

benzene-chloroform) it was possible to isolate 400 mg. of a substance shown to be identical to 2-methyl-4-phenyl-1,4-butanediol-(V) bis-3,5-dinitrobenzoate by comparison of the infrared spectra.

Reduction of α,β -Butenolide II with Excess Hydride: Preparation and Chromatography of 3,5-Dinitrobenzoates.—A mixture of α,β -butenolide II (4.9 g., 28.1 mmoles), LiAlH_4 (1.4 g., ca. 34 mmoles) and anhydrous ether (152 ml.) was allowed to stand at room temperature for 3 hr. The mixture was treated with moist ether, the precipitate was filtered and the ether was removed. The solid obtained in the filtration was suspended in chloroform and the suspension was shaken with dilute hydrochloric acid. Removal of the chloroform gave a residue which was combined with the previous portion obtained from the ether. The combined crystalline product (4.5 g., 92%) was dissolved in chloroform and treated, while hot, with carbon tetrachloride. Upon cooling several days in the refrigerator, 3.2 g. (65%) of crystalline *cis*-2-methyl-4-phenyl-2-butene-1,4-diol (VI), m.p. 146–147°, was collected. The mother liquid from which the unsaturated diol VI crystallized was evaporated to dryness and yielded 1.3 g. of material. This was treated with 3,5-dinitrobenzoyl chloride (2 g.) and pyridine (15 ml.). After 24 hr. at room temperature, the solution was poured into water and extracted with chloroform. Evaporation of the washed chloroform solution gave 2.1 g. of oily mixture of 3,5-dinitrobenzoates. The oil was taken in anhydrous benzene (75 ml.) and placed in a 20 × 5 cm. column of florisil. By successive elutions (benzene, 1:1 benzene-chloroform) it was possible to isolate 200 mg. of a substance shown to be identical to 2-methyl-4-phenyl-1,4-butanediol-(V)-bis-3,5-dinitrobenzoate by means of infrared spectra. Other fractions from the chromatogram had infrared spectra similar to but not identical with that of the saturated diol benzoate.

Reduction of One Mole of α,β -Butenolide II with 0.5 Mole of Hydride: Preparation and Chromatography of 2,4-Dinitrophenylhydrazones.—In the apparatus previously described, the α,β -butenolide (2.5 g., 14.4 mmoles) was

treated with 65 ml. of a 0.11 *M* LiAlH_4 solution in ether (7.2 mmoles of hydride). After 15 min. at room temperature moist ether was added. In the usual manner (moist ether hydrolysis), 1.9 g. (76%) of crystalline product was isolated. From the acidic treatment of the inorganic products of the hydrolysis, 0.61 g. (24%) of additional crystalline product was obtained. The 1.9 g. of product gave upon recrystallization from chloroform-carbon tetrachloride 0.4 g. (16%) of *cis*-2-methyl-4-phenyl-2-butene-1,4-diol (VI), m.p. 144–148°. The mother liquid was evaporated to dryness leaving 1.4 g. of gummy solid which was dissolved in methanol (10 ml.) and treated with a solution of 2,4-dinitrophenylhydrazinium sulfate in aqueous methanol. The red oil which formed was freed of liquid by centrifugation and decantation and was dried *in vacuo*. A solution of the 2,4-dinitrophenylhydrazone mixture in benzene was placed in a 9 × 3 cm. column of silicic acid (2 parts)-Celite (1 part). The column was eluted with benzene under a small positive pressure of nitrogen. From the first 50 ml. of benzene, a small amount of unreacted 2,4-dinitrophenylhydrazone was obtained. The second fraction (50 ml.) gave after evaporation, 0.14 g. of yellow crystalline solid (fraction A). Elution with more benzene (100 ml.) followed by 2:1 benzene-chloroform (250 ml.) gave no product. Elution with chloroform gave 0.175 g. of red oil (fraction B), $\lambda_{\text{max}}^{\text{CH}_1}$ 380 μ ; fraction B was rechromatographed from chloroform as before. In this manner fraction B yielded 0.135 g. of a red substance shown to be identical in all respects (m.p. 124–126°; no depression upon admixture with authentic sample; identity of infrared and ultraviolet spectra) with β -(hydroxymethyl)-butyrophenone-(IV)-2,4-dinitrophenylhydrazone previously reported.

Fraction A obtained above was recrystallized from chloroform-methanol to yield 75 mg. of yellow-orange crystals, m.p. 234.4–234.8°, $\lambda_{\text{max}}^{\text{CH}_1}$ 361 μ . *Anal.* Found: C, 50.5; H, 3.7; N, 20.8. This substance was not further investigated.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Metalation of 2,6-Diisopropylanisole and 1,3-Diisopropylbenzene¹

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Amylsodium with sodium *t*-pentoxide metalates 1,3-diisopropylbenzene and 2,6-diisopropylanisole in the ring positions *meta* to the alkyl groups. In separate metalations or in competition experiments the hydrocarbon is metalated more easily than the ether. Both 2,6-diisopropylanisole and triethylamine retard the metalation of 1,3-diisopropylbenzene. Electrostatic complexing of the sodium cation is postulated.

Introduction

Previous workers have shown that metalation of a heterosubstituted aromatic ring by organosodium reagents takes place *ortho* to the hetero atom if the position is available. Metalations of phenyl alkyl ethers,³ sodium and potassium phenoxides,⁴ sodium benzoate,⁵ sodium anilide⁶ and dimethylaniline⁷ by amylosodium took place in the *ortho* positions. This paper will discuss the effects of blocking the *ortho* positions of anisole with alkyl substituents. 2,6-Diisopropylanisole was chosen in the hope of

sterically preventing coordination at the ether oxygen and of limiting the position of metalation to the carbon atom *para* to the methoxy group. The isopropyl group of cumene severely restricts metalations at adjacent positions in the ring.^{8,9} The metalation of 1,3-diisopropylbenzene at the 5-position, which is sterically identical with the 4-position of 2,6-diisopropylanisole, also was studied for comparison purposes.

Metalation of 2,6-Diisopropylanisole.—This ether was prepared from the sodium salt of 2,6-diisopropylphenol¹⁰ by treatment with methyl *p*-toluenesulfonate. Bromination gave 2,6-diisopropyl-4-bromoanisole which was converted to the Grignard reagent and treated with carbon dioxide to give 3,5-diisopropyl-4-methoxybenzoic acid.

2,6-Diisopropylanisole was added to a slight excess of amylosodium containing sodium *t*-pent-

(1) This work was performed as a part of the research project sponsored by the Federal Facilities Corporation, Office of Synthetic Rubber, in connection with the Government Synthetic Rubber Program.

(2) B. B. Chemical Co., 784 Memorial Drive, Cambridge 39, Mass.

(3) A. A. Morton and A. E. Brachman, *THIS JOURNAL*, **76**, 2973 (1954).

(4) A. A. Morton and R. L. Letsinger, *ibid.*, **67**, 1537 (1945).

(5) A. A. Morton and F. Fallwell, Jr., *ibid.*, **60**, 1924 (1938).

(6) A. A. Morton and R. L. Letsinger, unpublished research.

(7) A. A. Morton and I. Hechenbleikner, *THIS JOURNAL*, **68**, 2599 (1936).

(8) A. A. Morton and J. L. Eisenmann, unpublished research.

(9) D. Bryce-Smith, *J. Chem. Soc.*, 1079 (1954).

(10) 2,6-Diisopropylphenol was kindly furnished by the Ethyl Corporation, to whom the author is grateful.

oxide¹¹ and the mixture was allowed to stand one week at room temperature before carbonation with Dry Ice. Short-path vacuum distillation provided 4.0% of 3,5-diisopropyl-4-methoxybenzoic acid.

Metalation of 1,3-Diisopropylbenzene.—The commercial product was purified by repeated fractionation in a glass-packed column until infrared examination showed the 1,4-isomer to be absent. The 1,3-diisopropylbenzene was metalated under conditions identical with those used for 2,6-diisopropylanisole. Carbonation and distillation afforded 16.8% of a carboxylic acid, m.p. 99.8–100.6° after recrystallization. Potassium permanganate oxidation failed to give an identifiable product. On the basis of the metalation of cumene, which failed to give major amounts of *ortho*- or α -metalation products, but produced much *m*-isopropylphenylsodium,^{8,9} the acid was assumed to be 3,5-diisopropylbenzoic acid. The infrared spectrum appeared to be compatible with this structure. The metalation product of 1,3-diisopropylbenzene underwent no reaction with 2,6-diisopropylanisole in one week. Similarly, the metalated 2,6-diisopropylanisole did not react with 1,3-diisopropylbenzene. Metalation of a mixture of the hydrocarbon and the ether therefore should give kinetically significant data.

Competition Experiments.—An equimolar mixture of 1,3-diisopropylbenzene and 2,6-diisopropylanisole was added to an amount of amylsodium (with sodium *t*-pentoxide) sufficient to monometalate one of the compounds completely. Carbonation after one week and distillation gave a mixture of acids which proved by infrared analysis to consist of a 1.4% yield of 3,5-diisopropyl-4-methoxybenzoic acid and 4.2% of 3,5-diisopropylbenzoic acid. The total metalation of 5.6% was slightly higher than that of 2,6-diisopropylanisole alone but considerably less than that of 1,3-diisopropylbenzene. The facts are inescapable not only that 2,6-diisopropylanisole was metalated more slowly than 1,3-diisopropylbenzene, but also that the presence of the former retarded the metalation of the latter. The conclusion seems justified that amylsodium formed an electrostatic complex of lowered reactivity with the ether oxygen. This conclusion negates any deductions that might be drawn concerning the comparative electrical effects of *para*-methoxy and -hydrogen in these metalations, but supports previously proposed mechanisms for amylsodium-ether interactions.³

To provide non-complexed 2,6-diisopropylanisole, a similar competition experiment was carried out with twice the amount of 2,6-diisopropylanisole needed to form a 1:1 complex with amylsodium. The products were 1.6% of 3,5-diisopropyl-4-methoxybenzoic acid and 3.2% of 3,5-diisopropylbenzoic acid. The total of 4.8% metalation was lower than in the previous experiment. A competition experiment containing a 4-fold excess of triethylamine, which might be expected to complex preferentially with amylsodium, gave 0.2% of 3,5-diisopropyl-4-methoxybenzoic acid and 0.8% of 3,5-diisopropylbenzoic acid. In these experi-

(11) Sodium *t*-alkoxides have been found to be efficient accelerators of metalation in the case of *t*-butylbenzene; A. A. Morton and C. E. Claff, Jr., *J. Org. Chem.*, **20**, 428 (1955).

ments, Lewis bases have decreased the metalating activity of amylsodium, possibly by coordinating with the sodium cation, and in their presence, a *para*-methoxy group adversely affected the rate of metalation. The facile *ortho*-metalation of anisole itself probably results from the proximity of aromatic carbon-hydrogen bonds to the site of coordination.³

Experimental

1,3-Diisopropylbenzene.—After two initial passes through a 4 ft. \times 1 in. glass helix-packed column at atmospheric pressure, Eastman Kodak Co. Practical grade *m*-diisopropylbenzene was refractionated and the center cut, which boiled constantly at 201° and with n_D^{20} 1.4860, was used in the experiments (recorded b.p. 203°, n_D^{20} 1.4860¹²). The strong infrared band of the *para* isomer at 12.05 μ was absent from the spectrum.

2,6-Diisopropylanisole.—Amylsodium was prepared in heptane in the usual way¹³ from 79.0 ml. (0.65 mole) of amyl chloride and 30.0 g. (1.31 g. atoms) of sodium. One hundred grams (0.56 mole) of 2,6-diisopropylphenol¹⁰ (n_D^{20} 1.5103) was added dropwise to the amylsodium at 15–20°. Methyl *p*-toluenesulfonate was redistilled and 105 g. (0.57 mole) was added dropwise at 30–40° to the stirred sodium 2,6-diisopropylphenoxide. After the mixture had been allowed to stand overnight, water was added very cautiously with stirring under nitrogen. The organic layer was dried and fractionated in a 6 \times 600 mm. Podbielniak Whirling Band column. There was obtained 77 g. (71%) of 2,6-diisopropylanisole, b.p. 57° (2.5 mm.), n_D^{20} 1.4913. The infrared spectrum showed no sign of the strong hydroxyl absorption band of 2,6-diisopropylphenol at 2.8 μ .

Anal. Calcd. for C₁₃H₂₀O: C, 81.26; H, 10.41. Found: C, 81.67; H, 10.55.

2,6-Diisopropyl-4-bromoanisole.—To 5 g. (0.026 mole) of 2,6-diisopropylanisole in 25 ml. of acetic acid was added 4.8 g. (0.030 mole) of bromine dissolved in acetic acid. The solution was heated to 50° for one hour, cooled, poured on ice, and extracted with carbon tetrachloride. The product was dried and fractionated in the Podbielniak column. The 2,6-diisopropyl-4-bromoanisole, 2.37 ml., boiled at 89–92° (2.5 mm.), and had n_D^{20} 1.5221.

Anal. Calcd. for C₁₃H₁₉OBr: Br, 29.47. Found: Br, 29.79.

3,5-Diisopropyl-4-methoxybenzoic Acid.—To a mixture of 1.41 g. (0.0052 mole) of 2,6-diisopropyl-4-bromoanisole and 0.2 g. (0.0082 mole) of magnesium turnings in 10 ml. of refluxing ethyl ether was added several drops of an ether solution of ethylmagnesium bromide. The mixture was refluxed two hours longer and poured over powdered solid carbon dioxide (Dry Ice). Acidification of the aqueous solution gave 0.37 g. (30%) of crude 3,5-diisopropyl-4-methoxybenzoic acid, m.p. 158.1–161.1°. The analytical sample was purified by vacuum sublimation and had m.p. 161.9–162.4°. The infrared spectrum in carbon tetrachloride showed strong absorption at 9.9 μ , and this peak was used for quantitative calculations.

Anal. Calcd. for C₁₄H₂₀O₃: C, 71.15; H, 8.53. Found: C, 71.15; H, 8.51.

3,5-Diisopropylbenzoic Acid.—Amylsodium was prepared¹³ from 60.5 ml. (0.5 mole) of amyl chloride and 23.0 g. (1.0 mole) of sodium sand in 500 ml. of heptane. To the amylsodium was added slowly 21.7 ml. (0.2 mole) of *t*-amyl alcohol. The mixture was diluted with heptane to 1000 ml. in a calibrated bottle. Aliquots of the amylsodium were withdrawn on the day of its preparation for the metalations described below. A 100-ml. aliquot was added to a 4-oz. bottle containing 4.05 g. (0.025 mole) of 1,3-diisopropylbenzene. After one week, during which time the bottle was occasionally shaken, the contents were poured over Dry Ice. The carboxylic acids were separated and caproic acid was removed by heating the acids at 110° (2 mm.). Short-path distillation at 150–160° (2 mm.) then gave 0.87 g. (16.8%) of carboxylic acids. Four recrystallizations from 50% aqueous ethanol gave 3,5-diisopropylbenzoic acid, m.p. 99.8–100.6°. The infrared ab-

(12) A. Newton, *THIS JOURNAL*, **65**, 320 (1943).

(13) A. A. Morton, *et al.*, *ibid.*, **72**, 3785 (1950).

sorption peak in carbon tetrachloride at 11.2μ was used for quantitative analysis.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.82. Found: C, 75.52; H, 8.78.

To an identical metalation mixture which had stood for 18 days to allow the amylsodium to decompose, was added 10 ml. of 2,6-diisopropylanisole. Carbonation of the mixture after one week gave 0.1 g. of distilled acids whose infrared spectrum showed no trace of an absorption peak at 9.9μ .

Metalation of 2,6-Diisopropylanisole.—To each of two bottles containing 4.80 g. (0.025 mole) of 2,6-diisopropylanisole was added a 100-ml. aliquot of the amylsodium preparation. Carbonation of a bottle after one week and short-path distillation of the acids gave 0.23 g. (4.0%) of product, m.p. 160.0 – 161.5° after two crystallizations from 50% aqueous ethanol. The material did not depress the melting point of 3,5-diisopropyl-4-methoxybenzoic acid.

After 18 days, the other bottle was treated with 10 ml. of 1,3-diisopropylbenzene. The contents were carbonated one week later. Infrared examination of the 0.41 g. of distilled acids disclosed no peak at 11.2μ .

A 100-ml. aliquot of amylsodium was added to a bottle containing 4.80 g. (0.025 mole) of 2,6-diisopropylanisole and 4.05 g. (0.025 mole) of 1,3-diisopropylbenzene. Carbonation after one week and distillation of the acids gave 0.30 g. of mixed acids which was found from the infrared spectrum to consist of 72% of 3,5-diisopropylbenzoic acid and 28% of 3,5-diisopropyl-4-methoxybenzoic acid. The same method of analysis applied to a known mixture of the two acids showed the probable error to be $\pm 2\%$.

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

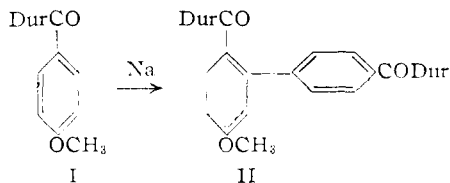
Conjugate Bimolecular Reduction of Hindered Ketones Involving Replacement of Methoxyl Groups. III¹

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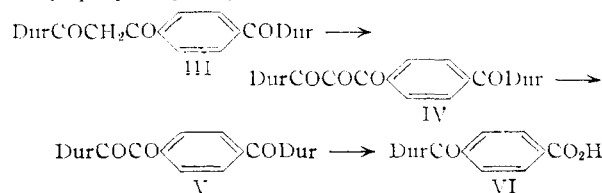
A number of hindered methoxy ketones have been shown to undergo bimolecular reduction with methoxyl group elimination when treated with sodium. Anisyl duryl ketone thus was converted to 2,4'-diduroyl-5-methoxy-3,4-dihydrobiphenyl (II, in text). Anisyl mesityl ketone reacted similarly. Structure proof of the reduction products was based primarily on the results of an alkaline permanganate oxidation. The two oxidation products which were isolated have been identified by comparison with authentic samples. Duryl *o*-methoxyphenyl ketone and mesityl *o*-methoxyphenyl ketone also underwent reduction to yield products analogous to those from the anisyl ketones.

Conjugate bimolecular reduction of duryl *o*-methoxyphenyl ketone with the binary mixture, $Mg + MgI_2$,⁴ has been shown to proceed with loss of methoxyl groups.⁵ We now have found that similar results can be obtained with metallic sodium. When anisyl duryl ketone (I) was treated with sodium in an ether-benzene solution, a product, which proved to be 2,4'-diduroyl-5-methoxy-3,4-dihydrobiphenyl (II), was obtained in 54% yield. Chromatographic adsorption yielded the reduction product in a state of high purity as well as a small amount of a high-melting by-product, the structure of which has not been investigated.



Treatment of the hydroaromatic diketone II with a palladium-on-charcoal catalyst converted it to the corresponding fully aromatic compound, which could be cleaved to a phenol; an attempted cleavage before aromatization gave a red resin. The hydroaromatic compound reacted with maleic

anhydride to form a Diels-Alder adduct and also absorbed two moles of hydrogen under mild conditions to produce the corresponding diketone containing a fully saturated ring. Alkaline permanganate oxidation of the dihydroaromatic compound gave *p*-duroylphenyl duryl diketone (V) and *p*-duroylbenzoic acid (VI), the structures of which have been proved by independent syntheses. It is assumed that destruction of the non-aromatic ring takes place and that the resulting tetraketone IV undergoes decarbonylation. Cleavage of the triketone V might be expected to yield *p*-duroylbenzoic acid (VI). The *p*-duroylbenzoic acid was obtained from the corresponding ethyl ester, prepared in turn either by condensation of *p*-carbethoxybenzoyl chloride with durene or by ethanolysis of duryl *p*-cyanophenyl ketone.



The tetraketone was synthesized by condensing *p*-duroylbenzoyl chloride with the bromomagnesium enolate of acetodurene and oxidizing the resulting triketone III with selenium dioxide. Because of its extreme sensitivity to heat and to alkali, the tetraketone could not be isolated in pure form. However, when treated with base, it did break down into the same mixture of products V and VI that was obtained by the permanganate degradation of the dihydroaromatic compound.

(1) This investigation was supported in part by a grant from the Office of Ordnance Research (Contract No. DA-11-022-ORD-874).

(2) National Science Foundation Fellow, 1952-1953; Allied Chemical and Dye Corp. Fellow, 1953-1954.

(3) Socony-Vacuum Oil Co. Fellow, 1954-1955.

(4) M. Gomberg and W. E. Bachmann, *THIS JOURNAL*, **49**, 236 (1927).

(5) R. C. Fuson and R. O. Kerr, *J. Org. Chem.*, **19**, 373 (1954).