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THE SYNTHESIS OF
BIPHENYL-4,4′-d_2

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NAA-SR-2147
CHEMISTRY-GENERAL
12 PAGES

THE SYNTHESIS OF BIPHENYL-4,4′-d_2

BY:

R. I. AKAWIE

ATOMICS INTERNATIONAL

A DIVISION OF NORTH AMERICAN AVIATION, INC.
P.O. BOX 309 CANOGA PARK, CALIFORNIA

CONTRACT: AT(11-1)-GEN-8

ISSUED: DECEMBER 15, 1957

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ABSTRACT

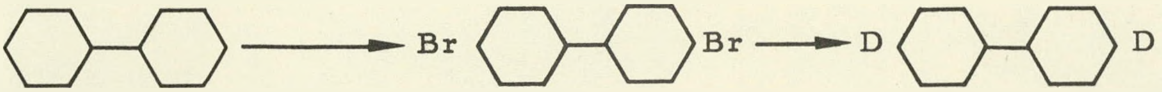
The synthesis of biphenyl-4, 4'-d_2 from biphenyl by bromination to 4, 4'-dibromobiphenyl, exchange with n-butylithium reagent, and hydrolysis with deuterium oxide, is described. The over-all yield was 44 per cent.

I. INTRODUCTION

Several analogues of biphenyl, labeled with deuterium in different positions on the rings, are needed to study the effects of radiation on biphenyl. One such analogue is the compound biphenyl-4, 4'-d_2 (see end formula in Reaction 1), in which the two para-hydrogen atoms of biphenyl are replaced with deuterium atoms. The synthesis of this compound is described in this report.

II. DISCUSSION OF RESULTS

The compound biphenyl-4, 4'-d_2 has been prepared by a two-step synthesis starting with biphenyl itself:



...(1)

Biphenyl was brominated with bromine vapor in a closed vessel at room temperature to 4, 4'-dibromobiphenyl, according to the procedure of Buckles and Wheeler.[1] The yield of purified material obtained was 70 per cent of theoretical.

Since Weldon and Wilson[2] used the reaction of Grignard reagents with deuterium oxide for the preparation of deuterated benzenes, efforts were first directed toward conversion of 4, 4'-dibromobiphenyl to its difunctional Grignard reagent, to be followed by reaction with deuterium oxide. Gibert[3] reported the formation of the di-Grignard reagent from 4, 4'-dibromobiphenyl by the entrainment method; Snyder, Weaver, and Marshall[4] converted 3, 3'-dibromobiphenyl to the di-Grignard reagent by a similar procedure. Two attempts to prepare the Grignard reagent from 4, 4'-dibromobiphenyl, with anhydrous magnesium iodide as promoter, were unsuccessful. A third attempt, using the entrainment method with ethyl iodide, was also without success, although ethylmagnesium iodide was formed.

The next method of attack involved application of the halogen-lithium exchange reaction.[5] Snyder, Weaver, and Marshall[4] succeeded in converting 3, 3'-dibromobiphenyl to the di-lithium compound; Gilman, Langham, and Moore[6] reported the conversion of 4, 4'-dibromobiphenyl to the corresponding di-lithium compound. In the latter case it was observed that a long reaction time in petroleum ether, as solvent, was necessary for exchange of both bromine atoms in the molecule. Consequently, the n-butyllithium reagent used for the exchange reaction was prepared in petroleum ether.[6] Yields of 46 and 50 per cent were obtained.

The first exchange reaction was performed in refluxing petroleum ether (bp 30-60 °C) for 16 hr, after which the solvent was evaporated and the solid residue was heated gradually to 102 °C during 8 hr. An impure oil was obtained after treatment with deuterium oxide; some deuterium was present in the oil as shown by its infrared spectrum in the region of 4.4 microns.

The second exchange reaction was performed in n-heptane; this solvent has a higher boiling point so that the reaction temperature can be controlled more easily than with petroleum ether. The petroleum ether from the n-butyllithium reagent was removed by distillation; then the reaction mixture was heated at 70-85 °C for 7.5 hr. After treatment with deuterium oxide, a small amount (12 per cent of the theoretical yield) of slightly impure biphenyl-4, 4'-d_2 (see end formula in Reaction 1) (white crystals, mp 61-64.5 °C) was isolated. This material was analyzed by gas chromatography and was shown to be essentially biphenyl-d_2, although the presence of small amounts of impurities was detected; the infrared spectrum was quite different from that of biphenyl, and absorption due to carbon-deuterium bonds at 4.4 microns was pronounced.

A third exchange reaction was performed in petroleum ether at 40-45 °C for 26 hr. Because of the milder reaction conditions, the product consisted of a mixture of biphenyl-4, 4'-d_2 and what was probably 4-bromobiphenyl-4'-d, with a small amount of 4, 4'-dibromobiphenyl.

Because Snyder, Weaver, and Marshall[4] had prepared a di-lithium compound from 3, 3'-dibromobiphenyl in ethyl ether, the next exchange was performed in that solvent. The n-butyllithium reagent was also prepared in ethyl ether;[5] because it decomposes on standing in this solvent, it was prepared just before the exchange reaction was performed. The yield of n-butyllithium was not determined; only the total amount of bases present in the ethyl ether solution was determined. Hence, twice the theoretically required base was employed for the exchange. The exchange was conducted at room temperature for 16 hr and then at the reflux temperature for 1 hr. Hydrolysis with deuterium oxide was quite vigorous. Two fractional distillations and one sublimation *in vacuo* gave biphenyl-4, 4'-d_2 (mp 68-69 °C, uncorrected); the yield was 63 per cent of theoretical. The product was analyzed by gas chromatography, and was free of impurities. Its infrared spectrum and mass spectrum were measured, the latter by Consolidated Electrodynamics Corporation. The mass pattern indicates the absence of any deuterated biphenyl other than biphenyl-4, 4'-d_2.[7] A final test of purity awaits the completion of an analytical unit for combustion of the solid and determination of the deuterium content of the resulting water by the falling drop method.[8]

III. EXPERIMENTAL

A. 4, 4'-DIBROMOBIPHENYL

A dish of bromine (78 gm, 24 ml, 0.48 mole) and a dish of finely powdered biphenyl (30.8 gm, 0.200 mole) were placed in a vacuum desiccator. The desiccator was vented to the atmosphere by means of a stopcock. After 48 hr at room temperature, the bromine had completely vaporized. The resulting pale yellow solid (63.0 gm) was recrystallized from 150 ml of benzene with the aid of decolorizing charcoal. After removal of the main crop of white crystals (39.4 gm; mp 161.5-163.5 °C, uncorrected) a second crop (4.4 gm) was obtained by concentrating the mother liquor. The combined yield (43.8 gm, 0.140 mole) is 70 per cent of theoretical.

B. n-BUTYLLITHIUM REAGENT

A one-liter, three-neck flask was fitted with a 500-ml, pressure-equalizing addition funnel, a stirrer, and a Liebig condenser through which a thermometer was suspended. Dry helium gas was passed through the funnel into the system and escaped through the condenser. Four hundred ml of anhydrous ethyl ether and 17.3 gm (2.5 gm-atoms) of lithium metal (which had been pounded flat with a hammer and then cut in narrow strips with scissors) were placed in the flask. A solution of 137.0 gm (105.4 ml, 1.00 mole) of anhydrous n-butyl bromide in 200 ml of anhydrous ethyl ether was placed in the addition funnel. Small amounts of the butyl bromide solution were added with stirring to the lithium metal until the reaction between the two substances began (as evidenced by the formation of white crystals of lithium bromide). The reaction mixture was cooled to -10 °C by immersing the flask in a dry ice and acetone bath kept at -40 °C. The remainder of the butyl bromide solution was added during a period of 40 min at -10 °C and stirring was continued for 2 hr while the reaction mixture warmed to 10 °C. Filtration through glass wool gave a bluish-purple filtrate which contained a finely divided solid. An aliquot of the filtrate was added to water and the resultant mixture was titrated with standard acid, using phenolphthalein as indicator; this determines the total bases present. The titration after reaction with benzyl chloride was not performed; this determines the total bases other than n-butyllithium present. The total bases present were 0.61 moles, which therefore is the maximum amount of n-butyllithium present.

C. BIPHENYL-4, 4'-d_2

A two-liter, three-neck flask was fitted with a 500-ml, pressure-equalizing addition funnel, a stirrer, and a reflux condenser. Dry helium gas was passed through the funnel into the system, and escaped through the condenser. Four hundred ml of anhydrous ethyl ether and 43.1 gm (0.138 mole) of 4, 4'-dibromobiphenyl were placed in the flask. Five hundred twenty ml of n-butyllithium reagent (containing 0.55 moles of total bases) was placed in the addition funnel. The butyllithium reagent was added rapidly to the stirred reaction mixture; the mixture refluxed slowly for a short time and the bluish-purple color introduced by the butyllithium reagent gradually disappeared. The reaction mixture was stirred for 17 hr at room temperature, refluxed for 1 hr, and treated, drop by drop, with approximately 20 ml of deuterium oxide (99.8 per cent pure). The reaction mixture refluxed during the hydrolysis; stirring was continued for a short time. The aqueous phase was discarded; the ether phase was filtered to remove a small amount of white solid, washed twice with water, and dried over anhydrous potassium carbonate. The solvent was distilled; the residual material was distilled *in vacuo* through a three-inch Vigreux column. The fraction collected distilled at 115-130 °C at 11-13 mm Hg and weighed 15.0 gm; some residue was noted. The distillate was redistilled and yielded 13.8 gm of white solid (bp 120-121 °C at 11.5 mm Hg; mp 64.5-66 °C, uncorrected). The solid was sublimed at approximately 1 mm Hg; the yield of 13.5 gm (0.0865 mole) of white crystals (mp 68-69 °C, uncorrected) is 63 per cent of theoretical.

D. INFRARED SPECTROMETRY

The infrared spectra were measured with a Perkin-Elmer, model-21, double-beam recording infrared spectrophotometer. Biphenyl and biphenyl-4, 4'-d_2 were dissolved in carbon tetrachloride at a concentration of 100 mg of solid to 641 mg of solvent (20 per cent, weight/volume, or 13.5 per cent, weight/weight), and were compared to pure carbon tetrachloride. There were appreciable differences between the spectra of the two biphenyls (see Fig. 1); the primary difference was the appearance of a large absorption peak at 4.40 microns in the spectrum of the deuterated compound. This peak is due to carbon-deuterium bond absorption.

E. GAS CHROMATOGRAPHY

Analysis for purity of the deuterated biphenyl was performed with a Perkin-Elmer, model-154B, Vapor Fractometer. Two columns were used: Column A is a two-meter column of didecyl phthalate on Celite; column C is a two-meter column of silicone oil on Celite. Column A, on which biphenyl (and biphenyl-4, 4'-d_2) has a retention time of about 41 min at 175 °C, was used to check for impurities more volatile than biphenyl. Column C, on which biphenyl has a retention time of about 2 min at 225 °C, was used to analyze for less volatile impurities such as 4-bromobiphenyl (which has a retention time of approximately 4.5 min) and 4, 4'-dibromobiphenyl (which has a retention time of approximately 9.5 min). Approximately 20 microliters of a 20 per cent, weight/volume, solution of biphenyl in carbon tetrachloride was used for each analysis.

F. MASS SPECTROMETRY

The mass spectra of biphenyl and biphenyl-4, 4'-d_2 were measured by Consolidated Electrodynamics Corporation (CEC) with their model 21-103C analytical mass spectrometer. The photographic records of the mass spectra were obtained from CEC, and the peak heights were measured in this laboratory. The relative peak heights, in the vicinity of the parent mass peak, are shown in Table I.

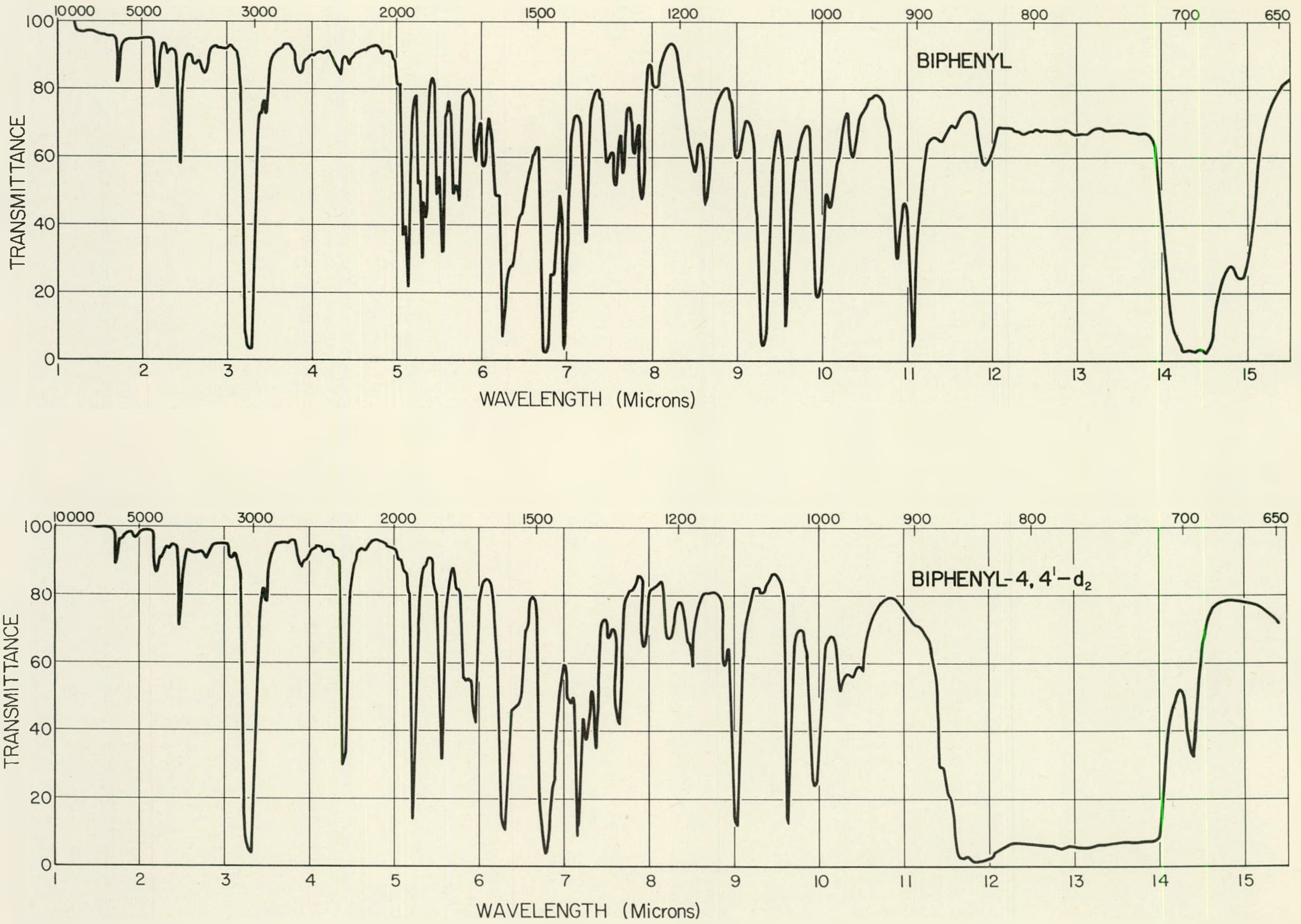


Fig. 1. Infrared Spectra of Biphenyl and Biphenyl-4, 4'-d_2
(Carbon Tetrachloride Solution)

TABLE I

MASS SPECTRA OF BIPHENYL AND BIPHENYL-4, 4'-d_2

Mass-charge Ratio	Biphenyl	Biphenyl-4, 4'-d_2
148	0.22	-
149	0.76	-
150	2.65	0.45
151	9.24	2.02
152	27.41	4.91
153	33.78	12.20
154	100.	26.52
155	13.06	31.39
156	1.89	100.
157	-	12.68
158	-	0.77

SUMMARY

The preparation of biphenyl-4, 4'-d_2 was performed by bromination of biphenyl to 4, 4'-dibromobiphenyl, followed by exchange with n-butyllithium reagent and hydrolysis of the resulting dilithium compound with deuterium oxide. The over-all yield was 44 per cent. The infrared spectrum and the mass spectrum of biphenyl-4, 4'-d_2 were obtained.

REFERENCES

1. R. E. Buckles and N. G. Wheeler, "4, 4'-Dibromobiphenyl," Organic Syntheses 31, 29 (1951)
2. L. H. P. Weldon and C. L. Wilson, "Structure of Benzene. XII. Preparation of Deuterated Benzenes by the Grignard Reaction. Mono- and 1, 4-Dideuterobenzene," J. Chem. Soc. 1946, 235
3. R. Gibert, "On the p, p'-Dimagnesium Reagents of Biphenyl. Favorable Role of Magnesium Iodide," Compt. rend. 205, 443 (1937)
4. H. R. Snyder, C. Weaver, and C. D. Marshall, "The Preparation of 3, 3'-Dibromobiphenyl and its Conversion to Organometallic Compounds," J. Am. Chem. Soc. 71, 289 (1949)
5. R. G. Jones and H. Gilman, "The Halogen-Metal Interconversion Reaction with Organolithium Compounds," Organic Reactions 6, 339 (1951)
6. H. Gilman, W. Langham, and F. W. Moore, "Some Interconversion Reactions of Organolithium Compounds," J. Am. Chem. Soc. 62, 2327 (1940)
7. J. G. Burr, R. I. Akawie, and J. M. Scarborough, "The Mass Spectra of Biphenyl, Biphenyl-4, 4'-d_2 and Biphenyl-2, 2', 4, 4', 6, 6'-d_6," NAA-SR-2146 (to be published)
8. R. F. Glascock, Isotopic Gas Analysis for Biochemists, (New York: Academic Press Inc., 1954), p 135-146