After this separation scheme was adopted, a somewhat similar plan was found to have been used by Low;[10] he had used chloroform instead of ether in the Soxhlet extractor. The latter was found to be a more selective solvent in this step. The terephthalaldehyde and terephthalaldehydic acid were then further purified by microsublimation at reduced pressure. Because of the aqueous insolubility of the acids produced, neutralization equivalents were found to be valid only if the acids were first dissolved in warm, standard alkali.

A detailed composite of the results of the isolation and identification of the DCX–HNO₃ reaction products is presented in Table II.

(10) W. Low, *Ann.*, **231**, 361 (1885).

Characterization and reactions of DCX. Table III summarizes the various reactions which were investigated with DCX. The most satisfactory derivative is α,α'-diphenoxy-p-xylene, p-C₆H₅OCH₂C₆H₄CH₂OC₆H₅; it is easily prepared and purified, and has a convenient melting point range.

Acknowledgment. I wish to thank the following Research Laboratory personnel for their invaluable assistance: Mr. Carl Hirt and Mrs. Florence Crouse for their aid in the interpretation and determination of infrared spectra, and Mrs. Joyce Northrup and Miss Beatrice Fey for their combustion analyses.

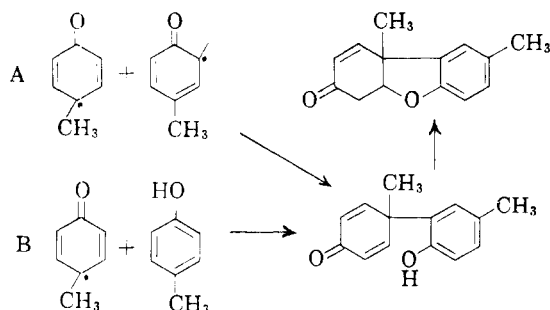# Oxidation of 3-Phenoxymesitol

THOMAS C. BRUICE

The synthesis of 3-phenoxymesitol (V) and the products of its alkaline ferricyanide oxidation are described.

The mold metabolite, usnic acid (I)[1,2] as well as the p-cresol oxidation product known as Pummerer's ketone (II)[2] are formed in one-electron
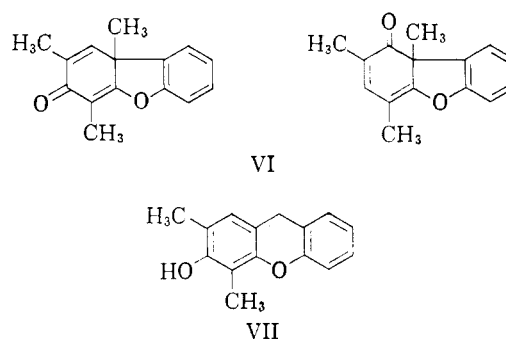

I   II

oxidation of methylphloracetophenone or p-cresol, respectively, by the pairing of radicals (A) or the substitution of one radical into a neutral phenol molecule followed by further oxidation (B).

A

B

In the free radical oxidation of 2,6-dialkyl-4-methylphenols the nature of the products suggests the transient existence of radicals IIIa and IVa.[3] If in the one-electron oxidation of 3-phenoxymesitol (V) there occurred an internal condensation

(1) D. H. R. Barton, A. M. Deflorin, and O. E. Edwards, *J. Chem. Soc.*, 530 (1956).

(2) V. Arkley, F. M. Dean, A. Robertson, and P. Sidisunthorn, *J. Chem. Soc.*, 2322 (1956).

(3) For discussion and general references see H. E. Hey and W. A. Waters, *J. Chem. Soc.*, 2754 (1955).

III   IV   V

a, R = R = alkyl; X = H
b, R = R = CH₃; X = —OC₆H₅

of the radicals IIIb and IVb as in reaction B there would be formed analogs of I (*i.e.*, VI) or the dibenzopyran VII.

VI

VII

The purpose of this study has been to ascertain whether the monomolecular ring closure of IIIb and or IVb could compete with the bimolecular dimerization and hydroxylation reactions which generally follow the formation of IIIa and IVa.

The synthesis of V was accomplished in the following manner. Bromonitromesitylene (IX), obtained by nitration of bromomesitylene,[4] was converted to nitrophenoxymesitylene by refluxing with sodium phenoxide and copper bronze in

(4) L. I. Smith, *Org. Syntheses*, **Coll. Vol. II** 95 (1943).
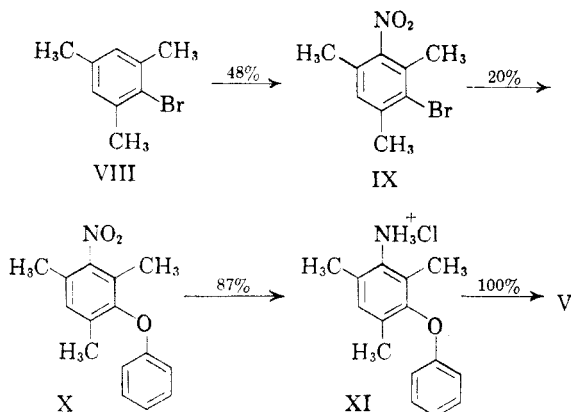
diethylene glycol diethyl e''ier. The period of reflux was found to be critical and the best yields were obtained when the reaction was run on a small scale. The nitrodiphenyl ether (X) was easily reduced to 3-phenoxymesidine (XI) by the general procedures of Furst[5] and XI converted to V by the general method of Lambooy.[6]

The oxidation of V by ferricyanide in water was found to occur only at high pH. When a 7% excess of ferricyanide was used and the reaction run in 5% aqueous potassium hydroxide solution at room temperature there was recovered 52% of the starting phenol (V), 14% of the pure benzyl alcohol XII, and 10% of the pure bibenzyl XIII. The
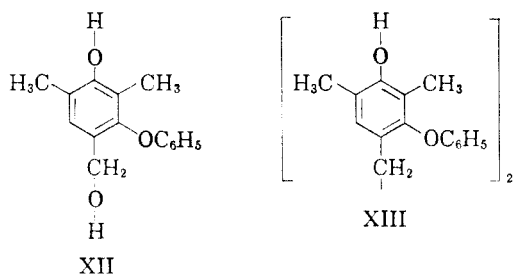
proposed structures XII and XIII are based on molecular weight and analytical data as well as infrared analysis. The positions of the —CH_2OH group in XII and of dimerization in XIII are assigned by analogy.[3]

Infrared analysis of the mixture of reaction products, prior to their fractionation, showed no absorbance between 4 and 7.7 μ, thus eliminating the presence of dienones (VI)[7] and there could not be isolated from the reaction mixture a fraction corresponding to VII. Thus, the internal condensation of the radicals IIIb and IVb does not appear to compete with the hydroxylation and pairing reactions which are the usual fate of IIIa and IVa.[3]

EXPERIMENTAL

Nitrobromomesitylene (IX). To 264 g. (1.33 mole) bromomesitylene[4] in 225 ml. acetic anhydride there was added,

(5) A. Furst, *J. Am. Chem. Soc.*, **75**, 4334 (1953).
(6) J. P. Lambooy, *J. Am. Chem. Soc.*, **72**, 5327 (1950).
(7) G. M. Coppinger, *J. Am. Chem. Soc.*, **79**, 2758 (1957).

with constant stirring, a solution of 83 ml. (2.0 mole) fuming nitric acid (sp. gr. 1.51) in 160 ml. of a 50% acetic acid–acetic anhydride mixture (15–20°). When addition was completed the reaction mixture was allowed to warm to room temperature and stand for several hours. The reaction mixture was then warmed to 50° for 15 min., cooled, and poured into 2.5 l. of cold brine. The organic layer was separated and the aqueous phase thoroughly extracted with ether. The organic phase and washings were combined, washed thoroughly with 5% sodium bicarbonate solution and the solvent removed on the steam bath. The residue was then fractionated by use of a three-foot helices packed column, b.p. 127° at 3 mm. Hg and a bath temperature of 180–195°. The solid distillate was melted and poured into 175 ml. of hot 95% ethanol and allowed to crystallize; 152–156 g. (47–48%) of IX, m.p. 54–56°. (lit.[8] 54°).

Nitrophenoxymesitylene (X). Phenol (33.8 g.; 0.36 mole) and sodium metal (7.2 g; 0.31 mole) were allowed to react to completion in 75 ml. of anhydrous diethylene glycol diethyl ether contained in a 200-ml. round bottom flask equipped with an air condenser with a takeoff 8″ above the solvent surface. To the suspension of sodium phenolate there was then added 0.9 g. copper-bronze and 29.4 g. (0.12 mole) of IX. After refluxing for 6 hr. the reaction mixture was cooled and poured into 200 ml. of 5% aqueous potassium hydroxide solution. The suspension was thoroughly extracted with petroleum ether which was then washed with a little water and dried over anhydrous sodium carbonate. After removal of solvent, over steam, the residue was distilled *in vacuo* using a modified Claisen head with a 5″ Vigreaux column heated at 70°. The fraction containing the product distilled at 140–155° at 1.1 mm. Hg and a bath temperature of 190–200°.

In practice it was found most convenient to repeat the above procedure a dozen times and then to recrystallize the pooled distillates three times from 95% ethanol. When this procedure was followed, and when the mother liquors from the recrystallizations of the product were added to the following batch, prior to distillation, then there was obtained 6.2 g. (20%) of X per batch, m.p. 66–68°. For analysis the compound was sublimed *in vacuo* (100° at 1.0 mm. Hg), m.p. 66–68°.

Anal. Calcd., for $C_{15}H_{15}O_3N$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.78; H, 6.02; N, 5.38.

3-Phenoxymesidine hydrochloride (XI). The nitrophenoxymesitylene (25.7 g.; 0.10 mole) was dissolved in 250 ml. of 95% ethanol to which was added 15 ml. of 100% hydrazine hydrate and a small quantity of Raney nickel. The suspension was warmed on a steam bath to initiate the reaction and then allowed to stand at room temperature for 60 min. Additional catalyst was then added and the flask heated to 50°. When ebullition had ceased the catalyst was removed by filtration and 13 ml. of concentrated hydrochloric acid added. After several hr. of refrigeration the amine hydrochloride was collected and dried *in vacuo* over $CaCl_2$. In this manner 22.2 g. (84%) of XI was obtained, m.p. 239–246°. For characterization the acetyl 3-phenoxymesidine was prepared and recrystallized from *n*-heptane and benzene and from ethanol and water, m.p. 168–169°.

Anal. Calcd. $C_{17}H_{19}O_2N$: C, 75.82; H, 7.11; N, 5.20. Found: C, 75.56; H, 7.17; N, 5.30.

3-Phenoxymesitol (V). By vigorous mechanical stirring, 5.27 g. (0.02 mole) of XI was dissolved in a solution composed of 80 ml. glacial acetic acid and 40 ml. *o*-phosphoric acid. The resultant clear solution was poured into a vigorously stirred solution of 800 ml. water and 64 ml. sulfuric acid. The fine suspension of the amine sulfate was then diazotized (0–5°) by the slow addition of a solution of sodium nitrite (2.76 g.; 0.04 mole) dissolved in 25 ml. water. When diazotization was completed (45 min.) excess nitrous acid was destroyed by addition of a solution of sulfamic acid.

(8) R. Fittig and J. Storrer, *Ann.*, **147**, 7 (1868).

The solution of diazonium salt was then added dropwise to a boiling solution of 80 ml. sulfuric acid in 340 ml. water, the phenol being continuously removed by steam distillation after the method of Lambooy,[6] in all, about 3.5 to 4 l. of distillate being collected. After addition of ammonium sulfate the distillate was extracted four times with benzene, the benzene dried over anhydrous sodium carbonate and evaporated *in vacuo* to yield the 3-phenoxymesitol as a colorless oil (4.5 g; 98%) which could not be induced to crystallize.

The phenol was characterized through its α-naphthylurethane which, for analysis, was chromatographed on acid washed alumina (benzene and *n*-heptane) and recrystallized from the same solvents, colorless needles melting at 173° *in vacuo.*

Anal. Calcd. for $C_{26}H_{23}O_3N$: C, 78.7; H, 5.84; N, 3.53. Found: C, 78.89; H, 5.96; N, 3.53.

Oxidation of V. To 3.31 g. of V (0.0145 mole) dissolved in 200 ml. of 5% potassium hydroxide solution there was added over a period of 30 min. and with rapid stirring, 5.1 g. (0.0155 mole) of potassium ferricyanide dissolved in 25 ml. 5% KOH solution. During the addition the solution acquired a bright violet color and then became milky in appearance. After an additional 2.5 hr. stirring the solution became clear and colorless. At this time the reaction mixture was neutralized with acetic acid, the precipitated oil extracted with benzene and the benzene solution washed with a little water and dried over Na_2CO_3. The yellow, viscous oil obtained by removal of solvent *in vacuo* was taken up three times in 25-ml. aliquots of boiling *n*-heptane, each time the solution was allowed to cool and the supernatant decanted. The combined supernatants were allowed to pass through (slight suction) a 6″ × 0.5″ acid washed alumina column previously wetted

with *n*-heptane. Evaporation of the column effluent yielded 1.7 g. (52%) of starting material (α-naphthyl urethane and infrared spectra). The oil remaining after extraction with *n*-heptane was dissolved in a minimum volume of benzene which was then passed through the column. The column was then washed with additional aliquots of benzene until a yellow band separated from the origin and traversed the length of the column. The benzene effluent when evaporated yielded a pale yellow glass which crystallized when stored at 40° under *n*-heptane (product A). The column was next washed with 25 ml. of a 10% ethanol-benzene mixture and the effluent evaporated to yield a yellow glass which also crystallized under *n*-heptane at 40° (product B).

On repeated recrystallization from benzene by addition of *n*-heptane, product A yielded 0.46 g. (14%) of 4,4'-dihydroxy-3,3',5,5'-tetramethyl-2,2'-diphenoxybibenzyl (XIII) as buttons of white needles, m.p. 154–155°.

Anal. Calcd. for $(C_{15}H_{15}O_2)_2$: C, 79.4; H, 6.66. Found: 79.23; H, 6.38. A Rast molecular weight determination could not be performed because of the reactivity of the product with camphor. A molecular weight by the isothermal distillation method of Childs:[9] Calcd. 454, found 436.

Recrystallization of product B from benzene and *n*-heptane mixtures yielded 0.33 g. (10%) of flat colorless plates of 2,6-dimethyl-1-hydroxy-3-phenoxybenzyl alcohol, m.p. 131–132°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.7; H, 6.59; mol. wt., 244. Found: C, 73.95; H, 6.68; mol. wt., 288 (Rast).

New Haven, Conn.

(9) C. E. Childs, *Anal. Chem.*, 26, 1963 (1951).

[Contribution from the Department of Chemistry, University of California, Berkeley]

1-Ketolilolidine and Some of Its Reactions

HENRY RAPOPORT and JAMES R. TRETTER

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Cyanoethylation of indoline gave 1-indolinepropionitrile which was cyclized directly to 1-ketolilolidine in very poor yield. However, hydrolysis to 1-indolinepropionic acid and heating this acid in polyphosphoric acid gave an excellent yield of cyclic ketone. Condensation with benzaldehyde or furfuraldehyde led to the α-ylidene ketone which was isomerized readily with alkali to the corresponding 4-quinolone.

As a possible entry to the difficulty prepared 7-substituted indoles and indolines, the synthesis of 1-ketolilolidine[1] (IV) was undertaken. Although its conversion to 7-substituted indolines as yet has not been achieved, a convenient preparation of the desired ketone (IV) and an account of some of its reactions are presented at this time.

Since acrylonitrile has been used to cyanoethylate numerous aromatic amines, the reaction of acrylonitrile and indoline was examined for the preparation of 1-indolinepropionitrile (I). Following the procedure which had been used successfully to

cyanoethylate tetrahydroquinoline,[2] indoline and acrylonitrile were heated in acetic acid. Some 1-indolinepropionitrile was obtained, but a by-product of major proportions was 1-acetylindoline. Similar difficulty had been encountered in the cyanoethylation of *o*-toluidine[3] and since it had been overcome by the addition of cuprous chloride, a comparable addition was made in the present case. As a result the formation of 1-acetylindoline was eliminated almost completely and 1-indolinepropionitrile (I) was obtained in excellent yield.

Cyclization to the ketone (IV) was considered first directly from the nitrile (I). Several examples of closely-related ring-closures have been re-

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(1) The nomenclature proposed by C. Y. Almond and F. G. Mann, *J. Chem. Soc.*, 1870 (1952), based on liline, liloline, and lilolidine has been used throughout the discussion with the usual delta designation for the position of the double-bond in liloline except when it is 1,2. In the experimental part, alternative names have been given for most compounds, derived from the *Chem. Abstr.* name for lilolidine, 1,4,5,6-tetrahydro-2*H*-pyrrolo[3,2,1-*ij*]quinoline.

(2) F. C. Whitmore, H. S. Mosher, R. R. Adams, R. B. Taylor, E. C. Chapin, C. Weisel, and W. Yanko, *J. Am. Chem. Soc.*, 66, 725 (1944).

(3) J. T. Braunholtz and F. G. Mann, *J. Chem. Soc.*, 1817 (1953).