ORGANIC AND BIOLOGICAL CHEMISTRY

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The Chemistry of Sulfur Tetrafluoride. II. The Fluorination of Organic Carbonyl Compounds[1]

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The selective replacement of oxygen atoms by fluorine in many types of organic compounds has been accomplished with SF_4. Typical reactions are the conversion of such groups as carboxyl to trifluoromethyl, carbonyl to difluoromethylene and hydroxyl to fluorine. These reactions provide direct syntheses of many hitherto inaccessible fluorine-containing compounds.

Sulfur tetrafluoride (SF_4), a relatively new chemical entity, has been found to be a remarkably effective reagent for the selective replacement of carbonyl oxygen in organic compounds with fluorine.[2] The reaction has broad scope and is effective with a variety of carbonyl compounds including aldehydes, ketones and carboxylic acids. Discovery of this reaction, one of few reactions useful for introduction of fluorine at a specific site in a molecule, makes available many new or relatively inaccessible fluorine compounds. Reactions of SF_4 with the various classes of organic carbonyl compounds are discussed in the following sections.

$$>C{=}O + SF_4 \longrightarrow\ >CF_2 + SOF_2$$

Carboxylic Acids.—In the reaction of a carboxylic acid with SF_4, the carboxyl group is converted to a trifluoromethyl group. This has proved to be the most general and direct method known for synthesizing compounds having CF_3 groups. Although a trifluoromethyl derivative can be obtained directly from a carboxylic acid, the reaction, illustrated below for benzoic acid, proceeds in two steps—formation of the acyl fluoride and replacement of the carbonyl oxygen.

$$C_6H_5COOH + SF_4 \longrightarrow C_6H_5COF + HF + SOF_2$$
$$C_6H_5COF + SF_4 \longrightarrow C_6H_5CF_3 + SOF_2$$

The first step occurs readily at or below room temperature, while the second step requires elevated temperatures. Table I lists a wide variety of aliphatic and aromatic carboxylic acids that react smoothly with SF_4. With polybasic acids, the degree of fluorination may be controlled by the amount of SF_4 used. Thus, from sebacic acid either 1,1,1,10,10,10-hexafluorodecane or 10,10,10-trifluorodecanoyl fluoride may be obtained as the principal product.

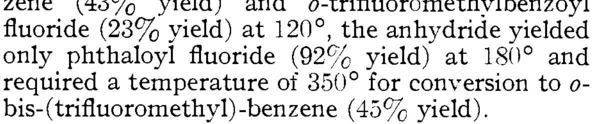
$$\begin{tikzcd}
HOOC(CH_2)_8COOH \arrow[r, "6SF_4"] \arrow[d, "3SF_4"] & \underset{87\%}{CF_3(CH_2)_8CF_3} \\
\ &
\end{tikzcd}$$
$$\underset{45\%}{CF_3(CH_2)_8COF} + \underset{27\%}{CF_3(CH_2)_8CF_3} + \underset{21\%}{FCO(CH_2)_8COF}$$

That the reaction of a carbonyl compound with SF_4 possesses an unusual degree of specificity is shown by the fact that olefinic and acetylenic bonds are unaffected by SF_4. As a result, trifluoromethylethylene and trifluoromethylacetylene are now easily accessible in good yield from acrylic and propiolic acids, respectively.

$$CH_2{=}CHCOOH \xrightarrow{SF_4} CH_2{=}CHCF_3$$
$$CH{\equiv}CCOOH \xrightarrow{SF_4} CH{\equiv}CCF_3$$

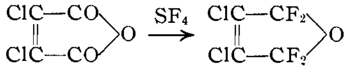
Other functional groups including fluoro, chloro, bromo, nitro and methoxycarbonyl usually are unaffected by SF_4 at temperatures up to 160°.

In some cases $\alpha,\alpha,\alpha',\alpha'$-tetrafluoro ethers have been isolated from reactions of carboxylic acids and SF_4. For example, diglycolic acid yielded 2,2,6,6-tetrafluorodioxane as well as 2,2,2-trifluoroethyl ether.

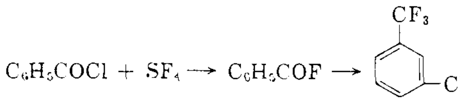


Acid Anhydrides, Salts and Acyl Halides.—Carboxylic acid anhydrides, salts and acyl halides react with SF_4 to give products like those from the acids (Table II), but more vigorous conditions are required for reaction. Whereas phthalic acid yielded a mixture of *o*-bis-(trifluoromethyl)-benzene (43% yield) and *o*-trifluoromethylbenzoyl fluoride (23% yield) at 120°, the anhydride yielded only phthaloyl fluoride (92% yield) at 180° and required a temperature of 350° for conversion to *o*-bis-(trifluoromethyl)-benzene (45% yield).

The anhydride ring may react without loss of the ring oxygen atom, *e.g.*, dichloromaleic anhydride and SF_4 gave 3,4-dichloro-2,2,5,5-tetrafluoro-2,5-dihydrofuran.



The reaction of an acyl fluoride with SF_4 proceeds in the expected manner to give a trifluoromethyl compound. The reaction of an acyl chloride and SF_4 is not so straight-forward, however. With benzoyl chloride, the initial reaction appears to be halogen exchange of Cl for F. This is followed by replacement of the carbonyl oxygen with two fluorine atoms and also by chlorination of the ring. The nature of the chlorinating agent is unknown.



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[1] For paper I of this series see C. W. Tullock, F. S. Fawcett, W. C. Smith and D. D. Coffman, THIS JOURNAL, **82**, 539 (1960).

[2] W. C. Smith, U. S. Patent 2,859,245 (November 4, 1958).

Table I

Reactions of Carboxylic Acids with SF_4

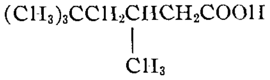
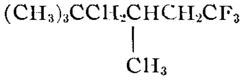
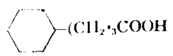
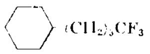
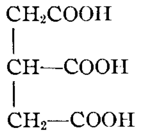
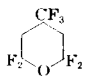
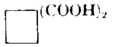
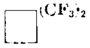
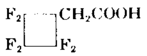
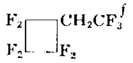
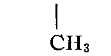
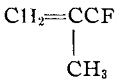
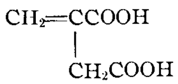
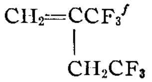
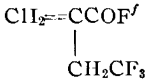
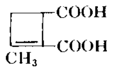
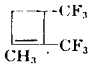
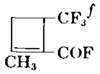
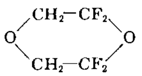
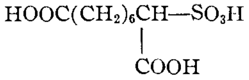
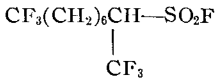
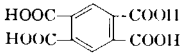
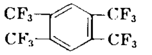
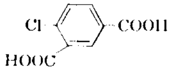
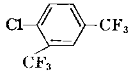
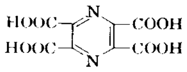
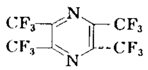
Starting material		Moles SF_4	Temp., °C.	Time, hr.	Products			Analyses, %					
								Calculated			Found		
Structure	Moles				Structure	Yield, %	Properties	C	H	F	C	H	F
CH_3CH_2COOH	0.60	1.82	150	8	$CH_3CH_2CF_3$[d]	89	....	Mass spectrometric analysis					
$CH_3(CH_2)_5COOH$	.20	0.65	130	6	$CH_3(CH_2)_5CF_3$	80	B.p. 101°, $n^{25}D$ 1.3449	54.5	8.5	37.0	54.8	8.7	37.1
$CH_3(CH_2)_{10}COOH$	.33	2.00	130	6	$CH_3(CH_2)_{10}CF_3$	88	B.p. 92° (12 mm.), $n^{25}D$ 1.3896	64.3	10.3	25.4	64.0	10.3	25.8
$CH_3(CH_2)_{16}COOH$	.35	2.13	130	6	$CH_3(CH_2)_{16}CF_3$	93	B.p. 107° (0.3 mm.), M.p. 28–30°, $n^{25}D$ 1.4148			18.5			18.5
 $(CH_3)_3CCH_2CH(CH_3)CH_2COOH$	.19	0.57	120	6	 $(CH_3)_3CCH_2CH(CH_3)CH_2CF_3$	64	B.p. 121–122°, $n^{25}D$ 1.3657			31.3			31.1
	.20	.60	120	10		80	B.p. 172–173°, $n^{25}D$ 1.3987	61.8	8.8	29.4	60.9	8.4	29.5
$HOOCCH_2COOH$	.30	.69	40	16	$FCOCH_2COF$	70	B.p. 92–94°						
$HOOCCH_2COOH$	.40	2.40	150	8	$CF_3CH_2CF_3$[d]	57	....	Mass spectrometric analysis					
$HOOC(CH_2)_2COOH$	.40	2.40	150	8	$CF_3CH_2CH_2CF_3$[d]	41	....	Mass spectrometric analysis					
$HOOC(CH_2)_4COOH$	.67	2.23	130	7	$CF_3(CH_2)_4CF_3$	19	B.p. 99–101°, $n^{25}D$ 1.3071	37.1	4.2	58.7	37.4	4.4	58.1
					$CF_3(CH_2)_4COOH$[e]	39	M.p. 36–38°	42.4	5.3	33.5	42.5	5.3	33.1
$HOOC(CH_2)_8COOH$	.15	0.46	120	6	$CF_3(CH_2)_8CF_3$	27	B.p. 90–96° (20 mm.), $n^{25}D$ 1.3519	48.0	6.4	45.6	48.4	6.7	45.4
					$CF_3(CH_2)_8COF$	45	B.p. 115–118° (20 mm.)	52.7	7.1	33.3	53.1	7.3	32.6
					$FCO(CH_2)_8COF$	21	B.p. 144–146° (20 mm.)						
 $CH_2(COOH)CH(COOH)CH_2COOH$	.07	0.63	130	10		20	B.p. 104–106°	31.9	2.2	58.8	32.2	2.5	58.2
$CH_2BrCHBrCH_2COOH$	.53	1.85	140	8	$CH_2BrCHBrCH_2CF_3$	54	B.p. 69–75° (58 mm.)	1.78	1.9	21.2	18.1	2.0	21.7
HCF_2CF_2COOH[a]	.15	0.48	250	8	$HCF_2CF_2CF_3$[d]	56	....	Mass spectrometric analysis					
	.28	2.32	150	6		43	B.p. 68–69°	37.6	3.1	59.4	37.9	3.2	59.1
	.08	0.30	160	16		51	B.p. 67°	29.3	1.2	69.5	29.8	1.4	68.5
$CH_2{=}CHCOOH$	.75	2.00	130	8	$CH_2{=}CHCF_3$[g]	45	B.p. −26°[i]	Mass spectrometric analysis					
 $CH_2{=}C(CH_3){-}COOH$	.75	2.00	130	8	 $CH_2{=}C(CH_3)CF_3$	54	B.p. 6°[j]	Mass spectrometric analysis					
$HOOCCH{=}CHCOOH$ (*trans*)	.55	2.78	130	9	$CF_3CH{=}CHCF_3$ (*trans*)[f,g]	95	B.p. 6°[k]	Mass spectrometric analysis					
$HOOCCH_2CH{=}CHCH_2COOH$	.10	0.55	130	10	$CF_3CH_2CH{=}CHCH_2CF_3$	58	B.p. 90–91°, $n^{25}D$ 1.3131			59.3			59.5
 $CH_2{=}C(CH_2COOH)COOH$	.62	2.80	160	10	 $CH_2{=}C(CH_2CF_3)CF_3$[f]	26	B.p. 47–49°	33.7	2.3	64.1	33.9	2.4	63.6
					 $CH_2{=}C(CH_2CF_3)COF$[f]	41	B.p. 90–95°	38.5	2.6	48.7	39.3	2.9	47.1

TABLE I (*Continued*)

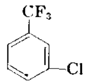
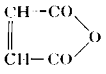
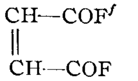
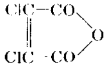
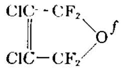
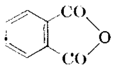
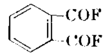
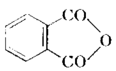
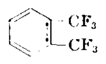
Starting material		Moles SF_4	Temp., °C.	Time, hr.	Products			Analyses, %					
Structure	Moles				Structure	Yield, %	Properties	Calculated			Found		
								C	H	F	C	H	F
	.149	0.89	120	4		31	B.p. 95–96°	41.2	3.0	55.8	41.3	3.3	55.8
					[f]	30	B.p. 160–161°	46.2	3.3	41.7	46.7	3.6	40.1
$HC\equiv CCOOH$	2.00	2.10	30–55	3	$HC\equiv CCOF$[f]	28	B.p. 22–23°						
$HC\equiv CCOOH$	0.27	0.78	120	3	$HC\equiv CCF_3$[f,h]	60	....	Mass spectrometric analysis					
$HOOCC\equiv CCOOH$[b]	.395	1.67	70	6	$FCOC\equiv CCOF$[f]	51	B.p. 40–45°						
$HOOCC\equiv CCOOH$[c]	.125	0.75	170	8	$CF_3C\equiv CCF_3$[d]	80	....	Mass spectrometric analysis					
$HOOCCH_2OCH_2COOH$	.50	3.00	130	7	$CF_3CH_2OCH_3CF_3$	35	B.p. 58–59°	26.7	2.2		27.4	2.6	
						14	B.p. 91°, n^{25}D 1.3262	30.0	2.5	47.5	30.6	2.8	47.5
$C_2H_5OOC(CH_2)_4COOH$	.77	2.00	130	7	$C_2H_5OOC(CH_2)_4CF_3$	14	B.p. 57–59° (11 mm.), n^{25}D 1.3725	48.5	6.6	28.8	48.5	6.7	28.8
					$HOOC(CH_2)_4CF_3$[e]	13	B.p. 110–111.5° (17 mm.) M.p. 37–38.5°						
$HOCH_2COOH$	.75	3.00	160	5	FCH_2CF_3[g]	48	B.p. −26.5°[l]	Mass spectrometric analysis					
					FCH_2COF	18	B.p. 51°[m]						
$HOOCCH_2SO_3H$	.2	0.69	180	6	$CF_3CH_2SO_2F$	41	B.p. 105–107°			45.8[v]			45.9
$HOOC(CH_2)_{10}SO_3H$	.083	0.41	130	8	$CF_3(CH_2)_{10}SO_2F$	42	B.p. 100–110° (0.10 mm.)	45.2	6.9	26.0[w]	44.8	6.9	26.0
 $HOOC(CH_2)_6\underset{\displaystyle COOH}{\underset{\mid}{C}}H{-}SO_3H$	.195	1.61	150	8	 $CF_3(CH_2)_6\underset{\displaystyle CF_3}{\underset{\mid}{C}}H{-}SO_2F$	33	B.p. 62–64° (0.15 mm.)	34.0	4.1	41.8[x]	34.4	4.1	41.8
C_6H_5COOH	.25	0.50	120	6	$C_6H_5CF_3$	22	B.p. 100–101°,[n] n^{25}D 1.4133			39.0			39.0
					C_6H_5COF	41	B.p. 155–156°[o]			15.3			14.8
$C_6H_5COCOOH$	.125	.51	100	6	$C_6H_5CF_3$	13	B.p. 45–55° (100 mm.)						
					C_6H_5COF	59	B.p. 92–94° (100 mm.)						
o-$C_6H_4(COOH)_2$	.10	.55	120	6	*o*-$C_6H_4(CF_3)_2$	43	B.p. 140–144°[p]			53.2			53.1
					o-$C_6H_4(COF)(CF_3)$	23	B.p. 175–178°[q]	50.0	2.1	39.5	50.5	2.3	39.1
p-$C_6H_4(COOH)_2$	.10	.60	120	6	*p*-$C_6H_4(CF_3)_2$	76	B.p. 113–115°, n^{25}D 1.3767[r]						
					p-$C_6H_4(COF)(CF_3)$	3	B.p. 156°[s]						
	.07	.83	150	6		77	M.p. 73–74°	34.3	0.6	65.1	34.7	0.7	64.2
p-$C_6H_4(COOCH_3)(COOH)$	.44	1.33	130	7	*p*-$C_6H_4(COOCH_3)(COF)$	63	B.p. 120–121° (13 mm.) M.p. 69–70.5°	59.2	3.9	10.4	59.4	4.2	10.7
p-$C_6H_4(NO_2)(COOH)$	.67	2.12	130	7	*p*-$C_6H_4(NO_2)(CF_3)$	72	M.p. 41–43°[t]	44.0	2.1[y]		44.4	2.2	
	.20	1.20	150	8		62	B.p. 147°, n^{25}D 1.4130[u]						
	.035	0.42	150	6		20	B.p. 129°	27.3	0.0	64.7	28.2	0.4	64.5

Footnotes In Table I

[a] BF_3 (0.03 mole) catalyst employed; at 180° without catalyst, only HCF_2CF_2COF obtained. [b] Sixty grams of methylcyclohexane employed as diluent. [c] TiF_4 (0.016 mole) catalyst employed. [d] Product purified by scrubbing with 40% aq. KOH. [e] Free acid formed in work-up procedure when crude product containing HF placed in glass equipment. [f] Infrared spectrum in agreement with structure shown. [g] Product purified by scrubbing with 20% aq. KOH, then distilled. [h] Product purified by scrubbing through buffer solution of pH 8.5 containing 450 g. $NaH_2PO_4 \cdot H_2O$ and 220 g. KOH in 4 liters of water. [i] Reported b.p. −24°; B. H. Robbins, *J. Pharmacol. Exptl. Therap.*, **86**, 197 (1946). [j] Reported b.p. 64°; F. Swarts, *Bull. acad. roy. Belg.*, **36**, 191 (1927). [k] Reported b.p. 85°; R. N. Haszeldine, *J. Chem. Soc.*, 2504 (1952). [l] Reported b.p. −26.1°; J. A. Cuculo and L. A. Bigelow, This Journal, **74**, 710 (1952). [m] Reported b.p. 51°; B. C. Saunders and G. J. Stacey, *J. Chem. Soc.*, 1773 (1948). [n] Reported b.p. 102°; H. S. Booth, H. M. Elsey and P. E. Burchfield, This Journal, **57**, 2066 (1935). [o] Reported b.p. 151°; C. E. Entemann, Jr., and J. R. Johnson, *ibid.*, **55**, 2900 (1933). [p] Reported b.p. 141.2°; P. E. Brown and T. DeVries, *ibid.*, **73**, 1811 (1951). [q] Reported b.p. 158–162°; U. S. 2,181,554 to General Aniline Works, Inc., 11-28-39. [r] Reported b.p. 117°, $n^{25}D$ 1.3767; reference cited in footnote *p*. [s] Reported b.p. 158–162°; reference cited in footnote *q*. [t] Reported m.p. 41.5°; H, Rouche, *Bull. sci. acad. roy. Belg.*, **13**, 346 (1927). [u] Reported b.p. 148°, $n^{25}D$ 1.4128; A. L. Meyers and T. DeVries, This Journal, **73**, 1813 (1951). [v] Calcd. for S, 19.3%, found 19.4%. [w] Calcd. for S, 11.0%; found 10.9%. [x] Calcd. for S, 10.1%; found 9.9%. [y] Calcd. for N, 7.3%; found 7.6%.

Table II

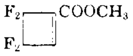
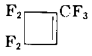
Reactions of Acyl Halides, Anhydrides and Carboxylic Acid Salts with SF_4

Starting material		Moles SF_4	Temp., °C.	Time, hr.	Products			Analyses, %							
								Calculated				Found			
Structure	Moles				Structure	Yield, %	Properties	C	H	F	Cl	C	H	F	Cl
C_6H_5COF[a]	0.145	0.30	120	6	$C_6H_5CF_3$	41	B.p. 100°, $n^{24.9}D$ 1.4124								
C_6H_5COCl[b]	.20	.80	150	8	C_6H_5COF	51	B.p. 149°								
C_6H_5COCl[c]	.20	.50	120	6		25	B.p. 138–139°, $n^{25}D$ 1.4459[g]	46.6	2.2	19.6	31.6	47.3	2.3	19.5	31.5
$(CH_3CO)_2O$	.30	.20	300	10	CH_3CF_3[e]	50	....	Mass spectrometric analysis							
	.30	.60	150	13	 $CH{-}COF \parallel CH{-}COF$[f]	71	B.p. 100–105°	40.0	1.7			40.4	1.9		
	.20	.47	300	10	[f]	46	B.p. 73–74°			36.0	33.6			36.0	33.7
	.20	.40	180	18		93	M.p. 40°[h]	56.5	2.4	22.4		56.9	2.5	23.1	
	.40	1.60	350	11		45	B.p. 143°	44.9	1.9			45.2	2.3		
C_6H_5COONa	.25	.50	120	6	C_6H_5COF	48	B.p. 152–155°								
$C_6H_5C{\equiv}CCOONa$[d]	.475	.52	45	6	$C_6H_5C{\equiv}CCOF$	71	B.p. 52–53° (2 mm.)	73.0	3.4			73.5	3.6		

[a] HF (0.05 mole) catalyst employed. [b] Under same conditions, with HF catalyst, the starting material charred. [c] HF (0.25 mole) catalyst employed. [d] This run included 100 ml. of cyclohexane as diluent. [e] Product purified by scrubbing through 10% aq. NaOH. [f] Infrared spectrum in agreement with structure shown. [g] Reported b.p. 138.4°, $n^{21.2}D$ 1.4466; H. S. Booth, H. M. Elsey and P. E. Burchfield, This Journal, **57**, 2066 (1935). [h] Reported m.p. 42–43°; A. T. Dann, A. N. Hambly, R. E. Paul and G. S. Semmers, *J. Chem. Soc.*, 15 (1933).

TABLE III

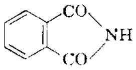
REACTIONS OF ESTERS WITH SF_4

Starting material		Moles	Catalyst,	Temp.,	Time,	Products		
Structure	Moles	SF_4	moles	°C.	hr.	Structure	Yield, %	Properties
$C_6H_5COOCH_3$[a]	0.30	0.60	....	300	6	$C_6H_5CF_3$	55	B.p. 98°
						C_6H_5COF	Trace	B.p. 151°
p-$C_6H_4(COOCH_3)_2$	.10	.60	BF_3, 0.03	130	8	p-$C_6H_4(CF_3)_2$	16	B.p. 113–116°
						p-$C_6H_4(COF)(CF_3)$	26	B.p. 154–158°
						p-$C_6H_4(COF)_2$	4	M.p. 122–124°
						CH_3F[b]	High	....
$HCOOCH_3$	.10	.32	HF, 0.05	200	6	CH_3F and CHF_3, yields high; HCF_2OCH_3, yield low[b]		....
	.20	.60	BF_3, 0.03	140	16		10	B.p. 42–43°

[a] At 250° for 6 hr., no reaction occurred. [b] Analysis by mass spectrometry.

TABLE IV

REACTIONS OF AMIDES WITH SF_4

Starting material		Moles	Catalyst,	Temp.,	Time,	Products		
Structure	Moles	SF_4	moles	°C.	hr.	Structure	Yield, %	Properties
$C_6H_5CONH_2$	0.20	0.41	....	150	8	$C_6H_5CF_3$	13	B.p. 36–38° (64 mm.) $n^{25}D$ 1.4150
$C_6H_5CONHCH_3$	.25	.50	BF_3, 0.015	60	4	C_6H_5COF	48	B.p. 90–94° (107 mm.)
$C_6H_5CON(CH_3)_2$	.25	.50	......	130	6	$C_6H_5CF_2N(CH_3)_2$[a]	17	B.p. 70–71° (15 mm.)
						C_6H_5COF	1.3	B.p. 50–55° (13 mm.)
	.20	.69	BF_3, 0.045	100	10	o-$C_6H_4(COF)(CF_3)$	58	B.p. 176–178°

[a] *Anal.* Calcd. for $C_9H_{11}NF_2$: C, 63.1; H, 6.5; N, 8.2; F, 22.2. Found: C, 64.0; H, 6.5; N, 8.0; F, 21.6.

TABLE V

REACTIONS OF ALDEHYDES WITH SF_4

Starting material		Moles	Temp.,	Time,	Products		
Structure	Moles	SF_4	°C.	hr.	Structure	Yield, %	Properties
CH_3CHO	0.60	0.75	50	14	CH_3CHF_2[b]	35	B.p. above −34°[g]
$CH_3(CH_2)_5CHO$	0.25	0.37	60	8	$CH_3(CH_2)_5CHF_2$	43	B.p. 118–119°, $n^{24}D$ 1.3688[h]
$(HCHO)_x$ (α-polyoxymethylene)	2.33	2.30	150	6	CH_2F_2[b]	49	B.p. −51.5°[i]
					FCH_2OCH_2F[c]	21	B.p. 32–34°
$H(CF_2)_4CHO$	0.25	0.28	100	10	$H(CF_2)_4CHF_2$[d]	55	B.p. 68–70°
C_6H_5CHO[a]	.30	0.60	150	6	$C_6H_5CHF_2$[e]	81	B.p. 130–135°[j]
p-$C_6H_4(CHO)_2$	.15	1.00	150	8	p-$C_6H_4(CHF_2)_2$	88	B.p. 54° (20 mm.)

[a] Under same conditions, with 0.30 mole SF_4, no distillable product obtained. [b] Analysis by mass spectrometry. [c] This product decomposes on storage, even at 4°. [d] *Anal.* Calcd. for $C_5H_2F_{10}$: F, 75.3. Found: F, 74.8. [e] *Anal.* Calcd. for $C_7H_6F_2$: F, 29.7. Found: F, 29.5. [f] *Anal.* Calcd. for $C_8H_6F_4$: F, 42.7. Found: F, 42.9. [g] Reported b.p. −26°; German Patent 641,878 to I. G. Farbenindustrie A.G., 1937. [h] Reported b.p. 120°, $n^{20}D$ 1.3710; A. L. Henne and E. P. Plueddeman, THIS JOURNAL, **65**, 587 (1943). [i] Reported b.p. −52°; E. H. Hadley and L. A. Bigelow, *ibid.*, **62**, 3302 (1940). [j] Reported b.p. 133.5°; F. Swarts, *Bull. acad. roy. Belg.*, 414 (1900).

Orientation of the chlorobenzotrifluoride was established by hydrolysis in concentrated sulfuric acid[3] to give m-chlorobenzoic acid in high yield.

Esters.—Carboxylic esters (Table III) require vigorous conditions for reaction with SF_4. Again, the products are trifluoromethyl compounds. Thus, methyl benzoate did not react at 250° but at 300° yielded benzotrifluoride and methyl fluoride.

$$C_6H_5COOCH_3 + 2SF_4 \longrightarrow C_6H_5CF_3 + CH_3F + 2SOF_2$$

α,α-Difluoro ethers and acyl fluorides appear to be intermediates in the conversion of an ester to the trifluoromethyl compound. Although methyl formate and SF_4 gave fluoroform and methyl fluoride as the major products, the presence of methyl difluoromethyl ether, HCF_2OCH_3, in the crude product was indicated by mass spectrometry. Also, very low conversion of ethyl acetate to a product thought to be ethyl 1,1-difluoroethyl ether, $CH_3CF_2OCH_2CH_3$, was indicated by the hydrogen and fluorine nuclear magnetic resonance spectra of the product, but the substance was not isolated in a pure state. Acyl fluorides, which could be formed either directly from the ester or by elimination of an alkyl fluoride from an α,α-difluoro ether, have been isolated in some cases from reactions of esters and SF_4.

Although esters will react with SF_4 at 130° when catalyzed by BF_3 or TiF_4, the presence of HF is without effect at temperatures to 170°. The latter fact has enabled us to prepare terminal trifluoro esters from monoesters of dibasic acids. For example, ethyl 6,6,6-trifluorohexanoate has been obtained from monoethyl adipate.

Amides.—In contrast to the sluggish behavior of the ester group with SF_4, the amide group is quite sensitive. Reactions of amides and SF_4 are listed in Table IV. Two types of amides may be distinguished: Those in which there is at least one N–H bond and those without an N–H bond. In

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(3) G. M. LeFave, THIS JOURNAL, **71**, 4148 (1949).

the first group, the carbonyl–nitrogen bond breaks to give an acyl fluoride, which may then undergo further reaction. Thus, benzamide and N-methylbenzamide yielded benzotrifluoride and benzoyl fluoride. With amides having no N–H bond, the carbonyl–nitrogen bond may or may not be broken. As examples, tetramethylurea yielded dimethylcarbamyl fluoride, and N,N-dimethylbenzamide yielded either benzoyl fluoride or N,N-dimethyl-α,α-difluorobenzylamine.

$$C_6H_5CON(CH_3)_2 \xrightarrow{SF_4} \begin{cases} C_6H_5COF \\ C_6H_5CF_2N(CH_3)_2 \end{cases}$$

The preparation of the difluoroamine could not be repeated consistently and could not be accomplished when the starting material contained small amounts of benzoic acid. These results suggest that the reaction of an amide with SF_4 in which the carbonyl–nitrogen bond is cleaved is catalyzed by trace amounts of HF.

Aldehydes and Ketones.—The action of SF_4 on aldehydes is typified by the preparation of benzal fluoride from benzaldehyde.

$$C_6H_5CHO \xrightarrow{SF_4} C_6H_5CHF_2$$

Table V lists reactions of aldehydes with SF_4. In general, aldehydes having no α-hydrogen atoms gave high yields of the expected difluorides. Aliphatic aldehydes which possess α-hydrogen are somewhat sensitive to SF_4 and the yields of the difluorides were correspondingly lower.

Reactions of ketones with SF_4 are listed in Table VI. Although ketones containing α-hydrogen are also sensitive toward SF_4, acetone gave a 60% yield of 2,2-difluoropropane. By carrying out the reaction below 50°, 1,1-difluorocyclohexane was obtained from cyclohexanone.

Benzophenone is quite resistant to reaction with SF_4 even at temperatures considerably higher than those employed for other ketones, a fact which probably reflects the steric hindrance of the carbonyl group. However, high yields of diphenyldifluoromethane were obtained from benzophenone and SF_4 when a catalyst was employed. When the catalyst used was BF_3, AsF_3 or TiF_4, the temperature of reaction had to be moderated to prevent complete charring of the benzophenone. With vicinal polyketones, such as benzil and diphenyltriketone, all of the ketonic oxygen atoms are replaced.

Quinones.—Some quinones, such as anthraquinone and chloranil, react in the same fashion as a ketone to yield products in which each carbonyl oxygen atom is replaced by two fluorine atoms. Other quinones are irregular in their behavior with

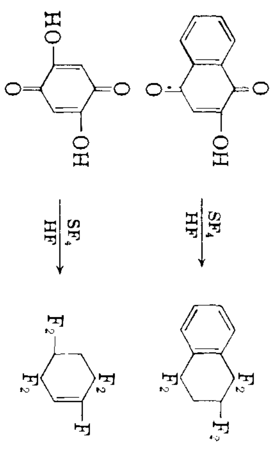
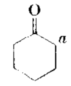
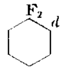
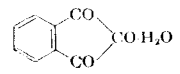
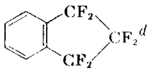
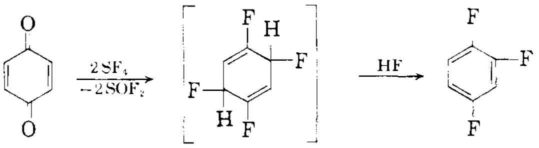


TABLE VI: REACTIONS OF KETONES WITH SF_4

Starting material		Moles SF_4	Temp., °C.	Time, hr.	Products			Analyses, %					
								Calculated			Found		
Structure	Moles				Structure	Yield, %	Properties	C	H	F	C	H	F
CH_3COCH_3	0.60	0.67	110	16	$CH_3CF_2CH_3$	60	B.p. −10° to −5°[e]	Mass spectrometric analysis					
 [a]	.40	.41	39	13	 [d]	31	B.p. 98–99°, $n^{25}D$ 1.3890	59.9	8.4	31.6	59.9	8.2	31.0
$C_6H_5COC_6H_5$[b]	.25	.50	180	6	$C_6H_5CF_2C_6H_5$	97	B.p. 114–115° (7.5 mm.), $n^{25}D$ 1.5351[f]						
$C_6H_5COCF_3$	.075	.22	100	8	$C_6H_5CF_2CF_3$	65	B.p. 115–116°[g]	49.0	2.6	48.4	49.6	2.9	47.8
$C_6H_5COCOC_6H_5$	.125	.50	180	5	$C_6H_5CF_2CF_2C_6H_5$[d]	34	M.p. 122–123°[h]			29.9			29.3
$C_6H_5COCOCOC_6H_5$	.075	.50	120	8	$C_6H_5CF_2CF_2CF_2C_6H_5$	50	B.p. 74–76° (0.24 mm.)	59.2	3.3	37.5	59.9	3.6	37.4
	.254	1.55	120	8	 [d]	25	B.p. 34° (4.5 mm.), 92–93° (70 mm.)	47.8	1.8	50.4	47.4	2.5	50.8
$(C_2H_5OOCCH_2)_2CO$	.25	0.50	80	6	$(C_2H_5OOCCH_2)_2CF_2$	29	B.p. 63–65° (2 mm.), $n^{25}D$ 1.4038	48.2	6.3	16.9	49.3	6.5	16.1
$CH_3COCH_2CH_2COOC_2H_5$[c]	.42	.48	95	10	$CH_3CF_2CH_2CH_2COOC_2H_5$	16	B.p. 70–72° (27 mm.), $n^{25}D$ 1.3798	50.6	7.3	22.8	51.5	7.6	22.6
$C_6H_5COCH{=}CHCOOCH_3$	.23	.48	160	10	$C_6H_5CF_2CH{=}CHCOOCH_3$	25	B.p. 102–103° (4.5 mm.), $n^{25}D$ 1.4861	62.3	4.8	17.9	62.5	4.9	18.0

[a] At 50° the starting material charred. [b] HF (0.05 mole) catalyst employed. [c] Water (0.028 mole) was added to this run; water gives HF catalyst by the reaction $H_2O + SF_4 \rightarrow 2HF + SOF_2$. [d] Infrared spectrum in agreement with structure shown. [e] Reported b.p. −0.1°; A. V. Grosse and C. B. Linn, THIS JOURNAL, **64**, 2289 (1942). [f] Reported b.p. 125° (10 mm.), $n^{20}D$ 1.5379; A. L. Henne and H. M. Leicester, *ibid.*, **60**, 864 (1938). [g] J. H. Simons and D. F. Herman, *ibid.*, **65**, 2064 (1943), report the synthesis of $C_6H_5CF_2CF_3$ from $C_6H_5CCl_2CCl_3$ and AgF_2 in 1.3% yield, and give a b.p. 128–129°. [h] U. S. Patent 2,238,242 to du Pont (April 15, 1941); a compound having m.p. 122–123°, prepared from $C_6H_5CCl_2CCl_2C_6H_5$ and HF and stated to be $C_6H_5CF{=}CFC_6H_5$, is probably identical with the substance reported here.

SF_4. Some hydroxyquinones yielded substances in which HF added to an unsaturated bond of the initial product. Thus, 1,1,2,2,4,4-hexafluoro-1,2,3,-4-tetrahydronaphthalene was obtained from 2-hydroxy-1,4-naphthoquinone and 1,3,3,4,4,6,6-heptafluorocyclohexene from 2,5-dihydroxyquinone. Quinone reacted with SF_4 and HF at 200° to give a 30% yield of 1,2,4-trifluorobenzene. This reaction may proceed by 1,4-fluorination of the α,β-unsaturated carbonyl groups, and then loss of a molecule of hydrogen fluoride. Reactions of quinones are listed in Table VII.



Syntheses of Carbon Tetrafluoride.—Several routes to carbon tetrafluoride from SF_4 (Table VIII) have been found. The oxygen atoms of carbon dioxide are replaced stepwise to give carbon tetrafluoride by way of carbonyl fluoride.

$$CO_2 \xrightarrow{SF_4} COF_2 \xrightarrow{SF_4} CF_4$$

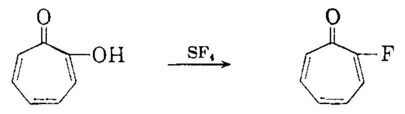
Phosgene also gave CF_4 by way of carbonyl fluoride, formed by an initial halogen exchange. A recent publication[4] notes a related reaction between phosgene and PF_5 to give difluorodichloromethane.

Another interesting route to CF_4 is provided by the reaction of carbon monoxide with SF_4. When approximately equimolar amounts of CO and SF_4 are used, up to 88% of the fluorine may be found in the product as CF_4, along with smaller amounts of carbon oxysulfide, carbonyl fluoride, thionyl fluoride and free sulfur. Two reactions shown to occur in this system are

$$3CO + SF_4 \longrightarrow 2COF_2 + COS$$
$$3CO + SOF_2 \longrightarrow COF_2 + COS + CO_2$$

Whereas temperatures near 500° are required for reaction of CO and SF_4 alone, high yields of CF_4 may be obtained at 150–250° by operating in liquid HF.

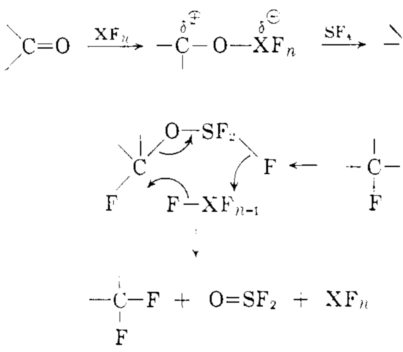
Hydroxylic Compounds.—Compounds containing hydroxyl groups react readily with SF_4 to introduce a fluorine atom at the site of the hydroxyl group (Table IX). As expected there is a rough correlation between the acidity of the hydroxyl group and the yield of product. The carboxylic and sulfonic acids, which possess very acidic hydroxyl groups, are easily converted in high yields to the acyl and sulfonyl fluorides. Moderate yields of fluorinated products are given by less acidic compounds such as tropolone, which is converted to α-fluorotropone.



Compounds even less acidic, such as methyl, ethyl and isopropyl alcohols, gave the corresponding alkyl fluorides, but in these cases a major by-product was the alkyl ether.

Catalysis and Mechanism.—The greater ease of reaction of a carboxylic acid with SF_4, as compared to the anhydride, to give a trifluoromethyl compound led to the discovery of catalysis of the reaction by hydrogen fluoride. Since it had been shown that a carboxylic acid reacted with SF_4 even at room temperature to give the acyl fluoride and hydrogen fluoride, it seemed reasonable that hydrogen fluoride was catalyzing the fluorination of the carbonyl group. Other evidence which pointed to the same conclusion was the fact that sodium benzoate yielded benzoyl fluoride, but no benzotrifluoride, under the same conditions that had been employed to convert benzoic acid to a mixture of benzotrifluoride and benzoyl fluoride. That hydrogen fluoride is actually a catalyst was proved when the yield of diphenyldifluoromethane from benzophenone and SF_4 was increased from 10 to 97% by addition of less than a stoichiometric amount of HF. Other fluorides, such as BF_3, AsF_3, PF_5 and TiF_4, subsequently proved to be even more potent in their ability to catalyze fluorinations by SF_4.

A possible route by which an oxygen atom is replaced by two fluorine atoms is indicated in the scheme



The initial step is thought to be coördination of the fluoride XF_n with the carbonyl compound to bring about a polarization of the carbonyl group. The complex may then react with SF_4 in the manner depicted. An alcohol probably reacts with SF_4 by elimination of HF to give an intermediate $R–O–SF_3$, which may further react with XF_n in a manner like that shown for $>CF–O–SF_3$. Although the role of XF_n may be assumed by SF_4, reactions proceed under milder conditions when XF_n is one of the catalysts, HF, BF_3, AsF_3, TiF_4 or PF_5. The ability of a substance to act as a catalyst can be correlated with its strength as a Lewis acid with respect to a carbonyl group. Fluorides which are not Lewis acids do not act as catalysts.

Additional evidence that the reaction may be initiated by coördination of a Lewis acid to the carbonyl group is provided by the behavior of compounds having two strongly electron-attracting groups attached to the carbonyl group. In such compounds the Lewis base character of the carbonyl group is so greatly reduced that coördination to the Lewis acid is significantly decreased. Reactions of such compounds should

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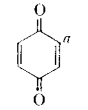
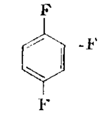
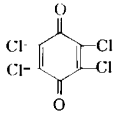
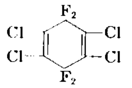
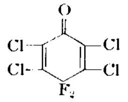
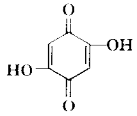
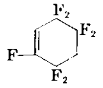
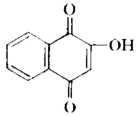
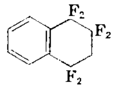
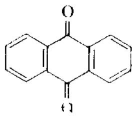
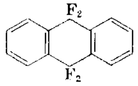
(4) R. N. Haszeldine and H. Iserson, *Nature*, **179**, 1361 (1957).

TABLE VII

REACTIONS OF QUINONES WITH SF_4

Starting material		Moles SF_4	Catalyst, moles	Temp., °C.	Time, hr.	Products[d]			Analyses, % Calculated				Found			
Structure	Moles					Structure	Yield, %	Properties	C	H	F	Cl	C	H	F	Cl
 [a]	0.20	0.35	HF, 0.35	200	4		30	B.p. 86.5°[e]	54.6	2.3	43.2		54.8	2.9	42.2	
	.14	.42	HF, 0.15	270	2.5		75	M.p. 45.5-46.5° B.p. 183-188°	24.9		26.2	48.9	25.0		26.2	48.9
							2	M.p. 104-107°	26.9		14.2	52.9	27.2		14.3	52.6
	.10	.55	HF, 0.10	60	8		40	B.p. 88-88.5°	34.6	1.5	63.9		35.2	1.7	62.5	
	.10	.50	(H_2O, 0.10)[c]	140	1.5		36	B.p. 91-95° (30 mm.)	50.0	2.5	47.5		50.6	2.7	47.0	
	.059	.28	HF, 0.05	255	8		78	M.p. 122-122.5°	66.7	3.2	30.1		67.7	3.4	29.0	

[a] Without catalyst, no reaction at 200°; charring at 250°, and a trace of impure 1,2,4-trifluorobenzene obtained at 240°. [b] At 220° only a trace of product formed. [c] Water gives HF catalyst ($H_2O + SF_4 \rightarrow SOF_2 + 2HF$). [d] Infrared spectra for all products in agreement with structures shown. [e] Reported b.p. 88°; G. Schiemann, *J. prakt. Chem.*, **140**, 97 (1934).

TABLE VIII

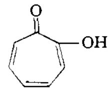
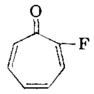
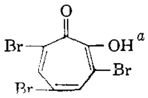
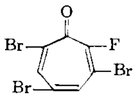
SYNTHESIS OF CARBON TETRAFLUORIDE

Starting material	Moles	Moles SF_4	Catalyst, moles	Temp., °C.	Time, hr.	Products, yield[a]
CO_2	0.11	0.20	....	500	2	CF_4, 80%; COF_2, 10%
$COCl_2$[b]	.10	.30	TiF_4, 0.026	250	4	CF_4, 90%; COF_2, 9%
CO	.2	.50	HF, 0.5	250	7	Based on CO: CF_4, 95%[c]
CO SOF_2	.75 .22	..	....	500	2	CO, 70%; COS, 13%; COF_2, 6%; CO_2, 11%

[a] Yields calculated from mass spectrometric analyses. [b] No reaction at 250° without catalyst. [c] The theoretical amount of sulfur, 0.10 mole, also formed, based on reaction $2CO + 3SF_4 \rightarrow 2CF_4 + 2SOF_2 + S$.

TABLE IX

REACTIONS OF HYDROXYLIC COMPOUNDS WITH SF_4

Starting material		Moles SF_4	Temp., °C.	Time, hr.	Products[b]			Analyses, %			
Structure	Moles				Structure	Yield, %	Properties	Calculated C	Calculated H	Found C	Found H
 [a]	0.02	0.065	60	10		28	M.p. 74–75°	67.7	4.0	67.7	4.3
 [a]	0.0033	0.02	60	8		57	M.p. 134–142°	23.2	0.6	23.4	0.9

[a] Experiment included 5 ml. of benzene as solvent; reaction run in a sealed platinum tube (capacity 15 ml.) which was heated while under nitrogen pressure in a shaker tube. [b] Infrared spectra of products in agreement with structures shown.

therefore require more vigorous conditions than those without electron-attracting groups, and such is found to be the case. Compounds having fluoroalkyl groups or fluorine atoms attached to the carbonyl group prove to be very sluggish in reactions with SF_4. A temperature of 250° and use of BF_3 catalyst was required to convert 2,2,3,3-tetrafluoropropionyl fluoride to 1H-perfluoropropane. Carbonyl fluoride similarly requires vigorous conditions for transformation to carbon tetrafluoride. The conditions required for reaction are far more vigorous than those necessary for acyl fluorides and ketones having electron-releasing groups attached to the carbonyl group.

Experimental

Details on the preparation and properties of SF_4 may be found elsewhere.[1]

The reactions with SF_4 were carried out in stainless steel- or "Hastelloy"-lined shaker tubes of 80-ml. to 1000-ml. capacity. Liquid or solid reactants were placed in the shaker tube under a nitrogen atmosphere, the head was screwed into place, the tube was cooled to solid carbon dioxide temperature, the nitrogen was removed with a vacuum pump and gaseous reactants (HF, BF_3, SF_4, etc.) were condensed into the shaker tube. After being heated for the prescribed period, the shaker tube was allowed to cool. In cases where the gaseous products were of interest, these were condensed into an evacuated stainless steel cylinder at liquid nitrogen temperature; otherwise, excess SF_4 and volatile by-products were vented from the tube. Liquid or solid products were recovered when the tube was opened, and pure products were obtained by the usual processes of distillation, recrystallization and sublimation. When it was necessary to remove HF from the crude mixture, this usually was accomplished by either (1) pouring the crude mixture into water and recovering the product by filtration, extraction or steam distillation, or (2) pouring the crude mixture into a suspension of sodium fluoride ($NaF + HF \rightarrow NaHF_2$) in an inert solvent having a boiling point considerably removed from that of the product desired, followed by filtration and fractional distillation. In some cases removal of HF from a solid or high boiling liquid was accomplished by vaporization of the HF and absorption into solid NaF or NaOH. Reaction times and temperatures, amounts of reactants, nature and amount of catalyst and identity and yield of products are given in the tables. Although the yields of products obtained vary widely, in very few specific cases has an effort been made to find optimum reaction conditions. Where infrared and mass spectrometric analyses were carried out, they are indicated in the tables and were in agreement with the structural assignments. In all cases the hydrogen and fluorine nuclear magnetic resonance spectra were in agreement with the structures of the products.

Acknowledgments.—We are indebted to Drs. F. S. Fawcett, R. J. Harder, J. F. Harris, C. M. Langkammerer, R. V. Lindsey, E. L. Muetterties, A. L. Oppegard, B. C. Pratt, R. E. Putnam, M. S. Raasch, J. C. Sauer, R. M. Scribner, W. A. Sheppard, O. W. Webster and B. D. Wilson for helpful discussions and for providing some of the experimental results listed in the tables.

WILMINGTON, DELAWARE

[CONTRIBUTION NO. 536 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND COMPANY]

Chemistry of Sulfur Tetrafluoride.[1] III. Organoiminosulfur Difluorides

BY WILLIAM C. SMITH, CHARLES W. TULLOCK, RONALD D. SMITH AND VAUGHN A. ENGELHARDT

RECEIVED JULY 17, 1959

An investigation of the chemistry of sulfur tetrafluoride has uncovered a new class of substances, the organoiminosulfur difluorides. These compounds, which have the general formula $RN{=}SF_2$, have been obtained by the reaction of sulfur tetrafluoride with organic and inorganic compounds having carbon–nitrogen multiple bonds. The chemical and physical data support the postulated iminosulfur difluoride structure for these substances The organoiminosulfur difluorides, unlike the unstable $C_6H_5N{=}SCl_2$, have high thermal stability, but the nitrogen–sulfur bond is unstable toward water and ethanol, and gross decomposition of the $-N{=}SF_2$ grouping takes place. Reaction of phenyliminosulfur difluoride, $C_6H_5N{=}SF_2$, with sodium methoxide and with phenyllithium was limited to the sulfur–fluorine bonds, however, and the new iminosulfur derivatives, $C_6H_5N{=}S(OCH_3)_2$ and $C_6H_5N{=}S(C_6H_5)_2$, were prepared. A direct synthesis of the trifluoromethyl derivative, $CF_3N{=}SF_2$, from an inorganic thiocyanate, chlorine and a metal fluoride also is described.

The synthesis of a compound having the empirical formula F_3NS has been reported by Glemser and Schröder.[2] This compound was assigned the structural formula $FN{=}SF_2$ on the basis of chemical evidence and was the first example of an iminosulfur difluoride. An organoiminosulfur dichloride

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[1] Paper II, W. R. Hasek, W. C. Smith and V. A. Engelhardt, THIS JOURNAL, **81**, 543 (1960).

[2] O. Glemser and H. Schröder, *Z. anorg. allgem. Chem.*, **284**, 97 (1956).