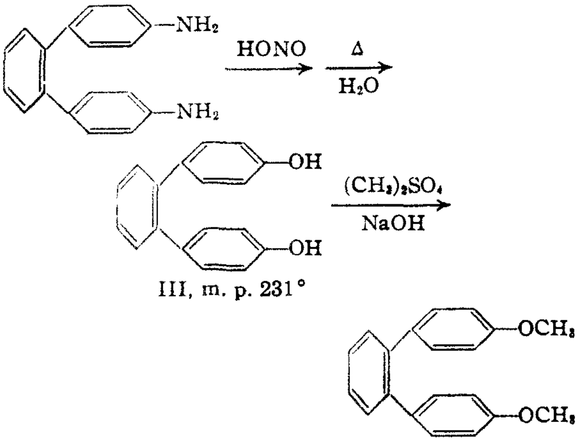
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Synthesis of Two Dihydroxyterphenyls

BY CHARLES C. PRICE AND GEORGE P. MUELLER[1]

In an attempt to prepare 1,2-di-(*p*-methoxyphenyl)-cyclohexane by the condensation of *p*-methoxyphenylmagnesium bromide with 1,2-dibromocyclohexane, the only products which were isolated in a pure state were 4,4′-dimethoxybiphenyl (I) and a substance (II), m. p. 273–275°, having the proper elementary analysis for a dimethoxyterphenyl.

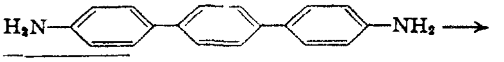
The possibility that this substance was the dimethoxy-*o*-terphenyl resulting from dehydrogenation of the desired 1,2-di-(4-methoxyphenyl)-cyclohexane was dispelled by synthesis of 4′,4″-dimethoxy-*o*-terphenyl (IV) through tetrazotization of the corresponding diamine, recently described by Allen and Pingert.[2] The hydrolysis with steam proceeded in practically quantitative yield. Methylation of the phenol, however, yielded an isomer of the product (II) from the Grignard condensation.

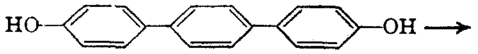


III, m. p. 231°

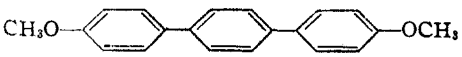
IV, m. p. 106°

Demethylation of the unknown dimethoxyterphenyl (II) followed by permanganate oxidation yielded terephthalic acid, which was identified as the dimethyl ester. The *p*-terphenyl derivative was, therefore, synthesized in the same manner[3-6] as the ortho isomer above and it proved to be identical with the Grignard condensation product.



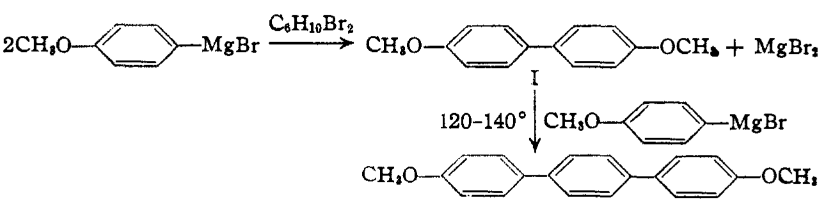


V, m. p. 375°



II, m. p. 273–275°

An experiment demonstrated that this dimethoxy-*p*-terphenyl could arise from a condensation of 4,4′-dimethoxybiphenyl and *p*-methoxyphenylmagnesium bromide.



This reaction recalls the formation of isoamylbenzene as a by-product in the demethylation of anisole with isoamylmagnesium bromide.[7,8] Coupling reactions of Grignard reagents with aryl ethers have also been reported by Fuson and Speck.[9]

Experimental[10]

4′,4″-Dihydroxy-*o*-terphenyl.—The tetrazotization of 4′,4″-diamino-*o*-terphenyl was carried out as prescribed by Allen and Pingert, using 2.6 g. (0.01 mole) of the diamine in 200 cc. of water, 17 cc. of 6 *N* hydrochloric acid solution and 1.38 g. (0.02 mole) of sodium nitrite in water. Apparatus had previously been arranged consisting of a 1-l. three-necked flask fitted with a 30-in. Allihn condenser, and a vertical glass tube measuring 2.5 by 100 cm. Into the top of the latter a 6-mm. glass tube projected 3 cm., and through this was passed steam from boiling, distilled water. Projecting exactly as far into the large tube was the tip of an addition funnel which had been drawn to a capillary at a slight angle so that the solution dripping therefrom would flow down the wall of the column instead of dropping through. This addition funnel was packed in an ice-bath. A little water was placed in the three-necked flask and this was kept boiling while, with the passage of steam down through the tube, the tetrazonium chloride solution was added very slowly. The flask had collected about 850 cc. of water by the time the addition was completed. White needles, sometimes containing an orange impurity, separated from the solution; the yield of the crude material, m. p. 223–228°, was 2.58 g. or 98%. Four recrystallizations from benzene gave colorless plates, m. p. 230.2–231.4° (cor.).

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.39; H, 5.62.

4′,4″-Diacetoxy-*o*-terphenyl.—By warming 0.5 g. of the diphenol with 2 g. of freshly-fused sodium acetate in 10 cc. of acetic anhydride for two and one-half hours, hydrolyzing the suspension in cold water and collecting the remaining solid, the theoretical quantity, 0.66 g., of crude, dry product was obtained, m. p. 175–183°. After four re-

---

[1] Eli Lilly and Company Fellow, 1941–1943.

[2] Allen and Pingert, THIS JOURNAL, **64**, 2639 (1942).

[3] Vorländer, *Z. physik. Chem.*, **106**, 449 (1927).

[4] U. S. Patent 1,993,771 (*Chem. Zentr.*, **106**, II, 3996 (1935)).

[5] (a) von Braun, *Ber.*, **60**, 1180 (1927); (b) France. Heilbron and Hey, *J. Chem. Soc.*, 1364 (1938).

[6] Künster and Schnitzler, *Z. physiol. Chem.*, **149**, 150 (1925).

[7] Späth, *Monatsh.*, **35**, 319 (1914).

[8] Lüttringhaus and Sääf, *Z. angew. Chem.*, **51**, 915 (1938).

[9] Fuson and Speck, THIS JOURNAL, **64**, 2446 (1942).

[10] Microanalyses by Miss Theta Spoor and Miss Dorothy Schneider.

crystallizations from 50% ethyl alcohol the tiny platelets melted at 186.0–186.4° (cor.).

Anal. Calcd. for $C_{22}H_{14}O_4$: C, 76.28; H, 5.24. Found: C, 76.43; H, 5.41.

4′,4″-Dimethoxy-*o*-terphenyl.—The diphenol, 0.20 g., was shaken at 80° with 2 cc. of dimethyl sulfate for a few minutes, 2 cc. of 20% sodium hydroxide solution was added and shaking was continued for a short time. This procedure was repeated three times and the mixture cooled and treated with an excess of aqueous ammonia. The product was collected and dried. The yield of crude material was 0.22 g., or the theoretical quantity. Five recrystallizations from ethyl alcohol produced long, flat needles, m. p. 104.8–106.4° (cor.).

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.90; H, 6.43.

4,4″-Diamino-*p*-terphenyl.—4,4″-Dinitro-*p*-terphenyl, 3.02 g., was suspended in 100 cc. of benzene and hydrogenated at 2000 lb. per sq. in. and 100° for two hours in the presence of Raney nickel. The white diamine crystallized in the bomb as beautiful leaflets, m. p. 240–244°.[11] The product was separated from the catalyst by diluting the mush to 200 cc. with benzene, filtering and concentrating. The recovery from two crops was 1.45 g. or 59%. The diamine was very slightly soluble in 5% hydrochloric acid solution; its solutions in organic solvents exhibited violet fluorescence.

4,4″-Diamino-*p*-terphenyl dihydrochloride was prepared by suspending some of the powdered diamine in 5% hydrochloric acid solution and heating at 95° for a few minutes. Its identity was confirmed by precipitation of the same product by the passage of hydrogen chloride through the benzene liquors containing the diamine. The white powder was nearly insoluble in water. It darkened at 315°; m. p. 355–370°, with decomposition.

4,4″-Dihydroxy-*p*-terphenyl.—4,4″-Diamino-*p*-terphenyl dihydrochloride, 1.56 g., was suspended in 200 cc. of water containing 10 cc. of concentrated hydrochloric acid solution and the mixture treated at 0° with 0.69 g. of sodium nitrite. After an hour of stirring, the excess nitrous acid was destroyed by the addition of urea and the suspension was filtered through an ice-cold Büchner funnel. The tetrazonium chloride was decomposed with steam as before and the pink micro-plates appearing were collected from the hot water. The yield of crude material was about 0.1 g. This is not surprising in view of the considerable residue remaining after filtration of the tetrazonium chloride solution. Purification was effected by shaking the diphenol with 6 cc. of 10% sodium hydroxide solution and 50 cc. of water, filtering, acidifying and centrifuging. This product was washed three times with water and recrystallized three times from ethyl alcohol. The fine, white plates melted at 375°. With very slow heating they melted below this temperature with decomposition. The diphenol is but slightly soluble in dilute alkali solutions, but these solutions show violet fluorescence.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.37; H, 5.45.

4,4″-Diacetoxy-*p*-terphenyl.—4,4″-Dihydroxy-*p*-terphenyl, 0.050 g., was warmed with acetic anhydride and fused sodium acetate in the usual way and the mixture hydrolyzed. The crude, dry product weighed 0.085 g., and, when recrystallized three times from ethyl alcohol, appeared as colorless plates, m. p. 244.3–245.3° (cor.).

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 76.30; H, 5.37.

4,4″-Dimethoxy-*p*-terphenyl.—The methylation was carried out as with the ortho isomer. The product was recrystallized three times from benzene. It formed white micro-plates, m. p. 273–275°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.89; H, 6.55.

Reaction of *p*-Methoxyphenylmagnesium Bromide with 1,2-Dibromocyclohexane.—*p*-Methoxyphenylmagnesium bromide was prepared from 14.6 g. (0.6 mole) of magnesium turnings, 100 cc. of dry ethyl ether and 112.4 g. (0.6 mole) of *p*-bromoanisole in 100 cc. of dry ether. The conventional Grignard-type apparatus with a 500-cc. addition funnel, a sealed stirrer and a condenser carrying a drying tube at the top, all attached to a 500-cc. three-necked flask, was used. After formation of the Grignard reagent was complete, 48.4 g. (0.2 mole) of 1,2-dibromocyclohexane was added at once, the condenser set downward for distillation and ether removed until the volume of the remaining solution was 200 cc. At this time 200 cc. of dry butyl ether was introduced, and the temperature of the mixture brought gradually to 120° where it was maintained for five and one-half hours with constant stirring. After standing at room temperature overnight the mixture was poured into one-half liter of crushed ice containing 35 cc. of concentrated sulfuric acid. A liter of ethyl ether was added, the water layer separated and extracted twice with ether. During these extractions a gray solid separated at the liquid–liquid interface. This was collected on a Büchner funnel and dried; it weighed 0.65 g. and sublimed at 250–300° (1 mm.) to yield clear, colorless plates which were recrystallized three times from benzene; m. p. 273–275°. This product proved to be 4,4″-dimethoxy-*p*-terphenyl. It did not depress the melting point of an authentic sample of this compound. The ether was heated in a steel bomb at 200° for twenty-four hours with 5 g. of potassium hydroxide and 20 cc. of ethyl alcohol. The product, 0.065 g. of the phenol from 0.10 g. of the ether, was soluble in alkali but insoluble in benzene, acetone and alcohol. It was warmed on a steam-bath in 5% sodium hydroxide while a 2% potassium permanganate solution was added until the green manganate color persisted; about 125 cc. was required. The resulting mixture was cooled, acidified and clarified with sodium bisulfite. The fine, white powder separating was collected on a 4-mm. filter. This was soluble in 5% sodium bicarbonate solution. It sublimed above 300°. The dimethyl ester was prepared,[12] m. p. 140–140.5°. Dimethyl terephthalate melts at 140–141° and a mixture of the two had the same melting point.

The ethereal filtrates from the original Grignard reaction were dried over anhydrous sodium sulfate and concentrated at reduced pressure in a dry air stream. The solid separating was collected, crystallized once from a mixture of benzene and petroleum ether (b. p. 95–96°), from which it separated as a mush. This was dried and sublimed at 150° (0.2 mm.) and recrystallized twice from methylcyclohexane. The compound, 4,4′-dimethoxybiphenyl, separated as plates from this solvent but as needles, m. p. 174.5–175.6°, from methyl alcohol.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59; mol. wt., 214.25. Found: C, 78.24; H, 6.68; mol. wt., 194, 208 (Rast).

Distillation of the ethereal liquors gave several liquid and solid fractions, one of which, 1.12 g., was collected at 135–146° (0.2 mm.) and proved to be more of the biphenyl making the total recovery of this product from the reaction 2.18 g.

Reaction of *p*-Methoxyphenylmagnesium Bromide and 4,4′-Dimethoxybiphenyl.—*p*-Methoxyphenylmagnesium bromide was prepared, as before, from 3.65 g. (0.15 mole) of magnesium turnings under 20 cc. of dry ether and 28.1 g. (0.15 mole) of *p*-bromoanisole in 25 cc. of dry ether. The mixture was stirred and warmed for half an hour after the Grignard formation seemed complete. 4,4′-Dimethoxybiphenyl, 2.0 g., and 50 cc. of dry butyl ether were added at once, the condenser set downward for distillation and the temperature of the stirred mixture raised slowly to 140° where it was maintained for eight hours. The mixture was cooled and held below 15° while 50 cc. of

---

[11] The sample of dinitroterphenyl used contained other isomeric nitroterphenyls which were not completely removed.

[12] Huntress and Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 178.

6 *N* sulfuric acid solution was slowly added. Ethyl ether was added, as before, and the solids separating were collected and dried. Sublimation of the 2.5 g. of crude products so obtained yielded 0.7 g. of 4,4′-dimethoxybiphenyl at a bath temperature up to 150° (0.005 mm.) and 0.1 g. of impure 4,4″-dimethoxyterphenyl up to 280°. The residue was infusible. The terphenyl fraction was recrystallized three times from toluene but still softened at 268° and was not entirely fused at 285° though most melting occurred at 275°. The presence of higher-melting impurities is thus indicated, probably the analogous dimethoxyquaterphenyls or even higher members.

Summary

4′,4″-Dihydroxy-*o*-terphenyl and 4,4″-dihydroxy-*p*-terphenyl, the dimethyl ethers and diacetates have been prepared and characterized.

The reaction between 4,4′-dimethoxybiphenyl and *p*-methoxyphenylmagnesium bromide has been found to form small amounts of 4,4″-dimethoxy-*p*-terphenyl.

URBANA, ILLINOIS RECEIVED DECEMBER 22, 1943

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

The Pinacols and Pinacolone from *p*-Methoxyacetophenone

BY CHARLES C. PRICE AND GEORGE P. MUELLER[1]

The successful dehydration of the pinacols from acetophenone[2,3] and *p*-hydroxyacetophenone[4] to the corresponding butadiene prompted an attempt to carry out a similar conversion for the two stereoisomeric pinacols from *p*-methoxyacetophenone. In every instance, however, dehydration resulted in rearrangement to the pinacolone.

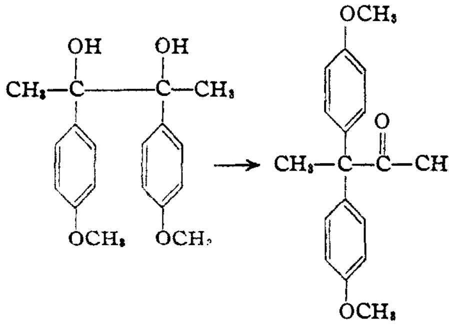
p-Methoxyacetophenone pinacol was prepared in 90% yields by electrolytic reduction of the ketone in potassium acetate, water and alcohol.[5] The crude product, upon repeated recrystallization from methyl alcohol or glacial acetic acid, gave the low- and high-melting isomers, respectively. The low-melting isomer showed some tendency toward solvate formation, the analyses of the compound indicating one-half molecule of methanol present before intensive drying. Also, recrystallization of this isomer, m. p. 122–123°, from ethylene glycol gave material melting at 111–113°; one recrystallization from methanol restored the melting point to its former value. The higher-melting isomer, m. p. 168–169°, was also obtained upon reduction of the ketone by aluminum amalgam in moist ether.

Oxidation of the low-melting isomer with lead tetraacetate yielded *p*-methoxyacetophenone, which was isolated quantitatively as the phenylhydrazone.

Several unsuccessful attempts were made to dehydrate this pinacol. Fraser[3] studied the yields obtained upon dehydration of acetophenone pinacol with acetyl chloride in terms of the time of reaction and found seven minutes at reflux with an equal weight of the acid chloride to be the optimum conditions. Such a reaction carried out with *p*-methoxyacetophenone pinacol (with a trace of hydroquinone present to inhibit polymerization) produced 74% of the pinacolone rather than the diene. A crystal of iodine dropped into the melted pinacol at 150° caused vigorous gas-evolution. The oil realized upon cooling did not show positive reactions either for an unsaturated or ketone derivative.

Both isomeric pinacols were treated repeatedly with fused sodium acetate in acetic anhydride, acetic anhydride and dry pyridine, and the high-melting isomer with benzoyl chloride and sodium hydroxide, but in no instance was esterification of the hydroxyl groups achieved. Any attempt to esterify these groups by an acidic reagent resulted in pinacolone rearrangement.

This rearrangement was conveniently carried out at room temperature in acetic anhydride, a trace of sulfuric acid serving as the catalyst. By analogy with 4,4-dianisyl-3-hexanone, which was obtained upon rearrangement of *p*-methoxypropiophenone-pinacol,[6] it was anticipated that this pinacolone should be 3,3-dianisyl-2-butanone.



This pinacolone did not undergo the iodoform reaction as modified by Fuson and Tullock.[7] This was not conclusive evidence for the absence of the acetyl grouping, however, for Poggi[8] has shown that pinacolone itself would not undergo the iodoform reaction when the procedure of Lieben[9] was

---

(1) Eli Lilly and Company Fellow, 1941–1943.

(2) Allen, Eliot and Bell, *Can. J. Research*, **17B**, 75 (1939).

(3) Fraser, Thesis, University of Illinois, 1939.

(4) Dodds, Golberg, Lawson and Robinson, *Proc. Roy. Soc.* (London), **127B**, 140 (1939).

(5) We are indebted to Professor Sherlock Swann of the Department of Chemistry for the preparation of this pinacol and to Mr. H. D. Marshall and Mr. H. Kerfman, who carried out the electrolytci reductions under his direction.

(6) Wessely, Kerschbaum, Kleedorfer, Prillinger and Zajic, *Monatsh.*, **73**, 127 (1940).

(7) Fuson and Tullock, THIS JOURNAL, **56**, 1638 (1934).

(8) Poggi, *Atti soc. ital. progresso sci.*, XXI Riunione, **2**, 576 (1933).

(9) Lieben, *Ann.*, VII Supplementband, 218 (1870).