

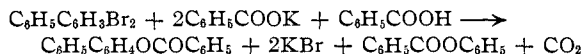
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Synthesis of 4- and 5-Phenylresorcinols. The "Positive" Bromine of the Dibromobiphenyls

BY C. M. SUTER AND PERRIN G. SMITH

Notwithstanding the profusion of resorcinol derivatives described in the literature, no account of the preparation or properties of the 4- or 5-phenylresorcinol has appeared.¹ Of the homonuclear dihydroxybiphenyls the 3,4-,² 2,5-,³ and 2,6-⁴ isomers are known. Including the compounds characterized in this investigation only the 2,3-dihydroxybiphenyl remains unreported.

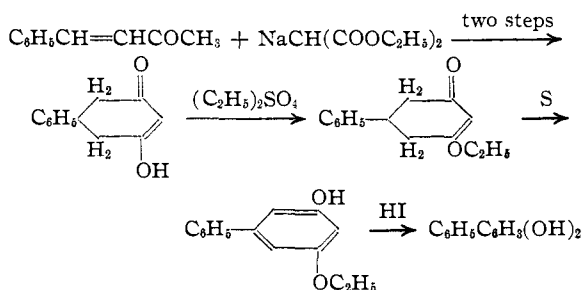
In the first method of synthesis investigated the attempt was made to replace the bromine atoms of 2,4- and 3,5-dibromobiphenyls by hydroxyls. When the 3,5-isomer was heated with potassium benzoate in boiling (250°) benzoic acid in the presence of a trace of copper and the resulting esters hydrolyzed, there were isolated an 82% yield of 3-hydroxybiphenyl and a small amount of phenol. Similar treatment of 2,4-dibromobiphenyl gave a 10% yield of *p*-hydroxybiphenyl and phenol. The over-all reaction may be written



The only aromatic compounds previously shown to contain "positive halogen" with the exception of iodomesitylene are bromine and iodine derivatives of phenols or amines in which the halogen is ortho or para to the hydroxy or amino group.⁵ It seems probable that whether or not a given halogen atom is "positive" will depend upon the solvent and reagent used in its solvolysis. Perhaps with potassium phenoxide in phenol, for example, the bromines would be replaced by phenoxy groups. The results obtained in this investigation serve to emphasize the suggestion of Nicolet that "Failure to react is no adequate indication of polar structure." It will be of interest to investigate the behavior of other comparatively inert compounds at high temperatures. The apparent oxidation of benzoic acid (or potassium benzoate) to phenol requires fur-

ther study before an adequate mechanism can be suggested.

Both phenylresorcinols were finally obtained by dehydrogenation methods. The 5-isomer resulted from the action of selenium or sulfur upon phenyldihydroresorcinol ethyl ether⁶ followed by deethylation. When sulfur was employed reaction occurred rapidly at 260–265°



whereas with selenium long heating at 285° was necessary and the yield was much lower. Since an attempt to dehydrogenate 4-cyclohexylresorcinol gave only tarry products it was necessary to make use of the dibenzoate. This with sulfur at 300° gave a product from which upon hydrolysis a 15% yield of 4-phenylresorcinol was isolated. With selenium none of the desired product could be obtained.

The two arylresorcinols are rather ineffective as bactericidal agents.⁷ Against *staphylococcus aureus* at 37° 4-phenylresorcinol gave a phenol coefficient of 14 while the value for the 5-isomer was less than 12. The stock solutions were made up in 20% ethanol.

Experimental

Dibromobiphenyls.—The synthesis of 2,4-dibromobiphenyl devised by Scarborough and Blakey⁸ necessitates no less than four steps and the first of these, the preparation of 3-nitrobiphenyl, gives only about a 15% yield. In the present investigation the dibromo compound was prepared directly from 2,4-dibromoaniline and benzene by a procedure similar to that developed by Gomberg and Bachmann⁹ for making 4-bromobiphenyl.

(6) Vorländer, *Ber.*, **27**, 2053 (1894); Michael and Freer, *J. prakt. Chem.*, [2] **43**, 390 (1891).

(7) We are indebted to Dr. Maurice L. Moore, Sharp and Dohme, for the bacteriological data presented here.

(8) Blakey and Scarborough, *J. Chem. Soc.*, 3000 (1927); see also Case, *This Journal*, **58**, 1247 (1936).

(9) Gomberg and Bachmann, *ibid.*, **46**, 2339 (1924).

(1) 4-Phenylresorcinol is mentioned in a recent patent (Christiansen, Moness and Harris, U. S. Patent 2,014,720, Sept. 17, 1935) but no information as to preparation or properties was supplied.

(2) Norris, Macintire and Corse, *Am. Chem. J.*, **29**, 125 (1903); Harvey, U. S. Patent 1,952,755; *C. A.*, **28**, 3426 (1934).

(3) Borsche, *Ann.*, **312**, 221 (1900).

(4) Kubota, Fujimura and Akashi, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **2**, 185 (1925); *C. A.*, **19**, 2334 (1925).

(5) Nicolet and co-workers, *This Journal*, **43**, 2081 (1921); **49**, 1796, 1801, 1806, 1810 (1927).

A mixture of 20 g. (0.08 mole) of 2,4-dibromoaniline and 17 ml. of concentrated hydrochloric acid was heated and then chilled rapidly to 0°. Over an eight-hour period there was added with stirring 5.5 g. (0.08 mole) of sodium nitrite in a little water. Then 250 ml. of benzene was added and 2% excess of 25% sodium hydroxide was dropped in at a rate just sufficient to keep the benzene from solidifying. The mixture was allowed to come slowly to room temperature and after removal of the excess benzene the residue was fractionated. There was obtained 5.5 g. (22%) of material distilling at 125° (2 mm.). Scarborough and Blakey report 235° (15 mm.). Other properties found were d_{25}^{25} , 1.7197; n_D^{25} , 1.6541; $[M]$ (calcd.) 65.94; $[M]$ (found) 66.50.

The 3,5-dibromobiphenyl was prepared according to the method of Scarborough and Waters¹⁰ from 4-aminobiphenyl in 76.5% yield. It distilled at 199° (11 mm.) and after two crystallizations from methanol melted at 41–41.5°. Scarborough and Waters reported a m. p. of 15°.

Action of Potassium Benzoate upon 3,5-Dibromobiphenyl.—To 135 g. (1.1 moles) of benzoic acid at 200° was added gradually 8.5 g. (0.15 mole) of potassium hydroxide. Upon raising the temperature to the boiling point (250°) a clear solution resulted. To this was added 11.2 g. (0.036 mole) of 3,5-dibromobiphenyl and 0.1 g. of copper powder; the mixture was refluxed for five hours and poured on a metal tray to cool. It was then ground in a mortar, the benzoic acid dissolved in dilute sodium hydroxide, and the esters extracted with benzene. The benzene was removed and the esters hydrolyzed with alcoholic sodium hydroxide, the hydrolysis mixture diluted with water, acidified, and extracted with ether. Benzoic acid was removed from the ether by washing with bicarbonate and the ether-soluble residue distilled. There were obtained 1.1 g. of phenol, identified as tribromophenol, m. p. 95°, and 5 g. (82%) of 3-hydroxybiphenyl,¹¹ m. p. 76°.

Not more than 10 g. of potassium hydroxide should be used for each 100 g. of benzoic acid as the reaction mixture then does not reflux smoothly and tar formation is noticeable.

Action of Potassium Benzoate upon 2,4-Dibromobiphenyl.—From 19 g. of 2,4-dibromobiphenyl, 160 g. of benzoic acid, 13 g. of potassium hydroxide and 0.1 g. of copper powder heated at 250° for four and one-half hours were obtained 2.0 g. of phenol, and on sublimation under high vacuum, 1.0 g. (9.7%) of 4-hydroxybiphenyl, m. p. 163°.

5-Phenyldihydroresorcinol Ethyl Ether.—To 250 ml. of an aqueous solution of 78 g. (0.415 mole) of 5-phenyldihydroresorcinol⁶ and 19 g. (0.475 mole) of sodium hydroxide at 100° was added slowly with stirring 73.1 g. (0.475 mole) of ethyl sulfate. The alkaline solution was extracted twice with ether and the extract fractionated at 1 mm. There was obtained 19.5 g. of the ether which solidified upon chilling and melted at 43°. Acidification of the alkaline solution remaining from the reactions gave 48 g. of unreacted 5-phenyldihydroresorcinol. The yield of the ethyl ether based upon unrecovered starting ma-

terial was 57%. Previously the ether has been obtained from heating the phenyldihydroresorcinol with alcohol and acid.⁶

5-Phenylresorcinol. A. By the Selenium Method.—Five reaction mixtures each consisting of 2 g. of 5-phenyldihydroresorcinol ethyl ether and 0.73 g. of selenium were heated together in a salt-bath at 285° for twelve hours when evolution of hydrogen selenide had practically ceased. Earlier experiments had shown that better yields were obtained when smaller amounts of materials were employed. The combined reaction mixtures were treated with hot benzene, filtered and the benzene removed. The residue was shaken with ether and dilute potassium hydroxide, the alkaline extract separated and acidified and the phenolic material removed by ether. The residue from the ether was refluxed with 40 ml. of glacial acetic acid and 15 ml. of 58% hydriodic acid for fifteen hours. By diluting with water, neutralizing until just acid to congo red and extraction with ether there was obtained a product which after two crystallizations from boiling water melted at 157°. The yield was 1.25 g. or 14.3% based upon the dihydroresorcinol ethyl ether.

B. By the Sulfur Method.—A mixture of 9.85 g. of the ethyl ether and 1.5 g. (2% excess) of sulfur was heated at 260–265° for seventy-five minutes when the evolution of hydrogen sulfide had practically ceased. By proceeding as under A there was obtained 2.8 g. of 5-phenylresorcinol, m. p. 156–157°, a yield of 33%. Further crystallization raised the melting point to 157–158°.

*Anal.*¹² Calcd. for C₁₂H₁₀O₂: C, 77.41; H, 5.41. Found: C, 77.19; H, 5.35.

4-Phenylresorcinol.—After an unsuccessful attempt to prepare 4-cyclohexylresorcinol by the method of Phillips¹³ it was obtained by an adaptation of the method employed by Chichibabin¹⁴ in the synthesis of various secondary and tertiary alkylphenols and resorcinols. To a solution of 110 g. (1 mole) of resorcinol in 250 g. of 85% phosphoric acid heated and stirred at 140° was added during one hour a solution of 100 g. (1 mole) of cyclohexanol in 225 g. of the phosphoric acid. After heating for three hours longer at 140°, the reaction mixture was diluted with water and extracted with benzene. The benzene solution was washed twice with 15% sodium hydroxide; this was then acidified and extracted and the product distilled under reduced pressure. Crystallization from chloroform gave 115 g. or 60% of the theoretical amount of material, m. p. 124°. The dibenzoate¹⁵ was prepared by the use of benzoyl chloride and pyridine. It melted at 88°.

A mixture of 2 g. of cyclohexylresorcinol dibenzoate and 0.48 g. of sulfur was heated at 300° for one hour. Five such mixtures were dissolved in hot alcohol, filtered and an equal volume of water containing 6 g. of sodium hydroxide added. After refluxing for two hours and ether extracting the mixture was acidified and the ether soluble product distilled with superheated steam. After removal of the benzoic acid at 120° the steam temperature was raised to 185° and the phenylresorcinol came over. After treat-

(12) We are indebted to Mr. Robert Schuetz for the carbon and hydrogen analyses.

(13) Phillips, U. S. Patent 1,650,036; C. A., **22**, 434 (1928).

(14) Chichibabin, *Compt. rend.*, **198**, 1239 (1934).

(15) Lilly and Garland, *This Journal*, **52**, 2112 (1930).

(10) Scarborough and Waters, *J. Chem. Soc.*, 557 (1926).

(11) Jacobsen and Loeb, *Ber.*, **36**, 4085 (1903); Errera and La Spada, *Gazz. chim. ital.*, **35**, II, 552 (1905); Colbert, Meigs and Jenkins, *This Journal*, **59**, 1122 (1937).

ment with petroleum ether to remove unchanged cyclohexylresorcinol and three crystallizations from carbon tetrachloride there was obtained 0.71 g. of product, m. p. 145°. The yield was 15%.

*Anal.*¹³ Calcd. for C₁₂H₁₀O₂: C, 77.41; H, 5.41. Found: C, 77.19; H, 5.65.

Summary

1. The action of potassium benzoate upon 3,5-

and 2,4-dibromobiphenyls gives monohydroxybiphenyl benzoates, one bromine being replaced by hydrogen.

2. 4-Phenylresorcinol and the 5-isomer have been synthesized by dehydrogenation reactions.

3. These resorcinol derivatives have but little activity as bactericidal agents.

EVANSTON, ILLINOIS

RECEIVED NOVEMBER 21, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

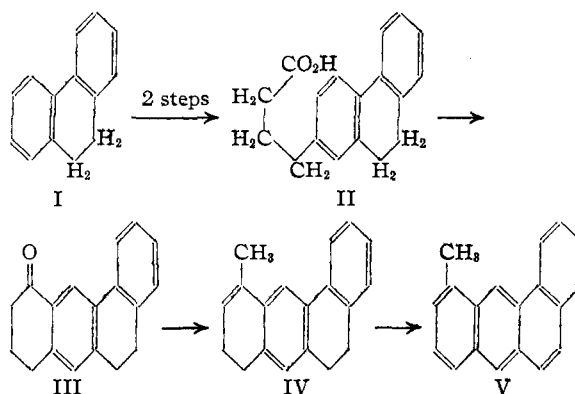
8-Methyl-1,2-benzanthracene

BY LOUIS F. FIESER AND WILLIAM S. JOHNSON¹

While one of two hydrocarbons recently described by Cook and Robinson² corresponds well in properties with the sample of 1'-methyl-1,2-benzanthracene previously synthesized in this Laboratory,³ the substance which they regard as 8-methyl-1,2-benzanthracene differs considerably from a hydrocarbon believed to have this structure which we had synthesized at the time of the appearance of their paper. After repeating the preparation with the same results and investigating the purity and identity of the intermediates, we are now placing our observations on record.

The starting material, 9,10-dihydrophenanthrene, was prepared according to Burger and Mosettig⁴ and Durland and Adkins⁵ by hydrogenation of phenanthrene over copper chromite catalyst. By conducting the reaction at 160° without solvent and avoiding the formation of the difficultly separated *s*-octahydride, it was found possible to obtain material of excellent purity (m. p. 32-33°) after a single fractionation at 7-8 mm. from unchanged phenanthrene. Condensation of this material with succinic anhydride in the Friedel and Crafts reaction gave the β -(9,10-dihydro-2-phenanthroyl)-propionic acid of Burger and Mosettig⁶ in a satisfactory condition in 96% yield. This was reduced to II as described by these authors, but since they had found cyclization with 85% sulfuric acid to give a low

yield (30%) of the ketone III, other methods were investigated. Ring closure with zinc chloride in



acetic acid-anhydride solution nearly doubled the yield, but it was found still more satisfactory to treat the acid in benzene with phosphorus pentachloride, followed by aluminum chloride.

The 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene (III) obtained easily by this method in 63% yield (pure) was found to exist in two polymorphic forms of different melting point, one of which corresponded to the sole product encountered by Burger and Mosettig, who established the structure of their substance by conversion to 1,2-benzanthracene. It seemed desirable to eliminate any doubt about the direction of ring closure under the conditions employed in the present work, and consequently a sample obtained with the use of phosphorus and aluminum chlorides was reduced and dehydrogenated. The sole product was 1,2-benzanthracene. It was also found that both crystalline modifications can be obtained from ketone prepared by cyclization with sulfuric acid and that the two forms

(1) Holder of the John Woodruff Simpson Fellowship from Amherst College.

(2) J. W. Cook and Mrs. A. M. Robinson, *J. Chem. Soc.*, 505 (1938).

(3) Fieser and Seligman, *This Journal*, **60**, 170 (1938).

(4) Burger and Mosettig, *ibid.*, **58**, 1857 (1936).

(5) (a) Durland and Adkins, *ibid.*, **59**, 135 (1937); (b) **60**, 1501 (1938).

(6) Burger and Mosettig, *ibid.*, **59**, 1302 (1937).