the appropriate chlorinated phenol (0.2 mole) was refluxed for 8 hr. The reaction mixture was then cooled to 25° and slowly reheated to reflux under reduced pressure (10–15 mm.) for 4 hr. to remove the last traces of hydrogen chloride and thus complete the reaction. The product was purified by distillation at reduced pressure through a short Claisen column.

Addition of about 0.1 g. of anhydrous magnesium chloride catalyzed the reaction of the chlorinated phenols and facilitated the removal of the hydrogen chloride.

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Organometallic Reactions of ω-Fluoroalkyl Halides. III.[1] ω-Fluoroalkyllithium Compounds

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In earlier reports[2,3] in this series have been described the preparation and reactions of ω-fluoroalkylmagnesium halides.[4] The present communication deals with a very brief examination of the corresponding ω-fluoroalkyllithium compounds. From a comparison of the yields obtained with the two metals, it seems reasonable to conclude that, with the one possible exception noted below, lithium is probably less effective than magnesium in syntheses involving organometallic derivatives of ω-fluoroalkyl halides.

The ω-fluoroalkyllithium compounds were prepared by standard procedures[5,6] and in the equipment previously described.[2] Petroleum ether[7] and ethyl ether[5,6] were examined as solvents; the latter appeared to be more satisfactory. Successful reactions included the following:

$$F(CH_2)_6Br \xrightarrow[C_6H_5CN]{Li} F(CH_2)_6COC_6H_5 \quad (47\%)$$

$$F(CH_2)_9Cl \xrightarrow[C_6H_5CN]{Li} F(CH_2)_9COC_6H_5 \quad (43\%)$$

$$F(CH_2)_{10}Cl \xrightarrow[(CH_2)_2O]{Li} F(CH_2)_{12}OH \quad (24\%)$$

There was no evidence of disubstitution products formed by replacement of both the fluorine and the halogen atoms; nor was there any sign of preferential replacement of fluorine, such as occurred when ω-fluoroalkyl bromides and iodides were treated with magnesium.[2] Nevertheless, it was apparent that considerable disruption of the ω-fluoroalkyl halides had occurred, since unreacted starting materials were seldom recovered.

The observation that preferential replacement of fluorine did not occur suggests the possible advantage of using lithium in place of magnesium in those instances in which the higher ω-fluoroalkyl bromides are more readily available than the corresponding ω-fluoroalkyl chlorides.

Under the same conditions, the lower ω-fluoroalkyl halides failed to give any of the expected products. Members examined included 3-fluoropropyl bromide, 4-fluorobutyl chloride, 4-fluorobutyl bromide, 5-fluoroamyl chloride, and 5-fluoroamyl bromide.

EXPERIMENTAL[8]

6-Fluorohexyl phenyl ketone. In the main reaction vessel,[2] cooled to −10° in a dry ice–acetone bath,[6] were placed lithium[9] (1.4 g., 0.20 g. atom) and anhydrous ethyl ether (25 ml.). Approximately 10 ml. of a solution of 6-fluorohexyl bromide (13.0 g., 0.071 mole) in ethyl ether (50 ml.) were added with stirring. There was evidence of a reaction almost immediately. The remainder of the fluorobromide solution was added dropwise over 1 hr. at a temperature of −10° or less. When the addition was complete, the mixture was stirred for 3 hr., while warming to 15°. The resultant organolithium solution was filtered under nitrogen pressure into the dropping funnel of the subsidiary vessel,[2] and was added (over 15 min.) at room temperature with stirring to a solution of benzonitrile (7.4 g., 0.072 mole) in ethyl ether (50 ml.). A vigorous reaction took place, and the color changed to orange. The mixture was gently refluxed for 1 hr. after the addition, and then allowed to stand overnight in an atmosphere of nitrogen. The mixture was cooled and hydrolyzed by the gradual addition of excess 10% sulfuric acid. The ether was removed on a water bath, and the residue was heated for a further 30 min. to ensure hydrolysis of the ketimine salt. The mixture was cooled and extracted with ether. The extracts were washed successively with water, 10% sodium carbonate, and water, and dried over magnesium sulfate. After removal of the ether, the residue on fractionation yielded 6-fluorohexyl phenyl ketone (6.9 g., 47%), b.p. 171–172° (13 mm.), 103° (0.15 mm.), m.p. 27–28° (corr.).

Anal. Calcd. for $C_{13}H_{17}FO$: C, 74.99; H, 8.17. Found: C, 75.02; H, 8.18.

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[1] Issued as DRB Report No. SW-34.

[2] F. L. M. Pattison and W. C. Howell, Part I, *J. Org. Chem.*, **21**, 879 (1956).

[3] W. C. Howell, W. J. Cott, and F. L. M. Pattison, Part II, *J. Org. Chem.*, **22**, 255 (1957).

[4] To avoid ambiguity, fluorine is not generally referred to as halogen in this communication.

[5] H. Gilman, E. A. Zoellner, and W. M. Selby, *J. Am. Chem. Soc.*, **55**, 1252 (1933).

[6] H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949).

[7] H. Gilman, F. W. Moore, and O. Baine, *J. Am. Chem. Soc.*, **63**, 2479 (1941).

[8] The microanalyses were performed by Mr. J. F. Alicino, Metuchen, N. J. and by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

[9] The lithium was obtained from the Lithium Corp. of America, Inc., Minneapolis, 2, Minn., in the form of 5 mm. ribbon, covered with a protective coating of vaseline. It was found that the average weight of a 10 cm. length of ribbon was 0.19 g. When the apparatus had been assembled, the appropriate length of ribbon was measured off and wiped as free as possible from vaseline. This length was then cut with scissors into small pieces (*ca.* 2–3 mm.) and transferred rapidly to the reaction vessel. All subsequent operations were conducted in an atmosphere of nitrogen. The lithium particles were washed with dry petroleum ether to remove the last traces of vaseline, and the washings were removed by filtration through the filter disc. The flask and lithium particles were then washed thoroughly with several portions of anhydrous ethyl ether, and the washings removed. The metal was then considered ready for reaction.

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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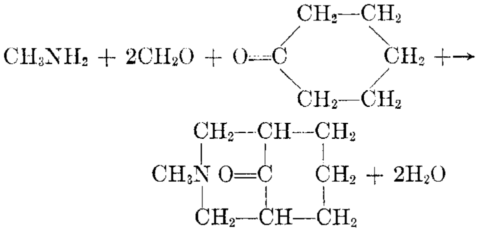
In 1920 Mannich and Braun[1] reported that cyclohexanone reacted readily with dimethylaminehydrochloride and formaldehyde to give an 85% yield of 2-(dimethylaminomethyl) cyclohexanone, but Mannich and Honig[2] found that when cyclohexanone was replaced with 4-methylcyclohexanone poor yields of the 2-dimethylaminomethyl-4-methylcyclohexanone 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.

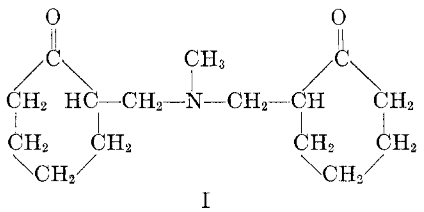
In this investigation condensation of methylaminehydrochloride, formaldehyde, and cyclohexanone in a 1:2:2 molar ratio, respectively, in methanol as a solvent gave a 19% yield of I. When the aminehydrochloride was replaced with the free base and an equivalent of concentrated hydrochloric acid added, 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



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