

ALIPHATIC FLUORIDES. I. ω, ω' -DIFLUOROALKANES

FRIEDRICH W. HOFFMANN

Received September 3, 1948

The strength of the carbon-fluorine bond, calculated by the postulate of the additivity of normal covalent bonds (1), is 61.1 kcal./mole. This is smaller by 45.9 kcal. than the somewhat empirical value of 107 kcal. given by Pauling for the actual bond strength. The additional energy is accounted for by the resonance theory, according to which structures of an ionic type as well as the covalent type contribute resonance energy (1). In accordance with these considerations, the high ionic resonance energy of the carbon-fluorine bond should lead us to expect a much greater stability for this bond than for the carbon-to-halogen bond of the other corresponding alkyl halides. However, Henne and Midgley (2) describe the *n*-alkyl fluorides as less stable, showing a tendency to lose hydrogen fluoride with formation of olefins. According to these authors, only the first members of the homologous series up to *n*-pentyl fluoride are described as stable to distillation at normal pressure. Higher members of this series exhibit a tendency to "decompose spontaneously to hydrogen fluoride and ethylenic hydrocarbons", an opinion which has found its way into several textbooks. This statement, however, is in contradiction to the observations of Desreux (3), who describes *n*-hexyl and *n*-heptyl fluoride as compounds which are completely stable to distillation at atmospheric pressure and are not attacked by sodium amalgam, concentrated alkali, or phosphorus pentoxide. They are affected only by concentrated sulfuric acid. As proof for the lower stability of *n*-alkyl fluorides, Henne and Midgley cite the toxicity of ethyl fluoride which, when applied as an inhalation anesthetic in large doses, causes fatal oedema in the lungs and the upper respiratory tract of animals similar to that caused by hydrogen fluoride. However, the physiological activity of any chemical compound should not be evaluated as proof of its instability, since living cells are able to perform chemical reactions which often cannot be reproduced *in vitro*.

The inertness of primary bound fluorine in aliphatic compounds toward sodium ethoxide, alkalies, and dilute acids has been observed frequently in connection with other problems. Under similar conditions the corresponding chlorine compounds have been found to be considerably more reactive. Ethylene fluoride is described (2) as decomposing spontaneously to hydrogen fluoride and butadiene at 0° and as hydrolyzing to glycol by merely passing it through water. Since no other members of the homologous series of the ω, ω' -difluoroalkanes of the general formula $F(CH_2)_{n>2}F$ have been described thus far, it appeared interesting to prepare some of the lower members and to determine their chemical and physical properties.

There exist a variety of methods for preparing these compounds by exchange of the halogen in the corresponding dichloro- or dibromo-alkanes with the fluorine in certain inorganic metal fluorides. Of these methods, the fluorination

with anhydrous potassium fluoride in glycol (4) was chosen, not only because of the availability of anhydrous potassium fluoride, but also because of the desirability of determining the scope of the application of this fluorinating agent.

The method can be applied successfully to the preparation of the desired difluoroalkanes except ethylene fluoride, which could not be prepared by this method. In addition to traces of vinyl fluoride, the only fluorination product of ethylene bromide is 1-bromo-2-fluoroethane which is obtained in about 24% yield. The main product of the reaction of potassium fluoride with ethylene bromide in glycol is vinyl bromide, formed by dehydrobromination of the starting material. Using ethylene chloride as reactant the results are even more unsatisfactory.

Since the fluorinated product is distilled off during the reaction at the same rate at which it is formed, and since the required reaction temperatures of 160–180° for chlorides and of 130–150° for the bromides do not allow much variation of the reaction conditions, it is necessary to add the aliphatic halides (especially

TABLE I
FLUORINATION OF DIHALOGENOALKANES

STARTING MATERIAL	REACTION TEMP. °C.	DIST. TEMP. °C.	DIFLUORO-ALKANE %	YIELDS OF HALOGENO-FLUORO-ALKANE %	FLUORO-ALKENE %
BrCH ₂ CH ₂ Br.....	150	40–50	—	23.7	—
BrCH ₂ CH ₂ CH ₂ Br.....	150	45–55	23.3	6.2	19.4
ClCH ₂ (CH ₂) ₂ CH ₂ Cl.....	170	104–116	44.2	6.6	2.2
ClCH ₂ (CH ₂) ₃ CH ₂ Cl.....	180	130–138	36.6	9.4	2.8
ClCH ₂ (CH ₂) ₄ CH ₂ Cl.....	185	140–150	30.0	—	2.5

the lower-boiling ones) slowly at the same rate at which they are consumed. Otherwise, the temperature of the reaction mixture is lower than the required reaction temperature and fluorination takes place only to a small extent.

Together with the desired difluoroalkanes, which are obtained in yields of 26–44%, there are also formed the monofluorinated derivatives in small amounts and traces of ω -fluoroalkene-1, formed by dehydrohalogenation of the monofluoro derivative. Table I shows the reaction temperatures, distillation temperatures, and yields of the various fluorine compounds for the fluorination of the homologous dibromo- or dichloro-alkanes.

The ω, ω' -difluoroalkanes are colorless liquids having an odor which resembles that of the lower liquid hydrocarbons. Their boiling points are in good agreement with the lowering of the boiling point (38° on the average) generally observed when chlorine is substituted by fluorine in aliphatic compounds. They are completely stable to distillation at atmospheric pressure and showed no sign of decomposition within a year's period. Chemically they are unreactive; they do not react at reflux temperature with magnesium in ether, sodium iodide in acetone, sodium ethoxide in absolute ethanol, aqueous-alcoholic potassium hydroxide, potassium carbonate in absolute ethanol, or dilute acids. An exception

is 1,3-difluoropropane, which shows considerable reactivity towards sodium ethoxide, whereas the higher homologs exhibit only negligible reactivity. However, the reactivity of difluoropropane is not more than 20% of that of the corresponding chlorine compound.

In order to compare the reactivity of primary bound fluorine with that of chlorine in aliphatic compounds, the corresponding difluoro- and dichloroalkanes have been treated with sodium ethoxide in ethanol and with aqueous-alcoholic potassium hydroxide under the same conditions, and the reacted halogen present as ions has been determined titrimetrically. In the first series of determinations, 0.01 mole of the substance was refluxed with 25 ml. of 1 *N* sodium ethoxide solution in ethanol for 30 minutes, and the mixture was then

TABLE II
REACTIVITY OF ω, ω' -DICHLORO- AND DIFLUORO-ALKANES

SUBSTANCE $X(CH_2)_nX$	1 <i>N</i> NaOEt		1 <i>N</i> KOH	
	X = Cl	X = F	X = Cl	X = F
n = 2	49.5 ^a	—	42.2 ^c	—
= 3	57.0	11.6 ^b	26.3	0.9 ^d
= 4	38.3	0.2	20.4	.2
= 5	31.4	0.1	15.4	.2
= 6	28.7	0.2	12.1	.2
$C_6H_{12}X$	21.2	traces	6.7	.2

^a Percentage of chlorine reacted after refluxing 0.01 mole of substance with 25 ml. of 1 *N* NaOC₂H₅ 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*.

diluted with water and the halogen ions titrated. In another series the halogen ions were determined after refluxing 0.01 mole of the substance with 25 ml. of 1 *N* potassium hydroxide solution in 70% ethanol. The results in Table II show the percentage of halogen present as ions after the reaction calculated on the total amount of halogen in the molecule. For comparison *n*-hexyl chloride and fluoride have been included in these two series.

As can be seen from Table II the reactivity of the C—Cl bond is increased by the presence of a second C—Cl bond in the molecule. While the dichloroalkanes from the C₂ to the C₆ members show a steady decrease in reactivity towards aqueous-alcoholic potassium hydroxide approaching the value of *n*-hexyl chloride, this decrease is interrupted by a maximum at the C₃ derivative in their reactivity towards sodium ethoxide. This increased reactivity of the chlorine might be caused by simultaneous dehydrochlorination of the molecule, together with the normal substitution reaction: $RCl + ^-OC_2H_5 \rightarrow ROC_2H_5 + Cl^-$. The hydrogen on the center carbon atom of this molecule is expected to be highly acid due to the inductive effect of the chlorine on both the adjacent carbon atoms.

1,3-Difluoropropane also shows an increased reactivity towards sodium ethoxide as compared to its higher homologs, because of the same reasons pointed out for 1,3-dichloropropane. The data obtained for the reactivity of the primary bound fluorine prove definitely that it is much more stable towards alkaline reactants than chlorine in the corresponding chlorine compounds. Ethylene fluoride has not been included in this investigation, since it could not be obtained by halogen exchange with potassium fluoride from ethylene bromide or chloride. By extrapolation from the reactivities of the higher difluorides and the dichlorides including ethylene chloride, however, the reactivity of ethylene fluoride should be expected not to exceed 10% of the total fluorine content of the molecule under the above described conditions. However, this is not in agreement with the reported properties of ethylene fluoride (2) and re-inves-

TABLE III
PHYSICAL CONSTANTS OF NEW COMPOUNDS

SUBSTANCE	B.P. AT 760 MM. °C.	d_4^{25}	d_4^{25}	t	n_D^t	MR_D^a	AR_F^b
$F(CH_2)_3F$	41.6	1.0057	0.9908	26.0	1.3190	15.77	0.96
$F(CH_2)_4F$	77.8	0.9767	0.9648	25.0	1.3433	20.38	.97
$F(CH_2)_5F$	105.5	0.9572	0.9463	23.8	1.3618	25.01	.96
$F(CH_2)_6F$	129.9	0.9407	0.9310	25.0	1.3739	29.65	.97
$F(CH_2)_3CH:CH_2$	61.9-62.1	—	—	—	—	—	—
$F(CH_2)_4CH:CH_2$	91-92	—	—	26.0	1.3869	—	—
$Br(CH_2)_3F$	101.4	1.542	1.525	23.0	1.4295	23.56	.82
$Cl(CH_2)_4F$	114.7	1.0627	1.0508	23.0	1.4025	25.31	.86
$Cl(CH_2)_5F$	143.2	1.0325	1.0219	23.0	1.4120	29.96	.90
$BrCH_2CHBrCH_2F^c$	162.5	2.089	2.082	23.0	1.5092	31.43	.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), and Br (8.865) from MR_D . ^c Reported by Meslans (5): b.p. 158-159°, d_4^{25} 2.09.

tigation of its stability seems necessary, since several compounds which have been described as decomposing spontaneously have been found in this laboratory to be completely stable.

Since the reactivity of the ω, ω' -difluoroalkanes is extremely low, an activating effect of the carbon-fluorine bonds on each other can only be observed in the trimethylene derivative. The values obtained for the reactivity of fluorine in the higher homologs fall within the limits of error of the method used, but they show definitely that the carbon-fluorine bond in these compounds is less reactive (by two orders of magnitude) than the primary aliphatic carbon-chlorine bond.

It is to be expected that the ω -halogeno-1-fluoroalkanes, which are formed as by-products in the preparation of the difluoroalkanes, can become the main reaction products of the fluorination of dihalogenoalkanes by proper choice of the reaction conditions. They are the first step of the fluorination, the second step of which is the formation of the difluoroalkanes. Dehydrohalogenation of

the intermediate, however, competes with this normal reaction and yields ω -halogeno-1-alkene as by-product. This side reaction prevailed in the fluorination of 1,3-dihalogenopropane, resulting in high yields of allyl fluoride which was characterized by its bromine addition product. The 1,2-dibromo-3-fluoropropane obtained had a somewhat higher boiling point than that given by Meslans (5) (158–159°). Its physical constants are listed in Table III. The dehydrohalogenation, which becomes of minor importance with the higher dihalides, is probably caused by the mutual influence of the two strongly electronegative substituents. The physical properties of the halogenofluoroalkanes are given in Table III together with those of the difluoroalkanes and two of the higher fluoroalkenes. A preliminary qualitative investigation of their chemical properties showed that the reactivity of the halogen atom corresponds to that of the halogen in the corresponding dihalides, while the carbon-fluorine bond exhibits approximately the same low reactivity as in the difluorides. Since the chlorofluoroalkanes are, therefore, valuable intermediates for the introduction of ω -fluoroalkyl groups into organic molecules, their preparation and chemical properties are under investigation and will be the subject of another paper.

EXPERIMENTAL PART

Materials. Potassium fluoride, KF. The anhydrous salt used as fluorinating agent was the commercial product in flakes procured from Harshaw Chemical Co. It was kept in a drying oven at 125° for 24 hours before grinding in a ball mill. The powdered salt was dried immediately before use in a vacuum oven at 150° for 24 hours in order to remove the last traces of moisture.

Ethylene glycol. To obtain the solvent for the potassium fluoride anhydrous, the commercial product (DuPont) was distilled at 50 mm. pressure until the boiling point was constant over a considerable period of time. About 10% of the commercial product was distilled off and discarded. The remaining part was used as the solvent in the fluorination reaction.

ω, ω' -Dihalogenoalkanes. All dihalogenoalkanes, except 1,6-dichlorohexane, used as starting materials for the preparation of the difluoroalkanes were commercial products which were distilled before use. 1,6-Dichlorohexane (b.p. 55° at 0.5 mm. pressure) was obtained by treatment of 1,6-hexanediol with thionyl chloride in the presence of pyridine.

Preparation of difluoroalkanes. Since the preparation of the difluoroalkanes is similar in all cases and differs only in the temperatures of the reaction mixture and the temperature at which the reaction product distills, the preparation of 1,5-difluoropentane is described as a typical example in the following. The total yield of fluorinated product is generally about 50% and consists mainly of ω, ω' -difluoroalkanes, varying quantities of 1-halogeno- ω -fluoroalkane, and a small amount of ω -fluoro-1-alkene. The reaction temperatures and yields of the various reaction products are given in Table I. The physical constants and analytical data of nine new primary aliphatic fluorides are listed in Table III.

Fluorination of 1,5-dichloropentane. A mixture of 290 g. (5 moles) of finely powdered, anhydrous potassium fluoride and 275 g. of ethylene glycol was heated at 180° in a 1-liter, 3-neck round-bottomed flask, fitted with a mercury-sealed stirrer, dropping-funnel, and a 12-cm. column with attached condenser and receiver. To the vigorously stirred reaction mixture there was added 281 g. of 1,5-dichloropentane in the course of 4 hours at such a rate that the reaction products distilled at 130–138°. After addition of the dichloropentane was complete, a slow stream of air was sucked through the apparatus for half an hour in order to distill off the reaction product completely. Together with the reaction products some glycol distilled over; the upper layer consisting of fluorinated product was separated

and treated with calcium chloride and sodium fluoride overnight. After filtration, the colorless liquid (137.2 g.) was fractionated at atmospheric pressure through a 75-cm. 3-step Vigreux column yielding 5.0 g. of 5-fluoro-1-pentene at 61–62.5°, 79.1 g. of 1,5-difluoropentane at 104–106°, 23.4 g. of 1-chloro-5-fluoropentane at 139–144°; 23.2 g. or 8.2% of unreacted 1,5-dichloropentane was recovered.

The analytical data of the new compounds are listed in Table IV.

TABLE IV
ANALYTICAL DATA OF NEW COMPOUNDS

SUBSTANCE	CALC'D C	FOUND C	CALC'D H	FOUND H	CALC'D F	FOUND F
F(CH ₂) ₃ F.....	45.0	44.6	7.6	7.4	47.5	47.4
F(CH ₂) ₄ F.....	51.1	51.1	8.6	8.5	40.4	40.3
F(CH ₂) ₅ F.....	55.5	55.5	9.3	9.3	35.1	35.0
F(CH ₂) ₆ F.....	59.0	58.8	9.9	9.8	31.1	30.9
F(CH ₂) ₃ CH:CH ₂	68.1	67.9	10.3	10.5	—	—
F(CH ₂) ₄ CH:CH ₂	70.5	70.2	10.9	10.6	18.6	18.5
Br(CH ₂) ₃ F.....	25.6	25.5	4.3	4.4	13.5	13.4
Cl(CH ₂) ₄ F.....	43.5	43.5	7.3	7.2	17.2	17.1
Cl(CH ₂) ₅ F.....	48.2	48.1	8.0	8.1	—	—

ACKNOWLEDGMENT

The author desires to express his appreciation to Messrs. C. A. Rush, S. Sass, T. M. Wooten, B. M. Zeffert, and P. B. Coulter for having contributed to the required analyses and physical measurements appearing in this report. The 1,6-hexanediol used in this work was obtained through the courtesy of Dr. E. Emmet Reid.

SUMMARY

Four members of the series of ω, ω' -difluoroalkanes of the general formula F(CH₂)_nF (n = 3, 4, 5, and 6) have been prepared and their chemical and physical properties determined. The primary carbon-fluorine bond in these compounds exhibits the stability expected according to considerations of the resonance theory.

The reactivity of primary bound fluorine in aliphatic compounds has been shown to be extremely low as compared to that of chlorine in the corresponding chlorine compounds.

1-Bromo-3-fluoropropane, 1-chloro-4-fluorobutane, 1-chloro-5-fluoropentane, 5-fluoro-1-pentene, and 6-fluoro-1-hexene have been obtained as by-products of the preparation of the difluoroalkanes. Their physical constants are tabulated.

ARMY CHEMICAL CENTER, MARYLAND.

REFERENCES

- (1) PAULING, "The Nature of the Chemical Bond", 2nd. ed., Cornell Univ. Press, Ithaca, New York, pp. 34–75 (1945).
- (2) HENNE AND MIDGLEY, *J. Am. Chem. Soc.*, **58**, 882 (1936).
- (3) DESREUX, *Bull. acad. roy. Belg., Cl. Sci.*, (5) **20**, 457 (1934).
- (4) HOFFMANN, *J. Am. Chem. Soc.*, **70**, 2596 (1948).
- (5) MESLANS, *Ann. chim.*, (7) **1**, 382 (1894).