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ALIPHATIC FLUORIDES. II. 1-HALOGENO-ω-FLUOROALKANES[1]

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The preparation of some members of the ω,ω′-difluoroalkane series from the corresponding dibromo- or dichloro-alkanes by halogen exchange with anhydrous potassium fluoride in glycol was recently described (1). In this reaction small quantities of 1-halogeno-ω-fluoroalkanes were obtained as by-products. It was expected that by proper alteration of the reaction conditions the fluorination of the dihalogenoalkanes could be stopped after exchange of one halogen atom thus leading to the formation of 1-halogeno-ω-fluoroalkanes as the main product of the reaction.

Synthesis of 1-halogeno-ω-fluoroalkanes. Complete substitution of the halogen of the dihalogenoalkanes by fluorine requires continuous removal of the low-boiling difluorides from the reaction mixture in order to maintain the necessary reaction temperature of 160–180° for the chlorides and 130–150° for the bromides. It was found that the first step of the fluorination takes place at a reasonable rate at lower temperatures. Satisfactory results were usually obtained at about 100° for replacement of bromine and approximately 130° for the exchange of one chlorine atom by fluorine. With the exception of 1-bromo-2-fluoroethane, 1-chloro-2-fluoroethane, and 1-chloro-3-fluoropropane the boiling points of the fluorohalogenoalkanes do not allow distillation of the reaction products from the mixture as the reaction proceeds. They are, therefore, best prepared by heating a mixture of the dihalogenoalkane, potassium fluoride, and ethylene glycol with vigorous stirring at the indicated temperatures for several hours with subsequent dilution of the reaction mixture with water and fractionation of the separated organic layer. The halogenofluoroalkanes are formed in about 20–40% yield together with 10–30% yields of the difluoroalkanes.

Formation of fluoroalkenes, which are obtained in traces as by-products of the preparation of the difluoroalkanes (1), was not observed. However, in all fluorinations with potassium fluoride in ethylene glycol, an appreciable amount of a high-boiling, fluorine-free by-product is formed. For example, in the preparation of *n*-amyl fluoride which was needed in this investigation for comparison of the relative reactivity of the primary-bound fluorine in alkyl fluoride and halogenofluoroalkane, this high-boiling by-product was isolated and identified as ethylene glycol mono-*n*-amyl ether. A solution of potassium fluoride in ethylene glycol reacts strongly basic behaving like alcoholic caustic. In competition with the ionic halogen-fluorine exchange a replacement of halogen by $HOCH_2CH_2O$— occurs to some extent, leading to the formation of glycol ethers. An equivalent amount of hydrogen ions is liberated, thus decreasing the alkalinity of the reaction mixture. If only a slight excess (10–20%) of potassium fluoride

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is used in the fluorination process, the reaction mixture soon becomes acid due to this side reaction. An ionic halogen-fluorine exchange alone should not render the reaction mixture acid. The formation of glycol ethers is believed to be responsible for the relatively low yields of fluorinated products.

The first four members of each of the bromo- and chloro-fluoroalkane series have been prepared. Data on the reaction temperature, reaction time, and yields of halogenofluoro- and difluoro-alkanes obtained in the fluorination of several dibromo- and dichloro-alkanes are listed in Table I. The three members of the series whose boiling points are considerably below the required reaction temperature are more favorably prepared from 2-fluoroethanol and 3-fluoropropanol, respectively. These two fluorinated alcohols are easily obtained from the corresponding chlorohydrins by the potassium fluoride-glycol method. The preparation of 3-fluoropropanol is described in detail in the experimental part of this paper; the 2-fluoroethanol was obtained according to directions previously given (2) and purified as described below.

TABLE I

FLUORINATION OF DIHALOGENOALKANES

STARTING MATERIAL	REACTION TEMP., °C.	REACTION TIME, HOURS	YIELDS OF	
			Halogenofluoroalkane, %	Difluoroalkane, %
$Br(CH_2)_2Br$	90	6	24	0
$Br(CH_2)_3Br$	80–100	7	31.0	10.2
$Br(CH_2)_4Br$	100–110	7	19.6	23.4
$Br(CH_2)_5Br$	100–110	6	31.4	25.0
$Cl(CH_2)_4Cl$	110	20	36.6	15.9
	125	20	34.2	29.3
$Cl(CH_2)_5Cl$	125	18	22.0	—
	130	7	38.5	14.1

1-Bromo-2-fluoroethane has been previously described in the literature (1, 3, 4). Physical data for 1-chloro-2-fluoroethane could not be found;[2] however, McCombie and Saunders have reported the preparation of this compound and its reaction with sodium phenoxide without giving experimental details (4). Therefore, it was included in Table II which lists the boiling points, densities, and refractive indices of several fluorinated compounds. The 1-halogeno-ω-fluoroalkanes are colorless liquids having a sweet odor which resembles that of the corresponding alkyl halides. They are stable to distillation at atmospheric pressure.

Reactivity of 1-halogeno-ω-fluoroalkanes. A comparison of the reactivity of the halogenofluoroalkanes towards alkaline reagents with that of the dihalogeno- and the difluoro-alkanes shows that in general the bromine or chlorine atom exhibits the same reactivity as in the di-bromides or -chlorides and that the fluorine is as unreactive as in the difluorides.

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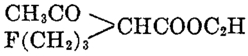
[2] Two recent articles on the preparation and properties of 1-chloro-2-fluoroethane came to the author's attention since this paper was submitted for publication (10, 11).

Alkyl fluorides are generally unable to form alkylmagnesium fluorides and only *n*-amyl fluoride has been reported (5) to yield pentane, decane, and *n*-amyl alcohol by prolonged refluxing with magnesium in ether and subsequent hydrolysis. Since the halogen atom in halogenofluoroalkanes was found to be of the same order of reactivity towards alkaline reagents, as that in alkyl halides, it was expected that bromofluoroalkanes would form ω-fluoroalkylmagnesium bromides with magnesium in ether. These Grignard reagents would be very valuable for further synthesis of organic fluorine derivatives. Although the bromofluoroalkanes react with magnesium in ether after initiation of the reaction with traces of iodine, no ω-fluoroalkylmagnesium bromides are formed, and treatment of the reaction mixture with ketone or phenyl isocyanate leads only to the formation of fluorine-free reaction products which have not been investigated further. Hydrolysis of a reaction product obtained from 1-bromo-5-fluoropentane and magnesium in ether and determination of fluoride ions in the hydrolysate showed that over 60% of the organic-bound fluorine was present in the ionic state. Since a preferred attack of the metallic magnesium on the fluorine atom seems improbable, it appears as if the fluoroalkylmagnesium bromide formed in the first step of the reaction exchanges to a large extent its bromine for fluorine from unreacted bromofluoroalkane or fluoroalkylmagnesium bromide. This assumption is supported by the fact that by reaction of phenylmagnesium bromide with 1-bromo-5-fluoropentane or with *n*-hexyl fluoride in equimolar quantities, the fluorine is found quantitatively as fluoride ion upon hydrolysis of the reaction mixture, whereas the amount of bromide ions is only about 60% of the bromine present in the phenylmagnesium bromide. The phenylmagnesium fluoride formed by halogen exchange between the phenylmagnesium bromide and the alkyl fluoride apparently reacts to some extent with the alkyl bromide formed during the reaction to yield an alkyl benzene. The reaction of aliphatic-bound fluorine

TABLE II

PHYSICAL CONSTANTS OF NEW COMPOUNDS

COMPOUND	B.P., °C.	d_4^{25}	d_4^{35}	n_D^{25}	MR_D [a]	AR_F [b]
$Cl(CH_2)_2F$	53.2	1.1675	—	1.3727	16.09	0.89
$Cl(CH_2)_3F$	82.1	1.0992	1.0862	1.3855[c]	20.66	.84
$Br(CH_2)_4F$	134.2	1.4443	1.4298	1.4372	28.13	.79
$Br(CH_2)_5F$	162.0	1.3604	—	1.4406	32.79	.83
 $\begin{matrix}CH_3CO\\F(CH_2)_3\end{matrix}{>}CHCOOC_2H_5$	105.2[d]	1.064	1.054	1.4237	—	–
$F(CH_2)_3CH(COOC_2H_5)_2$	122[e]	1.0764	1.0663	1.4176	51.52	.91
$F(CH_2)_5CH(COOC_2H_5)_2$	142[f]	1.0407	1.0314	1.4237	60.84	1.01
n-$C_5H_{11}F$	64.4	0.7852	0.7744	1.3569	25.14	.95

[a] MR_D is the molecular refraction for the sodium-D line calculated by the Lorentz-Lorenz equation. [b] AR_F is the atomic refraction for fluorine, computed by subtracting the increments for C (2.418), H (1.100), Cl (5.967), Br (8.865), O′ (1.1525), and O< (1.643) from MR_D. [c] at 27.2°. [d] 7 mm. [e] 11 mm. [f] 10 mm.

with the Grignard reagent can be summarized as follows:

$$R—F + C_6H_5MgBr \rightarrow C_6H_5MgF + R—Br \rightarrow C_6H_5—R + MgBrF.$$

The reaction 1 mole of 1-bromo-5-fluoropentane with 1 gram-atom of metallic sodium in absolute ether has been investigated quantitatively. After 24 hours of refluxing, the hydrolysate of the reaction mixture contained as ions 34% of the bromine and 25% of the fluorine originally present in the bromofluoropentane.

With alkali phenoxides, diethyl sodium malonate, and ethyl sodium acetoacetate, the halogen atom of the halogenofluoroalkane exhibits its normal reactivity, whereas the fluorine is not or only slightly attacked by these reactants. The first four members of the 1-bromo-ω-fluoroalkane series have been treated with sodium β-naphthoxide, yielding the crystalline ω-fluoroalkyl β-naphthyl ethers. Diethyl 3-fluoropropyl- and 5-fluoropentyl-malonate were obtained in 52 and 74% yield, respectively, by malonic ester synthesis, and ethyl α-(3-fluoropropyl)acetoacetate in 53% yield from ethyl sodium acetoacetate and 1-bromo-3-fluoropropane. The physical data of these esters are listed in Table II.

TABLE III

REACTIVITY OF ω,ω′-DIBROMO- AND 1-BROMO-ω-FLUOROALKANES

COMPOUND $X(CH_2)_nY$	1 *N* NaOEt			1 *N* KOH		
	X and Y = Br	X = Br and Y = F		X and Y = Br	X = Br and Y = F	
		Br^-	F^-		Br^-	F^-
n = 2	51[a]	45[a]	1[b]	50[c]	27[c]	2[e]
n = 3	85	82	0.5	70	31	0
n = 4	62	67	1.6	47	52	8
n = 5	58	57	0.5	37[d]	39	0
n-$C_5H_{11}Br$	–	47	–	–	23	–
n-$C_5H_{11}F$	–	–	trace	–	–	trace

[a] Percentage of bromine reacted after treatment of 0.01 mole of substance with 25 ml. of 1 *N* $NaOC_2H_5$ in ethanol at 35° for 4 hours. [b] Percentage of fluorine reacted under the same conditions as in [a]. [c] Percentage of bromine reacted after treatment of 0.01 mole of substance with 25 ml. of 1 *N* KOH in 70% ethanol at 35° for 5 hours. [d] In this run sufficient 95% ethanol (12.5 ml.) was added to obtain a homogeneous mixture. [e] Percentage of fluorine reacted under the same conditions as in [c].

The relative reactivities of the 1-bromo- and 1-chloro-ω-fluoroalkanes towards alkaline reagents are of interest for introducing ω-fluoroalkyl groups into organic molecules in reactions of the above-mentioned type. The halogenofluoroalkanes were therefore compared with the corresponding ω,ω′-dibromo- and dichloroalkanes on the basis of the percentage of reacted halogen after treatment with 1 *N* sodium ethoxide and 1 *N* 70% alcoholic KOH solutions as previously described for the difluoroalkanes (1). The reactions with the bromine derivatives were carried out at 35° for 4 and 5 hours, respectively, whereas the chlorine derivatives were treated with the same reagents at reflux temperature for 30 minutes. The results obtained are listed in Tables III and IV, in which the relative reactivities of *n*-amyl bromide, chloride, and fluoride have been included for comparison. The data show that the halogen in the dibromides and dichlorides exhibits a higher reactivity than in the corresponding *n*-amyl halides. The relatively large quantity of reacted halogen in the runs with the trimethylene derivatives and sodium ethoxide solution is probably due to a simultaneous dehydrohalogenation of the molecule competing with the normal substitution reaction, as was outlined in the first paper of this series. The halogenofluoroalkanes show a maximum reactivity at the C_3 derivatives for the bromine and chlorine, but the fluorine in these derivatives is very unreactive. 1,3-Difluoropropane was found to react to the extent of 11.6% of its fluorine by refluxing with 1 *N* NaOEt solution (1), but 1-bromo- and 1-chloro-3-fluoropropane react only to the extent of 0.5 and 0.7%, respectively, under the same conditions. In comparing the reactivities of the ethane derivatives, it is obvious that chlorine activates the fluorine on the adjacent carbon atom, since their reactivities are of the same order of magnitude, whereas bromine activates the neighboring fluorine only very slightly. The comparatively high reactivity of fluorine in the halogenofluorobutane derivatives towards KOH is presumably caused by the pronounced tendency of 4-fluorobutanol, formed by hydrolysis of the halogen, to eliminate hydrogen fluoride with ring closure to tetrahydrofuran (3c). The relatively high reactivity of the fluorine atom of 1-chloro-2-fluoroethane towards strong alkaline reagents makes the corresponding bromine derivative the preferred starting material for further synthetic reactions. 1-Bromo-2-fluoroethane retains the high reactivity of the bromine of an alkyl bromide without a pronounced increase in the reactivity of the fluorine over the normally low reactivity of primary fluorine. A number of interesting reactions using this reagent have been mentioned by McCombie and Saunders (4).

TABLE IV

REACTIVITY OF ω,ω'-DICHLORO- AND 1-CHLORO-ω-FLUORO-ALKANES

COMPOUND $X(CH_2)_nY$	1 *N* NaOEt			1 *N* KOH		
	X and Y = Cl	X = Cl and Y = F		X and Y = Cl	X = Cl and Y = F	
		Cl^-	F^-		Cl^-	F^-
n = 2	49[a]	18[a]	11[b]	39[c]	6[c]	6[d]
n = 3	61	52	0.7	23	19	0
n = 4	36	36	0.7	20	33	4
n = 5	30	26	1.6	15	14	0
n-$C_5H_{11}Cl$	–	23	–	–	9	–
n-$C_5H_{11}F$	–	–	traces	–	–	trace

[a] Percentage of chlorine reacted after refluxing 0.01 mole of substance with 25 ml. of 1 *N* $NaOC_2H_5$ in ethanol for 30 minutes. [b] Percentage of fluorine reacted under the same conditions as in [a]. [c] Percentage of chlorine reacted after refluxing 0.01 mole of substance with 25 ml. of 1 *N* KOH in 70% ethanol for 30 minutes. [d] Percentage of fluorine reacted under the same conditions as in [c].

EXPERIMENTAL PART

Materials. The commercial, anhydrous potassium fluoride (Harshaw Chemical Co.) and the ethylene glycol (Du Pont) were dried before use as previously described (1).

ω,ω'-Dihalogenoalkanes. The dichloroalkanes, ethylene bromide, and trimethylene bromide used as starting materials were commercial products. 1,4-Dibromobutane and 1,5-dibromopentane were obtained by reaction of tetrahydrofuran and tetrahydropyran, respectively, with hydrobromic acid according to the directions given for the preparation of 1,5-dibromopentane (6).

Purification of 2-fluoroethanol. The 2-fluoroethanol was prepared by fluorination of ethylene chlorohydrin with potassium fluoride in glycol (2). The crude product obtained from several runs was distilled through a 40 x 1.5 cm. column packed with $\frac{1}{8}''$ single-turn glass-helices at a reflux ratio of about 20:1. The fraction b.p. 103.0–103.8° was collected and redistilled through the same column which was also used in each of the following distillations. The fraction b.p. 103.1–103.8° was collected and about 5 vol.% of concentrated sodium bisulfite solution added to remove small amounts of crotonaldehyde [b.p. 104.0° (7)] which is formed in traces during the preparation of the alcohol (3*a*). After 48 hours at room temperature, and filtration, an equal volume of methylene chloride was added. The water was then removed by continuous, azeotropic distillation (b.p. of CH_2Cl_2–H_2O azeotrope: 38°). After removal of the solvent, the fluoroethanol was filtered from a small amount of crystalline precipitate and then distilled three times, collecting the distillate at 103.1–103.3°. During the third fractionation a mid-cut was taken at 103.3° for analysis and determination of the physical constants: n_D^{25} 1.3633, d_4^{25} 1.1002.

Anal. Calc'd for C_2H_5FO: C, 37.5; H, 7.9.
Found: C, 37.7; H, 8.0.

Preparation of 3-fluoropropanol. A mixture of 378 g. (4 moles) of trimethylene chlorohydrin, 350 g. (6 moles) of potassium fluoride, and 500 g. of ethylene glycol was heated at 175–180° with vigorous stirring. During the reaction the product was continuously distilled off between 130 and 154°. After 5 hours 186.9 g. of a colorless liquid was collected. Distillation through a 40-cm., packed column yielded 155.6 g. (49.8% yield) of 3-fluoropropanol, b.p. 126–128°. The crude 3-fluoropropanol was distilled twice through the same column and a constant-boiling mid-cut taken at 127.8° [b.p. 127.5–128° (3*c*)] for analysis and determination of the physical constants: n_D^{25} 1.3771, d_4^{25} 1.0390.

Anal. Calc'd for C_3H_7FO: C, 46.1; H, 9.0; F, 24.3.
Found: C, 45.9; H, 8.9; F, 24.1.

Preparation of 1-bromo-2-fluoroethane. (a) A mixture of 376 g. (2 moles) of ethylene bromide, 232 g. (4 moles) of potassium fluoride, and 400 g. of ethylene glycol was heated at 90° for 6 hours with vigorous stirring in a 2-liter round-bottom flask to which was attached a condenser with a receiver and a Dry Ice-acetone cold trap. In the receiver 7.1 g. of a colorless distillate (b.p. 32–42°) was collected. The cold trap contained 21.1 g. of a low-boiling liquid. After standing overnight the reaction mixture was diluted with 1000 ml. of water. The heavy, organic layer (225.7 g.) was separated, combined with the distillate and the cold trap condensate, and dried with 20 g. of calcium chloride. Distillation through a 40-cm., packed column yielded 38.4 g. of vinyl bromide boiling at 16–18°, 32.6 g. of 1-bromo-2-fluoroethane boiling at 70–74°, and 169.4 g. of unreacted ethylene bromide. Based on the reacted ethylene bromide the yield of 1-bromo-2-fluoroethane was 24%.

(b) To a refluxing mixture of 192 g. (3 moles) of 2-fluoroethanol and 10 g. of red phosphorus, 160 g. (1 mole) of bromine was added dropwise over a period of 3 hours through a dropping-funnel reaching to the bottom of the reaction flask. The mixture was then refluxed for 3 hours. Toward the end of the reaction a slight evolution of hydrogen fluoride and etching of the glass apparatus was noticed. Distillation of the reaction mixture yielded 265.9 g. of a pale-orange liquid boiling from 71° to 132°. The distillate was washed twice with 200-ml. portions of water and finally with sodium bicarbonate solution. The heavy, colorless layer was separated and dried with calcium chloride. Distillation through a 40-cm.

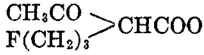
column yielded 129.4 g. of 1-bromo-2-fluoroethane boiling at 71–72°; yield based on bromine, 51%.

Preparation of 1-bromo-3-fluoropropane. (a) A mixture of 808 g. (4 moles) of trimethylene bromide, 350 g. (6 moles) of potassium fluoride, and 500 g. of ethylene glycol was heated with vigorous stirring at 80–100° for 7 hours. After 12 hrs., 1000 ml. of water was added to the reaction mixture. The heavy, organic layer was separated (490 g.) and dried with calcium chloride. Distillation through a 40-cm., packed column yielded after a forerun of 21.3 g. of trimethylene fluoride boiling at 41.0–41.2°, 113.4 g. of 1-bromo-3-fluoropropane boiling at 100–101.5°, and 283.4 g. of unreacted trimethylene bromide. The yield based on reacted starting material was 31.0%.

(b) To 100 g. of phosphorus tribromide (⅓ mole = 90.25 g.), cooled to −15° was added 78 g. (1 mole) of 3-fluoropropanol (b.p. 126–128°) in small portions in the course of 15 minutes. The temperature of the mixture was maintained between −5° and 0° until all of the fluoropropanol had been added. The reaction mixture was then allowed to warm to room temperature. After standing overnight it was refluxed for 1 hour and distilled. Between 100–114°, 146 g. of a colorless distillate was obtained, which was washed with 50 ml. of concentrated potassium carbonate solution and dried with calcium chloride. Distillation through a 40-cm., packed column gave 99.5 g. (70.6% yield) of 1-bromo-3-fluoropropane boiling at 100.5–101.5°. This material was used without further purification for the reactions with malonic and acetoacetic esters. For the quantitative measurements it was redistilled twice through a 40-cm., packed column and a mid-cut taken at 101.2° at 756 mm. [(b.p.$_{760}$ 101.4° (1)].

TABLE V

ANALYTICAL DATA OF NEW COMPOUNDS

COMPOUND	C		H		F	
	Calc'd	Found	Calc'd	Found	Calc'd	Found
$Cl(CH_2)_2F$	29.1	29.0	4.9	4.9	23.0	23.0
$Cl(CH_2)_3F$	37.3	37.3	6.3	6.1	19.7	19.7
$Br(CH_2)_4F$	31.0	30.9	5.2	5.2	12.3	12.2
$Br(CH_2)_5F$	35.5	35.7	6.0	6.1	11.2	11.3
 $\left.\begin{matrix}CH_3CO\\F(CH_2)_3\end{matrix}\right>CHCOOC_2H_5$	56.8	56.7	8.0	7.9	10.0	9.9
$F(CH_2)_3CH(COOC_2H_5)_2$	54.5	54.6	7.8	7.9	8.6	8.6
$F(CH_2)_5CH(COOC_2H_5)_2$	58.1	57.8	8.5	8.4	7.7	7.6
n-$C_5H_{11}F$	66.6	66.6	12.3	12.4	21.1	21.0

Preparation of 1-bromo-4-fluorobutane and 1-bromo-5-fluoropentane. These substances were prepared from the corresponding dibromoalkanes in essentially the same manner as described for 1-bromo-3-fluoropropane from trimethylene bromide. The reaction conditions and yields are listed in Table I, their physical data in Table II, and the analyses in Table V.

Reaction of 1-bromo-5-fluoropentane with phenylmagnesium bromide. To 4.23 g. (0.025 mole) of 1-bromo-5-fluoropentane was added a solution of 4.51 g. of phenylmagnesium bromide (0.025 mole, 4.53 g.) in 23.1 ml. of absolute ether. The mixture was refluxed for 20 hours and then hydrolyzed with 25 ml. of water and 100 ml. of 20% sulfuric acid. The aqueous layer was separated and after washing with 75 ml. of ether, aliquots were titrated for bromide and fluoride ions. *Found*: 0.49 g. F^-, 1.15 g. Br^-; Calc'd on charged bromofluoropentane: 0.48 g. F^-; on charged phenylmagnesium bromide: 1.99 g. Br^-.

Preparation of 1-chloro-2-fluoroethane. To 64 g. of 2-fluoroethanol was added dropwise in the course of 4 hours 131 g. (1.1 moles) of thionyl chloride, freshly distilled from linseed oil. After the addition was completed the reaction mixture was refluxed for 5 hours and then distilled through a 25-cm., 3-step Vigreux column. At 50–53.5°, 87.0 g. of a pale yellow liquid consisting of chlorofluoroethane and some thionyl chloride was collected. In order to remove the thionyl chloride, 5 ml. of water was added and the mixture shaken frequently. After standing overnight, anhydrous potassium carbonate was added in small portions until the evolution of carbon dioxide ceased. After two hours at room temperature the colorless liquid was decanted from the salt and distilled through a 40-cm., packed column; at 52–53.5°, 57.3 g. (69.4% yield) of chlorofluoroethane was collected. To remove traces of moisture from the product, it was dried with 4 g. of potassium carbonate for 18 hours. Redistillation through a 40-cm. column yielded, after a small forerun at 53.0–53.2°, pure 1-chloro-2-fluoroethane boiling at 53.2°. Physical data and analyses are given in Tables II and V, respectively.

Preparation of 1-chloro-3-fluoropropane. (a) To 104 g. (0.5 mole) of PCl_5 was added dropwise 78 g. (1 mole) of 3-fluoropropanol in the course of 45 minutes. The extremely vigorous reaction was moderated by occasional cooling of the reaction flask in a Dry-Ice-acetone bath. After the addition of 3-fluoropropanol was completed and the PCl_5 had gone into solution, the mixture was allowed to warm to room temperature and was finally refluxed for 3 hours. Distillation yielded 53.8 g. of a colorless liquid boiling at 82–96°, which was fractionated through a 40-cm., packed column, yielding 43.6 g. of crude 1-chloro-3-fluoropropane boiling at 79–81°. For further purification the product was washed with potassium carbonate solution, dried with calcium chloride, and redistilled twice through a 40-cm. column. A constant boiling mid-cut was taken at 79.9°. Physical data and analyses are listed in Tables II and V, respectively.

(b) To 44 g. (0.37 mole) of refluxing thionyl chloride was added dropwise 26.0 g. (0.33 mole) of 3-fluoropropanol in the course of 2 hours. After refluxing this mixture for 24 hours, the excess thionyl chloride was hydrolyzed with 10 ml. of water. The crude reaction product was then washed with water and finally with sodium bicarbonate solution, dried with calcium chloride, and distilled through a 40-cm., packed column. At 79–81°, 26.0 g. (81.3% yield) of 1-chloro-3-fluoropropane was obtained.

Preparation of 1-chloro-4-fluorobutane and 1-chloro-5-fluoropentane. Both substances were prepared in the same way as described for the corresponding bromine derivatives. The reaction conditions and yields are given in Table I.

Preparation of ω-fluoroalkyl β-naphthyl ethers. The β-naphthyl ethers described were all prepared in the same manner. A mixture of 0.03 mole each of 1-bromo-ω-fluoroalkane, β-naphthol, and sodium hydroxide in 50 ml. of 95% ethanol was refluxed for 3–4 hours. The mixture was then poured into 150 ml. of water and made distinctly alkaline with sodium hydroxide. The naphthyl ethers separated as oils, which crystallized on cooling, and were recrystallized from methanol or ethanol until a constant melting point was obtained. A Fisher-Johns melting point apparatus was used for the determination of the melting points.

2-Fluoroethyl ether. White crystals from 95% ethanol, m.p. 47.7° (uncorr.).

Anal. Calc'd for $C_{12}H_{11}FO$: C, 75.8; H, 5.8.
Found: C, 75.9; H, 5.8.

3-Fluoropropyl ether. White micro-plates from methanol after decolorization with Norit, m.p. 28.1°.

Anal. Calc'd for $C_{13}H_{13}FO$: C, 76.5; H, 6.4.
Found: C, 76.4; H, 6.4.

4-Fluorobutyl ether. White, glistening platelets from 95% ethanol, m.p. 47.6°.

Anal. Calc'd for $C_{14}H_{15}FO$: C, 77.0; H, 6.9.
Found: C, 76.7; H, 6.9.

5-Fluoropentyl ether. White micro-plates from methanol, m.p. 31.0°.

Anal. Calc'd for $C_{15}H_{17}FO$: C, 77.6; H, 7.4.
Found: C, 77.3; H, 7.5.

Preparation of diethyl 3-fluoropropylmalonate. To a warm solution of 27 g. (0.5 mole) of 96% sodium methoxide in 250 ml. of absolute ethanol was added 82.0 g. (0.51 mole) of diethyl malonate. To this solution was added 70.5 g. (0.5 mole) of 1-bromo-3-fluoropropane in the course of 10 minutes. The mixture was refluxed for 35 minutes, when it reacted neutral. The ethanol was distilled off and the residue taken up in 150 ml. of water. The upper, orange-yellow layer was separated and distilled through a 20-cm., packed column at reduced pressure. After a forerun of unreacted diethyl malonate, 56.9 g. (51.7% yield) of diethyl 3-fluoropropylmalonate was obtained, boiling at 124–127° at 13 mm. For analysis and determination of the physical constants the product was redistilled at 11 mm. and a mid-cut taken at 122°. The physical data and analyses are listed in the tables.

Preparation of diethyl 5-fluoropentylmalonate. The diethyl 5-fluoropentylmalonate was obtained from 1-bromo-5-fluoropentane in 74.3% yield using the same procedure as for the 3-fluoropropyl derivative. From the fraction boiling at 140–143° at 10 mm. pressure, a middle fraction was taken at 142° for analysis and determination of physical constants (Tables II and V).

Preparation of ethyl α-(3-fluoropropyl)acetoacetate. To a warm solution of 16.2 g. (0.3 mole) of sodium methoxide in 150 ml. of absolute ethanol was added 40 g. of ethyl acetoacetate and, after cooling to 45°, 42.3 g. (0.3 mole) of 1-bromo-3-fluoropropane. The mixture was refluxed for 6 hours, when it reacted neutral. The ethanol was removed *in vacuo* and the residue taken up in 60 ml. of water. The light, organic layer was diluted with 30 ml. of ether to facilitate separation. The ether was removed *in vacuo* and the residue, a yellow, oily liquid, was distilled through a 15-cm., packed column under reduced pressure. After a small forerun, 30.4 g. (53.2% yield) of ethyl α-(3-fluoropropyl)acetoacetate was obtained at 144–148° and 48 mm. The product was redistilled at 7 mm. and a mid-cut taken at 105.2° for analysis and determination of physical constants.

Preparation of n-amyl fluoride. A mixture of 290 g. (5 moles) of anhydrous potassium fluoride and 350 g. of ethylene glycol was heated to 120° with a mercury-seal stirrer, thermometer, dropping-funnel, and reflux still-head. *n*-Amyl bromide (453 g., 3 moles) was added dropwise in the course of 6 hours at such a rate that the reaction product distilled at 69–85°. The colorless distillate was treated with calcium chloride and sodium fluoride overnight, filtered, and distilled through a 40-cm., packed column. After a forerun of 12.1 g. of 1-pentene boiling at 40–45°, 136.3 g. (50.4%) of crude *n*-amyl fluoride boiling at 61–64.8° was obtained. For further purification the crude product was treated with bromine in order to remove small amounts of olefin still present. After one hour at room temperature, the pale-orange liquid was washed with 75 ml. of saturated sodium bicarbonate solution until it became colorless, and dried with calcium chloride overnight. It was distilled three times through a 40-cm. column. The pure substance boiled at 64.4° at 766 mm. This is somewhat higher than the boiling points reported in the literature: 62.8° (5); 62–63° (8). The physical constants were, therefore, determined and are included in Table II.

The contents of the reactor was diluted with 600 ml. of water. A pale-yellow, light layer separated, which was washed with 150 ml. of water and dried with silica-gel. Distillation through a 40-cm. column yielded a colorless liquid of pleasant fruity odor boiling at 70–72° and 8 mm. The substance was redistilled twice under reduced pressure through the same column: 68.5–69° at 6 mm. and 63.7–64.0° at 3 mm.; n_D^{25} 1.4229, d_4^{25} 0.8908; MR_D, Calc'd 37.69; Found 37.78.

Anal. Calc'd for $C_7H_{16}O_2$: C, 63.6; H, 12.2.
Found: C, 63.5; H, 12.2.

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SUMMARY

The first four members of each of the series of 1-bromo- and 1-chloro-ω-fluoroalkanes have been prepared. The physical properties, if not reported previously, have been tabulated and their chemical reactions are reported.

The reactivity of the halogen atoms in these compounds towards alkaline reagents is essentially the same as in the corresponding ω,ω′-dihalogenoalkanes; their fluorine atom exhibits the chemical stability of primary-bound fluorine.

The bromofluoroalkanes do not form fluoroalkylmagnesium bromides, and react with metallic sodium with simultaneous elimination of bromine and fluorine.

The ω-fluoroalkyl β-naphthyl ethers of the general formula $F(CH_2)_n—O—C_{10}H_7$ ($n = 2, 3, 4, 5$), diethyl 3-fluoropropyl- and 5-fluoropentyl malonate, and ethyl α-(3-fluoropropyl)acetoacetate have been synthesized.

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