[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, PENNSYLVANIA STATE UNIVERSITY]

ALKYLATION OF HYDROQUINONE AND ITS DERIVATIVES[1]

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Hydroquinone has been C-alkylated with tertiary butyl or amyl alcohols and/or their corresponding chlorides and olefins by several techniques (1–6). Cyclohexene has also been used to alkylate hydroquinone (7). In general only dialkyl derivatives were isolated. The one case where a monoalkylhydroquinone was found was in the reaction of hydroquinone with 2-propanol in the presence of HF. A 39% yield of 2-isopropylhydroquinone was reported (3). Surprisingly, under these conditions it was reported that attempts to prepare the dialkylated product led to elimination of a hydroxyl group and trialkylation to 2,4,6-triisopropylphenol (3).

The alkylation of hydroquinone and its derivatives does not seem to have been extended to other alkyl groups and one reference (4) specifically reports the failure of 1-methylcyclohexanol to alkylate hydroquinone or its diethyl ether. Other workers (7) have also reported difficulty in obtaining satisfactory yields in this type of reaction.

We have found that 1 and 2-methylcyclohexanol readily alkylate derivatives of hydroquinone in the presence of sulfuric acid. The structures of the products have been assigned on the basis of the well-known rules for aromatic substitution and no further structure proof has been attempted.

1,4-Dimethoxybenzene (II) was alkylated with 1-methylcyclohexanol (I) in sulfuric acid of concentrations ranging from 75–90% at a temperature of 0–5° to give 2,5-bis-(1′-methylcyclohexyl)-1,4-dimethoxybenzene. The yields based on I ranged from 41–69%. The best yield, described in the Experimental section, was obtained when the least amount of acid was used, so that it is probable that conditions could be found on further study for obtaining even higher yields. The dialkylated compound was the major product even when a two-fold excess of II was used. No monoalkylated product was isolated, and if any formed, the yield was less than 10%.

II was alkylated with 2-methylcyclohexanol to give the same product as was obtained when 1-methylcyclohexanol (I) was used as the alkylating agent. The yields were comparable. II was also alkylated with cyclohexene to give 2,5-dicyclohexyl-1,4-dimethoxybenzene, but the yield was only 21%.

Hydroquinone was dialkylated with I. Monoalkylated products were obtained by treating 2-methyl or 2-chloro-1,4-dimethoxybenzene with I.

Several reactions were run on the alkylated products. An unsuccessful attempt was made to convert the product from I and II to the product from I and hydroquinone by cleavage of the two methyl ether linkages using hydriodic acid. The ether linkages were cleaved but the reaction was accompanied by dealkyla-

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tion so that the sole product was hydroquinone in 90% yield. This reversal of the Friedel-Crafts alkylation is characteristic of highly-hindered *ortho*-substituted aromatic ethers (8).

An unsuccessful attempt was made to reduce the product from I and either II or its 2-methyl derivative by treating them with sodium and ethanol in liquid ammonia.

The product from I and hydroquinone was insoluble in aqueous alkali. It was easily oxidized to the corresponding quinone with silver oxide.

The following sequence of reactions shows promise of being a practical route to the synthesis of monoalkyl-1,4-dimethoxybenzenes. 2-Chloro-1,4-dimethoxybenzene was alkylated with I to give a 50% yield of distilled product which appeared to be a mixture of 5- and 6-(1′-methylcyclohexyl)-1,4-dimethoxybenzenes. It partially crystallized. The crystalline product (13%) was treated with sodium and alcohol which removed the chloro substituent. The monosubstituted dimethoxybenzene was not isolated in pure form but was realkylated with I to give 2,5-bis-(1′-methylcyclohexyl)-1,4-dimethoxybenzene identical to that obtained by direct alkylation of II.

EXPERIMENTAL

General method for the alkylations. The aromatic compound was dissolved in sulfuric acid and cooled to 0°. The alkylating agent was added dropwise to the stirred solution as rapidly as possible without raising the temperature above 5°. This order of mixing was originally chosen in an attempt to obtain monoalkylated products and is probably not optimum for obtaining the dialkylated products actually isolated. Stirring of the reaction mixture was continued unless the solution became homogeneous. The temperature was maintained at 0–5° throughout. After adding the reaction mixture to ice, the crude product was recrystallized if solid, and ether-extracted and distilled if an oil. The per cent yield is based on the alkylating agent unless otherwise noted.

Hydroquinone + I. I (3.1 g.) was added to a solution of an equimolar amount (3.0 g.) of hydroquinone in 15 ml. of 75% sulfuric acid. After one hr., the reaction mixture was added to ice. The crude product was 3.2 g. of white solid, m.p. 105–161°. Recrystallization from pentane gave 1.8 g. (44%) of 2,5-bis-(1′-methylcyclohexyl)-1,4-hydroquinone, m.p. 168–174°.

Anal. Calc'd for $C_{20}H_{30}O_2$: C, 79.4; H, 10.0.
Found: C, 79.1; H, 10.1.

2,5-Bis-(1′-methylcyclohexyl)-1,4-benzoquinone. A solution of 0.30 g. of 2,5-bis-(1′-methylcyclohexyl)-1,4-hydroquinone in 10 ml. of ether was shaken with 0.9 g. of freshly prepared silver oxide and 1.5 g. of anhydrous sodium sulfate for one hr. The solid was removed by filtration and washed with ether until the washings were no longer yellow. Removal of the ether left 0.224 g. (75%) of the corresponding quinone, m.p. 144–148.5°. Several recrystallizations from pentane-ethanol gave yellow needles, m.p. 148–149°.

Anal. Calc'd for $C_{20}H_{28}O_2$: C, 80.0; H, 9.4.
Found: C, 80.1; H, 9.0.

1,4-Dimethoxybenzene (II) + I. I (2.5 g.) was added to an equimolar amount (3.0 g.) of II dissolved in 5 ml. of 90% sulfuric acid. After 30 hrs. the reaction mixture was added to ice. The crude product was 6.6 g. of white solid, m.p. 57–102°. Recrystallization from aqueous ethanol gave 2.5 g. (69%) of white plates of 2,5-bis-(1′-methylcyclohexyl)-1,4-dimethoxybenzene, m.p. 128–130°. The highest m.p. observed was 130.5–131°.

Anal. Calc'd for $C_{22}H_{34}O_2$: C, 80.0; H, 10.4.
Found: C, 79.9; H, 10.3.

A solution of 0.5 g. of this compound in 6 ml. of hydriodic acid (*sp. gr.* 1.50) and 18 ml. of acetic acid was refluxed for three hrs. The solution was diluted with water and ether-extracted. The ether was removed and the crystals were washed with pentane leaving 0.15 g. (90%) of hydroquinone, m.p. 166–169°.

2-Methyl-1,4-dimethoxybenzene + I. I (10 g., 0.096 mole) was added to a solution of 12 g. of 2-methyl-1,4-dimethoxybenzene (0.079 mole) in 25 ml. of 85% sulfuric acid. After six hrs., the reaction mixture was added to ice and neutralized with base. The oily product was extracted with ether, dried over calcium chloride, and distilled. The yield of 5-(1′-methylcyclohexyl)-2-methyl-1,4-dimethoxybenzene, b.p. 179–182°/17 mm., was 12.1 g. (62% based on 2-methyl-1,4-dimethoxybenzene). An attempt to reduce this compound with sodium and ethanol in liquid ammonia resulted in purifying the compound so that it crystallized, m.p. 26–27°.

Anal. Calc'd for $C_{16}H_{24}O_2$: C, 77.4; H, 9.7.

Found: C, 77.2; H, 9.7.

2-Chloro-1,4-dimethoxybenzene + I. I (15 g., 0.13 mole) was added to a solution of 10 g. (0.058 mole) of 2-chloro-1,4-dimethoxybenzene in 50 ml. of 90% sulfuric acid. After nine hrs., the reaction mixture was added to ice. The crude oily product was extracted with benzene, dried over calcium chloride, and distilled. The yield of product, b.p. 208–216°/20 mm., was 7.8 g. (50%). The distilled product partially crystallized to give 2.8 g. (13%) of white crystals. The yields are based on 2-chloro-1,4-dimethoxybenzene. Two recrystallizations raised the m.p. to 65.5–67°.

Anal. Calc'd for $C_{15}H_{21}ClO_2$: C, 67.0; H, 7.9.

Found: C, 66.8; H, 7.7.

The distilled product is probably a mixture of 5- and 6-(1′-methylcyclohexyl)-2-chloro-1,4-dimethoxybenzenes. It is not known whether the crystalline product was the 5 or 6 isomer.

A solution of 0.27 g. of the crystalline product in 75 ml. of ethanol was refluxed while 7 g. of sodium was added in small pieces over three hrs. Water was added and the solution was neutralized with dilute hydrochloric acid. The solution was extracted with ether and dried over calcium chloride. Removal of the ether left a residual oil which is probably 2-(1′-methylcyclohexyl)-1,4-dimethoxybenzene. It was alkylated with I to give 0.15 g. (50%) of 2,5-bis-(1′-methylcyclohexyl)-1,4-dimethoxybenzene, identical with a sample prepared by direct alkylation of II.

1,4-Dimethoxybenzene (II) *+ 2-methylcyclohexanol.* 2-Methylcyclohexanol (2.5 g.) was added to an equimolar amount of II (3.0 g.) dissolved in 15 ml. of 90% sulfuric acid. After 20 hrs., the reaction mixture was added to ice yielding 4.1 g. of white solid, m.p. 79–100°. Recrystallization from ethanol gave 2.3 g. (64%) of 2,5-bis-(1′-methylcyclohexyl)-1,4-dimethoxybenzene identical with a sample prepared by alkylating II with I.

Cyclohexene + II. Cyclohexene (1.8 g.) was added to an equimolar amount of II (3.0 g.) dissolved in 15 ml. of 94% sulfuric acid. The reaction time was 30 min. The crude white crystals, 1.0 g., were recrystallized from ethanol to give 0.7 g. (21%) of 2,5-dicyclohexyl-1,4-dimethoxybenzene, m.p. 157–159°. Two recrystallizations raised the m.p. to 160–161° in agreement with the reported value of 162–162.5° (7).

SUMMARY

1,4-Dimethoxybenzene (II) and its 2-chloro and 2-methyl derivatives have been alkylated with 1-methylcyclohexanol (I) using sulfuric acid as the catalyst. Yields ranged from 40–70%. II gave only dialkylated product despite a choice of reaction conditions that would favor monoalkylation. The other two compounds gave monoalkylated products. An indirect method is presented for obtaining the monoalkylated product from II.

2-Methylcyclohexanol gave the same product with II as did 1-methylcyclohexanol (I) and in comparable yield.

Cyclohexene dialkylated II in 21% yield, and I dialkylated hydroquinone in 44% yield.

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