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Reactions of cycloalkanecarboxylic acids with SF_4. I. Fluorination of cyclopropanepolycarboxylic acids with SF_4*

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Abstract

Cyclopropanecarboxylic acids possessing more than one carboxylic group readily undergo fluorination when treated with SF_4 to yield the corresponding poly(trifluoromethyl)cyclopropanes and bicyclic ethers.

Keywords: Cycloalkanecarboxylic acids; Sulphur tetrafluoride; Poly(trifluoromethyl)cyclopropanes; Bicyclic ethers; NMR spectroscopy

1. Introduction

The fluorination of cyclopropanecarboxylic acid with SF_4 to give trifluoromethylcyclopropane only proceeds in the presence of excess HF [1]. This has been explained on the basis of the relative basicities of the COF group and the SF_4 molecule. In the system containing equimolar quantities of SF_4, HF and RCOF, the concentration of SF_3^+ cations may be related to the ratio of the equilibrium constants of competitive reversible reactions:

$$SF_4 + HF \overset{K_1}{\rightleftharpoons} \overset{\delta+}{S}F_4 \cdots \overset{\delta-}{H}F \overset{K_2}{\rightleftharpoons} SF_3^+ + HF_2^- \qquad (1)$$

$$RCOF + HF \overset{K_3}{\rightleftharpoons} R\overset{\delta+}{C}OF \cdots \overset{\delta-}{H}F \qquad (2)$$

The equilibrium constants K_1, K_2 and K_3 are related to the basic properties of SF_4 and RCOF. Two extreme cases may occur: (a) $K_1,K_2 > K_3$, i.e. acyl fluoride is a weaker base than SF_4, when equilibrium (1) is always displaced more to the right than reaction (2), leading to significant formation of the complex $SF_4 \cdot HF$ and SF_3^+ cations even at HF concentrations less than equimolar, and (b) $K_1,K_2 < K_3$, i.e. acyl fluoride is a stronger base than SF_4, when formation of the $RCOF \cdot HF$ adduct predominates and equilibrium (1) is predominantly to the left. In this case, the quantity of HF required to allow reaction (2) to proceed is greater than that consumed in the reaction [1].

Consequently, introduction of a second carboxylic group into the cyclopropane ring should lower the basicity of both fluorocarbonyl groups and also result in an increase in HF formed during the first fluorination step. Both trends should favour the fluorination of cyclopropanepolycarboxylic acids by SF_4.

2. Experimental

^1H, ^{13}C and ^{19}F NMR spectra were measured using a Bruker WP-200 NMR spectrometer with TMS and $CFCl_3$ as the respective internal standards, and $CDCl_3$ as the solvent (acetone-d_6 was employed as the solvent for compounds **15** and **16**). The upfield ^{19}F chemical shift values are negative. Gas–liquid chromatography was carried out with a Chrom 5 chromatograph using FID and helium as the carrier gas. A stainless-steel column (2500×3 mm) filled with 10% polyphenylmethylsiloxane on Chromatone AW (0.20–0.25 mm) was employed. Preparative GLC was carried out with 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) and helium as the carrier gas were used. All reported boiling and melting points are uncorrected.

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*Dedicated to Professor L.M. Yagupolskii on the occasion of his 70th birthday.

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Table 1
Reactions of cyclopropanecarboxylic acids with SF_4

Acids		SF_4 (mmol)	Reaction conditions		Reactions products [yield(%)]
Compound No.	mmol		Temp. (°C)	Time (h)	
1	61.5	507	125	5	**4** [48]
2	41.7	270	120	6	**5** [44]
3	100	454	120	4.5	**6** [53]
7	57	531	130	7	**8** [26]; **9** [26]
10	57	390	130	4.5	**11** [15]; **12** [60]
13	85	510	135	4	**14** [53]

2.1. Treatment of carboxylic acids with SF_4
General procedure

The 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. The gaseous products formed were released and the liquid residue poured into iced water. The organic layer was separated, dried over P_2O_5 and purified by distillation or preparative GLC, as appropriate. The physical properties and analyses of the products are given in Table 2 and the NMR data in Table 3.

1-Trifluoromethyl-cis-1,2-cyclopropanedicarboxylic acid (15)

A mixture consisting of 1,1,2-tris(trifluoromethyl)cyclopropane (**11**), 1-trifluoromethyl-2,2,4,4-tetrafluoro-3-oxa-bicyclo[3.1.0] hexane (**12**) (prepared by reaction of 1,1,2-cyclopropanetricarboxylic acid (**10**) with SF_4) and excess 10% oleum were heated at 120 °C (1 h) in a sealed tube and then cooled to room temperature. The colourless precipitate formed was collected by filtration and recrystallized from water. The product was identified as compound **15** by elemental analysis and ^{19}F NMR data.

1,1,2-Tris(trifluoromethyl)cyclopropane (11)

The organic layer containing **11** was separated from the filtrate obtained after the isolation of **15** above or by preparative GLC from the mixture of **11** and **12**.

1-Trifluoromethyl-3-aza-bicyclo[3.1.0]hexane-2,4-dione (16)

A solution consisting of 2 g (1 mmol) of compound **15** in ether was added to excess ether saturated with dry ammonia. The ammonium salt of compound **15** was collected by filtration and dried *in vacuo* at 100 °C. Cyclization occurred on heating at 185–200 °C (0.5 h). The residue thus obtained was sublimed *in vacuo* (20 mmHg) at 80–85 °C. Yield, 1.0 g (65%). Recrystallization of this product from benzene afforded **16** as colourless crystals.

trans-1,2-Bis(trifluoromethyl)-3-methylcyclopropane (5)

Hydrogen was bubbled through liquid *trans*-1,2-bis(trifluoromethyl)-3-methylenecyclopropane (**6**) and the resulting gas–vapour mixture passed through a quartz tube (800×10 mm) containing 13 g of freshly prepared 5% Pd/Al_2O_3 [2] heated at 100 °C. The hydrogenation product was collected in a trap, cooled to 195 K (Cardice) and identified as compound **5** (yield, 100%).

trans-1,2-Bis(trifluoromethyl)-3-chloro-3-chloromethylcyclopropane (17)

Chlorine at room temperature was bubbled through *trans*-1,2-bis(trifluoromethyl)-3-methylenecyclopropane (**6**) (1 g, 5 mmol) with constant illumination with a visible light lamp until the absorption of chlorine had ceased. The product was distilled under reduced pressure when 1.3 g of compound **17** was obtained in 95% yield.

1-Iodo-1-(2,2,2-trifluoroethyl)-trans-2,3-bis(trifluoromethyl)cyclopropane (18)

A mixture of CF_3I (13 g, 6.6 mmol) and compound **6** (5.3 g, 2.8 mmol) contained in a sealed tube (molybdenum glass) was irradiated by UV light (Hg lamp) at room temperature for 90 h. The volatile products were removed and the residue vacuum distilled when 2.3 g of compound **18** was obtained (yield, 21%).

Attempted reaction of 1,1-bis(trifluoromethyl)cyclopropane (14) with bromine

An equimolar mixture of compound **14** and bromine contained in a sealed tube (Pyrex glass) was irradiated by UV light (Hg lamp) at 120 °C (30 h) when only the unchanged starting materials were obtained.

3. Results and discussion

trans-Cyclopropane-1,2-dicarboxylic acid (**1**) and its methyl and methylene derivatives **2** and **3** readily react with SF_4 to yield the corresponding bis(trifluoromethyl)cyclopropanes **4**–**6** (Scheme 1).

Table 2
Physical properties of prepared compounds

Compound No.	B.p. [m.p.] (°C)	d_4^{22} (g cm^{-3})	n_D^{22}	Elemental analyses		
				Found (%)	Molecular formula	Calc. (%)
4	43[a]	1.331	1.291	C 33.6	$C_5H_4F_6$	33.7
				H 2.2		2.3
				F 63.8		64.0
5	63	1.273	1.306	C 37.3	$C_6H_6F_6$	37.5
				H 3.0		3.1
				F 58.9		59.4
6	52	1.288	1.312	C 37.6	$C_6H_4F_6$	37.9
				H 2.2		2.1
				F 59.3		59.4
8	65.5	1.543	1.293	C 29.2	$C_6H_3F_9$	29.3
				H 1.2		1.2
				F 69.5		69.5
9	83	1.565	1.317	C 32.2	$C_6H_3F_7O$	32.2
				H 1.4		1.4
				F 58.8		59.4
11	74	1.562	1.295	C 46.2	$C_6H_3F_9$	46.3
				H 1.1		1.2
				F 69.1		69.5
12	89	1.564	1.313	C 32.0	$C_6H_3F_7O$	32.1
				H 1.3		1.3
				F 59.1		59.4
14	45	1.362	1.296	C 33.8	$C_5H_4F_6$	33.7
				H 2.3		2.3
				F 63.7		64.0
15	[151]	–	–	C 36.4	$C_6H_5F_3O_4$	36.4
				H 2.5		2.5
				F 28.8		28.8
16	[103]	–	–	C 40.0	$C_6H_4F_3NO_2$	40.2
				H 2.2		2.2
				F 32.0		31.8
				N 7.9		7.8
17	127	1.558	1.366	C 27.6	$C_6H_4Cl_2F_6$	27.6
				H 1.5		1.5
				Cl 27.3		27.2
				F 43.6		43.7
18	60[b]	1.931	1.371	C 21.6	$C_7H_4F_9I$	21.8
				H 1.0		1.0
				F 44.1		44.3
				I 32.7		32.9

[a] Lit. value [3]: b.p. 38 °C.
[b] At 50 mmHg.

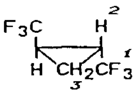
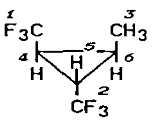
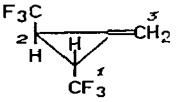
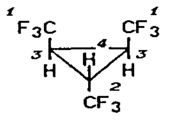
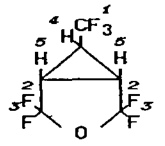
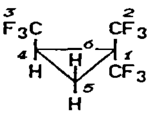
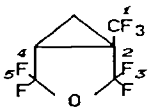
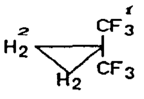
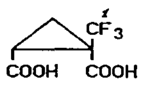
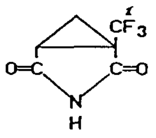
Fluorination of *cis*, *trans*-cyclopropane-1,2,3-tricarboxylic acid (**7**) and cyclopropane-1,1,2-tricarboxylic acid (**10**) with SF_4 resulted in the formation of the corresponding trifluoromethyl-substituted 2,2,4,4-tetrafluoro-3-oxa-bicyclo [3.1.0]hexanes **9** and **12**, in addition to the tris(trifluoromethyl)cyclopropanes **8** and **11** (Scheme 2).

It should be noted that 1,2,3-tris(trifluoromethyl)-cyclopropane (**8**) was not obtained by pyrolysis of tris(trifluoromethyl)pyrazoline or by the reaction of trifluoromethylcarbene with hexafluorobuthenes [4].

Like dimethylmalonic acid [5], when treated with SF_4 cyclopropane-1,1-dicarboxylic acid (**13**) readily undergoes fluorination to give 1,1-bis(trifluoromethyl)propane (**14**) (Scheme 3).

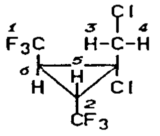
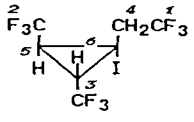
It is well known that cyclopropane rings resemble double bonds in some respects. Cyclopropane and alkyl-substituted cyclopropanes readily react with

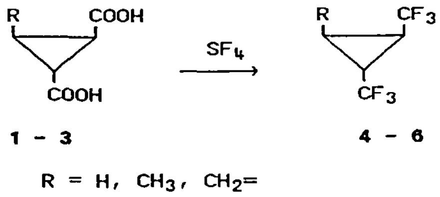
Table 3
NMR data of prepared compounds

Formula	Nucleus No.	Signal structure	Chemical shift (ppm)	Coupling constants (Hz)
 **4**	1	d	−68.32	$^3J_{1,2}=5.57$
	2	m	1.92	
	3	t	1.18	$^3J_{2,3}=8.0$
 **5**	1	d	−61.02	$^3J_{1,4}=7.3$
	2	d	−67.96	$^2J_{2,5}=5.9$
	3	d	1.22	$^3J_{3,6}=6.1$
	4	m	1.84	$^3J_{4,1}=7.3$; $^3J_{4,6}=7.2$
	5	q	1.74	$^2J_{5,2}=5.9$
	6	m	1.51	$^3J_{6,3}=6.1$; $^3J_{6,4}=7.2$
 **6**	1	m	−67.56	$^3J_{1,2}=5.6$
	2	d	2.51	$^3J_{2,1}=5.6$; $^4J_{2,3}=2.4$
	3	t	5.85	$^4J_{3,2}=2.4$
 **8**	1	m	−61.14	$^3J_{1,3}=3.9$; $^5J_{1,2}=0.5$
	2	d	−67.69	$^3J_{2,4}=5.9$
	3	m	2.23	$^3J_{3,1}=3.9$; $^3J_{3,4}=5.8$
	4	m	2.57	$^3J_{4,2}=5.9$; $^3J_{4,3}=5.8$
 **9**	1	m	−65.94	$^3J_{1,4}=6.2$; $^5J_{1,3}=2.1$
	2	AB	−79.91	$^2J_{2,3}=150$; $^3J_{2,5}=2.8$
	3	AB	−64.51	$^2J_{3,2}=150$; $^5J_{3,1}=2.1$
 **11**	1	q	−67.22	$^4J_{1,2}=8.6$
	2	m	−61.61	$^4J_{2,1}=8.6$; $^5J_{2,3}=11.4$
	3	m	−60.24	$^5J_{3,2}=11.4$; $^3J_{3,4}=7.5$
	4	m	2.78	$^3J_{4,3}=7.5$
	5, 6	m	1.98	
 **12**	1	d	−64.97	$^4J_{1,2}=13$
	2	AB	−70.57	$^2J_{2,3}=141.0$; $^4J_{2,1}=13$
	3	AB	−63.90	$^2J_{3,2}=141.0$
	4	AB	−81.55	$^2J_{4,5}=141.0$
	5	AB	−78.79	$^2J_{5,4}=141.0$
 **14**	1	m	−67.10	$^4J_{1,2}=0.6$
	2	bs	1.22	
 **15**	1	bs	−68.0	
 **16**	1	bs	−67.6	

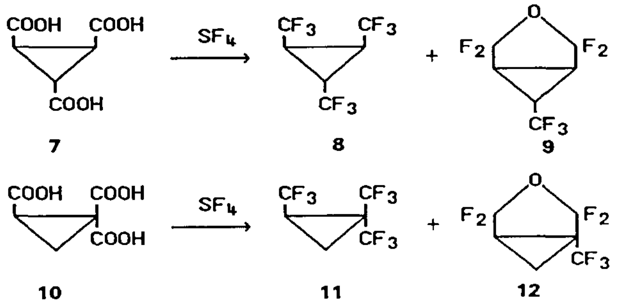
(continued)

Table 3 (*continued*)

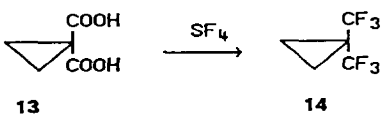
Formula	Nucleus No.	Signal structure	Chemical shift (ppm)	Coupling constants (Hz)
	1	m	−62.44	$^3J_{1,6}=7.0$; $^5J_{1,2}=0.9$
	2	m	−62.83	$^3J_{2,5}=6.1$; $^5J_{2,1}=0.9$
	3	d	3.82	$^2J_{3,4}=13.5$
	4	d	3.84	$^2J_{4,3}=13.5$
	5	m	2.78	$^3J_{5,2}=6.1$; $^3J_{5,6}=7.0$
17	6	m	2.66	$^3J_{6,5}=7.0$; $^3J_{6,1}=7.0$
	1	t	−63.05	$^3J_{1,4}=8.9$
	2	d	−61.31	$^3J_{2,5}=7.0$
	3	d	−63.90	$^3J_{3,6}=6.5$
18				



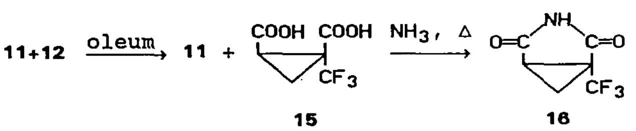
Scheme 1.



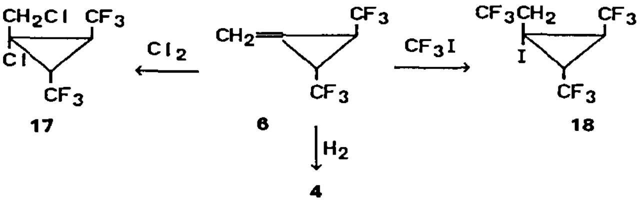
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

electrophilic reagents (e.g. H_2SO_4, HBr, Br_2) by ring opening, and undergo catalytic hydrogenating under mild conditions [6].

The introduction of trifluoromethyl groups into the cyclopropane ring results in the loss of cyclopropane-like properties and the properties of the trifluoromethylcyclopropanes are similar to those of the corresponding alkanes as may be illustrated by chemical properties of the compounds prepared. 1,1-Bis(trifluoromethyl)cyclopropane (**14**) does not react with bromine when heated under UV irradiation, and, as reported previously [7], does not undergo catalytic hydrogenation even under stringent conditions.

Treatment of the reaction mixture of 1,1,2-tris(trifluoromethyl)cyclopropane (**11**) and 1-trifluoromethyl-2,2,4,4-tetrafluoro-3-oxa-bicyclo[3.1.0]hexane (**12**) with oleum only leads to cleavage of the five-membered ring of the latter, but not the three-membered ring. 1-Trifluoromethylcyclopropane-1,2-dicarboxylic acid (**15**) has also been characterized in the form of its bicyclic imide **16** (Scheme 4).

trans 1,2-Bis(trifluoromethyl)-3-methylenecyclopropane (**6**) reacts at the exocyclic double bond with chlorine, hydrogen and trifluoroiodomethane without opening of the cyclopropane ring (Scheme 5).

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