FLUORINE-CONTAINING β-SULTONES

COMMUNICATION 18. DERIVATIVES OF DIFLUOROSULFOACETIC ACID

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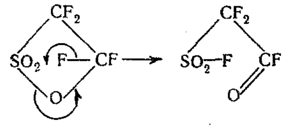
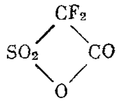
We have reported previously [1] that, when heated, tetrafluoro-1,2-ethanesultone is converted into difluoro(fluorosulfonyl)acetyl fluoride. The possibility of such rearrangement is determined by the high mobility of a fluorine atom in the α-position relative to an ester oxygen:

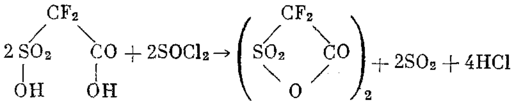


It was of interest to determine the stability of compounds of similar structural type which do not contain a mobile fluorine atom. It may be supposed that a simple compound of this type is the cyclic anhydride of difluorosulfoacetic acid:

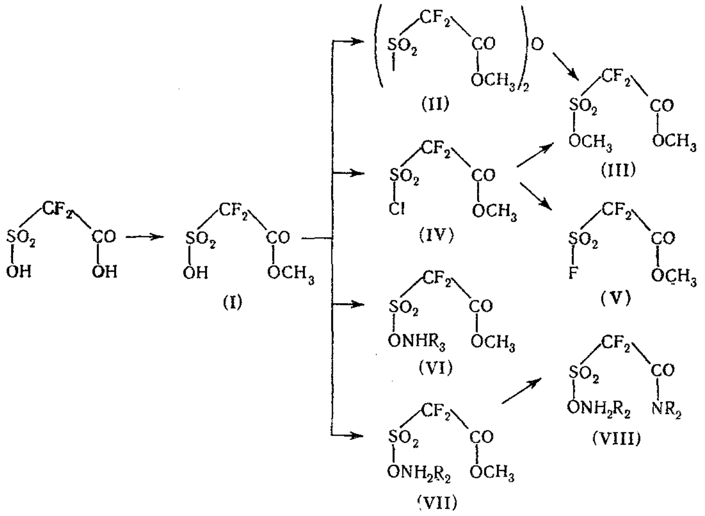


It was thought that this anhydride could be prepared by the dehydration of difluorosulfoacetic acid.

We were able to effect the dehydration of difluorosulfoacetic acid by treating it with thionyl chloride. The derivative then obtained corresponded in composition to the dimer of the anhydride:



In its chemical properties this compound is indeed a derivative of difluorosulfoacetic acid. Thus, in its treatment with methanol two molecular proportions of the monoester (I) is formed, and in treatment with a secondary amine—two molecular proportions of the dialkylammonium salt of the dialkylamide of difluorosulfoacetic acid (VIII). The structures of the latter compounds and thus the structure of the anhydride dimer were proved as follows:



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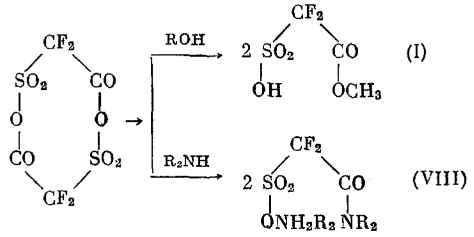
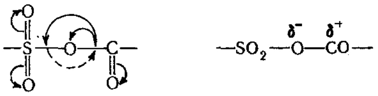
By the alcoholysis of difluorosulfoacetic acid we prepared an ester identical to the monoester (I) referred to above. By the dehydration of this compound with thionyl chloride we obtained the corresponding anhydro derivative (II), which by the action of dimethyl ether was converted into the previously described difluorosulfoacetic acid diester (III) [2]. It should be noted that under analogous conditions esters do not react with carboxylic acid anhydrides of the type difluoro(fluorosulfonyl)acetic anhydride [3], while on the other hand they react vigorously with anhydrides of sulfuric and sulfonic acids [4]. This fact indicates that the anhydridization of the monoester (I) is effected through the sulfo, and not the carboxy group, and that the monoester is the product of the esterification of the acid at the carboxy group.

By the action of phosphorus pentachloride the monoester of difluorosulfoacetic acid (I) is converted into the ester acid chloride (IV), and the alcoholysis of this gives the diester of the same acid, while treatment with antimony trifluoride gives the previously described methyl difluoro(fluorosulfonyl)acetate (V) [3]. It is therefore clear that the monoester is methyl difluorosulfoacetate. On reaction with amines the difluorosulfoacetic ester (I) is converted into the monoester ammonium salts (VI) and (VII), and when an excess of a secondary amine is used the salt of N,N-disubstituted difluorosulfoacetamide (VIII) is obtained and is identical to the compound prepared by the aminolysis of the anhydride dimer.

The formation of the monoester (I) and the difluorosulfoacetamide salt (VIII) as the sole products of the alcoholysis and aminolysis, respectively, of the anhydride dimer leaves no doubt about the structure of the latter compound. The dimer is a cyclic bisanhydride of difluorosulfoacetic acid in which the acid residues are linked in head-to-tail fashion:

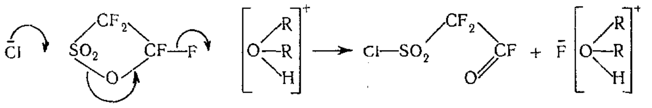


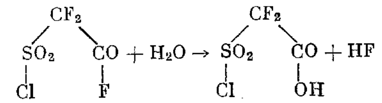
The reactivity of the bisanhydride is determined by the high lability of the anhydride groupings, which are polarized in accordance with the electron-acceptor properties of the sulfonyl and carbonyl groups:



The formation of the bisanhydride in the treatment of difluorosulfoacetic acid with thionyl chloride is probably a multistage process. In the first stage the mono[acid chloride] of the acid is formed, and this is then dehydrochlorinated and converted into the bisanhydride. Two courses are here possible: through the intermediate formation of a halosulfonyl carboxylic acid or of a haloformyl sulphonic acid. However, one of these courses, namely, that associated with the intermediate formation of the sulfonic acid chloride, must be excluded on the basis of the following considerations.

We have examined the stability of (chlorosulfonyl)difluoroacetic acid, prepared by the hydrochlorination of tetrafluoro-1,2-ethanesultone in moist ether and identified by its conversion into difluoro(fluorosulfonyl)acetic acid [3].



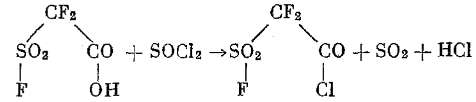


$$ClSO_2CF_2COF + H_2O \rightarrow ClSO_2CF_2COOH + HF$$

It was found that, like its analog difluoro(fluorosulfonyl)acetic acid, (chlorosulfonyl)difluoroacetic acid shows no tendency to undergo spontaneous dehydrohalogenation. When these acids are treated with thionyl chloride, not anhydrides, but acid chlorides of the acids are formed, e.g.,

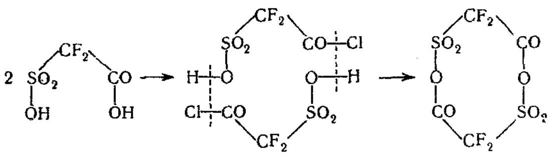
TABLE 1

Compound	M.p., °C	B.p., °C (p, mm)	d_4^{20}	n_D^{20}
$HOSO_2CF_2COOH \cdot 2H_2O$	46—47	—	—	—
$(—SO_2CF_2COO—)_2$	10—12	195 (2)	—	—
$HOSO_2CF_2COOCH_3$	—	98 (2)	1.4611	1.3601
$(—SO_2CF_2COOCH_2)_2O$	—	127 (2)	1.5585	1.4077
$ClSO_2CF_2COOCH_3$	—	63 (8)	1.5561	1.4111
$(C_2H_5)_3NHOSO_2CF_2COOCH_3$	37	—	—	—
$(C_2H_5)_2NH_2OSO_2CF_2COOCH_3$	26	—	—	—
$(C_2H_5)_2NH_2OSO_2CF_2CON(C_2H_5)_2$	44	—	—	—
$ClSO_2CF_2COOH$	—	71 (20)	1.4682	1.4095



On the other hand, sulfonic acids of analogous structure are readily anhydridized, which is shown by an examination of the above-examined example of the conversion of the difluorosulfoacetic ester (I) into (II).

There can be no doubt, therefore, that the formation of the bisanhydride of difluorosulfoacetic acid on treatment of this acid with thionyl chloride is effected through the intermediate formation of difluorosulfoacetyl chloride, which is then dehydrochlorinated with cyclodimerization of two anhydride residues:



The possibility of intramolecular dehydrochlorination with formation of a four-membered cyclic compound is probably excluded by steric hindrance. This conclusion is in accordance with known precedents. Thus, β-lactones and β-sultones cannot be prepared by the dehydration or dehydrochlorination of β-hydroxy acids or their acid chlorides, whereas the formation of the corresponding γ- and δ-cyclic compounds is effected comparatively readily. Finally, up to now no description has appeared in the literature of intramolecular anhydrides of malonic and methionic acids and their derivatives, which are close analogs of difluorosulfoacetic acid.

The physical properties of the derivatives of difluorosulfoacetic acid obtained are given in Table 1.

EXPERIMENTAL

Difluorosulfoacetic Acid. With cooling with ice and stirring, to 600 ml of water successive additions were made of 84 g of tetrafluoro-1,2-ethanesultone and of crystalline barium hydroxide until the mixture was weakly acid to Congo Red (275-280 g). The precipitate formed was filtered off, and the mother liquor was evaporated to dryness. The residue was dried by heating it at 80-100°. We isolated 126.5 g (88.5%) of the barium salt of difluorosulfoacetic acid. Found: C 7.51; F 12.44%. $C_2O_5F_2SBa$. Calculated: C 7.72, F 12.24%.

To an aqueous suspension of 124 g of the barium salt of difluorosulfoacetic acid we added sulfuric acid (sp.gr. 1.84) until no more precipitate came down (46 g). The precipitate was filtered off, and the mother liquor was evaporated at room temperature and a residual pressure of 10-12 mm. The highly concentrated solution (about 100 g) was dried in a vacuum desiccator over P_2O_5 for several days. The dry residue, which amounted to 81 g (91%), was difluorosulfoacetic acid dihydrate. Found: C 11.10; S 15.36%; equiv. wt. 109.5 (alkalimetry). $C_2H_2O_5F_2S \cdot 2H_2O$. Calculated: C 11.32; S 15.09%; equiv. wt. 106.1.

Difluorosulfoacetic Acid Bisanhydride. A mixture of 21.2 g of difluorosulfoacetic acid dihydrate, 50 ml of thionyl chloride, and 1 g of anhydrous potassium chloride was refluxed in a water bath for 6 h. By fractionation we then isolated 10.9 g (69%) of difluorosulfoacetic acid bisanhydride. Found: C 14.94; F 23.66; S 19.81%; mol. wt. 320.1; equiv. wt. 82. $C_4O_8F_4S_2$. Calculated: C 15.19; F 24.06; S 20.25%; mol. wt. 316.2; equiv. wt. 79. The bisanhydride is a viscous mass which becomes glassy when cooled; it is soluble in water, alcohol, and acetone, but insoluble in ether and chloroform.

By dissolution in methanol with subsequent fractionation we isolated methyl difluorosulfoacetate in 91% yield. By treating an ethereal suspension of the bisanhydride with diethylamine, filtering off the precipitate formed, washing it with ether, and drying it in a vacuum desiccator we isolated diethylammonium (diethylcarbamoyl)difluoromethanesulfonate in 94% yield.

Methyl Difluorosulfoacetate. 5 ml of methanol was added to 15 g of a concentrated aqueous solution of difluorosulfoacetic acid (concentration 56.8%). After two distillations of the mixture we isolated 6.3 g (74%) of methyl difluorosulfoacetate. Found: F 19.85; S 16.60%; mol. wt. 186.3. $C_3H_4O_5F_2S$. Calculated: F 19.98; S 16.85%; mol. wt. 190. The acid ester is of limited solubility in water and is hydrolyzed by boiling water; it is readily soluble in organic solvents.

2.5 g of triethylamine was added dropwise with stirring to a solution of 3 g of methyl difluorosulfoacetate in 10 ml of dry ether. The precipitate formed was filtered off, washed three times with ether, and left in a vacuum desiccator. We isolated 4.4 g (96%) of the triethylammonium salt of methyl difluorosulfoacetate in the form of white crystals. Found: N 4.57%; mol. wt. 287. $C_9H_{10}O_5NF_2S$. Calculated: N 4.81%; mol. wt. 291.

In an analogous way we obtained a 94% yield of the diethylammonium salt of methyl difluorosulfoacetate. Found: N 5.80%; mol. wt. 260. $C_7H_{15}O_5NF_2S$. Calculated: N 5.73%; mol. wt. 263.

Methyl Difluorosulfoacetate Anhydride. A mixture of 19 g of methyl difluorosulfoacetate, 15 ml of thionyl chloride, and 0.5 g of anhydrous potassium chloride was refluxed in a water bath for 4 h. By fractionation we then isolated 8.9 g (49%) of methyl difluorosulfoacetate anhydride. Found: C 20.02; H 1.88; F 20.66; S 17.50%; mol. wt. 358; equiv. wt. 92. $C_6H_6O_9F_4S_2$. Calculated: C 19.85; H 1.66; F 20.96; S 17.66%; mol. wt. 362; equiv. wt. 90.5.

Methyl (Chlorosulfonyl)difluoroacetate. A mixture of 3.2 g of methyl difluorosulfoacetate and 5.0 g of PCl_5 was heated in a water bath for 2 h. By fractionation we then isolated 3.0 g (69%) of methyl (chlorosulfonyl)difluoroacetate. Found: F 18.61; Cl 16.84%; equiv. wt. 71.5. $C_3H_3O_4F_2ClS$. Calculated: F 18.23; Cl 17.05%; equiv. wt. 69.5. The ester is sparingly soluble in water, but readily soluble in alcohol, acetone, ether, and benzene.

By heating this product with excess of antimony trifluoride in a water bath for 1 h and then fractionating the mixture we isolated methyl difluoro(fluorosulfonyl)acetate in 72% yield [3].

Difluorosulfoacetic Acid Dimethyl Ester. A mixture of 36 g of methyl difluorosulfoacetate and 10 g of dimethyl ether was heated in a sealed tube in a water bath for 2 h. In the subsequent fractionation we obtained 30.3 g (75%) of difluorosulfoacetic acid dimethyl ester [2].

A solution of sodium methoxide was added dropwise with stirring to a solution of methyl difluorosulfoacetate in dry methanol at -10°. The mixture was diluted with water and extracted with ether. The extract was dried with sodium sulfate and fractionated. We isolated difluorosulfoacetic acid dimethyl ester in 68% yield.

Diethylammonium (Diethylcarbamoyl)difluoromethanesulfonate. A mixture of 2.0 g of the diethylammonium salt of methyl difluorosulfoacetate and 10 ml of diethylamine was heated under reflux in a water bath for 2 h. The mixture was cooled and diluted with ether; the precipitate was filtered off, washed with ether, and left in a vacuum desiccator. We isolated 2.3 g (96%) of diethylammonium (diethylcarbamoyl)difluoromethanesulfonate in the form of white crystals. Found: N 9.13%. $C_{10}H_{22}O_4N_2F_2S$. Calculated: N 9.22%. A mixture with a sample prepared from difluorosulfoacetic acid bisanhydride melted without depression.

(Chlorosulfonyl)difluoroacetic Acid. 100 ml of ether containing 1.8 g of water was saturated with hydrogen chloride at 0°, and 18.0 g of tetrafluoro-1,2-ethanesultone was added dropwise with stirring. In the subsequent fractionation we isolated 15.6 g (80%) of (chlorosulfonyl)difluoroacetic acid as an oil which fumed in air. Found: F 19.10; Cl 17.86; S 16.21%; equiv. wt. 67.0. $C_2HO_4F_2ClS$. Calculated: F 19.51; Cl 18.19; S 16.47%; equiv. wt. 64.8.

By heating a solution of (chlorosulfonyl)difluoroacetic acid in hydrogen fluoride in an autoclave at 100° for 2 h with subsequent fractionation we isolated difluoro(flurosulfonyl)acetic acid in 63% yield [3]. By heating the latter with thionyl chloride in presence of potassium chloride until no more sulfur dioxide came off (about 1 h) with subsequent fractionation we isolated difluoro(fluorosulfonyl)acetyl chloride in 72% yield [3].

CONCLUSIONS

1. A number of derivatives of difluorosulfoacetic acid were prepared, and their mutual transformations were studied.

2. The mechanism of the formation of the bisanhydride of difluorosulfoacetic acid was examined.

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