Preparation of Halodifluoromethanesulfonic Acid Derivatives

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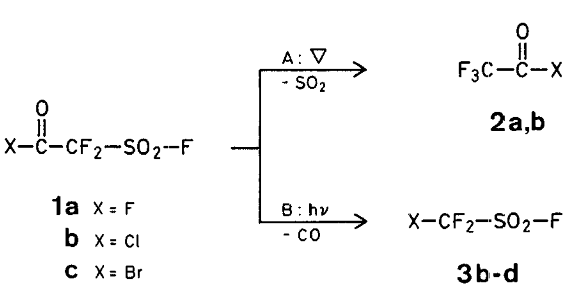
Trifluoromethanesulfonic acid and its derivatives have found extensive applications in synthetic chemistry[1]. However, methods for the synthesis of other halodifluoromethanesulfonic acids have not been reported.

It has been shown[2] that the 2-halo-2-oxodifluoroethanesulfonyl fluorides **1a** and **1b** decompose thermally with elimination of sulfur dioxide to give the trifluoroacetyl halides **2a** and **2b** (Scheme A, Route A). It could, therefore, be assumed that the photolysis of **1b-d** would proceed similarly. In fact, we have found that photolysis of **1b-d** occurs with quantitative elimination of carbon monoxide to give the halodifluoromethanesulfonyl fluorides **3b-d** in good yields (Scheme A, Route B).



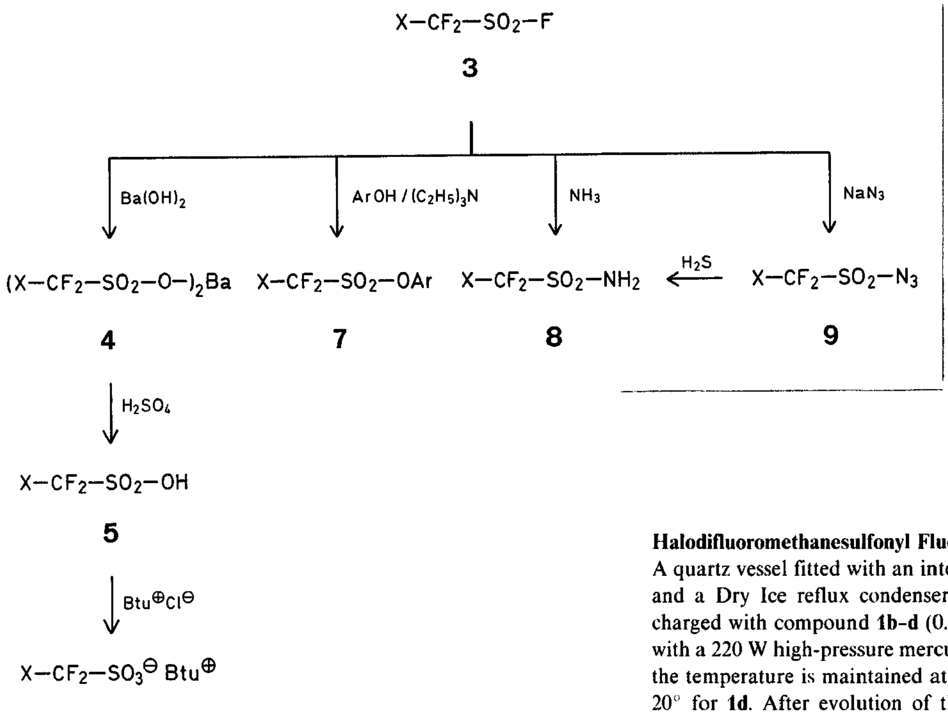
Scheme A

The ease of the photolytic transformation **1**→**3** increases in the order X = Cl < X = Br < X = J. Thus, photolysis of **1b** occurs at 80–90°, of **1c** at 50°, and of **1d** at room temperature.

The sulfonyl fluorides **3b-d** are key intermediates for the synthesis of various derivatives of halodifluoromethanesulfonic acids (Scheme **B**). Thus, hydrolysis of **3** with barium hydroxide yields the barium salts **4** which are converted to the free acids by treatment with sulfuric acid. The acids **5** are easily characterized as the *S*-benzylthiuronium (Btu) salts **6** which can be recrystallized from water. The ease of hydrolysis also increases in the order **3b** < **3c** < **3d**.

0039-7881/79/1232-0972 $ 03.00

The fluorides **3** are converted to aryl esters **7** by treatment with *m*- or *p*-fluorophenol/triethylamine, to sulfonamides **8** by treatment with ammonia, and to azides **9** by treatment with sodium azide. As direct ammonolysis of **3d** leads to the formation of tars, sulfonamide **8d** is better prepared by the mild hydrogen sulfide reduction of azide **9d**, which does not affect the iododifluoromethane group.



Scheme **B**

The pK_a values of the halodifluoromethanesulfonamides **8a-d** in water at 25° have been determined: **8a**, 6.45 (Lit. [3,4], 6.33, 5.8); **8b**, 6.50; **8c**, 6.53; **8d**, 6.79. It is interesting to note that, in the ^{19}F-N.M.R. spectra, the signals for the —SO_2—F fluorine atom also move to higher field as follows: **3a**, $\delta = -35.55$ ppm; **3b**, $\delta = -31.02$ ppm; **3c**, $\delta = -29.01$ ppm; **3d**, $\delta = -26.20$ ppm.

The 2-halo-2-oxodifluoroethanesulfonyl fluorides **1** used as starting materials are readily available on a laboratory scale. 2-Oxo-1,1,2-trifluoroethanesulfonyl fluoride (**1a**) is easily prepared by addition of sulfur trioxide to tetrafluoroethene and subsequent isomerization of 3,3,4,4-tetrafluoro-1,2-oxathietane 2,2-dioxide[4]. Reaction of sodium iodide with **1a** results in the formation of the iodo compound **1d**. However, carboxydifluoromethanesulfonyl fluoride[2] (**10**) is a more convenient starting material for the synthesis of **1b** and **1c**. Furthermore, the yield of **1d** can be substantially increased by reaction of **1b** with sodium iodide (Scheme C).

2-Bromo-2-oxodifluoroethanesulfonyl Fluoride (1c):

Method A: A mixture of 2-oxo-1,1,2-trifluoroethanesulfonyl fluoride[2] (**1a**; 10 g, 0.041 mol) and powdered anhydrous aluminium bromide (15 g, 0.083 mol) is heated under reflux with stirring for 5 h. The resultant mixture is then fractionally distilled to give **1c**; yield: 4.0 g (40%); b.p. 84–85°/760 torr.

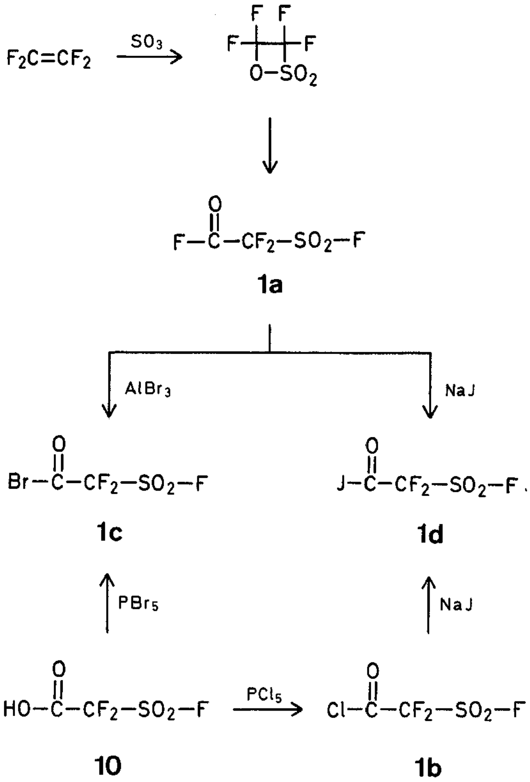
Method B: To phosphorus(III) bromide (27.1 g, 0.1 mol, freshly distilled over sulfuric acid), bromine (16.0 g, 0.1 mol), and fluoride **1a** (17.8 g, 0.099 mol) are added dropwise at 20°. The resultant mixture is heated under reflux at 80° for 1 h and the product fractionally distilled; yield: 22.9 g (95%).

2-Iodo-2-oxodifluoroethanesulfonyl Fluoride (1d):

To a suspension of sodium iodide (7.5 g, 0.05 mol) in anhydrous dichloromethane (10 ml) is added dropwise at room temperature **1b**[2] (9.8 g, 0.5 mol). The reaction mixture is heated under reflux for 5 h and then filtered to remove sodium fluoride. Solvent and unreacted **1b** are distilled and the product is obtained by distillation under reduced pressure; yield: 10 g (70%); b.p. 70°/190 torr.

Halodifluoromethanesulfonyl Fluorides 3b-d; General Procedure:

A quartz vessel fitted with an internal cooling coil, a thermometer, and a Dry Ice reflux condenser connected to an eudiometer, is charged with compound **1b-d** (0.05 mol). Irradiation is performed with a 220 W high-pressure mercury lamp 1 cm from the vessel and the temperature is maintained at 80–90° for **1b**, 40–50° for **1c**, or 20° for **1d**. After evolution of the theoretical amount of carbon monoxide (1120 ml), irradiation is stopped and the product fractionally distilled.



Scheme C

Table. 2-Halo-2-oxodifluoroethanesulfonyl Fluorides **1** and Halodifluoromethanesulfonic Acid Derivatives **3–9**

Product No.	X	Yield [%]	b.p./torr or m.p.	d_4^t	n_D (temp.)	Molecular formula[a]	I.R. (solvent) ν [cm^{-1}]
1c	Br	95	84.5–85°/760	1.9390	1.3790 (25°)	$C_2BrF_3O_3S$ (241.0)	1795; 1460; 1250; 1190; 1090; 1020; 920; 850; 800; 675; 630; 590 (CCl_4)
1d	J	70	70°/190	—	—	$C_2JF_3O_3S$ (288.0)	1910; 1860; 1780; 1620; 1460; 1380; 1340; 1300; 1200; 1200–1150; 1120; 1070; 1040; 1020; 995; 950; 930; 915; 830–770; 729; 670; 645; 615; 600–575
3b	Cl	83	26.5–27°/760	—	—	$CClF_3O_2S$ (168.5)	—
3c	Br	85	48–48.5°/760	1.9560	1.3492 (25°)	$CBrF_3O_2S$ (212.0)	1460; 1250; 1170; 1130; 1090; 920; 870; 795; 775; 685; 655; 585; 510; 500
3d	J	92	84.5–85°/760	2.2940	1.4050 (20°)	CF_3JO_2S (260.0)	1460; 1240; 1160; 1120; 930; 890; 810; 750; 645; 510; 495
5b	Cl	96	92°/15	1.7411	1.3850 (23°)	$CHClF_2O_3S$ (166.5)	—
6b	Cl	98	131–132°	—	—	$C_9H_{11}ClF_2N_2O_3S_2$ (332.8)	—
6c	Br	96	110–111°	—		$C_9H_{11}BrF_2N_2O_3S_2$ (372.2)	—
6d	J	96	88–89°	—	—	$C_9H_{11}F_2JN_2O_3S_2$ (424.2)	—
7b[b]	Cl	60	86°/13	1.5232	1.4586 (25°)	$C_7H_4ClF_3O_3S$ (260.6)	—
7b′[c]	Cl	57	90–91°/13	1.5332	1.4589 (25°)	$C_7H_4ClF_3O_3S$ (260.6)	—
8b	Cl	70	68–69°	—	—	$CH_2ClF_2NO_2S$ (165.5)	3470; 3365; 3295; 1590; 1530; 1400; 1200; 1150; 1120; 970; 930; 890; 840; 690; 675; 585; 550–470
8c	Br	40	53–54°		—	$CH_2BrF_2NO_2S$ (210.0)	3395; 3290; 1530; 1390; 1200; 1140; 1120; 980; 880; 655; 590; 510
8d	J	80	63–64°	—	—	$CH_2F_2JNO_2S$ (257.0)	3360; 3265; 1540; 1375; 1190; 1130; 1110; 930; 840; 670; 655; 505
9b	Cl	85	60–61°/175	1.6352	1.4070 (24°)	$CClF_2N_3O_2S$ (191.5)	2340–2280; 2150; 1420; 1200; 1160; 1110; 900; 790–760; 660; 650; 560
9c	Br	75	70°/220	1.9558	1.4462 (24°)	$CBrF_2N_3O_2S$ (236.0)	2340–2280; 2150; 1420; 1200; 1160; 1110; 900; 790–760; 660; 650; 560 (CCl_4)
9d	J	70	58°/12	2.2568	1.5011 (24°)	$CF_2JN_3O_2S$ (283.0)	2150; 1410; 1200; 1160; 1100; 800; 790; 770; 660; 655; 600; 560 (CCl_4)

[a] Halogen and nitrogen microanalyses were in satisfactory agreement with the calculated values (Cl ±0.12, F ±0.28, **Br** ±0.37, J ±0.10, N ±0.44); exceptions: **3d**, F −0.71; **5b**, F −0.57; **9d**, N +0.6.

[b] Ar = 3-F—C_6H_4.

[c] Ar = 4-F—C_6H_4.

Barium Chloro- (4b) and Bromodifluoromethanesulfonate (4c):

A mixture of **2b** or **2c** (0.047 mol), barium hydroxide (0.051 mol), and water (20 ml) is heated in a sealed tube for 6 h at 60° for **2b** or at 40° for **2c**. Excess barium hydroxide is neutralized with sulfuric acid, barium sulfate and barium fluoride are filtered off, and the filtrate is evaporated to dryness under reduced pressure to give **4b** or **4c**; yield: quantitative.

4b; I.R. (KBr): ν = 1290–1230; 1160; 1120; 1110; 1060; 940; 890; 690; 620; 565; 550 cm^{-1}.

4c; I.R. (KBr): ν = 1460; 1390; 1200; 1180; 1140; 1120; 980; 880; 655; 590; 510 cm^{-1}.

Barium Iododifluoromethanesulfonate (4d):

To a solution of barium hydroxide (2.5 g, 0.0146 mol) in water (10 ml) is added **3d** (7.2 g, 0.0277 mol) dropwise. The mixture is stirred at room temperature for 4 h and the product is then purified as described above; yield: 8.8 g (98%).

I.R. (KBr): ν = 1500; 1450; 1430; 1270; 1220; 1120; 1110; 1080; 1040; 920; 850; 760; 700; 685–670; 650; 590; 540 cm^{-1}.

Chlorodifluoromethanesulfonic Acid (5b):

A mixture of the barium salt **4b** (10 g, 0.02 mol) and sulfuric acid (13.2 g, 0.13 mol) is heated at 100° for 3 h. The product is isolated by distillation under reduced pressure; yield: 6.4 g (96%); b.p. 92°/15 torr.

Bromo- (5c) and Iododifluoromethanesulfonic Acid (5d):

To a solution of the barium salt **4c** or **4d** (0.01 mol) in water (10 ml) is added 2 normal sulfuric acid (10 ml) and the precipitate is filtered off. The aqueous solution is allowed to stand for 5 days and then a solution of *S*-benzylthiuronium chloride (4.1 g, 0.02 mol) and sodium carbonate (2.1 g, 0.02 mol) in water (5 ml) is added to precipitate the salt **6c** or **6d**; yield: 96%.

m- or *p*-Fluorophenyl Chlorodifluoromethanesulfonates 7b, 7b′:

m- or *p*-Fluorophenol ([illegible].9 g, 0.02 mol), triethylamine (10 ml, 0.07 mol), and the fluoride **3b** are stirred at 20° for 4 h. The resultant mixture is poured into water (20 ml), acidified with 10% hydrochloric acid (25 ml), and extracted with ether. The ether extracts are washed with water, dried with sodium sulfate, and the solvent removed under reduced pressure.

Chloro- (8b) and Bromodifluoromethanesulfonamide (8c):

Excess dry ammonia is bubbled into a solution of **3b** or **3c** (0.06 mol) in ether (15 ml) during 12 h. Excess hydrogen chloride is then passed through the mixture. The resultant mixture is filtered, the filtrate is evaporated, and the residue crystallized from benzene/hexane.

Iododifluoromethanesulfonamide (8d):

Excess hydrogen sulfide is slowly bubbled into a stirred solution of iododifluoromethanesulfonyl azide (**9d**; 4.2 g, 0.0148 mol; see below) in tetrahydrofuran (10 ml) at room temperature during 10 h. The precipitated sulfur is filtered off and the solvent removed by distillation. The product is recrystallized from hexane; yield: 3.0 g (80%); m.p. 63–64°.

Halodifluoromethanesulfonyl Azides 9b–d; General Procedure: These products are prepared from equimolar amounts of the fluoride **3** and sodium azide in methanol following the procedure[6] for trifluoromethanesulfonyl azide.

Received: July 31, 1979

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0039-7881/79/1232-0975 $ 03.00