New views on the fluorination of carbonyl compounds with SF_4

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Abstract

New data on the fluorination of some carbonyl compounds with SF_4 contradict present views on the mechanism of this reaction. Results of the present and earlier studies have been used to discuss the accepted reaction mechanism and to suggest a modified one.

Introduction

On treatment with SF_4 trichloroacetic acid yields to corresponding acyl fluoride, but no higher fluorinated products are formed even under forced conditions. Dmowski interpreted the low reactivity of trichloroacetic acid by the significant negative inductive effect of the trichloromethyl group [1].

We have found that tribromoacetic acid (**1**), which has a similar inductive effect of the tribromomethyl group as that of the trichloromethyl group (CBr_3: $\sigma_I = 0.25$, $pK = 0.66$; CCl_3: $\sigma_I = 0.29$, $pK = 0.65$ [2, 3]), yields a fully-fluorinated product, *i.e.* 1,2,2-tribromo-1,1,2-trifluoroethane (**2**). This result calls for a revision of the mechanism of the reaction of SF_4 with carbonyl compounds.

Experimental

^1H and ^{19}F NMR spectra were measured on a Bruker WP-200 NMR spectrometer using HMDS and $FCCl_3$ as the respective internal standards, and d_6-acetone as the solvent. The ^{19}F values were negative for upfield shifts. ^{13}C NMR spectra were measured on a Gemini-200 NMR spectrometer using $CDCl_3$ as the solvent. Gas–liquid chromatography was carried out on a Chrom-5 chromatograph with an FID using helium as the carrier gas and employing a stainless-steel column (2500×3 mm) filled with 10% polyphenylmethylsiloxane on Chromatone-AW (0.20–0.25 mm). Preparative GLC was carried out on a PACHV-07 chromatograph fitted with a thermal conductivity detector. A stainless-steel column (2600×12 mm) filled with 10% polyphenylmethylsiloxane on Chromatone-N-AW-HMDS (0.32–0.40 mm) was used with helium as the carrier gas.

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Treatment of carboxylic acids with SF_4

General procedure

A carboxylic acid and SF_4 were reacted in a stainless-steel cylinder using the relevant amounts of reactant, reaction time and temperature as indicated in Table 1. Volatile products were removed and the liquid was poured into iced water, separated, dried with P_2O_5 and purified by distillation or preparative GLC, as necessary.

TABLE 1

Reactions of carboxylic acids with SF_4

Acids		SF_4 (mol)	Reaction cond.		Reaction products and yield
No.	mol		Temp. (°C)	Time (h)	
1	0.03	0.09	25	45	**2**, 95%
5	0.0368	0.14	100[a]	4	**6**, 79%; **7**, 17%
8	0.058	0.46[b]	100	4	**9**, 60%
10	0.100	0.30	20	140	**11**, 64%; **12**, 16%
13	0.0378	0.23	140	4.5	**14**, 56%

[a]Reaction mixture initially stored at 20 °C for 17 h.
[b]Acid previously treated with 0.31 mol SF_4 at 25 °C.

TABLE 2

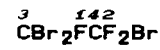
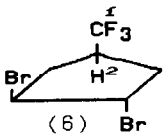
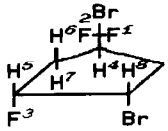
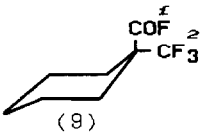
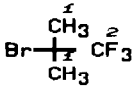
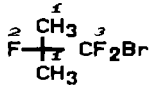
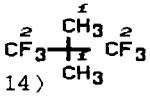
Physical properties of the prepared compounds

Compound No.	B.p. [m.p.] (°C)	d_4^{22}	n_D^{22}	Elemental analyses			
				El.	Found (%)	Molecular formula	Calc. (%)
2[a]	114	2.559	1.447	Br	74.21; 74.36	$C_2Br_3F_3$	74.74
6	193	1.948	1.475	C	24.12; 24.26	$C_6H_7Br_2F_3$	24.35
				H	2.23; 2.29		2.38
				Br	53.71; 53.85		54.00
				F	19.10; 19.18		19.26
9	152	1.262	1.382	C	48.57; 48.62	$C_8H_{10}F_4O$	48.49
				H	5.13; 5.25		5.09
				F	37.98; 38.13		38.35
11	66.5 [18]	1.517	1.365	Br	41.66; 41.81	$C_4H_6BrF_3$	41.85
				F	29.73; 29.92		29.85
12	74	1.538	1.369	Br	41.81; 42.11	$C_4H_6BrF_3$	41.85
				F	29.39; 29.46		29.85
14	39 [19]	–	–	C	33.12; 33.27	$C_4H_6F_6$	33.34
				H	3.21; 3.28		3.36
				F	63.04; 63.15		63.30

[a]Lit. [20]: b.p., 117 °C; d^7, 2.56656; n_{D^7}, 1.4666.

TABLE 3

NMR data of the prepared compounds

Formula	Nucl. No.	Signal struct.	Chem. shift (ppm)	Coupling constants (Hz)
 (2)	1	t	−71.58	$^3J_{1-2}=17.1$; lit. [21], 18
	2	d	−59.00	$^3J_{2-1}=17.1$
	3	d, t	89.18	$^1J_{3-1}=325$, $^2J_{3-2}=37$
 (6)	4	t, d	115.82	$^1J_{4-2}=315$, $^2J_{4-1}=35$
	1	d	−70.15	$^3J_{1-2}=9.8$
 (7)	1(2)	m	−48.12	$^2J_{1-2}=159.2$, $^3J_{1-4}=13.5$ $^5J_{1-3}=2.5$
	2(1)	m	−49.40	$^2J_{2-1}=159.2$, $^3J_{2-4}=13.5$ $^5J_{2-3}=2.5$
	3	m	158.84	$^2J_{3-5}=50$, $^3J_{3-8}=30$ $^3J_{3-6}=30$, $^3J_{3-7}=10$ $^5J_{3-1}=2.5$, $^5J_{3-2}=2.5$
 (9)	1	m	39.02	$^4J_{1-2}=8.8$
	2	d	−73.95	$^4J_{2-1}=8.8$
 (11)	1	q	1.82	$^4J_{1-2}=0.7$
	2	sept	−78.45	$^4J_{2-1}=0.7$
 (12)	1	d, t	1.53	$^3J_{1-2}=22.5$, $^4J_{1-3}=1.1$
	2	m	−148.7	$^3J_{2-1}=22.5$, $^3J_{2-3}=11.23$
	3	d	−61.5	$^3J_{3-2}=11.23$
 (14)	1	sept	1.34	$^4J_{1-2}=0.8$
	2	sept	−69.85	$^4J_{2-1}=0.8$

Results and discussion

The author of a recent review [1] has proposed a new mechanism for the reaction of SF_4 with carbonyl compounds in which it is postulated that

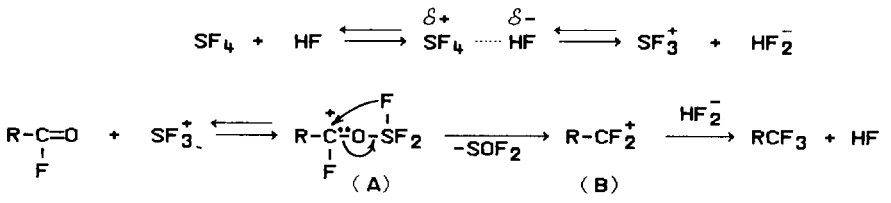
intramolecular rearrangement of the mesomerically stabilised carbocation (A) occurs initially, followed by the non-reversible formation of the carbocation (B) (Scheme 1).

According to this mechanism tribromoacetic and trichloroacetic acids should not be distinguished in their reactivity either at the reversible stage of carbocation (A) formation, or at the non-reversible stage of its intramolecular rearrangement to the carbocation (B), *i.e.* tribromoacetic acid should also give tribromoacetyl fluoride, but not a fully-fluorinated product.

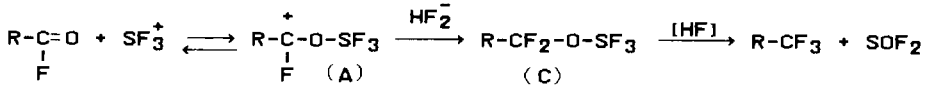
The contradiction vanishes if we exclude the non-reversible stage of the intramolecular rearrangement of the carbocation (A) to the carbocation (B) and return to the pioneering study by Martin and Kagan [4] (Scheme 2).

Scheme 2 suggests that the carbocation (A) takes part in the reaction without intramolecular rearrangement into the carbocation (B), and that it undergoes attack by the nucleophile to give the alkoxysulphur trifluoride (C) (Scheme 1).

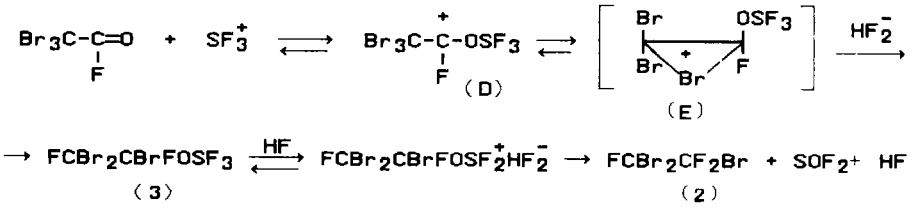
It is only the nature of (A) that determines the above reaction pathway. With all other conditions being the same as for trichloroacetic acid, the stage which allows the reaction of tribromoacetic acid to proceed is the formation of the cyclic bromonium cation (E). The latter undergoes nucleophilic attack by the HF_2^- anion and forms the alkoxysulphur trifluoride (**3**), which, in turn, in the presence of HF dissociates [5, 6] to give the final product, 1,2,2-tribromo-1,1,2-trifluoroethane (**2**) (Scheme 3).



Scheme 1.



Scheme 2.



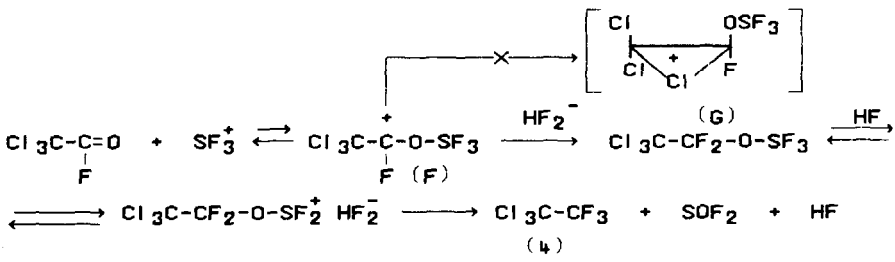
Scheme 3.

Despite the electrophilic nature of the carbocations (D) and (F), the latter is not able to form a cyclic chloronium cation (G) and, therefore, halogenotropism does not occur in the reaction of trichloroacetic acid. The reaction stops at the stage of trichloroacetyl fluoride or in the presence of excess HF yields 1,1,1-trifluoro-2,2,2-trichloroethane (**4**) [7] (Scheme 4).

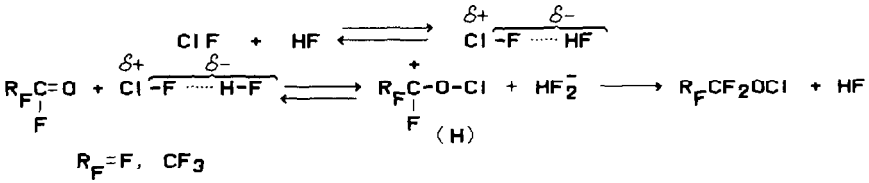
It should be noted that alkoxysulphur trifluorides are stable only in the absence of Lewis acids. 2-Fluoro-2,2-dinitroethoxysulphur trifluoride in the presence of HF at 25 °C gives 1,2-difluoro-1,1-dinitroethane in 30% yield [8]. 1,1,7-3*H*-Dodecafluoroheptyloxysulphonium difluoride is stable only up to −5 °C [5].

The possibility of neutralization of the slightly electrophilic carbocations (H) by the HF_2^- anion, similarly to (D) and (F), has been demonstrated by Young *et al.* [9] (Scheme 5).

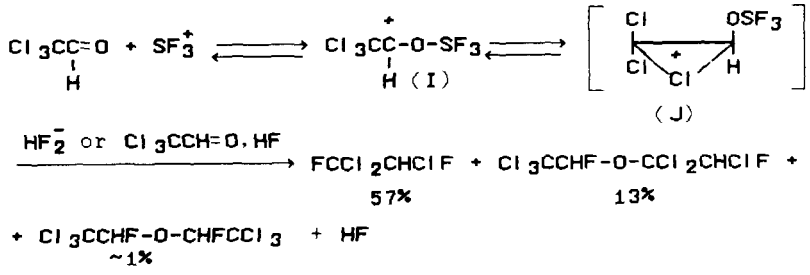
On the basis of Scheme 3, the fluorination of trichloroacetic aldehyde, which proceeds under mild conditions [10], may be represented by Scheme 6.



Scheme 4.



Scheme 5.

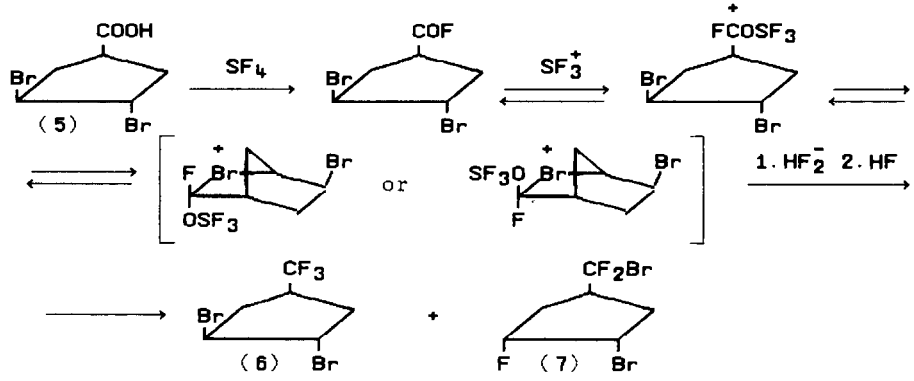


Scheme 6.

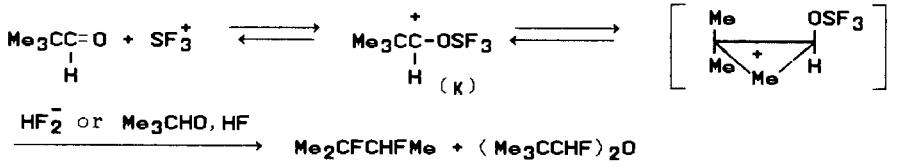
The electrophilicity of the mesomeric carbocation (I) is higher than that of (F) [11] and sufficient to form the cyclic chloronium cation (J). Hence, halogenotropism is observed. Further attack of nucleophiles on the cyclic cation (I), as in the case of tribromoacetic acid, is directed towards the carbon atom which is the most substituted with halogen atoms; the reaction possibly follows an S_N2 mechanism. The latter has been directly confirmed by the stereospecific substitution of fluorine for bromine in the reaction of *trans*-3,4-dibromocyclopentane-1-carboxylic acid (**5**) with SF_4 (Scheme 7).

The phenomenon of halogenotropism has also been observed in studies of the fluorination of other chlorine- and bromine-containing carbonyl compounds [12–14].

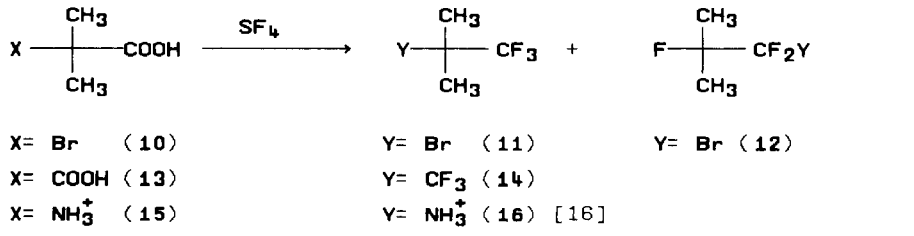
Migration of a methyl group to the electrophilic centre as observed in the reaction of pivalic aldehyde with SF_4 [1] (Scheme 8) can be regarded as analogous to the halogenotropism considered above.



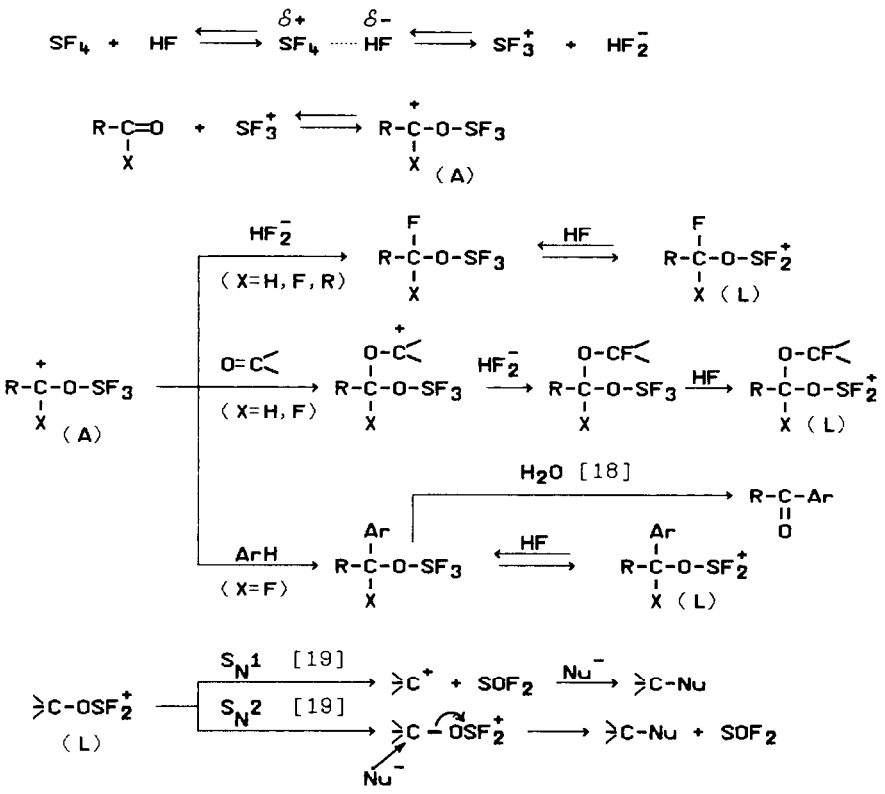
Scheme 7.



Scheme 8.



Scheme 9.



Scheme 10.

In contrast to pivalic aldehyde, pivalic acid is less reactive, *e.g.* 1,1,1-trifluoro-2,2-dimethylpropane was obtained in only 10% yield [7]. From our viewpoint, however, a difference in reactivity between these two sterically hindered carbonyl compounds is a result of the different behaviour of the methyl group in carbocations of type A. In the case of pivalic acid, despite the fact that the methyl group is an internal nucleophile, its migration is not possible owing to insufficient electrophilicity of the carbocationic centre. Similar instances of low reactivities are also known for methoxyacetic and 2-methoxy-2-phenylpropionic acids [7, 15]. In these cases, migration of the internal nucleophile, *i.e.* the methoxy group, is not possible.

Cyclohexane-1,1-dicarboxylic acid (**8**) reacts with SF_4 yielding 1-trifluoromethyl-1-fluoroformylcyclohexane (**9**) as the major product. In this case, structural factors favour methylene groups in 3,5 positions of the cyclohexane rings as the internal nucleophiles are again unable to migrate to the axially disposed carbocationic reactive centre.

It should be noted that acids like pivalic, in which one methyl group is substituted by an electronegative group (**10, 13, 15**), undergo fluorination readily when treated with SF_4 (Scheme 9).

The adjacent electronegative substituent reduces the nucleophilic ability of the methyl groups so that they no longer act as internal nucleophiles, and thus the reactivity of these acids is similar to that of sterically unhindered aliphatic acids.

In sterically hindered 1-adamantanecarboxylic acid which has a rigid skeleton, methylene fragments cannot act as internal nucleophiles in carbocations of type A, and fluorination of the carboxylic group proceeds readily [17].

In agreement with the present experimental data we propose the following general mechanism for the HF-catalyzed reaction of SF_4 with carbonyl compounds (Scheme 10).

This mechanism is sufficient to explain both simple and rearranged products.

References

1 W. Dmowski, *J. Fluorine Chem.*, *32* (1986) 255.
2 L. M. Yagupolskii, A. Ya. Il'chenko and N. V. Kondratenko, *Usp. Khim.*, *3* (1974) 64.
3 H. C. Brown, D. H. McDaniel and O. Hafliger, in E. A. Braude and F. C. Nachod (eds.), *Determination of Organic Structures by Physical Methods*, Academic Press, New York, 1955, Chapt. 14.
4 D. G. Martin and F. Kagan, *J. Org. Chem.*, *27* (1962) 3164.
5 V. E. Pashinnik, V. I. Tovstenko, L. S. Bobkova and L. N. Markovskii, *Zh. Org. Khim.*, *21* (1985) 2072.
6 J. Kollonitsch, *Isr. J. Chem.*, *17* (1978) 53.
7 W. Dmoswki and R. A. Kolinski, *Pol. J. Chem.*, *52* (1978) 547.
8 K. Baum, *J. Am. Chem. Soc.*, *91* (1969) 4594.
9 D. E. Young, L. R. Anderson and W. B. Fox, *Inorg. Chem.*, *9* (1970) 2602.
10 G. Siegemund, *Liebig's Ann. Chem.*, (1979) 1280.
11 R. H. Martin and R. W. Taft, *J. Am. Chem. Soc.*, *88* (1966) 1353.
12 V. V. Lyalin, R. V. Grigorash, L. A. Alekseeva and L. M. Yagupolskii, *Zh. Org. Khim.*, *17* (1981) 1774.
13 B. V. Kunshenko, S. O. Il'nitskii, L. A. Motnyak, V. V. Lyalin and L. M. Yagupolskii, *Zh. Org. Khim.*, *23* (1987) 833.
14 A. Haas, R. Plumer and A. Schiller, *Chem. Ber.*, *118* (1985) 3004.
15 L. Hub and H. S. Mosher, *J. Org. Chem.*, *35* (1970) 3691.
16 M. S. Raasch, *J. Org. Chem.*, *27* (1962) 1406.
17 A. M. Aleksandrov, G. I. Danilenko and L. M. Yagupolskii, *Zh. Org. Chem.*, *9* (1973) 951.
18 J. Wielgat and Z. Domagala, *J. Fluorine Chem.*, *35* (1982) 643.
19 L. S. German and S. V. Zemskov (eds.), *Novye Ftoriruyushchie Reagenty v Organicheskom Sinteze*, Novosibirsk, 1987, p. 228.
20 F. Swarts, *Chem. Zentralbl.*, *2* (1899) 281.
21 P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc.*, *79* (1957) 4565.