9-Fluorononyl phenyl ketone was prepared in essentially the same way (but without external cooling)[5] from 9-fluorononyl chloride (13.0 g., 0.072 mole), lithium (1.4 g., 0.20 g. atom), and benzonitrile (7.4 g., 0.072 mole), using anhydrous ethyl ether as solvent. The ketone was collected as a pale yellow oil, b.p. 124–126° (0.1–0.2 mm.), which solidified in long, needle-like crystals. These were dissolved in warm pentane; and the solution was filtered. The filtrate was concentrated and the resultant solid was dried in a vacuum desiccator. Recrystallization from methanol gave 9-fluorononyl phenyl ketone (7.8 g., 43%) as long, colorless, translucent needles, m.p. 36–36.5°.

Anal. Calcd. for $C_{16}H_{23}FO$: C, 76.76; H, 9.26. Found: C, 76.98; H, 9.35.

2,4-Dinitrophenylhydrazone, small, red prisms from ethyl acetate, m.p. 121.5–122°.

Anal. Calcd. for $C_{22}H_{27}FN_4O_4$: N, 13.02. Found: N, 13.18.

12-Fluorododecanol. The organolithium compound was prepared in essentially the same way from 10-fluorodecyl chloride (14.0 g., 0.072 mole) and lithium (1.4 g., 0.20 g. atom), using anhydrous ethyl ether as solvent. The resultant solution was filtered under nitrogen pressure into the subsidiary apparatus, in the dropping funnel of which had been placed ethylene oxide (13.2 g., 0.30 mole) in ethyl ether (50 ml.); the dropping funnel was cooled in a cardboard jacket containing Dry-Ice, and the reaction vessel was cooled in an ice-salt bath. The ethylene oxide solution was added over 30 min. with stirring. Stirring was continued in the cold for an additional 30 min. and then at room temperature for 2 hr. The mixture was added to crushed ice, and acidified with hydrochloric acid. The solution was then extracted with ethyl ether, and the extracts were dried over sodium sulfate. After removal of the ether, the residue on fractionation yielded unreacted 10-fluorodecyl chloride (1.5 g.) and then 12-fluorododecanol (3.1 g., 24%), b.p. 165–170° (12 mm.), n_D^{25} 1.4388. We have previously reported[10] b.p. 88–92° (0.15 mm.) and n_D^{25} 1.4391.

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Condensation of Methylamine, Formaldehyde, and Cyclohexanones. Improved Synthesis of Methyl-bis(2-cyclohexanonylmethyl)amine

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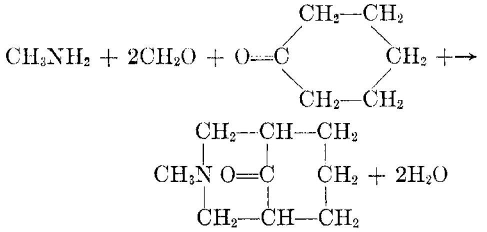
In 1920 Mannich and Braun[1] reported that cyclohexanone reacted readily with dimethylaminehydrochloride and formaldehyde to give an 85% yield of 2-(dimethylaminomethyl) cyclohexanone, but Mannich and Honig[2] found that when cyclohexanone was replaced with 4-methylcyclohexanone poor yields of the 2-dimethylaminomethyl-4-methylcyclohexanone were isolated. When Mannich[1] replaced dimethylaminehydrochloride with methylaminehydrochloride he obtained a small yield (2.4%) of methyl-bis(2-cyclohexanonylmethyl)amine (I). More recently Mannich and Hieronimus[3] indicated that unlike secondary amines, most primary amines, such as methylamine, react only poorly with formaldehyde and ketones to form 1,3-keto bases with a secondary nitrogen atom.

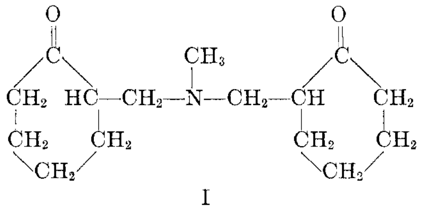
In this investigation condensation of methylaminehydrochloride, formaldehyde, and cyclohexanone in a 1:2:2 molar ratio, respectively, in methanol as a solvent gave a 19% yield of I. When the aminehydrochloride was replaced with the free base and an equivalent of concentrated hydrochloric acid added, a 45.2% yield of I was obtained. Similar condensations in which cyclohexanone was replaced with 3-methylcyclohexanone and 4-methylcyclohexanone yielded the corresponding derivatives of I. Condensations involving the free base, formaldehyde, and cyclohexanones without the addition of concentrated hydrochloric acid failed to give any crystalline products.

When methylamine, formaldehyde, cyclohexanone, and hydrochloric acid were condensed in an equimolar ratio with a view to obtaining 2-methylaminomethylcyclohexanone (II), a 31.8% yield of I was obtained. Condensations involving molar ratios of methylamine, formaldehyde, cyclohexanone, and hydrochloric acid of 2:2:1:2 gave 55% yields of I, but in no case was II isolated.

Many condensations have been carried out with methylamine, formaldehyde, cyclohexanone, and hydrochloric acid in a 1:2:1:1 molar ratio in meth-



III



I

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[2] C. Mannich and P. Honig, *Arch. Pharm.*, **265**, 598 (1927).

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anol solution with a view to obtaining 3-aza-3-methylbicyclo [3,3,1] nonan-9-one (III). When relatively concentrated solutions of the reactants in methanol were employed, instead of the desired cyclic product III, I was isolated. Replacement of cyclohexanone with 3-methylcyclohexanone and 4-methylcyclohexanone gave the corresponding bis derivatives. When condensations were effected in dilute solutions in methanol so as to favor the formation (intramolecular rather than bis formation) of III, no crystalline products were isolated.

EXPERIMENTAL[4]

Reaction 1: methyl-bis(2-cyclohexanonylmethyl)amine (I). To 3.88 g. of 40% methylamine (4.4 ml., 0.05 mole) in 15 ml. methanol was added dropwise, with agitation, at 15–18°, 7.5 ml. 37% formaldehyde (0.1 mole) dissolved in 10 ml. methanol. A solution of 9.8 g. of cyclohexanone (10.4 ml., 0.1 mole) in 25 ml. methanol was added with shaking, followed by the dropwise addition of 4.2 ml. 37% hydrochloric acid (0.05 mole). The flask was stoppered, shaken well for 2 min. and set aside at room temperature (25–28°) for 22 hr. The solution was decanted to a beaker and placed under a hood for 24 hr. The remaining liquid was treated with 25 ml. water and extracted with two 25 ml. portions of ether. The ether extracts were distilled at 34–35°, 755 mm. pressure, leaving only a trace of higher boiling material. To the aqueous extract after cooling on an ice bath was added 3.05 g. monoethanolamine (3 ml., 0.05 mole). A cloudiness appeared and after 3 hr. standing 4.78 g. white product, m.p. 152–161°, was removed by filtration. An additional 0.9 g. was obtained from the filtrate. The total crude yield was 45.2%. After five recrystallizations from ethyl acetate the compound melted at 163.5–164°.

Anal. Calcd. for $C_{15}H_{25}NO_2$: C, 71.64; H, 10.01; N, 5.57. Found: C, 71.52; H, 9.71; N, 5.60.

When reaction 1 was repeated using 4.9 g. cyclohexanone (0.05 mole) instead of 0.1 mole, 2.49 g., 39.6% yield, of I was obtained. When the latter condensation was repeated using a total of 500 ml. methanol instead of 50 ml., no crystalline product was isolated.

When reaction 1 was repeated using 3.38 g. methylaminehydrochloride (0.05 mole) in lieu of the 40% methylamine and hydrochloric acid, 2.38 g. of I, 18.9% yield, was isolated.

When reaction 1 was repeated but omitting the addition of 4.2 ml. 37% hydrochloric acid, no crystalline product was isolated.

When reaction 1 was repeated using 0.05 mole quantities of methylamine, formaldehyde, cyclohexanone, and hydrochloric acid, 1.94 g. of I, 30.9% yield, was obtained. When the latter reaction was repeated using 0.1 mole quantities of methylamine, formaldehyde, and hydrochloric acid, and 0.05 mole cyclohexanone, 3.48 g. of I, 55.4% yield, was secured.

Reaction 2: Methyl-bis(4-methyl-2-cyclohexanonylmethyl)-aminehydrochloride (IV). To 7.78 g. of 40% methylamine (8.8 ml., 0.1 mole) in 60 ml. of methanol at 15–18° was added 8.36 ml. 37% hydrochloric acid (0.1 mole). Over a period of 3 min. 15 ml. 37% formaldehyde (0.2 mole) was added with agitation. After adding 22.4 g. 4-methylcyclohexanone (24.6 ml., 0.2 mole), the resulting solution was gently refluxed for 2 hr. on a water bath. The solution was decanted to a beaker and placed under a hood to remove the solvents. The resulting solution was treated with 40 ml. water and 16.7 ml. concentrated hydrochloric acid. Small particles of white solid began to separate. After standing for 3 hr. 3.11 g., m.p. 185–187°, white solid was removed by filtration. The filtrate was extracted with three 15 ml. portions of ether, which after drying and distillation gave but a trace of high boiling material. The aqueous extracts after standing 2 days gave an additional 2.18 g. white solid, m.p. 185–187°. The total crude yield was 5.29 g. or 16.9%. Upon two recrystallizations from *n*-butyl alcohol, the hydrochloride melted at 193–195°.

Anal. Calcd. for $C_{17}H_{30}ClNO_2$: C, 64.64; H, 9.57; Cl, 11.22; N, 4.43. Found: C, 64.65; H, 9.69; Cl, 11.10; N, 4.22.

Repetition of reaction 2 in which the reactants were allowed to stand 46 hr. at 25–28° instead of refluxing for 2 hr. gave 6.17 g. of IV or 19.7% yield.

Methyl-bis(5-methyl-2-cyclohexanonylmethyl)amine or methyl-bis(3-methyl-2-cyclohexanonylmethyl)amine. (The structure of the compound is being investigated.) Repetition of reaction 1 using 0.1 mole of 3-methylcyclohexanone in lieu of 0.1 mole of cyclohexanone gave 1.45 g. white product, m.p. 164.5–166°, 10.5% yield.

Anal. Calcd. for $C_{17}H_{29}NO_2$: C, 73.07; H, 10.45; N, 5.01. Found: C, 72.80; H, 10.33; N, 5.15.

Each of the condensations mentioned above has been repeated at least five times with essentially the same yields.

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[4] Melting points are uncorrected.

2-Keto-1-methyl-$\Delta^{1(8)}$-tetrahydroindan[1]

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A synthesis of 2-keto-$\Delta^{1(8)}$-tetrahydroindan has been described in which sodio-2-carbethoxycyclohexanone (I) was alkylated with propargyl bromide, the triple bond hydrated, and the resulting diketoester cyclized and decarboxylated to yield the ketone in a 45% over-all yield.[2] This three step synthesis was evidently necessary as the authors reported that chloroacetone would not alkylate I. In an attempt to prepare the corresponding 1-methyl homolog (IV) it was found that 1-bromobutan-2-one was reactive enough toward I to give the diketoester (II) which was converted to the desired ketone (IV) in an over-all yield of 42%. The diketoester (II) was also cyclized with sodium ethoxide to the unsaturated ketoester (III) and then saponified and decarboxylated to give IV.

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