Journal of Fluorine Chemistry, *49* (1990) 281–291

Received: January 26, 1990; accepted: April 18, 1990

STUDIES ON DIRECT FLUORINATION OF STERICALLY HINDERED METHYL, ETHYL AND PROPYLENE GROUPS*

Wojciech DMOWSKI

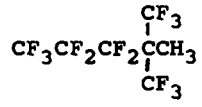
Institute of Organic Chemistry, Polish Academy of Sciences,
01-224 Warsaw (Poland)

SUMMARY

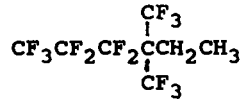
The action of elemental fluorine on fluorohydrocarbons R_FCH_3, $R_FCH_2CH_3$ and $R_FCH_2CH_2CH_2R'_F$, where $R_F = CF_3CF_2CF_2(CF_3)_2C$ and $R'_F = (CF_3)_2CF-$, was investigated. Numerous products of a stepwise substitution of fluorines for hydrogen atoms were isolated and identified by high resolution ^1H and ^{19}F NMR spectroscopy. The CH_3 group in compound R_FCH_3 has shown remarkable inertness towards elemental fluorine. The substitution pathways for other compounds investigated have been elucidated.

INTRODUCTION

A few years ago we synthesised branched fluorohydrocarbons **1** and **2** and we have found that the methyl and methylene groups adjacent to the perfluorinated part of these compounds exhibit high chemical inertness [1].



1



2

---

* Paper presented at the IXth European Symposium on Fluorine Chemistry, Leicester (U.K.), September 4 - 8, 1989.

0022-1139/90/$3.50

Attempted photochemical chlorination of **1** at the reflux temperature gave no trace of a chlorinated product and the gas-phase chlorination at 300°C resulted in less than 5% conversion to the monochloro derivative. Remarkable thermal stability of **1** was demonstrated by passing it in a stream of nitrogen through a quartz tube at 400°C; a colourless liquid was recovered without any trace of carbonisation. The photochemical chlorination of compound **2** proceeded exclusively at the terminal methyl group to give a mixture of mono-, di- and trichloroderivatives but the methylene group remained intact, independent of the reaction conditions.

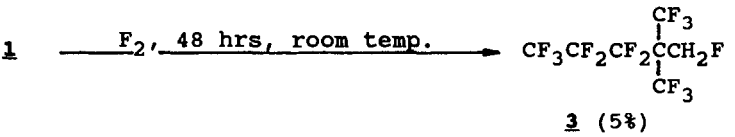
Therefore, it was deemed of interest to study the action of elemental fluorine on these two and similar fluorohydrocarbons. There was also thought that these compounds having only a few hydrogen atoms in their respective molecules could be particularly good substrates to follow the pathway of stepwise substitution of fluorines for hydrogen atoms.

RESULTS AND DISCUSSION

Lagow and co-workers [2,3] have found that the low temperature (-78°C) direct fluorination of branched aliphatic hydrocarbons, e.g. 2,2,4,4-tetramethylpentane and 2,2,5,5-tetramethylhexane, stops after the methyl groups become fully fluorinated; fluorination of the central methylene protons was achieved by continuing the reaction at room temperature or higher. By reason of that, we carried out fluorination reactions at ambient temperature (16 - 18°C). Practically, undiluted fluorine was used; only small amount of dry nitrogen was introduced just to keep a pressure of *ca.* 10 mm H_2O above atmospheric.

Compound **1** has shown remarkable inertness also towards elemental fluorine. After 48 hours in an atmosphere of undiluted fluorine most of the starting material remained unchanged; only *ca.* 5% converted to monofluoromethyl derivative **3**, but no trace of perfluorinated compound was detected. This is assumed to be a result of steric hindrances created by three bulky perfluoro-

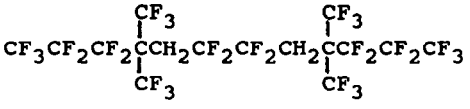
alkyl groups effectively shielding the hydrogens from the attack by fluorine.



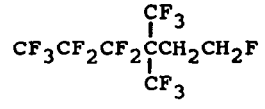
3 (5%)

Compound 2, albeit slowly, undergoes fluorination at room temperature to give a complex mixture of products. This mixture was found by GLC (Fig. 1) to contain four major components which were isolated by preparative GLC and subjected to the ^{1}H and ^{19}F NMR investigations (Table 1). Components A and B, with the retention time longer than that of the substrate, have been identified, respectively, as dimeric product 4 and 1-fluoroethyl compound 5. The GLC component C was found to consist of two unseparable compounds: 1,1-difluoroethyl derivative 6 and 1,1,2-trifluoroethyl derivative 7 in a 1 : 1.6 ratio. The most volatile major component D consisted mostly of 1,1,1-trifluoroethyl derivative 8 together with small amounts (5-8 %) of 1,1,1,2-tetrafluoroethyl and 1,1,2,2-tetrafluoroethyl compounds 9 and 10.

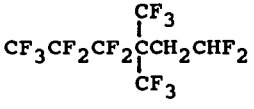
Products of the fluorination of compound 2:



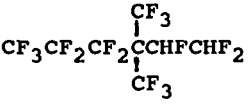
4



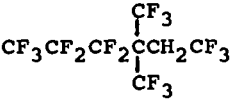
5



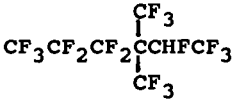
6



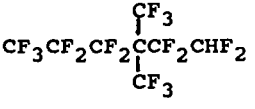
7



8



9



10

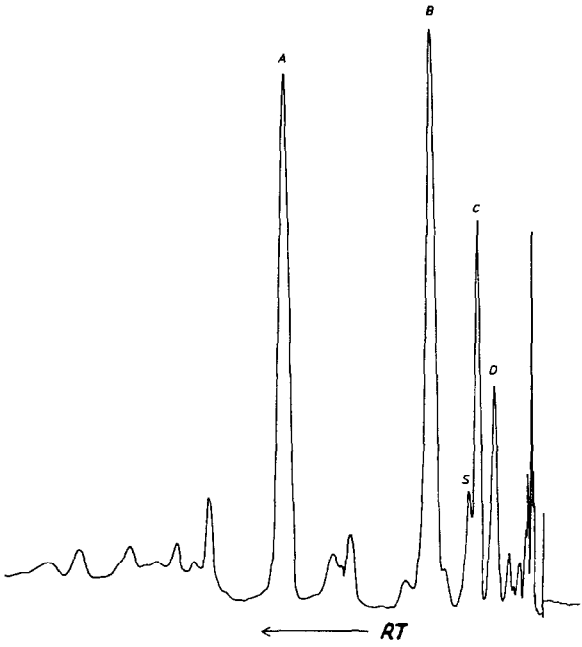


Fig. 1. The gas-liquid chromatogram of a mixture obtained from compound **2** after 30 hours fluorination.

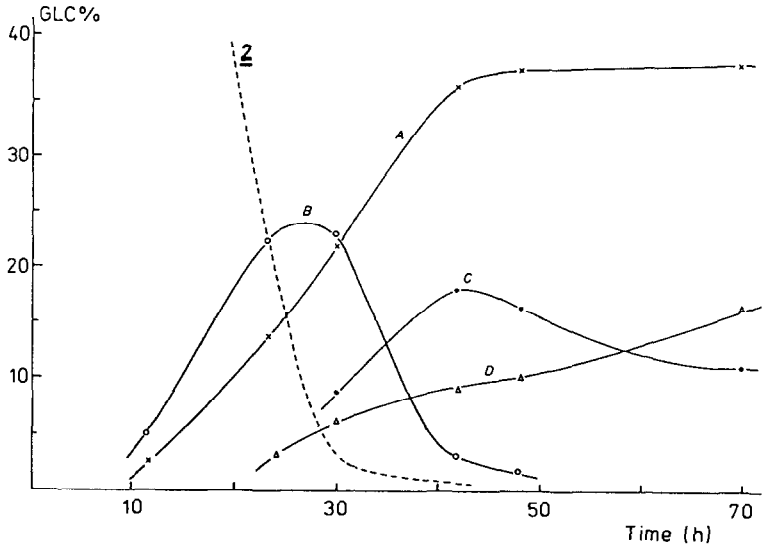
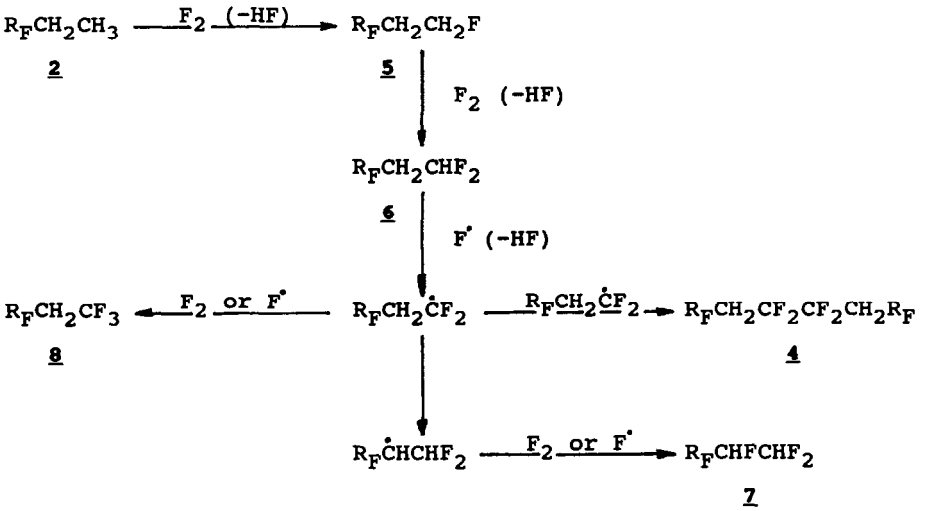


Fig. 2. Time-dependance of the composition of the fluorination products of compound **2**.

Monitoring the course of the fluorination of compound **2** by GLC (Fig. 2) gave evidence that compound **5** (or **B**) is the first intermediate: its concentration reached a maximum then fell practically to zero when the fluorination was continued. Also, at least one of the GLC components **C**, most probably compound **6**, is the next intermediate. It is also evident from Fig.2 that two other major compounds **4** and **8** (**A** and **D**) are final products, resistant to further fluorination.

Fluorination of ethyl derivative **2** gave considerable amounts of products fluorinated also at the sterically hindered methylene group. 1,1,2-Trifluoroethyl derivative **7** was one of the major components and detectable amounts of tetrafluoro derivatives **9** and **10** were formed. This result was rather unexpected, considering the high resistance of the methyl group in compound **1** towards fluorination.

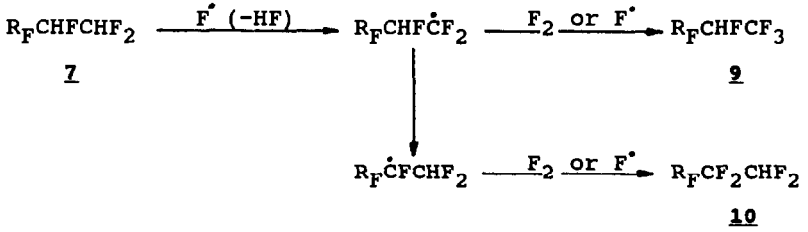
A logical explanation of this discrepancy could be that fluorination of the sterically shielded methylene group occurs via rearrangement of alkyl radicals involved, rather than by direct attack of fluorine on the methylene hydrogens. Such reasoning, and by considering compounds **5** and **6** as basic intermediates, suggests the main fluorination pathway of **2** as follows:



Introduction of the first two fluorine atoms occurs, as expected, at the terminal methyl group and due to the well known fact that the rate of fluorination decreases when an increasing number of fluorines has been introduced, the intermediate mono- and difluoromethyl derivatives **5** and **6** accumulate in the reaction mixture. Continued fluorination, albeit much slower, leads to the abstraction of the third hydrogen from the difluoromethyl group of **6** to give the primary difluoromethyl radical which can react further in three different ways:

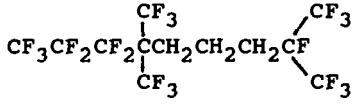
- two of these include the reaction with a fluorine molecule or radical to give 1,1,1-trifluoroethyl derivative **8**, or alternatively, coupling to form dimeric product **4**. Both of them are well known processes.
- the third possibility would involve a rearrangement of the primary radical to the secondary radical, followed by its fluorination to give the unexpected 1,1,2-trifluoroethyl compound **7** fluorinated at the sterically shielded methylene group.

Likewise, formation of both minor tetrafluoroethyl derivatives **9** and **10** can be understood by considering participation of primary and rearranged secondary radicals generated from 1,1,2-trifluoroethyl compound **7** as shown below:



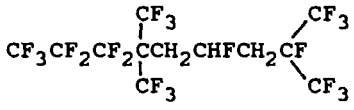
7 **9** **10**

The next object of investigation was the 1,3-bis(perfluoroalkyl)propane **11** containing a propylene group terminated at both sides by branched perfluoroalkyl substituents.

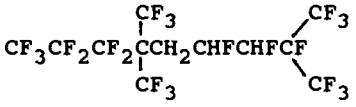


11

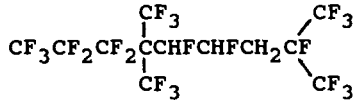
Fluorination of compound **11** gave a more complex mixture of products than that obtained from **2**. Monitoring the course of the reaction by GLC gave evidence for the participation of three intermediates and at least three main products which were resistant to further fluorination. Four GLC components of the reaction mixture were isolated but only the least volatile intermediate was found to be a single compound; it has been unambigously identified as monofluoroderivative **12** fluorinated at the central methylene group. Both proton and fluorine NMR spectra of another isolated intermediate revealed the presence of at least four non-equivalent CHF groups, therefore, this GLC component was assumed to be a mixture of diastereoisomers either of 1,2-difluoro- or 2,3-difluoropropylene derivatives **13** and **14** or both of them. The NMR spectra of higher fluorinated products were too complex to be resolved, nevertheless, the spectra had shown numerous signals characteristic of CH_2, CHF, and CF_2 groups.



12



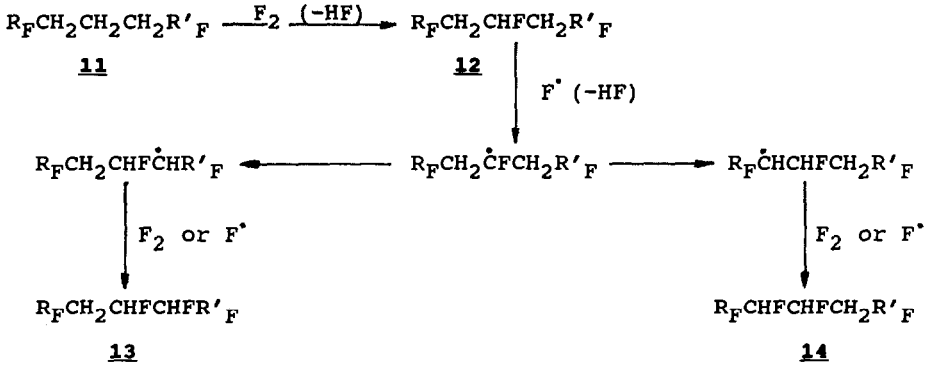
13



14

The results of the fluorination of 1,3-bis(perfluoroalkyl)-propane **11**, although only partial, support the suggestion that fluorination of sterically shielded carbon atoms proceeds via rearrangement of fluoroalkyl radicals.

Formation of compounds **12**, **13**, and **14** may proceed as shown in the scheme below:



CONCLUSIONS

- fluorination of a carbon-hydrogen bond is strongly hindered by the neighbouring bulky perfluoroalkyl groups
- even sterically shielded hydrogens may be replaced by fluorine atoms due to rearrangement of a radical initially formed on the adjacent non-shielded carbon.

It has been generally accepted [4] that the lack of selectivity in fluorination of hydrocarbons is due to very small differences in the activation energy for the abstraction of primary, secondary, and tertiary hydrogen atoms. The present results suggest that rearrangements of fluoroalkyl radicals might be an additional factor which contributes to this lack of selectivity.

EXPERIMENTAL

The GLC analyses were performed using a 1 m x 4 mm column packed with 4% of dinonyl phthalate on Chromosorb G. For the preparative work a 4.0 m x 10 mm column packed with Chromosorb G coated with 3% of Silicon Oil SE-52 was used. ^1H and ^{19}F NMR spectra were recorded in $CDCl_3$ solutions with a Brucker 500 MHz spectrometer. Chemical shifts are from internal TMS for the ^1H and from internal CCl_3F for the ^{19}F (positive upfield) spectra.

TABLE 1

^{1}H and ^{19}F NMR data for compounds **3** - **10** and **12**

$R_F = CF_3CF_2CF_2C(CF_3)_2-$

Compound	Chemical shift* δ(p.p.m.)	Coupling const. J(Hz)
1	2	3
R_FCH_2F **3**	CH_2 = 5.02 (d)	45.3
$R_FCH_2CF_2CF_2CH_2R_F$ **4**	CH_2 = 3.37 (m) CF_2 = 116 (m)	
b a $R_FCH_2CH_2F$ **5**	H_a = 2.65 (dt) H_b = 4.71 (dt)	H_aF_a = 45.7 H_aH_b = 7.3 H_bF_a = 15.8
b a $R_FCH_2CHF_2$ **6**	H_a = 6.17 (tt) H_b = 2.78 (td) F_a = 109.9 (dm)	H_aF_a = 54.5 H_aH_b = 4.0 H_bF_a = 14.6
b a $R_FCHFCHF_2$ **7**	H_a = 6.21 (tdd) H_b = 5.28 (dddd) F_a,F_a' = 122.3 and 129.0 (dd) F_b = 209.5 (m)	$H_aF_a = H_aF_a'$ = 53.0; H_aF_b = 7.8 H_aH_b = 3.2 F_aF_a' = 303.6 F_aH_b = 11.0 F_a,H_b = 7.9 H_bF_b = 42.3
b a $R_FCH_2CF_3$ **8**	H_b = 3.08 (q) F_a = 56.6 (m)	F_aH_b = 9.45

(continued)

TABLE 1 (cont.)

1	2	3
b a R_FCHFCF_3 **9**	H_b = 5.50 (dq) F_a = 60.5 (m) F_b = 202 (m)	H_bF_b = 41.2 H_bF_a = 5.9
b a $R_FCF_2CHF_2$ **10**	H_a = 6.16 (tt) F_a = 124.2 F_b - not found	H_aF_a = 52.2 H_aF_b = 5.7
e d c b a $R_FCH_2CHFCH_2CF(CF_3)_2$ **12**	F_a,F_a' = 77.4 and 77.5 (m) F_b = 172.0 (m) H_c,H_c' = 2.33 (d,) and 2.47 (dm) H_d = 5.35 (dm) F_d = 185.7 (m) H_e,H_e' = 2.65 (dm) and 2.76 (dm)	 H_cH_c' = 16.6 H_dF_d = 47.8 H_eH_e' = 17.0

* Chemical shifts for the R_F group: 60 -65 ppm (2 CF_3), 80.6 ppm (CF_3), 105 - 108.5 ppm (CF_2), 123 - 124 ppm (CF_2).

Syntheses of fluorohydrocarbons **1** and **2** were described previously [1]. Preparation of 1,3-bis(perfluoroalkyl)propane **11** will be published. Elemental fluorine was taken from a fluorine cell and freed from hydrogen fluoride by passing through a copper coil kept at -78°C. Nitrogen was dried by passing through a column filled with molecular sieves calcinated at 400°C.

Fluorinations were carried out using a simple apparatus consisting of a 5 cm diameter and 14 cm deep copper vessel fitted with a magnetic stirring bar, fluorine inlet tube (the

end of the tube was placed close to the surface of the fluorinated liquid), a tube for periodically withdrawing samples, and a copper reflux condenser surrounded by a wooden box filled with sufficient amount of dry ice to stay overnight. The efficient reflux condenser was necessary to minimize the loss of fluorinated substances.

General procedure

The apparatus was purged with dry nitrogen for at least one hour after which fluorinated compound (20 - 50 mmoles) was injected, then fluorine was introduced at a rate ca. 0.7 g per hour for 48 - 72 hours. The fluorinated material was magnetically agitated during the fluorination. Samples were taken periodically and analysed by gas-liquid chromatography. Finally, the fluorine flow was stopped, the reaction vessel was cooled with a dry ice-acetone bath, and the fluorine gas was removed with a stream of nitrogen. After warming up to ambient temperature the reaction mixture was transferred to a glass flask, sodium fluoride was added, all volatile material was distilled off under atmospheric pressure, then subjected to the preparative GLC separation and the ^{1}H and ^{19}F NMR investigations (Table 1).

ACKNOWLEDGMENT

This work has been supported by the Polish Academy of Sciences within the project CPBP-01.13.1.21.

REFERENCES

1 W.Dmowski and R.Woźniacki, J.Fluorine Chem., **36** (1987) 385.
2 L.A.Shimp and R.J.Lagow, J.Org.Chem., **42** (1977) 3437.
3 E.K.S.Liu and R.J.Lagow, J.Fluorine Chem., **13** (1979) 71.
4 W.A.Sheppard and C.M.Sharts, 'Organic Fluorine Chemistry', Benjamin, New York 1969, chapter 2.