

Reactions of cycloalkanecarboxylic acids with SF₄.

I. Fluorination of cyclopropanepolycarboxylic acids with SF₄[★]

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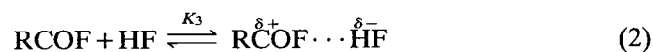
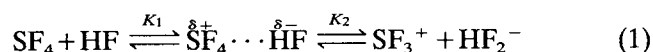
Abstract

Cyclopropanecarboxylic acids possessing more than one carboxylic group readily undergo fluorination when treated with SF₄ 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 SF₄ 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 SF₄ molecule. In the system containing equimolar quantities of SF₄, HF and RCOF, the concentration of SF₃⁺ cations may be related to the ratio of the equilibrium constants of competitive reversible reactions:



The equilibrium constants K_1 , K_2 and K_3 are related to the basic properties of SF₄ and RCOF. Two extreme cases may occur: (a) $K_1, K_2 > K_3$, i.e. acyl fluoride is a weaker base than SF₄, when equilibrium (1) is always displaced more to the right than reaction (2), leading to significant formation of the complex SF₄·HF and SF₃⁺ 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 SF₄, when formation of the RCOF·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 SF₄.

2. Experimental

¹H, ¹³C and ¹⁹F NMR spectra were measured using a Bruker WP-200 NMR spectrometer with TMS and CFCl₃ as the respective internal standards, and CDCl₃ as the solvent (acetone-*d*₆ was employed as the solvent for compounds **15** and **16**). The upfield ¹⁹F 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.

[★]Dedicated to Professor L.M. Yagupolskii on the occasion of his 70th birthday.

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Table 1
Reactions of cyclopropanecarboxylic acids with SF₄

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 SF₄

General procedure

The carboxylic acid and SF₄ 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 P₂O₅ 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 SF₄) 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 ¹⁹F 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/Al₂O₃ [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 CF₃I (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 SF₄ 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 ₅ H ₄ F ₆	33.7
				H 2.2		2.3
				F 63.8		64.0
5	63	1.273	1.306	C 37.3	C ₆ H ₆ F ₆	37.5
				H 3.0		3.1
				F 58.9		59.4
6	52	1.288	1.312	C 37.6	C ₆ H ₄ F ₆	37.9
				H 2.2		2.1
				F 59.3		59.4
8	65.5	1.543	1.293	C 29.2	C ₆ H ₃ F ₉	29.3
				H 1.2		1.2
				F 69.5		69.5
9	83	1.565	1.317	C 32.2	C ₆ H ₃ F ₇ O	32.2
				H 1.4		1.4
				F 58.8		59.4
11	74	1.562	1.295	C 46.2	C ₆ H ₃ F ₉	46.3
				H 1.1		1.2
				F 69.1		69.5
12	89	1.564	1.313	C 32.0	C ₆ H ₃ F ₇ O	32.1
				H 1.3		1.3
				F 59.1		59.4
14	45	1.362	1.296	C 33.8	C ₅ H ₄ F ₆	33.7
				H 2.3		2.3
				F 63.7		64.0
15	[151]	–	–	C 36.4	C ₆ H ₅ F ₃ O ₄	36.4
				H 2.5		2.5
				F 28.8		28.8
16	[103]	–	–	C 40.0	C ₆ H ₄ F ₃ NO 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 ₆ H ₄ Cl ₂ F 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 ₇ H ₄ F ₉ I	21.8
				H 1.0		1.0
				F 44.1		44.3
				I 32.7		32.9

^aLit. value [3]: b.p. 38 °C.

^bAt 50 mmHg.

Fluorination of *cis*, *trans*-cyclopropane-1,2,3-tricarboxylic acid (**7**) and cyclopropane-1,1,2-tricarboxylic acid (**10**) with SF₄ 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).

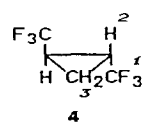
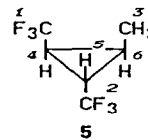
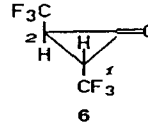
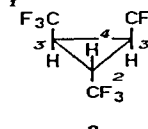
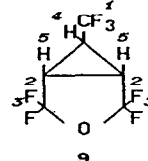
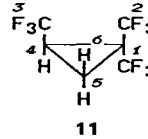
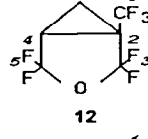
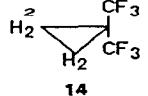
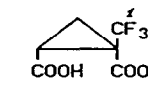
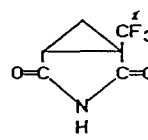
It should be noted that 1,2,3-tris(trifluoromethyl)-cyclopropane (**8**) was not obtained by pyrolysis of

tris(trifluoromethyl)pyrazoline or by the reaction of trifluoromethylcarbene with hexafluorobutenes [4].

Like dimethylmalonic acid [5], when treated with SF₄ cyclopropane-1,1-dicarboxylic acid (**13**) readily undergoes fluorination to give 1,1-bis(trifluoromethyl)propane (**14**) (Scheme 3).

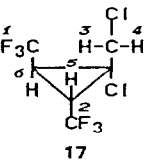
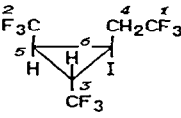
It is well known that cyclopropane rings resemble double bonds in some respects. Cyclopropane and alkyl-substituted cyclopropanes readily react with

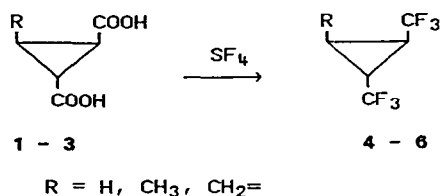
Table 3
NMR data of prepared compounds

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

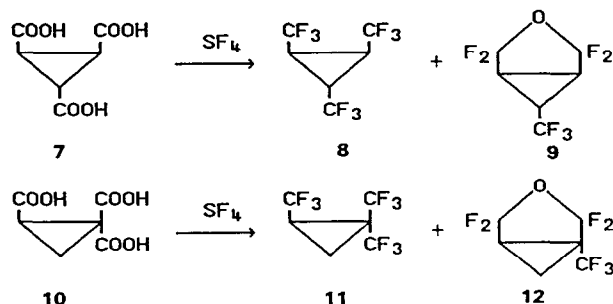
(continued)

Table 3 (continued)

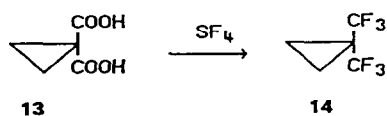
Formula	Nucleus No.	Signal structure	Chemical shift (ppm)	Coupling constants (Hz)
 17	1	m	–62.44	$^3J_{1,6} = 7.0$; $^5J_{1,2} = 0.9$
	2	m	–62.83	$^3J_{2,5} = 6.1$; $^5J_{2,1} = 0.9$
	3	d	3.82	$^2J_{3,4} = 13.5$
	4	d	3.84	$^2J_{4,3} = 13.5$
	5	m	2.78	$^3J_{5,2} = 6.1$; $^3J_{5,6} = 7.0$
	6	m	2.66	$^3J_{6,5}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



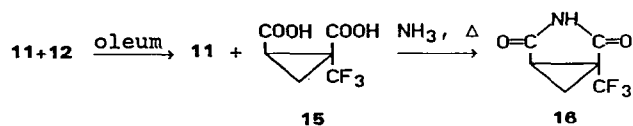
Scheme 1.



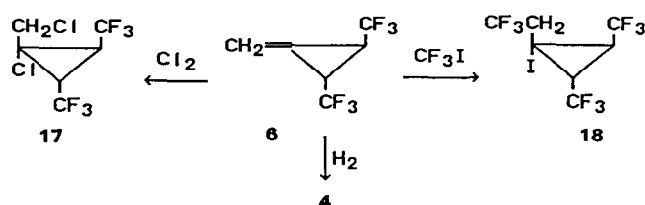
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

electrophilic reagents (e.g. H₂SO₄, HBr, Br₂) 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).

References

- [1] W. Dmowski and R.A. Kolinski, *Pol. J. Chem.*, 52 (1978) 547.
- [2] A.N. Alekseenko, L.B. Faryat'eva and V.P. Nazaretian, *Ukr. Khim. Zh.*, in press.
- [3] J.G. Shukys, F.M. Fiordalisi and L.S. Croix, *US Pat.* 2 727 900 (1955); [*Chem. Abs.*, 50 (1956) P15 584a].
- [4] R. Fields and R.N. Haszeldine, *J. Chem. Soc.*, (1964) 1881.
- [5] Yu.M. Pustovit and V.P. Nazaretian, *J. Fluorine Chem.*, 55 (1991) 29.
- [6] J.F. Stoddart, in D. Barton and W.D. Ollis (eds.), *Comprehensive Organic Chemistry*, Pergamon, Oxford, 1979, Vol. 1.
- [7] C. Groeger, H. Musso and I. Rossnagel, *Chem. Ber.*, 113 (1980) 3621.