

reddish, crystalline substance free of chlorine were obtained in this manner. The substance was dried *in vacuo* at 100° over phosphorus pentoxide. It gives positive color reactions with ninhydrin, with diazotized sulfanilic acid and with dichloroquinone chlorimide.

*Anal.* Calcd. for  $C_{11}H_{11}N_2O_2$ : C, 53.6; H, 5.6; N, 12.5; amino-N, 6.3. Found: C, 53.4; H, 5.6; N, 12.6; amino-N, 6.3 (Linderström-Lang titration).

The substance has no definite melting point.

**Formation of N-(*m*-Hydroxyphenyl)-glycine Anhydride from Glycylglycine and Resorcinol.**—To 25 g. of melted resorcinol was added 5 g. of glycylglycine. The mixture was heated for three hours in an oil-bath at a bath temperature of 175–185°. The limpid, hot solution was poured into a porcelain mortar and the solidified material was treated with ether. (No gas formation was observed on heating the dipeptide with resorcinol). After removing the ether by suction the remaining substance was washed with ether and dried; yield, 7.4 g. Five grams of this product was extracted with ethyl acetate for twenty-four hours in a Soxhlet apparatus. The yellowish product which appeared in the extract was filtered by suction, washed with ethyl acetate and dried. The substance (1.1 g.) was recrystallized from 30 cc. of water to which *carbo animalis* was added. On cooling, 250 mg. of a colorless substance was obtained in the form of glittering needles. The Millon reaction was positive. *Anal.* Found: N, 13.2. On benzylation of 200 mg. under the conditions previously described and on recrystallization from alcohol 170 mg. of a

product was obtained whose melting point (171°) was identical with the melting point of the product obtained by benzylation of N-(*m*-hydroxyphenyl)-glycine anhydride. The m. p. of a mixture of the two substances was also 171°.

*Anal.* Calcd. N, 9.0. Found: N, 9.2.

**Treatment of Glycine Anhydride with Hot Resorcinol.**—Glycine anhydride was heated for three hours with 5 parts of resorcinol at 175–185° in a similar manner to the treatment of glycine or glycylglycine. It dissolved in a short time. After solidification, the reaction mixture was treated with ether. The material obtained after drawing off the ether was boiled with 96% alcohol, filtered, washed with alcohol and dried. The product so obtained (80% of the original material) gave no color reaction with Millon reagent. It was recrystallized from water. *Anal.* Calcd. for glycine anhydride: N, 24.6. Found: N, 24.5.

### Summary

N-(*m*-Hydroxyphenyl)-glycine anhydride was isolated after treating glycine with hot resorcinol at 175–185°. The same product is formed when glycylglycine is heated with resorcinol.

Treating with sodium hydroxide converts N-(*m*-hydroxyphenyl)-glycine anhydride into glycyl-N-(*m*-hydroxyphenyl)-glycine.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## The Preparation of 3,3'-Dibromobiphenyl and its Conversion to Organometallic Compounds

BY H. R. SNYDER, CLAY WEAVER<sup>1,2</sup> AND CLIFFORD D. MARSHALL

Although the reactions of various dibromobiphenyls with magnesium<sup>3,4</sup> and with an alkyl-lithium<sup>5</sup> have been reported, 3,3'-dibromobiphenyl appears to have escaped such investigation. Since symmetrical difunctional organometallic compounds related to biphenyl have been of interest to us as possible intermediates<sup>6</sup> in the synthesis of biphenyldiboronic acids,<sup>7,8,9</sup> the behavior of 3,3'-dibromobiphenyl toward magnesium, lithium and *n*-butyllithium has been examined.

3,3'-Dibromobiphenyl was prepared from *o*-nitrobromobenzene by reduction to the hydrazo compound, rearrangement to the benzidine, and deamination of the tetrazonium salt with hypophosphorous acid.<sup>10</sup> The hydrazo compound and the benzidine thus prepared were found to

have melting points quite different from those observed on samples, obtained by processes involving the bromination of azobenzene<sup>11</sup> and of N,N'-diacetylbenzidine,<sup>12</sup> which have been considered<sup>13</sup> to have the structures of 2,2'-dibromohydrazobenzene and 3,3'-dibromobenzidine, respectively. The bromination of N,N'-diacetylbenzene was repeated, and a dibromobenzidine identical with our sample was the only product isolated in a pure state from the reaction mixture. In a Sandmeyer reaction with cuprous bromide the tetrazonium salt from our dibromobenzidine gave a product possessing the same melting point as the tetrabromobiphenyl<sup>14</sup> prepared by van Roosmalen from a dibromobenzidine obtained by the direct bromination method. Furthermore, our compounds had the expected compositions and yielded 3,3'-dibromobiphenyl of the correct properties.<sup>15</sup>

3,3'-Dibromobiphenyl did not react with magnesium under the usual conditions of Grignard preparations, but it did react in the presence of ethylmagnesium bromide. The difunctional Gri-

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- (3) Case, *THIS JOURNAL*, **58**, 1246 (1936).
- (4) Malinovskii and Pokrovskii, *Trudy Gor'kov. Gosudarst. Pedagog. Inst.*, No. 5, 51–53 (1940) [*C. A.*, **37**, 3077 (1943)].
- (5) Gilman, Langham and Moore, *THIS JOURNAL*, **62**, 2332 (1940).
- (6) Khotinsky and Melamed [*Ber.*, **42**, 3094 (1909)] first prepared boronic acids from alkyl borates and Grignard reagents.
- (7) Snyder and Weaver, *THIS JOURNAL*, **70**, 232 (1948).
- (8) Snyder, Weaver and Parmerter, *ibid.*, **70**, 773 (1948).
- (9) Snyder and Meisel, *ibid.*, **70**, 774 (1948).
- (10) "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 262.

- (11) Janowsky and Erb, *Ber.*, **20**, 364 (1887).
- (12) Levenstein, German Patent 97,101, *Chem. Zentr.*, **69**, II, 522 (1898); see *Frdl.*, **5**, 75 (1901).
- (13) Hellbron, "Dictionary of Organic Compounds," Vol. I, Oxford University Press, Oxford, 1934, pp. 429, 440.
- (14) van Roosmalen, *Rec. trav. chim.*, **53**, 371 (1934).
- (15) Ullmann, *Ann.*, **322**, 57 (1904).

gnard reagent so formed separated from the ether as a heavy oil. Because of the separation, and because of the presence of ethylmagnesium bromide in the solutions, it was not convenient to determine the extent of reaction of the dibromobiphenyl by titration. Carbonation of such solutions produced the known 3,3'-biphenyldicarboxylic acid which was further characterized as the methyl ester.<sup>16,17</sup> Since the yield of once-recrystallized dicarboxylic acid was moderately good (40%), the conversion of the dibromocompound to the Grignard reagent must have been high. When the Grignard preparation was carried out with only one equivalent of magnesium, both the mono- and difunctional organometallic compounds were formed, as shown by the conversion to 3'-bromo-3-biphenylcarboxylic acid and 3,3'-biphenyldicarboxylic acid. 3,3'-Dibromobiphenyl could not be induced to react with metallic lithium; however, it did react with *n*-butyllithium to produce the difunctional organometallic compound, the presence of which was demonstrated by carbonation.

### Experimental<sup>18</sup>

**2,2'-Dibromohydrazobenzene.**—The method of preparation was patterned after that used by Lukashevich<sup>18</sup> for the synthesis of the chloro analog. A mixture of 20 g. of *o*-nitrobromobenzene and 5 ml. of 50% aqueous sodium hydroxide was stirred at 60°, and zinc dust was added intermittently in small portions such that the temperature remained at 70–80°. After 15 g. of zinc had been added, the sludge was diluted with 50 ml. of water and 30 ml. of 20% aqueous sodium hydroxide. Then 20 g. of zinc was added rapidly, and the mixture was stirred at 70–80° until it was nearly colorless. The cooled mixture was poured slowly into 200 ml. of 25% sulfuric acid at 10°; the mixture was stirred for a few minutes and then filtered. The dry solid was extracted with three 30-ml. portions of ether, and the residue from the evaporation of the ether was recrystallized from petroleum ether (b. p. 40–60°), diluted with a little benzene, to give 10.8 g. (57%) of the hydrazo compound melting at 97–98°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>Br<sub>2</sub>N<sub>2</sub>: C, 42.1; H, 2.95. Found: C, 42.4; H, 3.30.

**3,3'-Dibromobenzidine.**—Method A: A solution of 4 g. of 2,2'-dibromohydrazobenzene in 50 ml. of ether was added slowly with shaking to 25 ml. of cold concentrated hydrochloric acid. Shaking was continued for one hour, and the dihydrochloride was separated by filtration and washed with ether. A suspension of the white product (wt., 4 g.) in excess 10% aqueous sodium hydroxide was heated on the steam-bath for one hour. The free base was extracted from the cooled mixture with ether, and the extracts were dried over calcium sulfate. The benzidine, recovered from the ether extracts, was recrystallized from ethanol to give 3 g. (75%) of a nearly white solid melting at 127–129°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>Br<sub>2</sub>N<sub>2</sub>: C, 42.1; H, 2.95. Found: C, 42.3; H, 3.27.

For the preparation of larger quantities of the dihydrochloride, essentially the same procedures were used but the intermediate hydrazo compound was not isolated. The yield of 3,3'-dibromobenzidine dihydrochloride from 61 g. of *o*-nitrobromobenzene was 35–40 g. (57–65%).

(16) Ullmann, *Ann.*, **322**, 71 (1904).

(17) Bulow and von Reden, *Ber.*, **31**, 2576 (1898).

(18) All melting points uncorrected.

(19) Lukashevich, *Azulinokrasochnaya Prom.*, **4**, 605 (1934) [*C. A.*, **29**, 2527 (1935)]

**Method B:** To a well-stirred suspension of 2.68 g. of *N,N'*-diacetylbenzidine in 100 ml. of water containing a trace of ferric bromide, 3 ml. of bromine was added over a two-hour period. The mixture was stirred for fifteen hours more and then permitted to stand for three days, at the end of which time a brown solid was removed by filtration, washed with water, and added to 40 ml. of 42% sulfuric acid. This mixture was gently refluxed for eighteen hours, cooled, diluted with water, and made alkaline with solid sodium carbonate. A dark solid was collected and extracted with ether. After treatment of the combined extracts with Darco, the ether was removed under reduced pressure. The dark solid so obtained was dissolved in a small amount of alcohol; careful addition of concentrated ammonia to the alcoholic solution produced, first, a very dark precipitate which was removed and discarded, and second, a light brown precipitate, which after separation and washing was dissolved in dilute sulfuric acid. This acidic solution, after decolorization with Darco, was made alkaline with ammonia and gently heated on a steam-bath for several minutes. A cream-colored precipitate was collected and washed with water; it was dissolved in alcohol and to the hot, filtered solution water was added to incipient cloudiness. From the cooled solution a finely crystalline precipitate was collected and washed with cold alcohol-water solution. The solid melted at 128–130° either alone or when mixed with a sample made by Method A, while admixture with benzidine caused a large depression in melting point.

**3,3',4,4'-Tetrabromobiphenyl.**—The procedure employed was essentially that of van Roosmalen<sup>14</sup>; a portion of 3,3'-dibromobenzidine prepared by Method A was used in the reaction. The product, recrystallized from benzene, melted at 166.5–168.5° (lit.<sup>14</sup> 169°).

**3,3'-Dibromobiphenyl.**—A mixture of 42 g. of 3,3'-dibromobenzidine dihydrochloride and 50 ml. of concentrated hydrochloric acid was diluted with 25 g. of ice and 25 ml. of water and tetrazotized by the addition of a solution of 14 g. of sodium nitrite in 50 ml. of water. The mixture was stirred for one hour after the addition of the nitrite and was then allowed to settle. The clear supernatant solution was added to 330 g. of 30% hypophosphorous acid at 10°; the small amount of residual solid was treated with 10 ml. of concentrated hydrochloric acid and sufficient sodium nitrite to cause complete solution, and this solution was also added to the hypophosphorous acid. The mixture was allowed to stand in the refrigerator for thirty hours and then in the room, with occasional shaking, for twenty hours. The mixture was then extracted with five 50-ml. portions of ether. The combined ether extracts were washed with two 50-ml. portions of 5% sodium hydroxide, followed by 50 ml. of water. The extracts were dried over potassium carbonate and the oil remaining after evaporation of the ether was distilled from a short-necked flask with a very wide side tube.<sup>20</sup> The yield of nearly colorless oil (b. p. 130–140° (2 mm.)), which soon solidified, was 22.0–25.2 g. (71–81%). A sample recrystallized from ethanol melted at 52–52.5° (lit.<sup>15</sup> 53°).

**3,3'-Biphenyldicarboxylic Acid.**—From the difunctional Grignard reagent: To 3.12 g. of 3,3'-dibromobiphenyl, 0.58 g. of magnesium, and 12 ml. of anhydrous ether, contained under a nitrogen atmosphere in a 3-necked 50-ml. flask equipped with a mercury sealed stirrer and a condenser, there was added an ethylmagnesium bromide solution prepared from 0.76 ml. of ethyl bromide, 0.28 g. of magnesium and 4 ml. of dry ether. After the mixture had been gently refluxed for eight hours, a heavy dark red oil had formed. The content of the flask was poured, portionwise with stirring, onto an excess of powdered Dry Ice contained in a flask toward whose mouth a vigorous stream of nitrogen was directed. After the carbonated mixture had been hydrolyzed with 20 ml. of 6 *N* sulfuric acid, a light yellow solid was removed by filtration and washed with several small portions of ether and

(20) The flask was of the type recommended by Koelsch, "Organic Syntheses," **20**, 20 (1940).

then with water (wt. of solid 1.60 g.). The ether layer of the filtrate was extracted with two 20-ml. portions of 5% sodium bicarbonate; acidification (congo red) of the combined bicarbonate washes with sulfuric acid gave a small amount of light yellow precipitate, which was collected and washed with water.

The solution of the two above precipitates in dilute sodium carbonate was decolorized with Darco. Acidification (congo red) of the solution with sulfuric acid produced a flocculent white solid, which was collected and washed with water. Recrystallization from dioxane gave a white powdery solid (wt. 0.97 g., 40%) melting at 330-332° (lit. 339-341°, 356-357°<sup>16</sup>) and containing no halogen.

**From 3,3'-biphenyldilithium:** To an ice-cold *n*-butyllithium solution in 24 ml. of dry ether, prepared from 0.56 g. of lithium and 3.4 g. of *n*-butyl chloride, contained in the apparatus described above and under an atmosphere of nitrogen, 2.34 g. of 3,3'-dibromobiphenyl in 12 ml. of dry ether was added by means of a dropping funnel over a thirty-minute period. The mixture was cooled and stirred for four hours and was then gently refluxed for one hour. After carbonation of the mixture, the acid was isolated and purified as above, m. p. 330.5-332° (wt. 0.83 g., 46%).

**Dimethyl Ester of 3,3'-Biphenyldicarboxylic Acid.**—The procedure of Bulow and von Reden<sup>17</sup> was employed. The dimethyl ester so obtained melted at 97.5-99° (lit.<sup>17</sup> 100-101°).

**3'-Bromo-3-biphenylcarboxylic Acid.**—To 3.20 g. of 3,3'-dibromobiphenyl, 0.24 g. of magnesium and 20 ml. of dry ether, contained in the apparatus previously described and under an atmosphere of nitrogen, approximately 0.005 mole of ethylmagnesium bromide in 5 ml. of dry ether was added; the mixture was stirred and gently heated for seven hours. The reaction mixture was carbonated and hydrolyzed as before.

From the hydrolysis mixture, 0.31 g. of light yellow solid (m. p. above 300°) was removed by filtration and washed with several small portions of ether. The separated ether layer was extracted with two 20-ml. portions of 5% sodium bicarbonate, then with two 20-ml. portions of 5% sodium hydroxide.

The combined sodium bicarbonate washes were decolorized with Darco, and acetic acid was added until the solution was almost neutral to litmus. A precipitate (A, wt.

0.59 g.) was collected and washed with water. Acidification (congo red) of the filtrate from A with sulfuric acid gave a second precipitate (B, wt. 0.13 g.). Similar treatment of the sodium hydroxide extracts with acetic acid gave a precipitate (C, wt. 0.37 g.); on further acidification of the filtrate no appreciable precipitate was obtained.

A portion of C was dissolved in dilute sodium carbonate and decolorized with Darco. Acidification of the filtered solution gave a white solid which was removed by filtration, washed with water and dried. The solid, which contained bromine, was recrystallized twice from benzene to give 3'-bromo-3-biphenylcarboxylic acid, melting at 190-191°.

*Anal.* Calcd. for C<sub>15</sub>H<sub>9</sub>O<sub>2</sub>Br: C, 56.34; H, 3.27. Found: C, 56.76; H, 3.54.

Precipitate A consisted primarily of the monobasic acid as shown by its almost complete liquefaction at a temperature of 190° and by its separation into the mono- and dibasic acids by stepwise acidification of its solution in dilute sodium carbonate. Precipitate B was primarily the dibasic acid as shown by the melting point, roughly determined as above 300°.

### Summary

3,3'-Dibromobiphenyl has been synthesized from *o*-nitrobromobenzene by zinc-alkali reduction to 2,2'-dibromohydrazobenzene, rearrangement of the hydrazo compound to 3,3'-dibromobenzidine, and deamination of the benzidine by reaction of the tetrazonium salt with hypophosphorous acid. A dilithium compound and a difunctional Grignard reagent were prepared from 3,3'-dibromobiphenyl. From the monofunctional Grignard reagent the new 3'-bromo-3-biphenylcarboxylic acid was obtained.

The melting points of the 2,2'-dibromohydrazobenzene and 3,3'-dibromobenzidine prepared in this work do not agree with those of substances previously considered to have these structures.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## The Stereochemical Course of Amine Replacement Reactions. Some Reactions of *d*-(+)-*N,N,N*-Trimethyl- $\alpha$ -phenylethylammonium Iodide

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Quaternary ammonium compounds containing benzyl groups can be used in the benzylation of the anions of such salts as sodiomalonic ester,<sup>2</sup> sodium cyanide,<sup>3</sup> sodium phenolate,<sup>3,4</sup> and the sodium salts of carboxylic acids<sup>3</sup> or of sulfur containing acids.<sup>3,5</sup> These reactions appear to be completely analogous to the formation of benzyl alcohol<sup>6</sup> and benzyl chloride<sup>7</sup> by thermal decom-

position of quaternary benzylammonium hydroxides and chlorides, and it would be expected that all of these processes occur by similar mechanisms.

Evidence has been presented to show that both methanol and benzyl alcohol are formed from benzyltrimethylammonium hydroxide by reactions having S<sub>N</sub>2 mechanisms.<sup>8,9</sup> Reactions proceeding by such mechanisms occur with complete inversion of configuration when they take place at an asymmetric carbon atom; other mechanisms result in partial or complete racemization or in retention of configuration.<sup>10</sup> Read and

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(2) Snyder, Smith and Stewart, *THIS JOURNAL*, **66**, 200 (1944).

(3) von Meyer, *Abhandl. math.-phys. Klasse sachs. Gesellschaft Wiss.*, **31**, 179 (1908); [*Chem. Zentr.*, **80**, II, 1800 (1909)].

(4) Hla Baw, *Quart. J. Indian Chem. Soc.*, **3**, 101 (1926); [*C. A.*, **20**, 3695 (1926)].

(5) Snyder and Speck, *THIS JOURNAL*, **61**, 668, 2895 (1939).

(6) von Braun, *Ann.*, **362**, 1 (1911).

(7) Michler and Gradmann, *Ber.*, **10**, 2078 (1877).

(8) Hughes and Ingold, *J. Chem. Soc.*, 69 (1933).

(9) Hughes, Ingold and Patel, *ibid.*, 526 (1933).

(10) Cowdrey, Hughes, Ingold, Masterman and Scott, *ibid.*, 1252 (1937).