[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

CERTAIN KETONIC MANNICH BASES DERIVED FROM 1- AND 2-ACETONAPHTHONE

S. W. PELLETIER[1]

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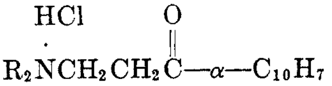
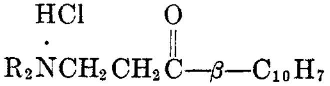
In connection with a study of the reduction of a series of β-aminoketones by lithium aluminum hydride, a number of Mannich bases derived from 1- and 2-acetonaphthone were prepared. Since Mannich bases of 1-acetonaphthone have not been previously described, it seemed useful to record the preparation and properties of a number of these compounds, along with several new derivatives of 2-acetonaphthone. Thus 1-α-naphthyl-3-dimethylaminopropanone-1 (Ia), 1-α-naphthyl-3-diethylaminopropanone-1 (Ib), 1-α-naphthyl-3-piperidinopropanone-1 (Ic), and 1-α-naphthyl-3-morpholinopropanone-1 (Id) were prepared in 25–46% yields[2] from 1-acetonaphthone, formaldehyde, and the appropriate tertiary amine hydrochloride. Similarly, from 2-acetonaphthone, 1-β-naphthyl-3-diethylaminopropanone-1 (IIa) and 1-β-naphthyl-3-morpholinopropanone-1 (IIb) were obtained in 46 and 76% yields,[2] respectively.



$$\overset{\mathrm{HCl}}{\underset{}{\cdot}}\,R_2NCH_2CH_2\overset{\mathrm{O}}{\overset{\|}{C}}—\alpha—C_{10}H_7$$

I

a. $R_2N = (CH_3)_2N$
b. $R_2N = (C_2H_5)_2N$
c. $R_2N =$ piperidino
d. $R_2N =$ morpholino



$$\overset{\mathrm{HCl}}{\underset{}{\cdot}}\,R_2NCH_2CH_2\overset{\mathrm{O}}{\overset{\|}{C}}—\beta—C_{10}H_7$$

II

a. $R_2N = (C_2H_5)_2N$
b. $R_2N =$ morpholino

The products derived from 1-acetonaphthone (I) were always obtained in lower yields than the corresponding ones from 2-acetonaphthone (II). This is probably due to the greater solubility of the 1-derivatives. The diethyl derivative of each series (Ib, IIa) was obtained in a low yield and was particularly difficult to purify. The bases were isolated and purified as the hydrochlorides.

EXPERIMENTAL[3]

The Mannich bases were prepared by the usual method, but since the yields were observed to be greatly affected by the choice of reaction and isolation conditions, the following directions are reported as giving the desired products in optimum yields.

Acetonaphthones. Eastman Kodak Practical grade 1-acetonaphthone was distilled *in vacuo*, discarding the first 10% and leaving a similar quantity of residue. The portion boiling at 105–110°/0.5 mm. was collected. Eastman Kodak "White Label" 2-acetonaphthone m.p. 53–55°, was used without further purification.

1-α-Naphthyl-3-dimethylaminopropanone-1 hydrochloride (Ia). A mixture of 8.2 g. (0.10

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[1] Present address: The Rockefeller Institute for Medical Research, New York, N. Y.

[2] Yields are based on the quantity of once-recrystallized material isolated.

[3] Melting points are corrected. Analyses are by Emily Davis, Jean Fortney, and K. Pih.

mole) of dimethylamine hydrochloride, 4 g. (0.13 mole) of paraformaldehyde, 17 g. (0.10 mole) of 1-acetonaphthone, 10 ml. of absolute ethanol, and 0.5 ml. of concentrated hydrochloric acid was boiled under reflux for four hours. After cooling to room temperature, a quantity of acetone equal to one-half the volume of the mixture was added slowly and the mixture was allowed to stand overnight in the refrigerator. The amorphous product which separated was collected and washed with cold acetone until free of yellow color. The yield of material melting at 135–144° was 14.0 g. The crude product was dissolved in 30 ml. of boiling absolute ethanol; the resulting solution was treated with Norite, filtered, and reheated to boiling. After adding 60 ml. of boiling ethyl acetate to the solution, it was allowed to cool slowly to room temperature in a beaker of hot water. Yield, 10 g. (38%) of white needles, m.p. 149–152.4°. Three more recrystallizations from absolute ethanol-ethyl acetate furnished pure Ia melting at 156.8–158.1°.

Anal.[4] Calc'd for $C_{15}H_{17}NO\cdot HCl$: C, 68.30; H, 6.88; N, 5.31.
Found: C, 68.08; H, 7.12; N, 5.35.

1-α-Naphthyl-3-diethylaminopropanone-1 hydrochloride (Ib). This compound was prepared by the method described for Ia except that 13 ml. of absolute ethanol was used as solvent and a 4½ hour reflux time was employed. After diluting with acetone and cooling in an ice-bath, a few crystals had formed. Ether was added to incipient turbidity and the mixture allowed to stand overnight in the refrigerator. The crude product which separated (10.5 g.) was recrystallized from a mixture of 1 part absolute ethanol and 2 parts ethyl acetate. The yield was 7.3 g. (25%) of white crystals melting at 141–142°. This compound was prepared in better yield by using isoamyl alcohol as the solvent. Boiling under reflux for 30 minutes and working up the mixture as described gave 15.5 g. (53%) of the crude product. Repeated recrystallization from a minimum of ethyl alcohol-ethyl acetate furnished material of constant m.p. 139–140°.

Anal. Calc'd for $C_{17}H^{21}NO\cdot HCl$: C, 69.97; H, 7.60; N, 4.80.
Found: C, 69.72; H, 7.78; N, 4.72.

1-α-Naphthyl-3-piperidinopropanone-1 hydrochloride (Ic). A finely powdered mixture of 12.2 g. (0.10 mole) of piperidine hydrochloride, 4 g. (0.13 mole) of paraformaldehyde, and 17 g. (0.10 mole) of 1-acetonaphthone in 15 ml. of absolute ethanol was boiled under reflux for one hour. Hydrochloric acid (0.5 ml.) was then added and boiling continued one hour. Another gram of paraformaldehyde was added and the mixture boiled an additional two hours. After cooling, 15 ml. of acetone was added and the mixture stored in the refrigerator overnight. The crude product was washed free of colored materials with acetone to give 17.6 g. (58%) of white crystals; m.p. 173–176°. Recrystallization of 31 g. from hot ethanol gave 18.3 g., m.p. 176–179°. Concentration of the mother liquor afforded an additional 9 g. of less pure material. Repeated recrystallization furnished pure white crystals; m.p. 180.3–182.3°.

Anal. Calc'd for $C_{18}H_{21}NO\cdot HCl$: C, 71.15; H, 7.30; N, 4.61.
Found: C, 71.07; H, 7.27; N, 4.67.

1-α-Naphthyl-3-morpholinopropanone-1 hydrochloride (Id). This compound was prepared by the method described for Ia except that 18 ml. of absolute ethanol was used as solvent, and a three-hour reflux time was employed. There was obtained 23.5 g. (77%) of yellow crystals; m.p. 158.5–163.5°. One recrystallization from ethanol afforded a 60% recovery of material melting at 163–165°. Repeated recrystallization from ethanol gave material melting at 166–169°, but which did not give a satisfactory analysis. (The analytical data for this material are given in parentheses.) An analytical sample was prepared by recrystallization from a mixture of methanol and acetone; m.p. 175–178°.

Anal. Calc'd for $C_{17}H_{19}NO_2\cdot HCl$: C, 66.77; H, 6.59; N, 4.58.

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[4] Analytical samples were dried at 0.5 mm. over P_2O_5 as follows: Ia, 1 hour at 75°; Ib, 2 hours at 75°; Ic and IIb, 3 hours at 100°; Id, 2 hours at 100°; and IIa, 1 hour at 100°. Drying times longer than those indicated engendered sufficient decomposition to vitiate the analyses.

Found: C, (66.24), 66.99; H, (6.73), 6.64; N, (4.46), 4.67.

1-β-Naphthyl-3-diethylaminopropanone-1 hydrochloride (IIa). This compound was prepared from 11 g. of diethylamine hydrochloride, 4 g. of paraformaldehyde, and 17 g. of 2-acetonaphthone by the method described for Ia except that 24 ml. of ethanol and a reflux time of six hours was employed. When dilution with acetone and standing overnight at 10° did not induce crystallization, dry ether was added slowly to the mixture. White crystals of IIa, m.p. 148.8–149.5°, were thereby obtained; yield 16.8 g. (57%). This compound was also prepared by refluxing the reactants for one-half hour in 25 ml. of isoamyl alcohol. Working up the reaction mixture gave 17 g. of material, m.p. 144–146°. Recrystallization from absolute ethanol (80% recovery) furnished white crystals of constant m.p. 147.3–147.8°, which failed to give a satisfactory analysis. An analytical sample was prepared by dissolving the crude material in the minimum of hot methanol and diluting this solution with a large volume of hot acetone. When cooled, the solution deposited fine white needles; m.p. 147.1–148.3°. Subsequent recrystallization did not alter the melting point.

Anal. Calc'd for $C_{17}H_{21}NO \cdot HCl$: C, 69.97; H, 7.60; N, 4.80.

Found: C, 70.44, 70.69; H, 7.67, 7.69; N, 4.88.

1-β-Naphthyl-3-morpholinopropanone-1 hydrochloride (IIb). A mixture of 59.4 g. (0.5 mole) of morpholine hydrochloride, 15 g. (0.5 mole) of paraformaldehyde, and 68 g. (0.4 mole) of 2-acetonaphthone in 100 ml. of absolute ethanol was boiled under reflux a half-hour, after which 1 ml. of hydrochloric acid was added. Boiling was continued for an hour and a half when the mixture was allowed to cool to room temperature. Occasionally the product began to separate before the heating period was completed. There was collected 103 g. (85%) of a white amorphous solid; m.p. 195.5–200.5° dec. The product is only slightly soluble in cold water, methanol, or ethanol. It may be recrystallized from hot methanol in 90% yield. Three such recrystallizations furnished the pure hydrochloride; m.p. 200–201.5° dec.

Anal. Calc'd for $C_{17}H_{19}NO \cdot HCl$: C, 66.77; H, 6.59; N, 4.58.

Found: C, 67.29; H, 6.73; N, 4.78.

SUMMARY

Optimum conditions are described for the synthesis of six new 1-naphthyl-3-alkylaminopropan-1-ones by the Mannich reaction on 1- and 2-acetonaphthone. The products were isolated as the hydrochlorides.

URBANA, ILLINOIS