anhydride under reflux for 5 hr. Distillation of the reaction mixture gave 4.1 g. of a colorless oil; b.p. 61–62° at 0.5 mm., n^{20}_{D} 1.4997

Anal. Calcd. for $C_8H_9NO_2$: C, 63.56; H, 6.00. Found: C, 63.47; H, 6.22.

Acid Hydrolysis of 2-Acetoxy-3-methylpyridine (VIII).—A 1.0-g. sample of 2-acetoxy-3-methylpyridine (VII) was hydrolyzed following the same procedure described previously for the preparation of 2,6-di-(hydroxymethyl)-pyridine. The product was obtained, after recrystallization from a benzene–hexane mixture, as light tan crystals, m.p. 138–140°.[33] The ultraviolet absorption spectrum of this material is very similar to that of 2-pyridone in that it has absorption maxima at 230 (log ε 3.83) and 289 mμ (log ε 3.83), whereas 2-pyridone has its maxima at 227 (log ε 4.00) and 297 mμ (log ε 3.80).[11]

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[33] H. L. Bradlow and C. A. VanderWerf (*J. Org. Chem.*, **14**, 509 (1949)) give 138–139.5° as the m.p. of 3-methyl-2-pyridone.

ROCHESTER, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF UTAH]

Condensation of 2-Naphthol with Acetaldehyde Ammonia

BY WILLIAM J. BURKE AND RICHARD J. REYNOLDS[1]

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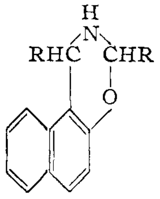
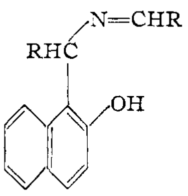
Condensation of 2-naphthol with acetaldehyde ammonia resulted in a high yield of 1,2-dihydro-1,3-dimethyl-3H-naphth-[1.2-e]-*m*-oxazine (Ib). Evidence is presented for the structure assigned. Hydrolysis of Ib yielded 1-α-aminoethyl-2-naphthol (IIIb). Reactions of Ib and IIIb were studied.

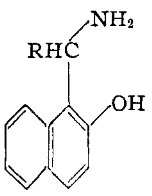
Betti[2] reported that 2-naphthol reacted with aldehydes and ammonia in a molar ratio of 1:2:1 to yield crystalline products, which were assigned either a *m*-naphthoxazine (I) or isomeric Schiff base structure II on the basis of a ferric chloride test. Related compounds were obtained when the product III of the condensation of equimolar quantities of the reactants was condensed with a second molecule of an aldehyde. Aromatic aldehydes were reported to yield the corresponding Schiff base II upon reaction with IIIa, while naphthoxazines were obtained when aliphatic aldehydes were employed.[3]



I



II



III

Ia, R = C_6H_5 IIa, R = C_6H_5 IIIa, R = C_6H_5
Ib, R = CH_3 IIb, R = CH_3 IIIb, R = CH_3

Ahmed, Hemphill and Ray[4] uncovered evidence to show that the product from the condensation of 2-naphthol, benzaldehyde and ammonia in a molar ratio of 1:2:1 was the *m*-naphthoxazine (Ia). Betti initially[2b] proposed this structure but later[5] assigned the Schiff base formula IIa to the product.

Considering the attention given to the condensation of hydroxyaromatic compounds with aldehydes and amines or ammonia, it is rather surprising that products from such reactions involving the use of acetaldehyde ammonia have not been described in the literature. This general type of reaction has provided a convenient route to a variety of complex substances difficultly accessible by other methods. It has been found that the course of the condensation and the type of products obtained depend upon several factors including the nature of the hydroxyaromatic compounds,[2a,6] amine[2d,7] and aldehyde components,[3,8,9] their ratio in the reaction system[2,6] and the particular conditions employed.[7,10,11] The lack of sufficient experimental evidence has frequently prohibited the definite assignment of structure to the resulting condensates. In view of these factors, the present study of the condensation of 2-naphthol with acetaldehyde ammonia was undertaken.

2-Naphthol and acetaldehyde ammonia in a molar ratio 1:2.4 reacted readily in refluxing benzene to give a 74% yield of 1,2-dihydro-1,3-dimethyl-3H-naphth[1.2-e]-*m*-oxazine (Ib) with the liberation of ammonia. A reaction time in excess of 45 minutes did not result in a higher yield, but the use of benzene rather than ethanol as a solvent was advantageous. The conversion to Ib was over 95% based on the 2-naphthol consumed. Ib was appreciably less sensitive to acids than the corresponding 1,3-benzoxazines,[12] derived from phenols, formaldehyde and primary amines, and formed a stable hydrochloride. In a refluxing solution of propanol-2 in the presence of hydrochloric acid, Ib was converted smoothly to 1-α-aminoethyl-2-naphthol (IIIb) hydrochloride, which upon treatment with 2-aminoethanol yielded the crystalline free base. The latter, however, was unstable and slowly liberated ammonia. Reaction of IIIb in ether solution with acetaldehyde at room temperature re-

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[2] (a) M. Betti, *Gazz. chim. ital.*, [II] **30**, 310 (1900); *J. Chem. Soc.*, **80**, 81 (1901); (b) M. Betti, *Gazz. chim. ital.*, [I] **31**, 377 (1901); *J. Chem. Soc.*, **80**, 611 (1901); (c) M. Betti and A. Torricelli, *Gazz. chim. ital.*, [I] **33**, 1 (1903); *J. Chem. Soc.*, **84**, 480 (1903); (d) M. Betti, *Gazz. chim. ital.*, [I] **33**, 17 (1903); *J. Chem. Soc.*, **84**, 510 (1903).

[3] M. Betti and V. Foa, *Gazz. chim. ital.*, [I] **33**, 27 (1903); *J. Chem. Soc.*, **84**, 511 (1903).

[4] N. Ahmed, M. G. Hemphill and F. E. Ray, THIS JOURNAL, **56**, 2403 (1934).

[5] M. Betti, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 381.

[6] W. J. Burke, R. P. Smith and C. Weatherbee, THIS JOURNAL, **74**, 602 (1952).

[7] W. J. Burke, M. J. Kolbezen and C. W. Stephens, *ibid.*, **74**, 3601 (1952).

[8] M. Betti, *Gazz. chim. ital.*, [I] **34**, 212 (1904); *J. Chem. Soc.*, **86**, 581 (1904).

[9] F. W. Holly and A. C. Cope, THIS JOURNAL, **66**, 1875 (1944).

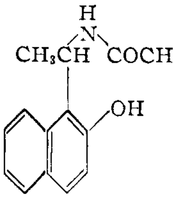
[10] J. C. Duff and E. J. Bills, *J. Chem. Soc.*, 1307 (1934).

[11] J. C. Duff and U. I. Furness, *ibid.*, 1512 (1951).

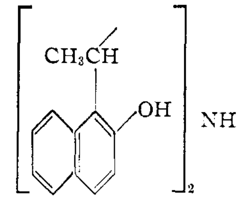
[12] (a) W. J. Burke, THIS JOURNAL, **71**, 609 (1949); (b) W. J. Burke and C. W. Stephens, *ibid.*, **74**, 1518 (1952).

sulted in the regeneration of Ib in essentially quantitative yield. Acetaldehyde ammonia was also used to convert IIIb to Ib but in this case heating was required and the yield was lower.

Acetylation of IIIb yielded 1-α-acetamidoethyl-2-naphthyl acetate which upon treatment with dilute potassium hydroxide at 0° was converted to 1-α-acetamido-2-naphthol (IV). Reaction of Ib with acetic anhydride in pyridine resulted in an acetyl derivative, which liberated acetaldehyde upon acid hydrolysis to form IV. The product from the acetylation of Ib was recovered unchanged after subjection to sodium hydroxide in hot methanol, indicating the presence of an N- rather than an O-acetyl group. These results are consistent with a naphthoxazine (Ib) but not with the isomeric Schiff base structure IIb for the condensation product from 2-naphthol and acetaldehyde ammonia. Assignment of the new carbon to carbon bond at the 1-position of Ib appeared reasonable in view of related studies on the structure of the products from the condensation of 2-naphthol and formaldehyde with primary[7] and secondary[13] amines.



IV



V

The attempted direct synthesis of IIIb by condensation of equimolar quantities of 2-naphthol and acetaldehyde ammonia resulted in a high yield of the addition product of Ib with 2-naphthol. This adduct was also obtained in essentially quantitative yield by reaction of Ib with 2-naphthol in benzene solution. The addition product showed unusual stability in that its composition was not changed by repeated recrystallization or by sublimation under reduced pressure. However, it was readily decomposed in sodium hydroxide or hydrochloric acid solutions to yield Ib and 2-naphthol. It is interesting to note that while 2- or 4-alkylaminomethylphenols are readily obtained directly from equimolar quantities of phenols, formaldehyde and primary amines,[12] efforts to prepare the related 1-alkylaminomethyl-2-naphthols by an analogous procedure resulted in the corresponding bis-(2-hydroxy-1-naphthylmethyl)-alkylamines.[7]

In view of the instability of IIIb, a study of its decomposition was undertaken. When an ethanol solution of IIIb hydrochloride was heated under reflux in the presence of an equivalent quantity of potassium hydroxide a 93% conversion to Ib along with a 7% conversion to α,α-bis-(2-hydroxy-1-naphthylethyl)-amine (V) was effected. Only the naphthoxazine (Ib) was isolated in attempts to prepare V directly by reaction of 2-naphthol with acetaldehyde ammonia in a molar ratio of 2:1, respectively.

Acknowledgment.—The financial assistance given by the Research Corporation under a Frederick Gardner Cottrell Grant is gratefully acknowledged.

Experimental

1,2-Dihydro-1,3-dimethyl-3H-naphth[1.2-e]-*m*-oxazine (Ib).—2-Naphthol (28.8 g., 0.2 mole) and acetaldehyde ammonia (29.3 g., 0.48 mole) were added to 200 ml. of benzene. The mixture was refluxed gently for two hours while being stirred vigorously. After two hours, the light brown benzene solution was washed successively with water, 10% sodium hydroxide and water and then dried over anhydrous sodium sulfate. Benzene was removed from solution under reduced pressure. The resulting viscous amber colored oil was taken up in half its volume of methanol and allowed to crystallize at −20° overnight. The colorless prismatic crystals were collected on a filter and washed twice with a small volume of cold methanol; yield 26.5 g., m.p. 97.5°. An additional 5.0 g. of product was obtained from the mother liquor; m.p. 93–96°, total yield 74%. The combined 10% sodium hydroxide extracts were acidified, extracted with ether and evaporated to yield 6.5 g. of solid; m.p. 117–120°. The product melted at 122° upon recrystallization from chloroform, and did not depress the m.p. of 2-naphthol. The conversion to naphthoxazine was 95.5%, based on the 2-naphthol consumed. The yield of oxazine was not materially increased by use of as much as 100% excess of acetaldehyde ammonia, nor was it greatly affected by variation of the reaction time from 45 minutes to two hours. Lower yields were obtained when benzene was replaced with ethanol as a solvent.

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.85; H, 7.09; N, 6.57. Found: C, 78.39; H, 7.11; N, 6.69.

The hydrochloride was deposited quantitatively as colorless needles from an acetone solution of Ib by treatment with a 50% excess of concentrated hydrochloric acid; m.p. 195° dec.

Anal. Calcd. for $C_{14}H_{16}ClNO$: Cl, 14.20. Found: Cl, 14.15.

The naphthoxazine (Ib) was the only product isolated when a benzene solution of 2-naphthol and acetaldehyde ammonia in a molar ratio of 2:1 was heated under reflux for two hours.

1-α-Aminoethyl-2-naphthol (IIIb) Hydrochloride.—Twenty-five grams of Ib (0.117 mole) was dissolved in 200 ml. of boiling propanol-2. Concentrated hydrochloric acid (18 ml.) followed by 12.5 ml. of water was added quickly to the boiling solution. The mixture was refluxed vigorously for two hours. The acetaldehyde liberated was identified as the 2,4-dinitrophenylhydrazone. After refluxing, the mixture was slowly distilled until the crystals which had formed were barely covered by liquid. Acetone (30 ml.) was added to the cooled mixture. The resulting colorless plate-like crystals were collected on a filter and washed several times with cold acetone and finally with ether; yield 25.0 g. (95%), m.p. 207° dec.

Anal. Calcd. for $C_{12}H_{14}ClNO$: Cl, 15.85. Found: Cl, 15.83.

When 5.0 g. of Ib in 50 ml. of methanol containing 5.0 ml. of concentrated hydrochloric acid was heated under reflux for one hour, the hydrochloride of Ib was recovered.

Ten grams of IIIb hydrochloride was added to 100 ml. of water, 150 ml. of ether and 20 ml. of 2-aminoethanol in a separatory funnel. After this mixture was shaken thoroughly, the ether layer was washed three times with 100-ml. portions of water and then dried over sodium sulfate. The ether was removed by evaporation at room temperature. The *free base* (8.4 g.) crystallized as colorless needles in essentially quantitative yield; m.p. 74–76°. The compound decomposed slowly with the liberation of ammonia and attempts to recrystallize it were not successful.

Reaction of 1-α-Aminoethyl-2-naphthol (IIIb) with Acetaldehyde.—Ten grams of IIIb hydrochloride (0.0447 mole) was combined with 100 ml. of water and 150 ml. of ether in a separatory funnel and shaken with 20 ml. of 2-aminoethanol (0.335 mole). The ether solution was washed three times with water and dried. Acetaldehyde (7.56 ml., 0.134 mole) was added and the mixture was kept at room temperature for one week. The solid (9.6 g.) obtained upon evaporation of the ether melted at 97.5–98° after recrystallization from methanol and did not depress the m.p. of Ib. The conversion to naphthoxazine was

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[13] W. T. Caldwell and T. R. Thompson, This Journal, 61, 2354 (1939).

quantitative. Although acetaldehyde ammonia was successfully used as a source of acetaldehyde in this ring closure, refluxing was required and the yield was lower.

1-α-Acetamidoethyl-2-naphthyl Acetate.—Ten grams of IIIb hydrochloride (0.0447 mole) was combined with water and ether in a separatory funnel and treated with 2-aminoethanol in the usual fashion. The ether solution of the free base was added to 25 ml. of acetic anhydride in 30 ml. of pyridine. After standing overnight, the mixture was concentrated to a volume of 20 ml. and poured into water. The crystals were collected on a filter; yield 10.8 g. (90%), m.p. 147–149°. After recrystallization from dry benzene, the product melted at 149–149.5°.

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.82; H, 6.32. Found: C, 71.20; H, 6.36.

Conversion of 1-α-Acetamidoethyl-2-naphthyl Acetate to IV.—1-α-acetamidoethyl-2-naphthyl acetate (1.5 g., 0.0055 mole) was dissolved in 150 ml. of acetone and cooled to 0°. This solution was treated with 100 ml. of 0.10 *N* potassium hydroxide solution and allowed to stand 2.5 hours at 0°. The solution was then acidified and concentrated under reduced pressure. The product crystallized from the residue at 0°; yield 1.1 g. (87%), m.p. 212.5° after recrystallization from methanol.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.60. Found: C, 73.04; H, 6.46.

1,2-Dihydro-1,3-dimethyl-2-acetyl-3H-naphth[1.2-e]-*m*-naphthoxazine Picrate.—Two grams of Ib was treated with 5 ml. of acetic anhydride in 10 ml. of pyridine for 24 hours. The colorless oil which separated when the pyridine solution was poured into a mixture of ice and water was washed thoroughly with water and taken up in methanol. Addition of a saturated methanol solution of picric acid brought about the rapid separation of an orange picrate; 3.0 g., m.p. 146–147°.

Anal. Calcd. for $C_{16}H_{17}NO_2 \cdot C_6H_3N_3O_7$: C, 54.55; H, 4.16; N, 11.57. Found: C, 54.53; H, 4.19; N, 11.6.

IV from Acetyl Derivative of Ib.—The picrate of acetylated Ib (1.9 g.) was decomposed with ammonium hydroxide in the usual fashion and the resulting oil dissolved in 20 ml. of propanol-2. After addition of 2 ml. of concentrated hydrochloric acid and 1.5 ml. of water, the mixture was refluxed for two hours, evaporated to a small volume, and poured into water. The water was extracted with ethyl acetate and the solution evaporated to an oil (0.75 g.). The oil was dissolved in benzene and crystallized upon addition of petroleum ether. After one recrystallization from methanol, the product melted at 211–212° and did not depress the melting point of IV prepared by deacetylation of 1-α-acetamidoethyl-2-naphthyl acetate.

Stability of Acetyl Derivative of Ib to Basic Hydrolysis.—The picrate of acetylated Ib (4.5 g.) was decomposed by extracting an ether solution three times with dilute ammonium hydroxide and washing with water. The oil remaining after removal of ether was dissolved in 125 ml. of 10% potassium hydroxide in methanol and the resulting solution was heated under reflux for one hour. Solvent was removed by evaporation under reduced pressure and the organic material extracted from the residue with ether. After drying, the ether was removed from solution and evaporated to an oil weighing 2.34 g.; 99% recovery of acetylated Ib. The oil was combined with 2.35 g. of picric acid and warmed with alcohol until solution was complete. On cooling to room temperature, an orange picrate (3.5 g.) separated, m.p. 147.5–148°. The melting point of a mixture of the product and the picrate of acetylated Ib was undepressed.

Anal. Calcd. for $C_{16}H_{17}NO_2 \cdot C_6H_3N_3O_7$: neut. equiv., 484. Found: neut. equiv., 490.

Addition Compound of Ib with 2-Naphthol. Procedure A.—A mixture of 14.4 g. of 2-naphthol (0.1 mole) and 6.1 g. of acetaldehyde ammonia (0.1 mole) in 300 ml. of benzene was refluxed for 45 minutes while being stirred vigorously. As the reaction progressed, the acetaldehyde ammonia slowly went into solution with the liberation of ammonia. The benzene solution was washed several times with water and dried. Benzene was evaporated from this solution under reduced pressure until the product began to separate. Petroleum ether was added and the mixture cooled; yield 12.8 g. (72%), m.p. 108–109° after recrystallization from benzene. The product was recovered unchanged after sublimation at 90° (0.1 mm.).

Anal. Calcd. for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 80.34; H, 6.41; N, 3.88.

Procedure B.—Ib (1.80 g., 0.00845 mole) was combined with 1.22 g. of 2-naphthol (0.00845 mole) and 10 ml. of benzene and the mixture warmed until solution was complete. An equal volume of petroleum ether (b.p. 30–80°) was added, and upon cooling a crystalline product (2.91 g.) was obtained; yield 96%, m.p. 107–108.5°. When recrystallized from benzene the product melted at 107–109° and did not depress the melting point of the adduct prepared directly from acetaldehyde ammonia and 2-naphthol according to procedure A.

The addition product (1.47 g., 0.00412 mole) was dissolved in ether in a separatory funnel and shaken with two 50-ml. portions of 10% sodium hydroxide solution. The ether solution was washed with water and dried. The crystals (0.85 g.) obtained upon removal of ether melted at 94–96°; 97% yield of Ib. When recrystallized twice from methanol, the product melted at 96.5–98° and did not depress the melting point of Ib. Acidification of the basic extracts and cooling resulted in the separation of 0.52 g. of solid, m.p. 120–122°. The product did not depress the m.p. of 2-naphthol (89% recovery).

Ten grams of the addition product (0.028 mole) was dissolved in 25 ml. of acetone and 3.7 ml. of concentrated hydrochloric acid was added to the solution at room temperature. After 40 hours, the resulting crystalline hydrochloride (6.7 g.) was removed by filtration. Treatment with 2-aminoethanol yielded the free base, which was crystallized from methanol; yield 4.5 g.; m.p. 96–97.5°. The melting point of the product was not depressed by admixture with Ib. 2-Naphthol (3.8 g.) was obtained from the acetone mother liquor; 94% recovery.

Conversion of IIIb to Ib and V.—Ten grams of IIIb hydrochloride (0.0447 mole) was combined with 2.8 g. of 85% potassium hydroxide in 50 ml. of alcohol and heated at reflux for 2.5 hours. Solvent was removed from the solution by evaporation under reduced pressure and the residue transferred with ether to a separatory funnel. The ether solution was extracted twice with 100 ml. of 10% aqueous sodium hydroxide and then washed twice with 100 ml. of water. The dry ether solution upon evaporation deposited a crystalline product; yield 4.41 g. (93%), m.p. 88–92°. Upon recrystallization from methanol, the product had a m.p. of 96.5–97.5° and did not depress the melting point of Ib. The aqueous and basic extracts were acidified and then neutralized with sodium bicarbonate and extracted with two 200-ml. portions of ethyl acetate. The ethyl acetate solution was dried, and evaporated under reduced pressure to an oil which was crystallized from alcohol; yield 0.67 g. (7%), m.p. 141.5–143°. Upon two crystallizations from alcohol the product had a m.p. of 147–148°.

Anal. Calcd. for $C_{24}H_{23}NO_2 \cdot C_2H_5OH$: C, 77.39; H, 7.24; N, 3.47. Found: C, 77.61; H, 7.17; N, 3.43.

The alcohol of crystallization was removed by distilling a benzene solution of the product. The crystalline material V which separated in quantitative yield melted at 152°.

Anal. Calcd. for $C_{24}H_{23}NO_2$: N, 3.92. Found: N, 3.88.

The hydrochloride of V melted at 191–192° dec.

Anal. Calcd. for $C_{24}H_{24}ClNO_2$: Cl, 9.00. Found: Cl, 9.00.

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