

final quaternary through this series of reactions is hereafter denoted as Procedure A.

With easily hydrolyzable esters contact with alkali was avoided and the amino alcohols were esterified in the form of their quaternized salts (Procedure B, compounds 13 and 14).

EXPERIMENTAL

Acids. β -Truxinic acid was prepared according to Bernstein and Quimby^{5,6} in a 14% yield, m.p. 206–209°. DL- α -Methylsuccinic acid, m.p. 111°, *racemic*-2,5-diethyladipic acid, m.p. 68–69°, *meso*-2,5-diethyladipic acid, m.p. 136–137°, and *racemic*-2,5-diphenyladipic acid, m.p. 207–208° were a gift of the U.S.I. division of National Distillers and Chemicals Co.

Acid chlorides. Succinyl chloride was Eastman Kodak 2281. The adipyl chlorides were prepared from the corresponding acid and thionyl chloride. The remaining acid chlorides were prepared from the acid and phosphorous pentachloride. No attempt was made to isolate and purify the acid chloride.

Amino alcohols. 2-Dimethylaminoethanol was a redistilled Dow sample, $b_{750\text{ mm}}$ 134–135°. 2-*N*-Methylanilinoethanol was Eastman Kodak 3709. 3-Hydroxypyridine and 2-pyridinemethanol were obtained from Sapon Laboratories. Other amino alcohols were prepared by known procedures from the commercially available amine and ethylene chlorohydrin.

Procedure A. Two moles of the amino alcohol were added dropwise with agitation to a chilled ether solution of one mole of acid chloride. The precipitate was dissolved in water, the aqueous solution was saturated with sodium chloride and made strongly alkaline, and the alkaline solution was then extracted with ether. The ether extracts were dried over Drierite and were treated with excess organic halide. The product was usually crystallized from methanol ether or methanol ethyl acetate to yield a sample suitable for pharmacological assay. Over-all yields amounted to 5–10%. No attempt was made to optimize the yields.

Procedure B. The amino alcohol was allowed to react with excess organic halide, in ether or acetone. The product was isolated and purified. Two moles of the quaternary salt were combined with one mole of succinyl chloride in toluene and refluxed until the evolution of hydrogen chloride had almost ceased. Although the system was heterogeneous, the reaction proceeded at a reasonable rate at the reflux temperature of toluene. The product was crystallized from methanol ether or methanol ethyl acetate to yield an analytical sample. In the case of compounds 13 and 14, purification was hampered by apparent decomposition in air or light. Over-all yields were about the same as secured by Procedure A.

Iodides. In those cases where a chloride was used for quaternization (compounds 1, 5, and 12), the product was converted to the iodide by treatment with an acetone solution of sodium iodide.

Perchlorates. The crude iodide was dissolved in a minimal amount of water and treated with 70% perchloric acid dropwise until precipitation was complete. The product was crystallized from methanol ether.

The pharmacology of all these compounds is being examined by the Wm. S. Merrell Co.

(5) H. I. Bernstein and W. C. Quimby, *J. Am. Chem. Soc.*, **65**, 1845 (1943).

(6) E. H. White and H. C. Dunathan, *J. Am. Chem. Soc.*, **78**, 6055 (1956).

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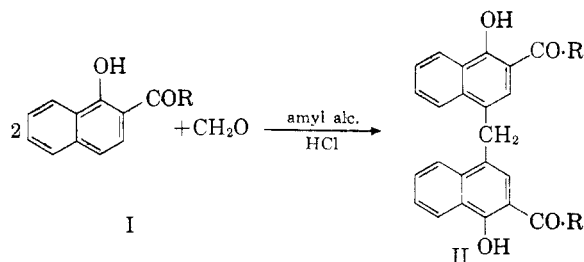
Studies on Sterically Hindered Phenols II.¹ Overcrowded Phenols Obtained by Condensation of Aldehydes with Alkyl Hydroxynaphthyl Ketones

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In general, phenols react readily with formaldehyde in the presence of both alkaline and acidic catalysts, producing a variety of substances ranging from simple methylene derivatives to complex resins. Very little seems to be known about the action of formaldehyde on alkyl hydroxynaphthyl ketones in an acidic medium.

We have investigated the condensation of paraformaldehyde with 2-acetyl-1-naphthol (Ia),² 2-propionyl-1-naphthol (Ib)³ and 2-butyryl-1-naphthol (Ic)⁴ and found that almost quantitatively the 3,3'-diacyl-4,4'-dihydroxydinaphthylmethanes IIa-IIc were formed.



(I) and (II):
(a) R = CH₃
(b) R = CH₂-CH₃
(c) R = CH₂-CH₂-CH₃

IIa gave diacetyl and dibenzoyl derivatives and a color reaction with ferric chloride.⁵ The dioxime of IIb was prepared. The fact that 2-acetyl-4-bromo-1-naphthol⁶ (III) does not condense with

(1) Part I: A. Schönberg, A. Mustafa, and A. Shalaby, *J. Am. Chem. Soc.*, **77**, 5756 (1955).

(2) E. J. Chu, Z. Shen, T. Chien, and T. S. Tuan, *J. Am. Chem. Soc.*, **66**, 653 (1944).

(3) C. M. Brewster and G. G. Watters, *J. Am. Chem. Soc.*, **64**, 2578 (1942).

(4) Yuoh Fong Chi, *J. Am. Chem. Soc.*, **61**, 2487 (1939).

(5) The tests with ferric chloride mentioned in this paper were carried out by adding a few drops of an aqueous ferric chloride solution to the alcoholic solution of the substance to be investigated.

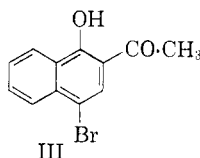
(6) M. Akram, R. D. Desai, and Ahmad Kamal, *Proc. Indian Acad. Sci.*, **11A**, 139 (1940).

TABLE I
 CONDENSATION OF PARA-FORMALDEHYDE WITH HYDROXYNAPHTHYL KETONES

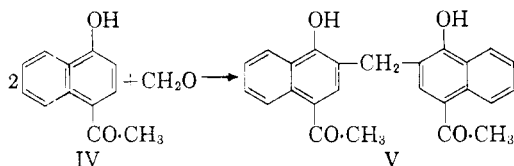
Ketone	Color of Product, Yield, g.	Color Test		M.P., °C.	Formula	Analyses, %
		(a) FeCl ₃	(b) Concd. H ₂ SO ₄			
Ia (3 g.)	Yellow	(a) Green		228	C ₂₅ H ₂₀ O ₄	Calcd.: C, 78.1; H, 5.2
1 g. ^a	3.0	(b) Orange			IIa	Found: C, 78.1; H, 5.2
Ib (1 g.)	Yellow	(a) Green		187	C ₂₇ H ₂₄ O ₄	Calcd.: C, 78.6; H, 5.9
0.3 g. ^a	1.0	(b) Orange			IIb	Found: C, 78.2; H, 5.9
Ic (1 g.)	Yellow	(a) Green		168	C ₂₉ H ₂₈ O ₄	Calcd.: C, 79.1; H, 6.4
0.3 g. ^a	1.0	(b) Orange			IIc	Found: C, 79.0; H, 6.8
IV (3 g.)	Yellowish	(a) No		245	C ₂₅ H ₂₀ O ₄	Calcd.: C, 78.1; H, 5.2
1 g. ^a	2.9	(b) Yellow			V	Found: C, 78.4; H, 5.8

^a Amount of paraformaldehyde used.

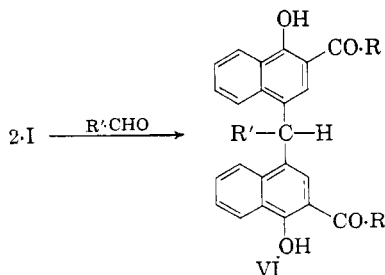
paraformaldehyde is in agreement with the supposed condensation in the *p*-position with respect to the hydroxyl groups.



The condensation of 4-acetyl-1-naphthol⁷ (IV) with paraformaldehyde yielded V, the proposed orientation being in agreement with the fact that 2-bromo-4-acetyl-1-naphthol⁷ did not condense with paraformaldehyde under the same experimental conditions. V forms a diacetate derivative.



We found that Ia did not condense with benzaldehyde under conditions which led to the formation of IIa. However, condensation occurred when the ketone and the aldehyde were dissolved in glacial acetic acid, treated with a few drops of concentrated sulfuric acid and the solution kept at 5° for a few days. Thus Ia, b, c reacted with benz-



- (a) R = CH₃; R' = C₆H₅
 (b) R = CH₂·CH₃; R' = C₆H₅
 (c) R = CH₂·CH₂·CH₃; R' = C₆H₅
 (d) R = CH₃; R' = C₆H₄·NO₂ (*p*)
 (e) R = CH₂·CH₃; R' = C₆H₄·Cl (*o*)

(7) M. Akram and R. D. Desai, *Proc. Indian Acad. Sci.*, 11 A, 149 (1940).

aldehyde, *p*-nitrobenzaldehyde, and *o*-chlorobenzaldehyde to yield VIa-e.

The overcrowded sterically hindered phenols V and VIa-VIe are insoluble in aqueous sodium hydroxide. Similar insolubilities of phenols of this type have been reported in the case of 2,6-di-*t*-alkylphenols, 2,4-dimethyl-6-*t*-butyl phenol⁸ and of 1-triphenylmethyl-2-naphthol.¹ The sterically hindered phenols IIa-IIc are insoluble in cold aqueous alkali; on heating yellow or yellow-orange solutions are obtained.

EXPERIMENTAL

Condensation of paraformaldehyde with hydroxynaphthyl ketones. To a solution of the ketone and paraformaldehyde⁹ in 10 ml. of amyl alcohol (in case of Ia and IV 20 ml. of amyl alcohol were used), 1 ml. of concentrated hydrochloric acid was added, and the mixture was heated under reflux for 3 hr. The condensation product that separated on cooling was filtered and purified by crystallization from benzene or petroleum ether (b.p. 100-120°). V was crystallized from ethyl alcohol (Table I).

Benzoylation of IIa. The general procedure for carrying out a Schotten-Baumann reaction was followed. The dibenzoyl derivative was crystallized from benzene as colorless crystals, m.p. 251°. It is insoluble in aqueous sodium hydroxide solution, dissolves in concentrated sulfuric acid with orange color and gives no color with ferric chloride.

Anal. Calcd. for C₂₉H₂₂O₆: C, 79.0; H, 4.8. Found: C, 79.3; H, 4.7.

Acetylation of IIa. IIa (1 g.) was boiled for 2 min. with a mixture of anhydrous sodium acetate (1 g) and 2 ml. of acetic anhydride. While hot the solution was poured into cold water. The diacetyl derivative that separated (0.9 g.) was crystallized from benzene as colorless crystals; m.p. 200°. It gives an orange color with concentrated sulfuric acid.

Anal. Calcd. for C₂₉H₂₄O₆: C, 74.4; H, 5.2. Found: C, 74.4; H, 5.4.

Benzoylation of IIb. The dibenzoyl derivative crystallizes from benzene as colorless crystals, m.p. 179°. It is insoluble in aqueous sodium hydroxide solution, dissolves in concentrated sulfuric acid with orange color, and gives no color with ferric chloride.

Anal. Calcd. for C₄₁H₃₂O₆: C, 79.3; H, 5.2. Found: C, 79.6; H, 5.5.

(8) G. H. Stillson, D. W. Sawyer, and C. K. Hunt, *J. Am. Chem. Soc.*, 67, 303 (1945).

(9) The paraformaldehyde was prepared by the evaporation of the commercial 40% formaldehyde solution on the water bath.

TABLE II
 CONDENSATION OF HYDROXYNAPHTHYL KETONES WITH AROMATIC ALDEHYDES

Ketone	Wt. of Aldehyde, ^a G.	Yield, G. Color React. with Concd. H ₂ SO ₄	M.P., °C.	Formula	Analyses, %
Ia	0.3 (A)	0.9 Orange	268	C ₃₁ H ₂₄ O ₄ VIa	Calcd.: C, 80.9; H, 5.3 Found: C, 80.9; H, 5.4
Ib	0.3 (A)	0.7 Orange	202	C ₃₃ H ₂₈ O ₄ VIb	Calcd.: C, 81.1; H, 5.8 Found: C, 81.0; H, 5.8
Ic	0.3 (A)	0.5 Orange	122	C ₃₅ H ₃₂ O ₄ VIc	Calcd.: C, 81.4; H, 6.2 Found: C, 81.4; H, 6.3
Ia	0.4 (B)	1.2 Deep brown	310	C ₃₁ H ₂₃ NO ₆ VI d	Calcd.: C, 73.7; H, 4.6; N, 2.8 Found: C, 74.3; H, 4.7; N, 2.9
Ib	0.4 (C)	0.8 Orange	228	C ₃₃ H ₂₇ ClO ₄ VIe	Calcd.: C, 75.8; H, 5.2; Cl, 6.8 Found: C, 75.7; H, 5.4; Cl, 6.9

^a A, Benzaldehyde; B, *p*-nitrobenzaldehyde; C, *o*-chlorobenzaldehyde.

Dioxime of I**b** crystallizes as yellow crystals from dilute ethyl alcohol, m.p. 235–236°. It is soluble in sodium hydroxide solution, dissolves in concentrated sulfuric acid yielding yellowish green solution and its alcoholic solution gives deep green color with ferric chloride solution.

Anal. Calcd. for C₂₇H₂₆N₂O₄: C, 73.3; H, 5.9; N, 6.3. Found: C, 73.4; H, 6.2; N, 6.1.

Acetylation of V. The diacetyl derivative was crystallized from benzene as colorless crystals, m.p. 194°. It gives yellow color with concentrated sulfuric acid.

Anal. Calcd. for C₂₉H₂₄O₆: C, 74.3; H, 5.2. Found: C, 74.7; H, 5.4.

Condensation of hydroxynaphthyl ketones with aromatic aldehydes. The ketone (I) (1 g.) and the aromatic aldehyde were dissolved in 30 ml. of glacial acetic acid. The solution was cooled to about 5°, and four drops of concentrated sulfuric acid were added. The solution was kept at about 5° in a tightly stoppered flask for 7 days. The yellow solid that separated was filtered and washed with hot ethyl alcohol and crystallized from benzene (b.p. 100–120°). VI d was crystallized from toluene. VIa–VIe are insoluble in aqueous sodium hydroxide solution and give a green color with ferric chloride solution.

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Absolute Configuration of 1,1'-Bi-2-naphthylamine¹

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According to a recently formulated optical displacement rule,² the fact that (+)-1,1'-bi-2-naphthylamine (I) gives the strongly levorotatory bridged derivative³ II suggests that (+)-I has the (*R*)-configuration.⁴ This conclusion is buttressed

(1) Configurational Studies in the Biphenyl Series. VIII. Part VII: Ref. 8.

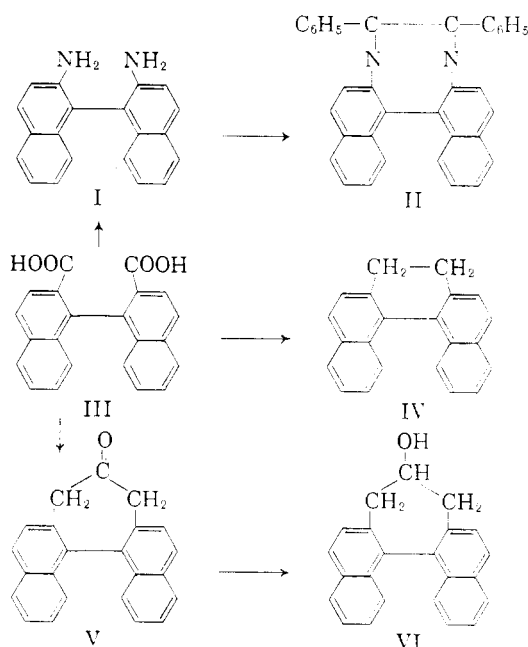
(2) D. D. Fitts, M. Siegel, and K. Mislow, *J. Am. Chem. Soc.*, **80**, 480 (1958).

(3) R. Kuhn and P. Goldfinger, *Ann.*, **470**, 183 (1929).

(4) Nomenclature according to R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

by the observation³ that both (+)-I and (+)-(*R*)-6,6'-dimethyl-2,2'-biphenyldiamine⁵ change optical sign in acidic solvents. In the present work we have provided sound support for this configurational assignment.

The absolute configuration of 1,1'-binaphthalene-2,2'-dicarboxylic acid (III) has previously been secured by three independent lines of evidence. First, the (*R*)-configuration has been established² for (–)-IV, a derivative⁶ of (+)-III, on the basis of arguments arising out of the polarizability theory of optical activity. Second, (–)-VI, a derivative of (+)-III, has been assigned⁷ the (*R*)-configuration on the basis of the fact that a partial Meerwein-



(5) F. A. McGinn, A. K. Lazarus, M. Siegel, J. E. Ricci, and K. Mislow, *J. Am. Chem. Soc.*, **80**, 476 (1958).

(6) D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 1242 (1955).

(7) K. Mislow and F. A. McGinn, *J. Am. Chem. Soc.*, in press.