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A FACILE PHENOL SYNTHESIS.

AN IMPROVED ROUTE TO 6-METHOXY-2-TETRALONE.

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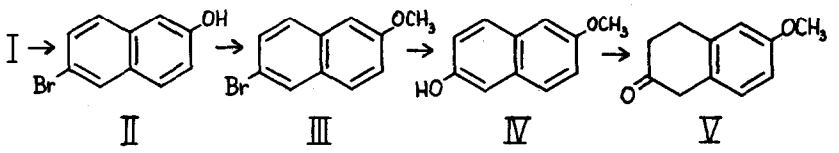
The oxidation of alkyl boranes produced from the hydroboration of an olefin is a familiar reaction (1). Arene boronic acids undergo a similar reaction to yield a phenol (2). Although the reaction has existed for some time no synthetic use has been made of it. We wish to report on this reaction as a useful phenol synthesis applied to the preparation of 6-methoxy-2-tetralone.

Derivatives of 2,6-dihydroxynaphthalene have been valued as starting material for natural product syntheses. The original synthesis of this valuable material was a potassium hydroxide fusion of the sulfonic acid salt (3). Since then other methods have appeared (4). We have also developed several routes (5) to the desired naphthalene intermediate but will discuss only the following scheme at this time.



II III IV V

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The readily available starting material, 6-bromo-2-naphthol (II) was prepared from 144 g of 2-naphthol (I) according to published procedures (6). The crude product contained some tin salts but these did not interfere with subsequent reactions.

Methylation of the crude solid was accomplished by dissolving the solids in 1 liter of 1.5 N sodium hydroxide. The solution was filtered, placed in a 4 liter beaker and cooled. To the cold solution was added with stirring 95 ml of dimethyl sulfate in one portion. After a few minutes the product precipitated out as a solid mass. This was broken up and washed with 500 ml of 1N NaOH. The filtrates were combined and treated with 20 ml of dimethyl sulfate. After thirty minutes the product was collected and combined with the previous material. The product (III) was dried azeotropically with benzene and then distilled through a short path tube. A 71.8% yield of white solid 6-methoxy-2-naphthol (III) was obtained, m.p. 100-103; lit. (4b): 102-104. This was sufficiently pure for the subsequent reaction.

Arene boronic acids have been prepared from the reaction of a Grignard reagent and a borate ester (7). Although modifications were introduced (8) to increase the yield of phenyl boronic acid isolated, we found that a simplified procedure could be used since the boronic acid was not isolated. A further modification in the preparation of the Grignard reagent from (III) was made. Whereas ethyl ether has been the solvent employed to date (9) we found the bromide to be relatively insoluble in this solvent and thus used tetrahydrofuran. This solvent also has the advantage of rendering the subsequent oxidation more homogeneous.

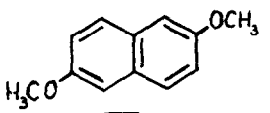
The Grignard of the methoxybromide (III) was prepared from 23.7 g (0.10 mole) III and 3.6 g (0.15 mole) magnesium which were placed in a reaction flask. The tetrahydrofuran was refluxed over lithium aluminum hydride and distilled into the flask containing the solids until 100 ml had

been added. The reaction began immediately and continued for a half hour. Additional heat was applied for another half hour to reflux the mixture. The resulting black solution was filtered into a dropping funnel.

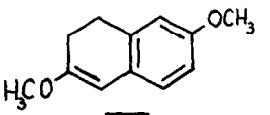
The boronic acid was prepared and oxidized to the phenol without isolation of the acid. The Grignard solution was added over ten minutes to an ice cold solution of 15 ml trimethyl borate in 50 ml of anhydrous ethyl ether. The trimethyl borate had previously been purified with lithium chloride (10). The reaction immediately formed a white paste which was stirred for fifteen minutes.

Basic oxidations of this solution yielded very little product. Thus we turned to mildly acidic oxidations (11). To the cold boronic ester mixture was added a cold solution of 300 ml of 15% hydrogen peroxide containing 20 g of ammonium chloride. The reaction mixture was stirred for one hour while the volatile solvents were removed with an aspirator thereby cooling the solution. A white precipitate separated. This was collected by filtration. The product was purified by dissolving it in aqueous base, filtering and precipitating the phenol with carbon dioxide. The solids were collected and dried giving 14.0 g (80.5%) of 6-methoxy-2-naphthol (IV), m.p. 145-147; lit.: 150-151 (4b). The NMR spectrum in deutero-chloroform showed absorption centered at δ = 3.93 (singlet, OCH_3), 4.9 (broad peak, OH), 7.4 (broad multiplet 7.0-7.8, six aromatic protons). The phenol could be methylated in the usual fashion to give 2,6-dimethoxynaphthalene (VI), m.p. 151-152 (golden plates); lit.: 150 (3).

The reduction of 2,6-dimethoxynaphthalene has been reported to give conjugated enol ether (VII) (4a). We have confirmed this by examining the NMR spectrum in carbon tetrachloride of the product (VII) from sodium reduction in 2-methoxyethanol. The spectrum showed absorption centered at δ = 2.5 (symmetrical multiplet A_2B_2-CH_2-CH_2-), 3.57 and 3.63 (singlets, two -OCH_3 groups), 5.32 (singlet, CH-) and 6.54 (broad multiplet 6.28-6.80,



VI



VII

three aromatic protons). The enol ether could be hydrolyzed to the desired tetralone (V).

Starting with 20 g of 2,6-dimethoxynaphthalene dissolved in 200 ml of boiling 2-methoxyethanol and 30 g of sodium, which was added over fifteen minutes, there was obtained 8.72 g of tetralone (V) upon hydrolysis of the enol ether. This product distilled at b.p. 117-119 /0.5 mm; lit.: 111-114.5 /0.2 mm (4d). The liquid crystallized on standing. This gave a positive "tetralone blue test" (12).

A greater simplification was achieved by the direct reduction of the phenol (IV) to the ketone (V). Using the procedure of Nelson et. al (4d), 6-methoxy-2-naphthol was reduced to 6-methoxy-2-tetralone in 70% yield.

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REFERENCES

(1) H. C. Brown, Hydroboration, W. A. Benjamin, Inc., New York (1962).

(2) A. D. Ainley and F. Challenger, J. Chem. Soc., 2171 (1930).

(3) R. Willstatter and J. Parnas, Ber., 40, 1406 (1907).

(4)a. R. Robinson and F. Weygand, J. Chem. Soc., 386 (1941).

b. H. E. French and K. Sears, J. Am. Chem. Soc., 70, 1279 (1948).

c. M. Gates and W. G. Webb, J. Am. Chem. Soc., 80, 1186 (1958).

d. N. A. Nelson, R. S. P. Hsi, J. M. Schuck and L. D. Kahn, J. Am. Chem. Soc., 82, 2573 (1960).

e. J. H. Burckhalter and J. R. Campbell, J. Org. Chem., 26, 4232 (1961).

(5) R. L. Kidwell and R. E. Cosgrove, Unpublished results.

(6) C. F. Koelsch, Organic Synthesis Vol. 20, p. 18, John Wiley and Sons, Inc., New York (1940).

(7) E. Khotinsky and M. Melamed, Ber., 42, 3090 (1909).

(8) F. R. Bean and J. R. Johnson, J. Am. Chem. Soc., 54, 4415 (1932).

(9) L. Horner, K. Teichmann, K. Weber and E. Geyer, Ber., 98 (2), 1233 (1965).

(10) H. I. Schlesinger, H. C. Brown, D. L. Mayfield and J. R. Gilbreath, J. Am. Chem. Soc., 75, 213 (1953).

(11) H. G. Kuivila, J. Am. Chem. Soc., 76, 870 (1954).

(12) J. W. Cornforth, R. H. Cornforth and R. Robinson, J. Chem. Soc., 689 (1942).