161°. A mixture melting point with an authentic specimen was not depressed.

For a duplicate reaction 3.73 g. (88%) of triphenyl-2-furyltin was recovered, melting at 159–160°.

*Acknowledgment.* This investigation was aided by a fellowship from The National Medical Fellowships, Inc., through funds appropriated by The National Foundation for Infantile Paralysis. One of us (L.A.G.) wishes to express his appreciation for this assistance.

AMES, IOWA

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO]

# Organometallic Reactions of ω-Fluoroalkyl Halides. II.[1,2] Reactions of ω-Fluoroalkylmagnesium Chlorides

W. C. HOWELL, W. J. COTT, AND F. L. M. PATTISON

*Received September 14, 1956*

The study of Grignard reagents formed from ω-fluoroalkyl halides has been extended to include a variety of typical reactions through the use of such reagents as acid chlorides, acid anhydrides, ethylene oxide, benzonitrile, and triethyl orthoformate. This has led to new methods for preparing ω-fluorocarboxylic esters, ω-fluoroalkyl ketones, ω-fluoroalcohols and ω-fluoroaldehydes, all of which are of pharmacological interest.

In the preceding paper of this series[2] a general method was outlined for the preparation of Grignard reagents from various ω-fluoroalkyl halides. From this study, the longer chain ω-fluoroalkyl chlorides ($C_6$–$C_{10}$) emerged as potentially valuable intermediates in the synthesis of new ω-fluoroalkylated derivatives. At that time, however, it was established only that these Grignard reagents reacted with carbon dioxide. To determine the general usefulness of the method, other reactions have been examined both for the diversity of reaction type, and for possible pharmacological interest of the products. The reactants selected were: (*a*) *Ethyl chloroformate:* reaction of a carbonyl halide; formation of ω-fluorocarboxylic esters.[3,4] (*b*) *Acid chlorides:* reaction of a carbonyl halide; formation of ω-fluoroalkyl ketones.[5] (*c*) *Carboxylic anhydrides:* addition to a carbonyl group; formation of ω-fluoroalkyl ketones.[5] (*d*) *Ethylene oxide:* cleavage of an epoxide; formation of ω-fluoroalcohols.[6] (*e*) *Benzonitrile:* addition to an unsaturated C—N system; formation of ω-fluoroalkyl phenyl ketones.[5] (*f*) *Triethyl orthoformate:* cleavage of an ether-acetal; formation of ω-fluoroaldehydes.[7]

First to be examined were the reactions of ω-fluoroalkylmagnesium chlorides with ethyl chloroformate[8–10] giving rise to ω-fluorocarboxylic esters. A large excess of chloroformate was used and the reaction was completed by heating for a short time under reflux; by this means, tertiary alcohol formation was minimized, but ketones were occasionally isolated, formed by reaction of excess Grignard reagent with the main product. A representative example is described in the Experimental section, and results are summarized in Table I. Similar conditions were found to be satisfactory for the use of acid chlorides[11] in the preparation of ω-fluoroalkyl ketones, although tertiary alcohol formation appeared to occur to a greater extent than in the reactions with ethyl chloroformate. The lower ω-fluorocarboxylic acid chlorides failed to react under the conditions employed; thus fluoroacetyl chloride, 3-fluoropropionyl chloride, 4-fluorobutyryl chloride and 5-fluorovaleryl chloride gave none of the desired ketones. The successful reactions are shown in Table I.

The use of carboxylic anhydrides[12–16] for the preparation of ketones was next investigated. A series of ω-fluoroalkyl methyl ketones (Table I)

---

[1] (*a*) Issued as DRB Report No. SW-29. (*b*) To avoid ambiguity, fluorine is not generally referred to as halogen in this communication.

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

[3] F. J. Buckle, F. L. M. Pattison, and B. C. Saunders, *J. Chem. Soc.*, 1471 (1949).

[4] F. L. M. Pattison, S. B. D. Hunt, and J. B. Stothers, *J. Org. Chem.*, **21**, 883 (1956).

[5] R. R. Fraser, J. E. Millington, and F. L. M. Pattison, *J. Am. Chem. Soc.*, in press.

[6] F. L. M. Pattison, W. C. Howell, A. J. McNamara, J. C. Schneider, and J. F. Walker, *J. Org. Chem.*, **21**, 739 (1956).

[7] J. F. K. Wilshire and F. L. M. Pattison, *J. Am. Chem. Soc.*, **78**, 4996 (1956).

[8] J. Houben, *Ber.*, **36**, 3087 (1903).

[9] R. Gaertner, *J. Am. Chem. Soc.*, **73**, 3934 (1951).

[10] A. I. Krutman, *J. Gen. Chem.* (*U.S.S.R.*), **22**, 1385 (1952) (Engl. translation).

[11] W. C. Percival, R. B. Wagner, and N. C. Cook, *J. Am. Chem. Soc.*, **75**, 3731 (1953).

[12] Tissier and Grignard, *Compt. rend.*, **132**, 683 (1901).

[13] H. Fournier, *Bull. soc. chim. France*, [3], **31**, 483 (1904); [3], **35**, 19 (1906); [4], **7**, 836 (1910).

[14] M. S. Newman and W. T. Booth, *J. Am. Chem. Soc.*, **67**, 154 (1945).

[15] M. S. Newman and T. J. O'Leary, *J. Am. Chem. Soc.*, **68**, 258 (1946).

[16] M. S. Newman and A. S. Smith, *J. Org. Chem.*, **13**, 592 (1948).

TABLE I

GRIGNARD REACTIONS OF ω-FLUOROALKYL CHLORIDES

| ω-Fluoro-alkyl Chloride | Reagent | Product | Yield, % | Disubstitution Product | Yield, % |
|---|---|---|---|---|---|
| $F(CH_2)_6Cl$ | $ClCOOEt$ | Ethyl 7-fluoroheptanoate<br>$F(CH_2)_6COOEt$ | 48 | Diethyl suberate[a]<br>$EtOOC(CH_2)_6COOEt$ | 6 |
| $F(CH_2)_7Cl$ | $ClCOOEt$ | Ethyl 8-fluoroöctanoate<br>$F(CH_2)_7COOEt$ | 49 | Diethyl azelate[a]<br>$EtOOC(CH_2)_7COOEt$ | 8 |
| $F(CH_2)_8Cl$ | $ClCOOEt$ | Ethyl 9-fluorononanoate<br>$F(CH_2)_8COOEt$ | 54.5 | Diethyl sebacate[a]<br>$EtOOC(CH_2)_8COOEt$ | 10 |
| $F(CH_2)_9Cl$ | $ClCOOEt$ | Ethyl 10-fluorodecanoate[b]<br>$F(CH_2)_9COOEt$ | 61 | Diethyl undecanedioate[a]<br>$EtOOC(CH_2)_9COOEt$ | 6 |
| $F(CH_2)_{10}Cl$ | $ClCOOEt$ | Ethyl 11-fluoroundecanoate[c]<br>$F(CH_2)_{10}COOEt$ | 54 | Diethyl dodecanedioate[a]<br>$EtOOC(CH_2)_{10}COOEt$ | 4 |
| $F(CH_2)_6Cl$ | $CH_3COCl$ | 8-Fluoro-2-octanone<br>$F(CH_2)_6COCH_3$ | 47 | | |
| $F(CH_2)_6Cl$ | $CH_3(CH_2)_4COCl$ | 12-Fluoro-6-dodecanone<br>$F(CH_2)_6CO(CH_2)_4CH_3$ | 49 | | |
| $F(CH_2)_6Cl$ | $F(CH_2)_5COCl$ | 1,12-Difluoro-6-dodecanone[d]<br>$F(CH_2)_6CO(CH_2)_5F$ | 51 | | |
| $F(CH_2)_6Cl$ | $F(CH_2)_6COCl$ | 1,13-Difluoro-7-tridecanone[e]<br>$F(CH_2)_6CO(CH_2)_6F$ | 55 | | |
| $F(CH_2)_6Cl$ | $(CH_3CO)_2O$ | 8-Fluoro-2-octanone<br>$F(CH_2)_6COCH_3$ | 59 | 2,9-Decanedione[f]<br>$CH_3CO(CH_2)_6COCH_3$ | 17 |
| $F(CH_2)_7Cl$ | $(CH_3CO)_2O$ | 9-Fluoro-2-nonanone<br>$F(CH_2)_7COCH_3$ | 64 | 2,10-Undecanedione[f]<br>$CH_3CO(CH_2)_7COCH_3$ | 16 |
| $F(CH_2)_8Cl$ | $(CH_3CO)_2O$ | 10-Fluoro-2-decanone<br>$F(CH_2)_8COCH_3$ | 68 | 2,11-Dodecanedione[f]<br>$CH_3CO(CH_2)_8COCH_3$ | 19 |
| $F(CH_2)_9Cl$ | $(CH_3CO)_2O$ | 11-Fluoro-2-undecanone<br>$F(CH_2)_9COCH_3$ | 65 | 2,12-Tridecanedione[f]<br>$CH_3CO(CH_2)_9COCH_3$ | 21 |
| $F(CH_2)_{10}Cl$ | $(CH_3CO)_2O$ | 12-Fluoro-2-dodecanone<br>$F(CH_2)_{10}COCH_3$ | 64 | 2,13-Tetradecanedione[f]<br>$CH_3CO(CH_2)_{10}COCH_3$ | 22 |
| $F(CH_2)_6Cl$ | $[F(CH_2)_5CO]_2O$ | 1,12-Difluoro-6-dodecanone[d]<br>$F(CH_2)_6CO(CH_2)_5F$ | 47 | | |
| $F(CH_2)_6Cl$ | $(CH_2)_2O$ | 8-Fluoroöctanol<br>$F(CH_2)_8OH$ | 46 | 1,10-Decanediol<br>$HO(CH_2)_{10}OH$ | 4 |
| $F(CH_2)_8Cl$ | $C_6H_5CN$ | 8-Fluorooctyl phenyl ketone<br>$F(CH_2)_8COC_6H_5$ | 70 | 1,8-Dibenzoyloctane[g]<br>$C_6H_5CO(CH_2)_8COC_6H_5$ | 10 |
| $F(CH_2)_8Cl$ | $HC(OC_2H_5)_3$ | 9-Fluorononanal<br>$F(CH_2)_8CHO$ | 37[h] | Sebacaldehyde<br>$OHC(CH_2)_8CHO$ | 43[i] |

[a] Identified by hydrolysis to the corresponding acid, followed by mixed melting point determination with authentic sample. [b] Also isolated was 1,19-difluoro-10-nonadecanone, $F(CH_2)_9CO(CH_2)_9F$ (11% yield), formed by reaction of excess Grignard reagent with the main product. [c] Also isolated was 1,21-difluoro-11-heneicosanone, $F(CH_2)_{10}CO(CH_2)_{10}F$ (4% yield), formed by reaction of excess Grignard reagent with the main product. [d] Also isolated was 5-fluoroamyl-*bis*-6-fluorohexylcarbinol, $F(CH_2)_5C(OH)[(CH_2)_6F]_2$ (10% yield), formed by reaction of excess Grignard reagent with the main product. [e] Also isolated was *tris*-6-fluorohexylcarbinol, $[F(CH_2)_6]_3COH$ (11% yield), formed by reaction of excess Grignard reagent with the main product. [f] Identified by melting point and formation of 2,4-dinitrophenylhydrazone. [g] Identified by melting point and formation of dioxime. [h] Total yield of free aldehyde and corresponding diethyl acetal; yield of pure, free aldehyde was 25%. [i] High yield of disubstitution product was possibly due to prolonged refluxing with excess magnesium.

was prepared by the interaction of the appropriate ω-fluoroalkylmagnesium chloride with acetic anhydride under essentially the same conditions as those recommended by Newman and Smith.[16] Of the ω-fluorocarboxylic anhydrides examined, fluoroacetic anhydride and 3-fluoropropionic anhydride failed to react under the conditions employed, but 6-fluorohexanoic anhydride formed the expected 1,12-difluoro-6-dodecanone in 47% yield.

Several reactions were studied in less detail. The use of ethylene oxide for forming primary alcohols[17] was illustrated by the conversion of 6-fluorohexyl chloride to 8-fluorooctanol. 8-Fluorooctyl phenyl ketone was prepared from 8-fluorooctylmagnesium chloride by treatment with benzonitrile; this procedure afforded a general route to the new series of ω-fluoroalkyl phenyl ketones, the pharmacological properties of which could be compared with the corresponding ω-fluoroalkyl methyl ketones.[5] Finally, the Bodroux-Tschitschibabin synthesis[18,19] was examined as a means of preparing ω-fluoroaldehydes, which have been obtained only with difficulty by other conventional methods.[7] Treatment of 8-fluorooctylmagnesium chloride with triethyl orthoformate in the usual manner[20,21]

---

(17) R. C. Huston and C. C. Langham, *J. Org. Chem.*, **12**, 90 (1947).

(18) F. Bodroux, *Compt. rend.*, **138**, 92, 700 (1904).

(19) A. E. Tschitschibabin, *Ber.*, **37**, 186, 850 (1904).

(20) L. I. Smith and M. Bayliss, *J. Org. Chem.*, **6**, 437 (1941).

(21) L. I. Smith and J. Nichols, *J. Org. Chem.*, **6**, 489 (1941).

TABLE II

PHYSICAL CONSTANTS AND ANALYTICAL DATA

| Compound | Boiling Point °C. | Boiling Point Mm. | $n_D^{25}$ or M.P., °C. | C, % Calcd. | C, % Found | H, % Calcd. | H, % Found | N, % Calcd. | N, % Found |
|---|---|---|---|---|---|---|---|---|---|
| $F(CH_2)_6COOEt$ | 97–97.5 | 11 | 1.4111 | 61.34 | 61.32 | 9.72 | 9.52 | | |
| $F(CH_2)_7COOEt$[a] | 106.5–107 | 9 | 1.4158 | 63.13 | 63.08 | 10.07 | 9.72 | | |
| $F(CH_2)_8COOEt$ | 120–120.5 | 9 | 1.4191 | 64.67 | 64.42 | 10.36 | 10.16 | | |
| $F(CH_2)_9COOEt$[b] | 136–136.5 | 11 | 1.4228 | 66.02 | 65.62 | 10.62 | 10.32 | | |
| $F(CH_2)_{10}COOEt$[c] | 145–146 | 9 | 1.4257 | 67.20 | 67.19 | 10.85 | 10.74 | | |
| $F(CH_2)_6COCH_3$ | 87–88 | 11 | 1.4132 | 65.73 | 65.65 | 10.34 | 10.11 | | |
| DNP[d,e] | | | 82 | | | | | 17.17 | 17.12 |
| $F(CH_2)_7COCH_3$ | 98–98.5 | 9 | 1.4180 | 67.45 | 67.73 | 10.70 | 10.92 | | |
| DNP[e] | | | 65 | | | | | 16.47 | 16.65 |
| $F(CH_2)_8COCH_3$ | 113–113.5 | 9 | 1.4213 | 68.92 | 68.60 | 10.99 | 10.98 | | |
| DNP[e] | | | 83.5 | | | | | 15.81 | 15.57 |
| $F(CH_2)_9COCH_3$ | 126–126.5 | 9.5 | 1.4258 | 70.16 | 69.84 | 11.24 | 11.00 | | |
| DNP[e] | | | 70 | | | | | 15.21 | 15.48 |
| $F(CH_2)_{10}COCH_3$ | 138–138.5 | 9.5 | 1.4288 | 71.24 | 71.07 | 11.46 | 11.44 | | |
| DNP[e] | | | 87.5 | | | | | 14.65 | 14.44 |
| $F(CH_2)_6CO(CH_2)_4CH_3$ | 138.5–139 | 13 | 1.4278 | 71.24 | 71.38 | 11.46 | 11.45 | | |
| DNP[e] | | | 47.5 | | | | | 14.65 | 14.43 |
| $F(CH_2)_6CO(CH_2)_5F$ | 136–136.5 | 4 | 1.4254 | 65.42 | 65.44 | 10.07 | 10.15 | | |
| DNP[e] | | | 41 | | | | | 14.00 | 14.24 |
| $F(CH_2)_6CO(CH_2)_6F$ | 99–99.5 | 0.18 | 1.4292<br>23 | 66.62 | 66.58 | 10.33 | 10.23 | | |
| DNP[e] | | | 21 | | | | | 13.52 | 13.45 |
| $F(CH_2)_9CO(CH_2)_9F$[f] | | | 59 | 71.64 | 71.60 | 11.40 | 11.53 | 318.5[g] | 313[g] |
| $F(CH_2)_{10}CO(CH_2)_{10}F$[f] | | | 64.5 | 72.78 | 73.04 | 11.63 | 11.56 | 346.5[g] | 337[g] |
| $F(CH_2)_8CHO$ | 99–100 | 9 | 1.4220 | 67.50 | 67.54 | 10.70 | 10.82 | | |
| DNP[e] | | | 101.5 | | | | | 16.46 | 16.36 |
| $F(CH_2)_8COC_6H_5$[h] | 134–137 | 0.7 | 1.4983 | 76.23 | 76.30 | 8.96 | 8.80 | | |
| DNP[i] | | | 129.5 | | | | | 13.46 | 13.82 |
| $F(CH_2)_8OH$[j] | 106–108 | 9 | 1.4248 | | | | | | |
| $F(CH_2)_5C(OH)[(CH_2)_6F]_2$[f] | | | 72 | 66.68 | 66.69 | 10.80 | 10.78 | | |
| $[F(CH_2)_6]_3COH$[f] | | | 74 | 67.46 | 67.52 | 10.95 | 10.77 | | |

[a] Buckle *et al.*[3] report b.p. 191°. [b] Buckle *et al.*[3] report b.p. 135–138° (10 mm.). [c] Buckle *et al.*[3] report b.p. 140–141° (11 mm.). [d] DNP = 2,4-dinitrophenylhydrazone. [e] Recrystallized from methanol. [f] Recrystallized from petroleum ether (30–60°). [g] Molecular weight (Rast). [h] M.p. *ca.* 20°. [i] Recrystallized from ethanol. [j] Pattison *et al.*[6] report b.p. 111.5–112° (12 mm.) and $n_D^{25}$ 1.4248.

gave a low yield of 9-fluorononanal. Hydrolysis of the acetal formed in the initial reaction proved difficult, with the result that a pure sample of aldehyde was obtained only after several distillations. Results of the above reactions are shown in Table I.

From this work, it is evident that Grignard reagents formed from ω-fluoroalkyl chlorides undergo the normal reactions in satisfactory yield. As observed in the carbonation reaction previously described,[2] moderate amounts of material formed by replacement of both fluorine and chlorine were obtained from the distillation residues (Table I); a few of the residues were not examined, since disubstitution in the case of 6-fluorohexyl chloride had already been fully substantiated in this and earlier work. It is hoped that some theoretical aspects of this problem will be discussed in another communication. In conformity with previous work,[22] the new compounds have been submitted for pharmacological examination, the results of which will be reported elsewhere.[5] Physical constants and analytical results are shown in Table II.

## EXPERIMENTAL[23]

*Materials.* ω-Fluoroalkyl halides were prepared in the usual manner.[24] ω-Fluorocarboxylic acid chlorides and anhydrides were prepared as described previously[25]; using the isopropenyl acetate method,[26] improved yields were obtained for fluoroacetic anhydride (79%) and for 3-fluoropropionic anhydride (75%). Commercial samples of ethyl chloroformate, acetic anhydride, benzonitrile, and triethyl orthoformate were fractionated prior to use. Ethylene oxide, Eastman Reagent, was used directly from a fresh ampoule.

*Grignard reagents.* In each case, the ω-fluoroalkyl chlorides were converted to the corresponding Grignard reagents in the apparatus and under the conditions described in Part

---

[22] F. L. M. Pattison, *Nature*, **172**, 1139 (1953); **174**, 737 (1954). See also *J. Org. Chem.*, **21**, 739 (1956) and subsequent papers in the series.

[23] (a) The microanalyses were performed by Mr. J. F. Alicino, Metuchen, N. J., and by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. (b) Melting points and boiling points are uncorrected, unless specified.

[24] F. L. M. Pattison and W. C. Howell, *J. Org. Chem.*, **21**, 748 (1956).

[25] F. L. M. Pattison, R. R. Fraser, G. J. O'Neill, and J. F. K. Wilshire, *J. Org. Chem.*, **21**, 887 (1956).

[26] H. J. Hagemeyer and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949).

I of this series.[2] The subsequent reactions were usually carried out in the subsidiary apparatus.[2]

*Grignard reactions.* Most of the reactions were carried out only once, hence the yields reported are not necessarily the highest obtainable. The experimental conditions were uniform for each type of reaction, of which the following examples are representative.

(*a*) *Ethyl 7-fluoroheptanoate.* The Grignard reagent was prepared from 6-fluorohexyl chloride (10.0 g., 0.072 mole), ether (70 ml.) and magnesium (3.0 g., 0.124 g. atom). After filtration under nitrogen pressure, the Grignard solution was added dropwise over 1.75 hr. to a stirred solution of ethyl chloroformate (42.0 g., 0.40 mole) in 75 ml. of ether. The reaction vessel was cooled to −75° in a Dewar flask containing a slurry of powdered Dry-Ice in acetone. Stirring was continued for an additional hour and then the mixture was allowed to stand overnight in the cold. The clear yellowish solution was then stirred while warming to room temperature. During this period a fine white precipitate gradually separated. The reaction was completed by gentle refluxing for 1 hr. After cooling and addition of excess 10% sulfuric acid, the product was separated by ether extraction. The extract was washed successively with water, 10% sodium carbonate solution, and again with water. After drying over magnesium sulfate, the extract was concentrated and the residue fractionated. Excess ethyl chloroformate and unreacted 6-fluorohexyl chloride (1 g.) were recovered. Further distillation yielded 5.5 g. (48%) of ethyl 7-fluoroheptanoate. Distillation of the residue under high vacuum gave two fractions, (*a*) b.p. 56–57° (0.1 mm.), $n_D^{25}$ 1.4212 and (*b*) b.p. 82–84° (0.1 mm.), $n_D^{25}$ 1.4302. Hydrolysis of fraction (*b*) with alkali gave a small quantity (6%) of suberic acid, m.p. 140–141°.

(*b*) *1,13-Difluoro-7-tridecanone.* The Grignard reagent, prepared from 6-fluorohexyl chloride (10.0 g., 0.072 mole), ether (70 ml.) and magnesium (3.0 g., 0.124 g. atom), was filtered from the excess magnesium and added fairly rapidly (over about 15 min.) to a mixture of 7-fluoroheptanoyl chloride (30 g., 0.18 mole) and anhydrous, resublimed ferric chloride (0.27 g.) in ether (25 ml.); the reaction vessel was cooled by means of an acetone–dry ice bath. The mixture was stirred for 1 hr. further and then was allowed to stand overnight in the cold. The cold bath was removed and the mixture was allowed to warm to room temperature. After being stirred for 30 min., the mixture was hydrolyzed with ice water. The resultant mixture was neutralized with sodium carbonate, and extracted several times with ether. The extracts were washed with water and dried over sodium sulfate. After removal of the ether, the residue on fractionation gave 0.9 g. of unreacted 6-fluorohexyl chloride, followed by 1,13-difluoro-7-tridecanone (8.5 g., 55%).

The *2,4-dinitrophenylhydrazone* was recrystallized from methanol as orange microcrystals.

The distillation residue solidified to pale yellowish crystals. Recrystallization from petroleum ether (30–60°) gave colorless crystals of *tris-6-fluorohexylcarbinol* (1.2 g., 11%).

(*c*) *11-Fluoro-2-undecanone.* The Grignard reagent, prepared from 9-fluorononyl chloride (13.0 g., 0.072 mole), ether (75 ml.) and magnesium (3.0 g., 0.124 g. atom), was filtered from the excess magnesium and added dropwise over 1.5 hr. to a stirred solution of acetic anhydride (21.0 g., 0.21 mole) in 50 ml. of ether cooled in an acetone–dry ice bath. Stirring was continued for an additional hour. After standing overnight in the cold, the reaction mixture was allowed to warm to about 0° and then was hydrolyzed by addition of a minimum quantity (10–14 ml.) of saturated ammonium chloride solution. The product was extracted with ether, and the extracts, after successive washings with water, 5% sodium hydroxide and water, were dried over sodium sulfate or magnesium sulfate. Fractionation of the product gave 2.86 g. of unchanged 9-fluorononyl chloride, followed by 11-fluoro-2-undecanone (6.88 g., 65%).

The *2,4-dinitrophenylhydrazone* was recrystallized from methanol as long orange needles.

The distillation residue (2.49 g.) solidified to pale yellowish crystals. Recrystallization from petroleum ether (30–60°) gave colorless prisms of 2,12-tridecanedione, m.p. 71–72° (corr.). (Canonica and Bacchetti[27] report m.p. 72°.) The *bis*-2,4-dinitrophenylhydrazone, m.p. 165.5–166.5° (corr.) was recrystallized from pyridine as orange microcrystals.

(*d*) *8-Fluorooctanol.* The Grignard reagent was prepared from 6-fluorohexyl chloride (10.0 g., 0.072 mole), ether (70 ml.) and magnesium (3.0 g., 0.124 g. atom). When the reaction of the fluorochloride with the magnesium appeared to be complete (7 hr.), 50 ml. of ether were distilled into the dropping funnel around which had been fitted a cardboard jacket filled with powdered dry ice. Cold ethylene oxide (8 ml., 7 g., 0.16 mole) was quickly added to the ether. The reaction vessel was cooled in an ice-salt bath while the ether solution of ethylene oxide was added over 15 min. to the stirred Grignard solution. The ice bath was removed and the reaction mixture was stirred for 1 hr. at room temperature. After decantation of the product onto ice and cautious acidification with hydrochloric acid, the organic layer was separated and the aqueous layer extracted with additional quantities of ether. The extracts were combined, washed successively with water, 10% sodium carbonate and water, and dried over sodium sulfate. The dried extracts were concentrated and the residue was fractionated under reduced pressure. After a large forerun (*ca.* 4 g.) of ethylene chlorohydrin, b.p. 30–32° (10 mm.), unreacted 6-fluorohexyl chloride (1.15 g.) was collected at b.p. 52–60° (9 mm.), followed by 8-fluorooctanol (4.37 g., 46%). From the semisolid distillation residue was isolated a small quantity (4%) of 1,10-decanediol by crystallization from benzene, m.p. 68–70°. No depression in melting point was observed when mixed with an authentic sample.

(*e*) *8-Fluorooctyl phenyl ketone.* A solution of benzonitrile (7.4 g., 0.072 mole) in 15 ml. of ether was added rapidly with stirring at room temperature to the Grignard reagent prepared from 8-fluorooctyl chloride (12.0 g., 0.072 mole), ether (70 ml.) and magnesium (3.0 g., 0.124 g. atom). Stirring was continued and during the next 10 min. an exothermic reaction took place accompanied by the formation of a colorless precipitate. When this reaction abated, the mixture was boiled gently for 1 hr. After standing overnight at room temperature, the vessel was cooled while the complex was hydrolyzed with excess 10% sulfuric acid. To complete the hydrolysis of the ketimine salt, the ether solvent was distilled off through an inverted Friedrichs condenser, and the residue heated on the water bath for 20 min. The resultant yellow oily layer was extracted with ether. After washing and drying, fractionation of the product gave unreacted benzonitrile and unreacted 8-fluorooctyl chloride (1.4 g.), followed by 8-fluorooctyl phenyl ketone (10.5 g., 70%).

The *2,4-dinitrophenylhydrazone* was recrystallized from ethanol as small red plates.

The solid distillation residue (2 g.) was recrystallized from carbon tetrachloride, giving colorless plates of 1,8-dibenzoyloctane, m.p. 93–93.6°. (Borsche and Wollemann[28] report m.p. 91–92°.) The dioxime, m.p. 121–123°, was recrystallized from methanol. (Ponzio and Biglietti[29] report m.p. 125–126°; Borsche and Wollemann[28] report m.p. 120–121°.)

(*f*) *9-Fluorononanal.* The Grignard reagent from 8-fluorooctyl chloride (12.0 g., 0.072 mole), ether (70 ml.) and magnesium (3.0 g., 0.124 g. atom) was treated with a solution of triethyl orthoformate (12.0 g., 0.081 mole) in

---

[27] L. Canonica and T. Bacchetti, *Atti accad. nazl. Lincei, Rend., Classe sci. fis., mat. e nat.*, **10**, 479 (1951).

[28] W. Borsche and J. Wollemann, *Ber.*, **44**, 3185 (1911).

[29] G. Ponzio and F. Biglietti, *Gazz. chim. ital.*, **64**, 861 (1934).

50 ml. of ether. There were no apparent signs of any reaction. After heating under reflux for a total of 6 hr., the reflux condenser was replaced by an inverted Friedrichs condenser and the ether removed. The viscous residue was cooled and treated with 100 ml. of 5*N* hydrochloric acid, thus forming a yellow oily layer. The mixture was warmed on a water bath for 20 min. to complete the hydrolysis of the acetal. The product was extracted with ether, and the extracts were washed successively with water, saturated sodium bicarbonate solution and water. After drying over sodium sulfate, distillation of the product gave two fractions: (*a*) 2 g. (17%) of b.p. 98–103° (9 mm.), which readily formed a yellow, crystalline derivative with 2,4-dinitrophenylhydrazine; and (*b*) 3.3 g. (20%) of b.p. 122–124° (9 mm.), which formed a 2,4-dinitrophenylhydrazone only after prolonged boiling. The residue (5.3 g.), a sweet-smelling, yellow, viscous liquid, was impure sebacaldehyde. Fraction (*b*), thought to be unhydrolyzed acetal, was boiled for 1 hr. with 7% sulfuric acid (25 ml.) and dioxane (12 ml.). Distillation of the hydrolyzate gave two fractions, which had boiling points identical to those of fractions (*a*) and (*b*) above. Combination of the two samples of b.p. 98–103° (9 mm.) followed by several fractionations gave pure 9-fluorononanal (2.9 g., 25%).

The *2,4-dinitrophenylhydrazone* was recrystallized from methanol as long yellow needles.

*Acknowledgments.* The work described herein was carried out under Contract (DRB X-24) with the Defence Research Board of Canada, to whom grateful acknowledgement is made for financial assistance, and for permission to publish this work. The authors wish also to express their indebtedness to the National Research Council of Canada for the awards of a Fellowship (W.C.H.) and a Bursary (W.J.C.).

LONDON, ONTARIO, CANADA

---

[CONTRIBUTION FROM THE WILLIAM H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

# Addition of Ethylenediamine to Methyl Methacrylate and to Acrylonitrile. Reactions of the Adducts

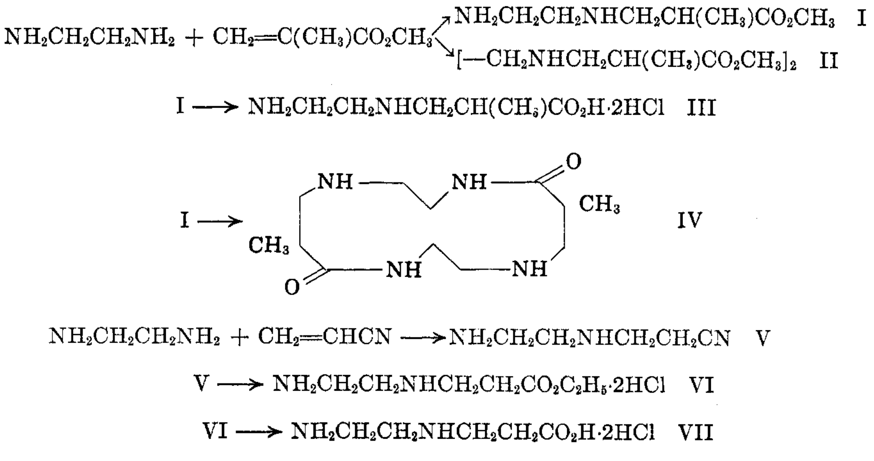
S. CARLTON DICKERMAN AND JULIUS SIMON

*Received September 14, 1956*

Ethylenediamine has been added to methyl methacrylate and to acrylonitrile. Several diamino esters, diamino acids, and derivatives of these have been prepared. Aged samples of one of the adducts have yielded a substance believed to be 1,5,8,12-tetraza-3,10-dimethyl-2,9-cyclotetradecanedione.

During the course of another investigation certain diamino acids were needed as reference compounds. The simplest representatives of this particular group might be prepared from ethylenediamine and derivatives of acrylic acid. Accordingly such reactions have been studied.

The accompanying flowsheet indicates that both 1:1 and 1:2 adducts, I and II, were obtained from ethylenediamine and methyl methacrylate. The proportions of these adducts were controlled by the ratio of reactants as illustrated in Table I. The formation of adducts which contain only one



$$NH_2CH_2CH_2NH_2 + CH_2{=}C(CH_3)CO_2CH_3 \rightarrow NH_2CH_2CH_2NHCH_2CH(CH_3)CO_2CH_3 \quad \text{I}$$
$$\rightarrow [-CH_2NHCH_2CH(CH_3)CO_2CH_3]_2 \quad \text{II}$$

$$\text{I} \longrightarrow NH_2CH_2CH_2NHCH_2CH(CH_3)CO_2H{\cdot}2HCl \quad \text{III}$$

$$\text{I} \longrightarrow \text{IV}$$

$$NH_2CH_2CH_2NH_2 + CH_2{=}CHCN \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CN \quad \text{V}$$

$$\text{V} \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CO_2C_2H_5{\cdot}2HCl \quad \text{VI}$$

$$\text{VI} \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CO_2H{\cdot}2HCl \quad \text{VII}$$