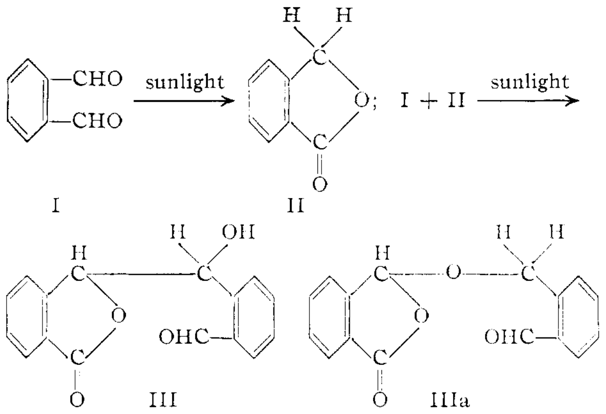
in a strained ring; at 3465, 1420, 1309 and 1070 cm.$^{-1}$ from a secondary alcohol in which the –OH group is free and non-bonded as indicated by the high frequency and the sharpness of the 3465 cm.$^{-1}$ band; at 1333 and 1344 cm.$^{-1}$ from the two → C–H groupings; and at 1611, 1597, 1498, 1196, 1112, 1022, 967, 766, 763 and 704 cm.$^{-1}$ from *o*-disubstituted benzene groupings, the doublet at 766 and 763 cm.$^{-1}$ indicating that two such groupings are present. These groupings are compatible with formula III, but not with formula IIIa, since they do not contain an aliphatic ether (C–O–C) grouping.

The photochemical addition of I to II yielding III is parallel to the photochemical addition of diphenylmethane to benzophenone,[2] xanthene to benzophenone, and xanthene to xanthone.[3] In all these cases the hydrogen of a methylene group migrates under the influence of sunlight to a carbonyl group. The formation of II from III by the action of heat is comparable to the formation of xanthene from the xanthene–xanthone adduct, corresponding to III, under similar conditions.



Experimental

Action of Sunlight on *o*-Phthalaldehyde (I).—The air in a Schlenk tube,[4] containing 1 g. of I[5] in 25 ml. of dry, thiophene-free benzene, was displaced by dry carbon dioxide and the tube sealed. The reaction mixture was exposed to sunlight for one day (July). The colorless crystals that separated during exposure melt at around 184° (dec., yellow melt).[6] Crystals from xylene contained xylene of crystallization which was readily lost when the sample was dried at 100° for 6 hr. The yield was almost quantitative.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.5; H, 4.4. Found: C, 71.3; H, 4.3.

Compound III is soluble in hot xylene, but difficultly soluble in cold benzene, ethyl alcohol and ether; it gives an orange color with sulfuric acid. III (0.2 g.) was heated (steam-bath) with 2 ml. of phenylhydrazine for 0.5 hr.; the resulting colorless crystals were washed with ether and recrystallized from xylene; yield 0.12 g., m.p. 220° (yellow melt).

Anal. Calcd. for $C_{22}H_{18}N_2O_3$: C, 73.7; H, 5.0; N, 7.8; mol. wt., 358. Found: C, 73.4; H, 4.9; N, 7.7; mol. wt. (micro-Rast), 365.

The addition of a few ml. of ether to the filtrate of the reaction mixture gave more of the hydrazone derivative.

A solution of 0.3 g. of III and 0.2 g. of hydroxylamine hydrochloride in 30 ml. of ethyl alcohol, containing a few drops of pyridine, was refluxed for 3 hr. The reaction mixture was set aside overnight at room temperature, rendered just acidic with dilute hydrochloric acid and concentrated. The oily residue was then washed several times with light petroleum (b.p. 50–60°) and the resulting solid crystallized from dilute alcohol; yield 0.18 g., m.p. 139°.

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.8; H, 4.6; N, 4.9. Found: C, 67.3; H, 4.5; N, 4.7.

Thermal Decomposition.—The pyrolysis was carried out in a 15-ml. flask which was connected to a working oil-pump through a delivery tube containing two bulbs which were cooled externally. When the reaction flask, containing 1 g. of III, was heated at 150° (bath-temp.), colorless crystalline sublimate was formed. Upon recrystallization from petroleum ether (b.p. 50–60°), the sublimate yielded 0.31 g. of phthalide which was identified by m.p. and mixed m.p. The residual mass in the reaction vessel was crystallized from benzene as almost colorless crystals, m.p. 278°.

Spectra.—The rock salt infrared (2 to 15 μ) spectrum of the photo-dimer was measured in the solid state as a Nujol mull of capillary thickness with a Perkin–Elmer model 21 double beam, automatic recording infrared spectrophotometer.

Acknowledgment.—The authors are indebted to Dr. David N. Kendall for the infrared spectrum and its interpretation.

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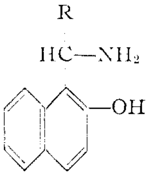
Studies on Sterically Hindered Phenols. I. Instability of 1-Triphenylmethyl-β-naphthol toward Acids

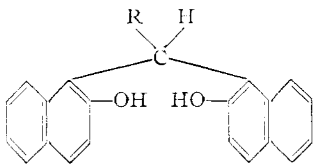
BY ALEXANDER SCHÖNBERG, AHMED MUSTAFA AND AHMED FATHY ABDEL MAUGOUD SHALABY

RECEIVED APRIL 25, 1955

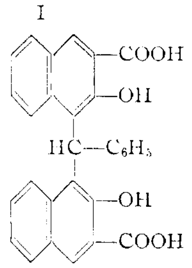
Some derivatives of 1-methyl-2-hydroxynaphthalene are readily hydrolyzed with the rupture of the C–C bond between the naphthalene ring and the methyl carbon atom. Thus, compounds of types I and II were hydrolyzed to yield naphthol and the corresponding aldehyde[1,2]; III yielded 2-hydroxy-3-naphthoic acid and benzaldehyde.[3]



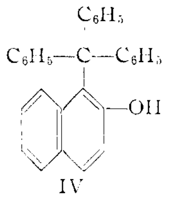
I



II



III



IV

Since all three types of substances (I, II, III) have one or two hydroxyl groups and one hydrogen atom

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[2] E. Paternò and G. Chieffi, *Gazz. chim. ital.*, **39**, II, 419 (1909).

[3] A. Schönberg and A. Mustafa, *J. Chem. Soc.*, 67 (1944).

[4] W. Schlenk and A. Thal, *Ber.*, **46**, 2840 (1913).

[5] *o*-Phthalaldehyde obtained from Dr. Theodor Schuchardt (Munich) was crystallized from light petroleum (b.p. below 40°) m.p. 57°.

[6] The control experiment which was run in the dark, but otherwise under identical conditions, showed no reaction.

[1] M. S. Kharasch and L. B. Howard, THIS JOURNAL, **56**, 1370 (1934).

[2] M. S. Kharasch and J. Porsche, *J. Org. Chem.*, **1**, 265 (1936).

[3] K. Brass and J. Fiedler, *Ber.*, **65**, 1654 (1932).

attached to the central methyl group, the question arises whether these two types of hydrogen atoms are necessary for the facile rupture of the C–C bond. In the case of the phenolic hydrogen, the answer is in the negative as 1,1′-benzal-bis-1-(2-methoxynaphthalene)—the dimethyl ether of II—yielded benzaldehyde and 2-methoxynaphthalene.[2]

To determine whether the hydrogen in the methyl group is essential, we investigated the hydrolysis of 1-triphenylmethyl-2-naphthol (IV)[4] which was prepared by the action of phenylmagnesium bromide on *o*-naphthofuchsone. When IV was heated with hydrochloric acid, it behaved like II, yielding β-naphthol and triphenylcarbinol. IV was acylated with *p*-nitrobenzoyl chloride; this and the fact that it gives the Platkovskaya test[5] for hindered phenols indicates that IV exists in the phenolic form, although it is practically insoluble in aqueous alkali. It is similar, therefore, to 2,4-dimethyl-6-*t*-butylphenol[6] which is also insoluble in alkali (10%), unstable in acid, and gives a positive Platkovskaya test[6]; both substances are soluble in Claisen solution.[6]

Experimental

1-Triphenylmethyl-2-naphthol (IV).—To an ethereal solution of phenylmagnesium bromide (prepared from 0.9 g. of magnesium, 8 g. of bromobenzene and 40 ml. of dry ether) was added a suspension of 1 g. of *o*-naphthofuchsone[7] in 30 ml. of benzene. The reaction mixture was refluxed (steam-bath) for three hours, set aside at room temperature and then decomposed with cold, saturated aqueous ammonium chloride solution containing a few ml. of hydrochloric acid. The reaction mixture was extracted with ether; the ethereal layer was dried (Na_2SO_4) and allowed to evaporate slowly. The solid residue was washed with 25 ml. of cold ethyl alcohol and crystallized from petroleum ether (b.p. 100–120°).

Compound IV (m.p. 155°) is soluble in hot benzene; its alcoholic solution gives no color when treated with alcoholic ferric chloride solution. It is almost insoluble in aqueous sodium hydroxide solution (10%) and gives no color when treated with sulfuric acid.

Anal. Calcd. for $C_{29}H_{22}O$: C, 90.1; H, 5.7; active H, 0.26. Found: C, 90.1; H, 6.1; active H, 0.28.

Compound IV was recovered unchanged from a mixture of 0.2 g. of IV, 0.1 g. of hydroxylamine hydrochloride, 0.2 g. of sodium acetate and 20 ml. of ethyl alcohol which had been refluxed for 6 hours.

Acylation.—To a solution of 0.5 g. of IV in 20 ml. of pyridine was added 0.5 g. of *p*-nitrobenzoyl chloride. The reaction mixture was heated (steam-bath) for 4 hr., then cooled and poured into ice-water. The resulting solid was washed with aqueous sodium carbonate solution and crystallized from acetic acid, m.p. 200°.

Anal. Calcd. for $C_{36}H_{25}NO_4$: C, 80.7; H, 4.7. Found: C, 80.3; H, 4.6.

Hydrolysis.—A stream of hydrogen chloride gas was passed intermittently into a heated mixture of 1 g. of IV and 25 ml. of concentrated hydrochloric acid. After a heating period of 16 hr., IV, which had been suspended, was transformed into an oily substance. After cooling, the oily layer was decanted and set aside overnight at room temperature; colorless crystals (A) separated leaving an oily residue (B). After crystallization from petroleum ether (b.p. 50–60°) (A) (0.2 g., m.p. 121°) were identified as β-naphthol (m.p., mixed m.p. and ready solubility in aqueous sodium hydroxide solution).

(B), which solidified on standing and cooling, was dissolved in ether; the ethereal solution was washed with cold aqueous sodium hydroxide solution (10%) followed by water, and dried. The ether was evaporated and the solid residue, upon crystallization from carbon tetrachloride (0.4 g., m.p. 160°), was identified as triphenylcarbinol.

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[4] D. V. N. Hardy's (*J. Chem. Soc.*, 1000 (1929)) syntheses of this substance (m.p. 228°) has been disproved by the fact that his compound couples with the anti-diazotate of 2,5-dichloroaniline (see ref. 2), and by our results.

[5] V. M. Platkovskaya and S. G. Vatkina, *J. App. Chem.* (*U.S.S.R.*), **10**, 202 (1937); *C. A.*, **31**, 4232 (1937).

[6] G. H. Stillson, D. W. Sawyer and C. K. Hunt, THIS JOURNAL, **67**, 303 (1945).

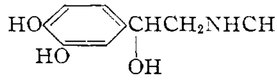
[7] M. Gomberg and F. W. Sullivan, *ibid.*, **42**, 1864 (1920).

Synthesis of Compounds Related to Epinephrine

BY JAMES R. VAUGHAN, JR., AND JACK BLODINGER[1]

RECEIVED JULY 5, 1955

In a program designed to develop more active bronchodilators for the treatment of asthma, several modifications of the structure of the natural product, epinephrine, were synthesized and tested.



The synthetic scheme followed is illustrated in the diagrams on the following page.

1-(3,4-Dimethoxyphenyl)-2-methylaminoethanol hydrochloride (II) was prepared by causing α-bromo-3,4-dimethoxyacetophenone to react with benzylmethylamine, followed by hydrogenation of this compound I using palladium catalyst, to yield the desired product II plus a minor amount of III. The observations of Suter and Ruddy[2] concerning the difficulties encountered in using ammonia or primary aliphatic amines in this condensation were substantiated. Use of their modified procedure in this and the following examples, however, gave excellent results.

1-(3,4-Ureidophenyl)-2-methylaminoethanol (VI) was synthesized by the following scheme. 5-Acetylbenzimidazolone-2 (IV) was prepared both by the Friedel–Crafts reaction between benzimidazolone-2 and acetyl chloride and by the action of phosgene on 3,4-diaminoacetophenone. Both products were identical. This product was then brominated in the side chain and caused to react with benzylmethylamine to give V. This on catalytic reduction, using palladium catalyst in aqueous solution, gave the desired product VI. In ethanol solution, however, the reduction stopped after the hydrogenolysis step and the product isolated was the corresponding ketone VII.

The analog 1-(3,4-ureidophenyl)-2-amino-1-butanol (X) was prepared as follows: benzimidazolone-2 was caused to react with butyryl chloride by the Friedel–Crafts reaction to give VIII. This was side-chain brominated and caused to react with benzohydrylamine to give IX. Catalytic hydrogenation of this in the presence of palladium in ethanol solution led to the preparation of X. This product was further characterized by conversion to the diacetyl derivative XI.

The analog 1-(2-methyl-5-benzimidazolyl)-2-methylaminoethanol dihydrochloride (XV) was

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[1] Pharmaceutical Product Development Section, Research Division, American Cyanamid Co., Pearl River, N. Y.

[2] C. M. Suter and A. W. Ruddy, THIS JOURNAL, **66**, 747 (1944).