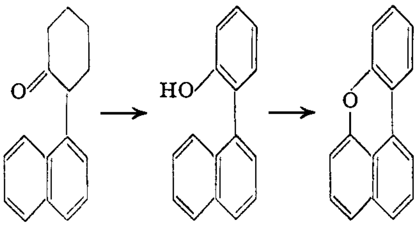
[CONTRIBUTION FROM THE CENTRAL EXPERIMENT STATION, U. S. BUREAU OF MINES]

Aromatic Cyclodehydrogenation. VI. Synthesis of Ring Oxygen Compounds[1]

BY MILTON ORCHIN[2]

In an effort to confirm the structure of 2-(1-naphthyl)-cyclohexanone, I, required in another investigation, this compound was dehydrogenated with palladium-on-charcoal in the liquid phase in an attempt to obtain the known 1-phenylnaphthalene. The benzene solution of the product from the reaction fluoresced in ordinary light and showed a brilliant blue fluorescence in ultraviolet light. The strongly fluorescent material was separated by chromatographic adsorption and it was possible to isolate from this fraction a colorless crystalline compound, $C_{16}H_{10}O$, melting point 108°; picrate, deep red needles, melting point 123°. The intense fluorescence of the compound, its melting point and composition, and the color and melting point of its picrate all correspond exactly to the properties of 1,9-benzoxanthene, III, isolated from coal tar by Kruber.[3] Kruber's proof of structure consisted of hydrogenation of the benzo ring followed by oxidative degradation of it to the known xanthone.

The formation of III from I can be explained by presuming the intermediate formation of 2′-hydroxy-1-phenylnaphthalene, II, followed by the unusual loss of hydrogen between the hydroxyl group and position 8 of the naphthalene nucleus

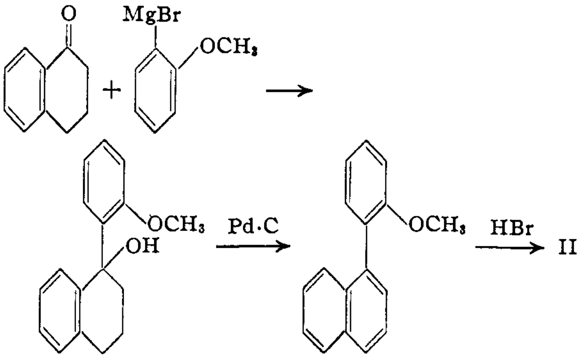


I II III

In order to substantiate this mechanism, 2′-hydroxy-1-phenylnaphthalene, II, was synthesized and treated with palladium-on-charcoal under the same conditions as prevailed in the similar treatment of I. The compound presumed to be 1,9-benzoxanthene, identical with that obtained from I, was isolated from the reaction mixture.

The intramolecular loss of hydrogen between a suitably situated hydroxyl group and an aromatic nucleus presents interesting synthetic possibilities. In an extension of the reaction, *o*-phenylphenol was treated with palladium-on-charcoal and diphenylene oxide was isolated in 8% yield from the products of the reaction. Diphenyl was also present in the products, indicating that the hydrogen liberated in the ring closure was utilized in a hydrogenolysis reaction. When the reaction was carried out in a sealed tube a 14% yield of diphenylene oxide and an 8% yield of diphenyl were obtained.

The synthesis of 2′-hydroxy-1-phenylnaphthalene was achieved by a three-step process, starting with the reaction between *o*-anisylmagnesium bromide and 1-tetralone



IV V

The carbinol, IV, was obtained in 74% yield. One-step dehydration–dehydrogenation with palladium-on-charcoal gave V directly in excellent yield. The over-all yield was not improved by the isolation of the intermediate 1-*o*-anisyl-3,4-dihydronaphthalene. Both the methyl ether, V, and the hydroxy compound, II, formed two different crystalline modifications. II was not extracted from its benzene solution by aqueous alkali.

Experimental[4]

2-(1-Naphthyl)-cyclohexanone, I.—1-Naphthylmagnesium bromide was prepared from 105 g. 1-bromonaphthalene (purified by fractionation), 13 g. magnesium, 200 cc. of dry ether and 350 cc. dry benzene. To this Grignard reagent there was added, with stirring, 66.0 g. of *o*-chlorocyclohexanone.[5] The dropwise addition of the ketone caused a vigorous reaction. After all the ketone was in, the mixture was refluxed for sixteen hours, then poured onto ice and steam distilled. Twenty-nine grams of naphthalene was collected in the distillate. The residue was a tacky red solid. It was taken up in ether, the ether solution washed with hydrochloric acid and water, dried, and the ether evaporated. The residue was distilled and 50 g. of a very viscous oil was collected between 170–240° (1 mm.). Since attempts to obtain crystalline material from this residue were unsuccessful, the mixture was dissolved in alcohol and treated with 25 g. of semicarbazide hydrochloride and 18.3 g. of sodium acetate. From the more soluble fractions of the semicarbazone mixture, 4.86 g. of semicarbazone, m. p. 213–215°, was obtained. To 4.5 g. of this semicarbazone there was added 25 cc. of water and 50 cc. of concentrated hydrochloric acid, and the mixture was refluxed for one hour. The aqueous solu-

---

[1] Published by permission of the director, U.S. Bureau of Mines, Department of the Interior. Not copyrighted.

[2] Organic chemist, Synthetic Liquid Fuels, Research and Development Division, U. S. Bureau of Mines.

[3] Kruber, *Ber.*, **70**, 1556 (1937).

[4] All melting points corrected. Analyses marked (a) by Arlington Laboratories, (p) by Mr. G. L. Stragand of the University of Pittsburgh.

[5] Secured from the Farchan Research Laboratories, 609 E. 127th Street, Cleveland 8, Ohio.

tion was decanted from the oil on the sides of the flask, the oil washed with water, and the water decanted completely. The oil was refluxed with benzene, the benzene solution concentrated, and petroleum ether added. On cooling, 3.25 g. of crystalline material, m. p. 81–84°, was obtained. The sample for analysis was crystallized twice from petroleum ether and had melting point 83.5–85.0°. *Anal.*[4a] Calcd. for $C_{16}H_{18}O$: C, 85.7; H, 7.2. Found: C, 85.9; H, 7.2. The semicarbazone of the pure 2-(1-naphthyl)-cyclohexanone was obtained from dioxane–ethanol as a white powder, m. p. 213–215° (put in the bath at 204°). *Anal.*[4a] Calcd. for $C_{17}H_{19}N_3O$: N, 15.8. Found: N, 15.3.

1,9-Benzoxanthene from 2-(1-naphthyl)-cyclohexanone.—A mixture of 1.0 g. of the ketone, I, and 0.1 g. of 30% palladium-on-charcoal[6] was heated at 310–320° for forty minutes and at 325–340° for about twenty minutes. During this time about 133 cc. (N. T. P.) of hydrogen was evolved (1.4 moles of hydrogen per mole compound). The mixture was dissolved in benzene, filtered, and the filtrate extracted with aqueous potassium hydroxide. Acidification of the alkaline extract gave a trace of material which was discarded. The neutral fraction was chromatographed. Two brands were observed in the column. The less strongly adsorbed band fluoresced brilliantly in ultraviolet light; it was separated and eluted with benzene. The benzene was replaced with methanol and on cooling the solution about 60 mg. of colorless needles, m. p. 107–108°, was obtained. Recrystallization from methanol gave fine needles, m. p. 107.4–108.0°. The picrate was crystallized from ethanol and had the melting point 123.0–123.8°. The complex with *s*-trinitrobenzene was obtained as beautiful, brilliant red crystals (from methanol), melting point 147.8–148.4°. *Anal.*[4a] Calcd. for $C_{16}H_{13}N_3O_7$: N, 9.7. Found: N, 10.4. The ultraviolet absorption spectrum[7] of III (Fig. 1), its melting point, the melting points of the picrate and *s*-trinitrobenzene complex, were identical with those of III obtained from II as described below.

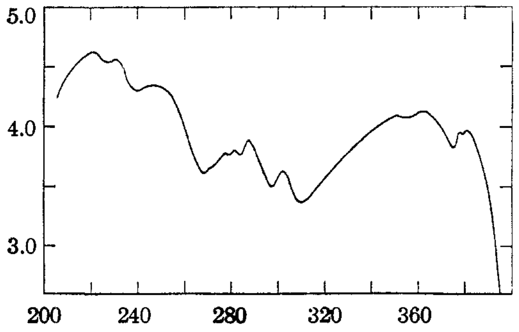


Fig. 1.—Ultraviolet absorption spectrum of 1,9-benzoxanthene.

1-*o*-Anisyl-1-hydroxy-1,2,3,4-tetrahydronaphthalene, IV.—*o*-Anisylmagnesium bromide was prepared in quantitative yield (titration) from 82.2 g. of freshly distilled *o*-anisyl bromide, 12.0 g. of magnesium and 325 cc. of dry ether. To the clear brown-black solution there was added dropwise, with stirring, a solution of 64.0 g. of pure vacuum fractionated 1-tetralone in 150 cc. of dry ether.[8] After all of the tetralone was added the mixture was refluxed for seventeen hours; during this time about 200 cc. of ether was replaced with an equivalent volume of benzene. The mixture was poured onto ice and ammonium chloride. The organic layer was separated, washed well with water and saturated sodium chloride solution, and filtered through sodium sulfate. After removal of most of the solvent *in vacuo*, beautiful colorless crystals separated; these weighed 30.58 g. and melted at 96.0–100.2°. Concentration of the mother liquor gave 47.04 g. of additional carbinol of the same melting point. The mother liquor was evaporated and the residue distilled. The fraction of distillate boiling at 145–160° (2 mm.) was dehydrogenated with sulfur and 4.61 g. of 1-*o*-anisylnaphthalene, V, identical with that prepared below, was obtained. The total yield of carbinol, IV, was thus 74%. The sample of IV taken for analysis was crystallized from petroleum ether and had melting point 98.5–100.0°. *Anal.*[4a] Calcd. for $C_{17}H_{18}O_2$: C, 80.3; H, 7.1; methoxyl, 12.2. Found: C, 80.5; H, 6.9; methoxyl,[9] 12.2.

1-*o*-Anisyl-3,4-dihydronaphthalene.—A mixture of 10 g. of IV and 50 cc. of 90% formic acid was refluxed for one hour. Separation and distillation of the dihydro compound gave 7 g. of a colorless glass, boiling point 160–162° (2–3 mm.), n^{20}_{D} 1.6265. Scratching caused crystallization and after recrystallization from petroleum ether the compound was obtained as thick, colorless crystals, m. p. 66.6–67.6°. *Anal.*[4a] Calcd. for $C_{17}H_{16}O$: C, 86.4; H, 6.8; methoxyl, 13.4. Found: C, 85.9; H, 6.9; methoxyl,[9] 13.2.

1-*o*-Anisylnaphthalene.—(a) A mixture of 30.0 g. of the carbinol, IV, and 1.0 g. of 30% palladium-on-charcoal[6] was heated with stirring at 240–250° for two hours, and for forty-five minutes at 250–300°. About 2 g. of water distilled from the mixture. The mixture was dissolved in benzene and filtered, and the benzene replaced with alcohol. Concentration of the alcohol solution gave 25.5 g. of colorless crystalline material, m. p. 87–90°. The mother liquor gave 0.3 g. additional material, thus making the total yield of crude material 93.5%. Recrystallization from alcohol gave crystals, m. p. 91.2–92.6°. *Anal.*[4a] Calcd. for $C_{17}H_{14}O$: C, 87.2; H, 6.0; methoxyl, 13.2. Found: C, 86.5; H, 5.9; methoxyl,[9] 13.2. During a recrystallization of this material from petroleum ether it was noted that the crystals appeared different from those previously obtained. These crystals had melting point 98.6–99.8°. When some of the low-melting form was dissolved in ethanol and the solution seeded with the high-melting form, material of melting point 98.6–99.8° was obtained. When the high-melting form was dissolved in ethanol and the solution seeded with the low-melting form, material of melting point 91.2–92.6° was obtained. When the low-melting form was melted and allowed to cool, the melting point of the solidified material was 91.0–98.5°.

(b) A mixture of 2.0 g. of 1-*o*-anisyl-3,4-dihydronaphthalene and 0.2 g. of palladium-on-charcoal[6] was heated at 280–320° for ninety minutes. During this time the theoretical quantity of hydrogen was evolved. Distillation of the mixture gave 1.77 g. of oil which crystallized on standing. Crystallization from benzene–ethanol gave material, m. p. 90.8–92.4°, identical with that obtained from the one step dehydration–dehydrogenation of IV.

2′-Hydroxy-1-phenylnapthalene, II.—A solution of 8.84 g. of V in 250 cc. of acetic acid and 90 cc. of 48% hydrobromic acid was refluxed for five hours. The solution was poured onto ice and the mixture extracted with ether–benzene. The organic layer was washed successively with water, sodium bicarbonate, water, and saturated sodium chloride solution. After drying the solvent was evaporated and the residue distilled to give 7.85 g. (94.5%) of colorless oil, boiling point 163–170° (3 mm.). The oil was crystallized with difficulty by cooling and scratching. On attempted recrystallization the compound separated in beautiful needles from alcohol or petroleum ether, but as soon as the solvent was removed the crystals lost their shape and became semi-fluid. If the resulting sticky material was scratched and allowed to stand, firm crystalline material was again obtained which had melting point 55–60°. A small sample was purified by chromatography on alumina–celite and the pure sample

---

(6) Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

(7) We wish to thank Dr. R. A. Friedel for the spectrum data.

(8) We wish to thank Dr. Gilbert Thiessen and The Koppers Company for a generous gift of 1-tetralone.

(9) We wish to thank Mr. E. O. Woolfolk for this analysis and for valuable assistance with a portion of the experimental work.

recrystallized twice from petroleum ether by seeding with previously crystallized material. The final sample had melting point 60–61.5°. *Anal.*[4p] Calcd. for $C_{16}H_{12}O$: C, 87.2; H, 5.5. Found: C, 86.7; H, 5.8.

In one demethylation experiment the benzene solution of the products was extracted with alkali. Acidification of the alkaline extract gave only a small quantity of II; the bulk of II was found in the neutral fraction.

An infrared absorption spectrum showed a strong band in the 2.8 micron region, thus establishing the presence of a hydroxyl group.[7]

1,9-Benzoxanthene from 2′-Hydroxy-1-phenylnaphthalene.—A mixture of 3.0 g. of II and 0.3 g. of palladium-on-charcoal[6] was heated in a nitrogen atmosphere for two hours at 320–350°. The mixture was treated with benzene and filtered. To the concentrated benzene solution there was added 0.7 g. of 2,4,7-trinitrofluorene.[10] On cooling there separated 1.3 g. of dark brown crystals, m. p. 178–190°. Recrystallization from acetic acid gave 1.0 g. of the crystalline complex of 1,9-benzoxanthene and 2,4,7-trinitrofluorenone, m. p. 214.0–214.6°. The complex was dissolved in benzene and the solution poured onto a column of activated alumina. The benzoxanthene was eluted with benzene and the benzene solution evaporated to dryness, leaving 0.41 g. (13.5%) of III. Two crystallizations from ethanol gave the compound in long needles, m. p. 107.5–108.0°. *Anal.*[4p] Calcd. for $C_{16}H_{10}O$: C, 88.1; H, 4.6. Found: C, 87.8; H, 4.6.

Diphenylene Oxide from *o*-Phenylphenol.—A mixture of 5.00 g. of *o*-phenylphenol[11] was heated with 0.5 g. of 30% palladium-on-charcoal catalyst at 285–290° for three hours. The mixture was treated with petroleum ether and filtered. The filtrate was washed with aqueous alkali; acidification of the alkaline extract gave 4.25 g. of recovered phenylphenol. The petroleum ether solution containing the neutral material was dried and chromatographed on a mixture of activated alumina and celite. The components of the mixture were selectively eluted from the column by using mixtures of petroleum ether-benzene containing increasing quantities of benzene; percolate receivers were changed at 100-cc. intervals. The solutions in all receivers were separately evaporated to dryness and the residue, if any, weighed and its melting point determined. The first fractions gave a total of 140 mg. of material, m. p. 66–69°; mixed melting point with diphenyl gave no depression. The later fractions gave a total of 400 mg. (8%) of diphenylene oxide, m. p. 81.5–83.0°; mixed melting point with authentic diphenylene oxide gave no depression. When 5.0 g. of phenylphenol was heated in a sealed tube at 315° for fourteen hours with 0.5 g. of palladium charcoal, a yield of 14% pure diphenylene oxide and 8% diphenyl was obtained. The balance of the material was unconverted phenylphenol.

Summary

Liquid phase treatment of 2-(1-naphthyl)-cyclohexanone with palladium-on-charcoal gave a small yield of a compound whose properties were identical with those reported for 1,9-benzoxanthene. 2′-Hydroxy-1-phenylnaphthalene was probably the intermediate in this conversion since on similar treatment it also gave the compound presumed to be 1,9-benzoxanthene.

o-Phenylphenol when treated with palladium-on-charcoal gave diphenylene oxide. The intramolecular loss of hydrogen between an aromatic hydroxyl group and a suitably situated aromatic nucleus appears to be a general reaction.

1-*o*-Anisylnaphthalene was synthesized in 69% yield in two steps by condensing 1-tetralone with *o*-anisylmagnesium bromide and treating the resulting carbinol with palladium-on-charcoal.

PITTSBURGH, PENNSYLVANIA RECEIVED MAY 2, 1947

---

(10) Orchin and Woolfolk, THIS JOURNAL, **68**, 1727 (1946).

(11) Gift from the Dow Chemical Company.

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

The Preparation of Some 6-Substituted-2-thiouracils[1]

BY MARY JACKMAN, A. J. BERGMAN AND S. ARCHER

Recently Astwood[1a] has shown that certain 6-alkyl- and 6-aralkyl-2-thiouracils, prepared by Anderson and co-workers[2] were powerful goitrogens. In the 6-alkyl-2-thiouracil series maximum activity was reached when the substituents ranged from ethyl through butyl and then dropped off rapidly. The most potent compounds, 6-*n*-propyl-2-thiouracil and 6-benzyl-2-thiouracil (an aralkyl derivative) appeared to be about ten times as active as thiouracil, heretofore considered to be the best antithyroid drug. Astwood screened only one 6-cycloalkyl derivative, namely, 6-cyclohexyl-2-thiouracil, and found that it was equal to thiouracil in effectiveness.

In the course of our work in this field we had occasion to prepare and test some thiouracils joined at the six position, either directly or through an aliphatic chain to alicyclic, heterocyclic and aromatic rings. In addition, 6-methylthiomethyl-2-thiouracil was prepared. The β-keto esters required for condensation with thiourea were prepared by one of the methods given below, depending upon the availability of the starting materials.

$$\mathrm{RCOOC_2H_5 + CH_3COOC_2H_5 \xrightarrow{NaOC_2H_5} RCOCH_2COOC_2H_5} \quad \text{(A)}$$

$$\mathrm{RCOCl + CH_3COCHNaCOOC_2H_5 \longrightarrow RCOCH(COCH_3)\,COOC_2H_5 \xrightarrow{NH_3} RCOCH_2COOC_2H_5} \quad \text{(B)}$$

$$\mathrm{RCOCH_3 + (C_2H_5)_2CO_3 \xrightarrow{NaNH_2} RCOCH_2COOC_2H_5} \quad \text{(C)}$$

Ethyl furoylacetate[3] and ethyl nicotinoylacetate[4] were prepared according to method A and then condensed with thiourea to form the corresponding

---

(1) Presented at the Atlantic City meeting of the American Chemical Society, April, 1947.

(1a) Astwood, Bissell and Hughes, *Endocrinology*, **37**, 460 (1945).

(2) Anderson, Halverstadt, Miller and Roblin, THIS JOURNAL, **67**, 2197 (1945).

(3) Wahl and Dahl, *Bull. soc. chim.*, [4] **13**, 279 (1913).

(4) Strong and McElvain, THIS JOURNAL, **55**, 818 (1933).