1.60)	0.39 (0.38-0.41)	0.91 (0.81-1.05)

[a]Each animal (5 animals per time point) received 5.34 μCi of [^{125}I]10 by tail injection.



Scheme V

AGENTS FOR MEDICAL COOPERATIVE PROGRAMS

Osmium-191

Eight shipments of ^{191}Os-potassium osmate were made to the Medical Cooperative Programs for further development of the ^{191}Os→^{191m}Ir generator system and to study clinical applications of ^{191m}Ir ($T_{1/2}$ = 4.96 s). Applications being studied include first-pass radionuclide angiographic evaluation of intracardiac shunts and measurement of left ventricular ejection fraction. One shipment was made to the Children's Hospital Medical Center in Boston, MA (Drs. S. Treves and A. Packard), two shipments to the Cyclotron Center, University of Liege, Belgium (Drs. C. Brihaye and M. Guillaume), one shipment to George Washington University, Washington, D.C. (Dr. B. Wessels), two shipments to the University of Bonn, Federal Republic of Germany (Dr. S. Reske), and two shipments to Massachusetts General Hospital, Boston, MA (Dr. H. W. Strauss).

Platinum-195m

Three shipments of ^{195m}Pt-labeled cis-dichlorodiammineplatinum(II) (cis-DDP) were supplied to collaborators to study the pharmacokinetic properties and mode of antitumor activity of this agent. Investigators at the Harvard Medical School, Boston, MA (Dr. A. Jones), City of Hope Medical Center, Duarte, CA (Dr. K. Scanlon) and Memorial Sloan-Kettering Hospital, New York, NY (Dr. J. S. Laughlin) received one shipment each.

Copper-64

One shipment of ^{64}Cu was made to collaborators at Oak Ridge Associated Universities, Oak Ridge, TN (Dr. J. Crook).

PAPERS AND PUBLICATIONS

Papers

C. Brihaye, M. Guillaume, F. E. Delcourt, H. Ham, F. F. Knapp, Jr., and T. A. Butler "Clinical Potential of a New High Performance ^{190}Os-^{191m}Ir Generator," European Nuclear Medicine Congress 1985, London, England, Sept. 3-6, 1985.

R. Dudczak, P. Angelberger, R. Schmoliner, K. Kletter, F. F. Knapp, Jr., and M. M. Goodman "Myocardial Scintigraphy Using 15-p-(I-123)-Iodophenyl-β-methyl-pentadecanoic Acid (βMPPA), European Nuclear Medicine Congress 1985, London, England, Sept. 3-6, 1985.

F. F. Knapp, Jr., M. M. Goodman, and K. R. Ambrose "Effects of 3-Methyl-Branching on Heart Uptake and Metabolism of 15-(p-Iodophenyl)pentadecanoic Acid Analogues," European Nuclear Medicine Congress 1985, London, England, Sept. 3-6, 1985.

Reports

F. F. Knapp, Jr., K. R. Ambrose, M. M. Goodman, and P. C. Srivastava, Nuclear Medicine Progress Report for Quarter Ending June 30, 1985, ORNL/TM-9707.

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