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cis- and *trans-*1,4-Bis-(*p*-methoxyphenyl)-cyclohexane

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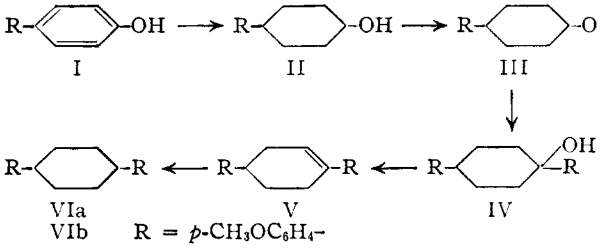
4-*p*-Methoxyphenylcyclohexanone has been synthesized and from it the carbinol, 1,4-bis-(*p*-methoxyphenyl)-cyclohexanol. The latter was dehydrated and hydrogenated to give *cis-* and *trans-*1,4-bis-(*p*-methoxyphenyl)-cyclohexane.

With the preparation of these compounds we have characterized five of the six geometric isomers of bis-(*p*-methoxyphenyl)-cyclohexane. The crystalline 1,2-[1] and 1,3-[2,3] isomers and an oily 1,3-[2] isomer have been reported previously.

Although the 1,4-diarylcyclohexanes might have been expected[4] from the acid-catalyzed condensation of anisole with cyclohexene derivatives, none was obtained.[2] More recently an attempt to promote self-condensation of ethyl anisylsuccinate, followed by cyclization, with sodium ethoxide or sodium failed to yield the desired intermediate, 2,5-dicarbethoxy-3,6-dianisylcyclohexanedione.[5] Again we have found addition of a Grignard reagent to the properly substituted cycloalkanones to be the best synthetic route to these compounds.



It was expected that hydrogenation of I in the presence of Raney nickel would afford the most likely method of preparing one or both cyclohexanols, II. This expectation was based on the more stringent conditions required for reduction of simple phenolic ethers vis-a-vis the parent phenols,[6,7] coupled with the increased preference for reduction of the phenolic nucleus in polynuclear phenols where strong base is an adjunct to the nickel catalyst.[7–10] Our results showed, however, that about 15% of the unchanged phenol remained after the theoretical quantity of hydrogen had been absorbed and that the yield of the higher-melting 4-(*p*-methoxyphenyl)-cyclohexanol averaged 27% in three trials.

We found the copper–chromium oxide catalyst, which has been useful for reduction of the phenolic ring in other systems,[11] to be superior here in spite of the higher temperatures and pressures required. The reaction stopped with the reduction of one ring; no phenolic material was recovered and the crystalline cyclohexanol was isolated in 46% yield.

4-(*p*-Methoxyphenyl)-cyclohexanone was obtained by dichromate or Oppenauer oxidation of II. This ketone and *p*-methoxyphenylmagnesium bromide afforded, in one instance, a 23% yield of 1,4-bis-(*p*-methoxyphenyl)-cyclohexanol. The carbinol, IV, was dehydrated in phosphoric acid, yielding 1,4-bis-(*p*-methoxyphenyl)-cyclohexene (V). The latter occurred also as the principal product in subsequent attempts to prepare IV. Although the phenylcycloalkyl carbinols appear to be stable,[12] this is the first instance in which we have isolated one of the *p*-methoxyphenylcarbinols in Grignard reactions.

The structures of the *cis* and *trans* isomers, VIa and VIb, have been assigned on the grounds that the higher melting compound is probably the more symmetrical *trans* isomer. The appearance of both isomers is unusual in that hydrogenation of the diarylcycloalkanes in this series has heretofore yielded only one of the stereoisomers.

Experimental

4-Methoxy-4′-hydroxybiphenyl.—*p*, *p*′-Biphenol was methylated in alkaline dimethyl sulfate by the procedure described,[13] affording a 36% yield of the monomethyl ether, m.p. 183.5–184.0°.[14] The acetate, obtained with acetic anhydride and purified three times from alcohol, melted at 112–113°. *Anal.* Calcd. for $C_{15}H_{14}O_3$: C, 74.37; H, 5.83. Found: C, 74.12; H, 5.52. This was somewhat higher than van Alpen's value of 101°. The benzoate was prepared from 0.5 g. of the phenol and 2.5 ml. of benzoyl chloride in pyridine and crystallized several times from alcohol; m.p. 156.5–157°. *Anal.* Calcd. for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.79; H, 5.18.

Attempts to prepare 4-methoxy-4′-hydroxybiphenyl by treating phenol with *p*-methoxybenzenediazonium sulfate[15] gave only 1.2% of this product. Similarly, 1.5% of the pure product resulted from treatment of the zinc chloride double salt of *p*-methoxybenzenediazonium chloride with an excess of molten phenol.[16]

4-(*p*-Methoxyphenyl)-cyclohexanol.—The phenol was purified for hydrogenation by refluxing an alcoholic solution with Raney nickel. The resulting material, 6.5 g., was hydrogenated for three hours at 245° and 6000 p.s.i. over 3 g. of copper–chromium oxide catalyst in 60 ml. of purified dioxane. An ethereal solution of the concentrated filtrate was washed with 5% sodium hydroxide solution. One of

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(1) G. P. Mueller and R. May, THIS JOURNAL, **71**, 3313 (1949).

(2) C. C. Price and G. P. Mueller, *ibid.*, **66**, 628 (1944).

(3) G. P. Mueller and C. B. Honaker, *ibid.*, **73**, 2377 (1951).

(4) C. D. Nenitzescu and D. Curcaneanu, *Ber.*, **70B**, 346 (1937); B. B. Corson and V. N. Ipatieff, THIS JOURNAL, **60**, 747 (1938).

(5) Unpublished work from the thesis submitted by Donald Pickens to the Committee on Graduate Study of the University of Tennessee in partial fulfillment of the requirements for the M.S. degree.

(6) H. Adkins, "Reactions of Hydrogen with Organic Compounds Over Copper–Chromium Oxide and Nickel Catalysts," University of Wisconsin Press, Madison, Wis., 1937, p. 58.

(7) H. E. Ungnade and A. D. McLaren, THIS JOURNAL, **66**, 118 (1944).

(8) G. Stork, *ibid.*, **69**, 576 (1947).

(9) H. Adkins and G. Krsek *ibid.*, **70**, 412 (1948).

(10) H. E. Ungnade, *J. Org. Chem.*, **13**, 361 (1948).

(11) D. M. Musser and H. Adkins, THIS JOURNAL, **60**, 664 (1938); A. L. Wilds and W. B. McCormack, *ibid.*, **70**, 4127 (1948); H. J. Dauben, Jr., B. C. McKusick and G. P. Mueller, *ibid.*, **70**, 4170 (1948).

(12) *Cf.* G. P. Mueller, J. G. Fleckenstein and W. H. Tallent, *ibid.*, **73**, 2651 (1951).

(13) J. van Alpen, *Rec. trav. chim.*, **50**, 657 (1931).

(14) All melting points were obtained on the Kofler block and are corrected.

(15) J. F. Norris, B. G. MacIntire and W. N. Corse, *Am. Chem. J.*, **29**, 120 (1903).

(16) H. H. Hodgson and C. K. Foster, *J. Chem. Soc.*, 581 (1942).

the cyclohexanols crystallized from a ligroin solution of the oily mixture; it melted at 134–137° and appeared in 46% yield. The filtrate gave 45% of an oily product which contained some cyclohexanol, since dichromate oxidation analogous to that described below yielded 20% of 4-(*p*-methoxyphenyl)-cyclohexanone. The high-melting 4-(*p*-methoxyphenyl)-cyclohexanol was purified by further recrystallization from methanol; m.p. 143.5–145°. *Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.60, 75.71; H, 8.69, 8.80. The benzoate was prepared in pyridine but resisted all ordinary attempts at crystallization. It finally crystallized after standing for a year and was crystallized further from aqueous alcohol with ease; m.p. 103.4–103.6°. *Anal.* Calcd. for $C_{20}H_{22}O_3$: C, 77.39; H, 7.15. Found: C, 77.55; H, 7.28. An attempt to prepare the 3,5-dinitrobenzoate by heating 0.1 g. of the cyclohexanol with 0.1 g. of 3,5-dinitrobenzoyl chloride in 1 ml. of pyridine for five minutes and pouring the mixture into water gave an orange precipitate. This was washed with 2% sodium bicarbonate and recrystallized several times from aqueous alcohol (charcoal), yielding colorless needles, m.p. 91.0–91.5°. This compound did not contain nitrogen and appeared to be the isomeric 4-(*p*-methoxyphenyl)-cyclohexanol. *Anal.* Found: C, 75.34; H, 8.74.

4-(*p*-Methoxyphenyl)-cyclohexanone.—Oxidation of a 2-g. sample of the crystalline cyclohexanol with sodium dichromate was accomplished by the procedure used for the preparation of 4-phenylcyclohexanone.[13] The ketone was purified through its bisulfite. It crystallized from aqueous alcohol as colorless plates, m.p. 76.0–76.2°. *Anal.* Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.42; H, 7.92. The yield of 0.3 g. (15%) was small, and 0.5 g. (25%) of pure 4-(*p*-methoxyphenyl)-cyclohexanol was recovered.

Oxidation of 7.5 g. of the cyclohexanol for 10 hours in 200 ml. of acetone and 200 ml. of benzene with 10.9 g. of aluminum *t*-butoxide[17] gave a slightly better yield, 2 g. (27%) of ketone, but with only 7% recovery of starting material.

4-(*p*-Methoxyphenyl)-cyclohexanone oxime crystallized as colorless needles from aqueous alcohol; m.p. 121.5–122°. *Anal.* Calcd. for $C_{13}H_{17}O_2N$: C, 71.20; H, 7.82. Found: C, 71.33; H, 7.38. The 2,4-dinitrophenylhydrazone was prepared and recrystallized from ethyl acetate. It appeared as yellow-orange plates, m.p. 199.2–199.8°. *Anal.* Calcd. for $C_{19}H_{20}O_5N_4$: C, 59.37; H, 5.25. Found: C, 59.42; H, 4.86.

1,4-Bis-(*p*-methoxyphenyl)-cyclohexanol.—The Grignard reagent prepared under nitrogen from 1.1 g. (0.006 mole) of *p*-bromoanisole in 25 ml. of absolute ether was treated with a solution of 1.0 g. (0.005 mole) of 4-(*p*-methoxyphenyl)-cyclohexanone in 75 ml. of absolute ether. The addition was completed in 20 minutes and after an additional two hours at reflux the mixture was left overnight. It was then hydrolyzed with saturated ammonium chloride while being cooled in an ice-bath. A yellow oil obtained by ether extraction crystallized in part from an alcoholic solution, giving 0.33 g. (23%) of a product, m.p. 120–143°. After purification from ligroin this crystallized as long, white needles, m.p. 146–148°, $\lambda^{\text{alc}}_{\text{max}}$ 224 mμ (ϵ 18,000) and 275 mμ (ϵ 3,250). *Anal.* Calcd. for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.70; H, 7.72.

1,4-Bis-(*p*-methoxyphenyl)-cyclohexene.—Dehydration of 0.07 g. of 1,4-bis-(*p*-methoxyphenyl)-cyclohexanol was accomplished by heating with 5 ml. of 85% phosphoric acid on a steam-bath for three hours. Dilution with water and extraction with benzene gave a yellow oil. This crystallized from petroleum ether and was recrystallized several times from alcohol. The compound was 1,4-bis-(*p*-methoxyphenyl)-cyclohexene, m.p. 150–151°. It was identical with the product obtained from attempts to repeat the foregoing preparation of 1,4-bis-(*p*-methoxyphenyl)-cyclohexanol. In one of these experiments 0.9 g. of the ketone yielded 0.27 g. (21%) of faintly yellow crystals, m.p. 140–143°, which were purified from alcohol, giving long, white needles, m.p. 150–151°, $\lambda^{\text{alc}}_{\text{max}}$ 253 mμ (ϵ 16,240). *Anal.* Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.64; H, 7.60. A small amount (3%) of pure 1,4-bis-(*p*-methoxyphenyl)-cyclohexanol was also isolated from the alcoholic mother liquors.

***cis*- and *trans*-1,4-Bis-(*p*-methoxyphenyl)-cyclohexane.**—A mixture of 0.16 g. of 1,4-bis-(*p*-methoxyphenyl)-cyclohexene and 0.04 g. of palladium-on-charcoal catalyst[18] in 50 ml. of acetone was shaken under 40 p.s.i. of hydrogen for 24 hours. The acetone filtrate was evaporated, and the remaining solid crystallized by slow cooling of its solution in 15 ml. of alcohol. The initial crop of crystals, m.p. 164.5–165°, 0.05 g. (32%), was recrystallized several times from alcohol; the pure *trans*-1,4-bis-(*p*-methoxyphenyl)-cyclohexane crystallized as needles, m.p. 171.2–172.0°, $\lambda^{\text{alc}}_{\text{max}}$ 222 mμ (ϵ 20,020), 226 mμ (ϵ 20,400) and 278 mμ (ϵ 3,590). *Anal.* Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.99; H, 8.02.

The original alcoholic liquors were concentrated to one-fourth their volume and chilled, yielding 0.08 g. (51%) of platelets, m.p. 75–76°. Further purification of these from alcohol gave *cis*-1,4-bis-(*p*-methoxyphenyl)-cyclohexane, m.p. 80.5–81.5°, $\lambda^{\text{alc}}_{\text{max}}$ 223 mμ (ϵ 19,100), 226 mμ (ϵ 20,000) and 278 mμ (ϵ 3,660). *Anal.* Found: C, 81.11; H, 8.15.

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[17] *Cf.* L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Company, New York, N. Y., 1941, p. 444.

[18] Reference 20, p. 459.