Dinitrofluoroethyl Derivatives

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Reported here is the synthesis of dinitrofluoroethyl amines, by the Mannich condensation of 2,2-dinitro-2-fluoroethanol with various primary amines, and dinitrofluoroethyl carbamates by the addition of 2,2-dinitro-2-fluoroethanol to isocyanates. Selected N-nitro and N-cyano derivatives were prepared. The preparation of aliphatic, aromatic, and heterocyclic esters of 2,2-dinitro-2-fluoroethanol is also described.

In previous papers (*1-3*) we have reported the synthesis of trinitroethyl amines, by the Mannich condensation of 2,2,2-trinitroethanol with various primary amines, and trinitroethyl carbamates by the addition of 2,2,2-trinitroethanol to isocyanates. This work has now been extended to the preparation of the corresponding dinitrofluoroethyl derivatives.

2,2-Dinitro-2-fluoroethanol, 1, was condensed with methyl amine, trifluoroethyl amine, and ethylene diamine to give 1,1-dinitro-1-fluoro-3-azabutane, 2a; 1,1-dinitro-1,5,5,5-tetrafluoro-3-azapentane, 2b; and 1,1,8,8-tetranitro-1,8-difluoro-3,6-diazaoctane, 2c. Cyanogenation of 2a yielded 1,1-dinitro-1-fluoro-3-cyano-3-azabutane, 3a. Nitration of 2b and 2c gave 1,1,3-trinitro-1,5,5,5-tetrafluoro-3-azapentane, 3b, and 1,1,3,6,8,8-hexanitro-1,8-difluoro-3,6-diazaoctane, 3c, respectively:

$$\underset{1}{FC(NO_2)_2CH_2OH} \xrightarrow{CH_3NH_2} \underset{2a}{FC(NO_2)_2CH_2NHCH_3} \xrightarrow{CNBr}$$

$$\xrightarrow{CF_3CH_2NH_2} \underset{2b}{FC(NO_2)_2CH_2NHCH_2CF_3} \xrightarrow{HNO_3}$$

$$\xrightarrow{NH_2CH_2CH_2NH_2} \underset{2c}{[FC(NO_2)_2CH_2NHCH_2]_2} \xrightarrow{HNO_3}$$

$$\underset{3a}{FC(NO_2)_2CH_2N(CN)CH_3}$$

$$\underset{3b}{FC(NO_2)_2CH_2N(NO_2)CH_2CF_3}$$

$$\underset{3c}{[FC(NO_2)_2CH_2N(NO_2)CH_2]_2}$$

Compound 1 reacted readily with methyl isocyanate, phenyl isocyanate, and methylene diisocyanate to give *N*-methyl 2,2-dinitro-2-fluoroethyl carbamate, 4a; *N*-phenyl 2,2-dinitro-2-fluoroethyl carbamate, 4b; and methylene-bis-(2,2-dinitro-2-fluoroethyl)dicarbamate, 4c, respectively:

$$1 \xrightarrow{CH_3NCO} \underset{4a}{CH_3NHCO_2CH_2C(NO_2)_2F} \xrightarrow{HNO_3}$$

$$\xrightarrow{C_6H_5NCO} \underset{4b}{C_6H_5NHCO_2CH_2C(NO_2)_2F} \xrightarrow{CH_2[NCO]_2}$$

$$\underset{4c}{CH_2[NHCO_2CH_2C(NO_2)_2F]_2}$$

$$\underset{5a}{CH_3N(NO_2)CO_2CH_2C(NO_2)_2F}$$

Nitration of 4a gave *N*-methyl-*N*-nitro-2,2-dinitro-2-fluoroethyl carbamate, 5a. The properties of the dinitrofluoroethyl amines and carbamates are summarized in Table I.

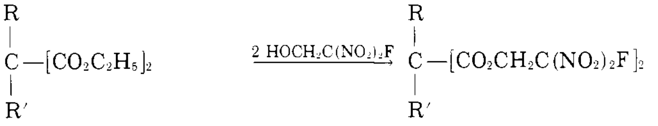
A series of aliphatic dinitrofluoroethyl esters was prepared by the reaction of the diacid chlorides with 1:

$$R[COCl]_2 \xrightarrow{2\ HOCH_2C(NO_2)_2F} R[CO_2CH_2C(NO_2)_2F]_2$$

$R = O$, 6a 7a
$R = CH_2$, 6b 7b
$R = CH{=}CH$, 6c 7c

The synthesis of 7b and 7c has recently been reported (*4*).

The synthesis of other members of the malonic ester series, 6b—i.e., nitro, fluoronitro, and dinitromalonate—was attempted by the transesterification of the diethyl esters of the substituted malonic acids with 1:



$$\begin{array}{c} R \\ | \\ C{-}[CO_2C_2H_5]_2 \\ | \\ R' \end{array} \xrightarrow{2\ HOCH_2C(NO_2)_2F} \begin{array}{c} R \\ | \\ C{-}[CO_2CH_2C(NO_2)_2F]_2 \\ | \\ R' \end{array}$$

$R = H, R' = NO_2$, 8a 9a
$R = F, R' = NO_2$, 8b 9b
$R = NO_2, R' = NO_2$, 8c 9c

Diethylnitromalonate, 8a, and diethyl fluoronitromalonate, 8b, were prepared by the procedure of Adolph et al. (*5*). Attempts to prepare diethyl dinitromalonate, 8c, included oxidative nitration of diethyl nitromalonate, reaction of silver nitrite with diethylbromonitromalonate, and nitration of diethyloximinomalonate. None of the attempts was successful. The transesterification reaction between 8a and 1 in 1 to 1 96% H_2SO_4:30% fuming H_2SO_4 at 0° C was unsuccessful, as 8a was unstable in the reaction medium. An alternate route to synthesize 9a through the nitration of 7b was also unsuccessful. Treatment of 8b with 1 in fuming sulfuric acid gave 7a, rather than the desired 9b.

It was of interest to prepare bis(2,2-dinitro-2-fluoroethyl)difluoromalonate, the fluoro analog of 7b. To do so, it was necessary to synthesize the intermediate difluoromalonic acid, 10. Several methods for the preparation of 10 have been reported. These include the hydrolysis of 2,2-dichloro-1,1,2-trifluoropropionic acid (*6*), the oxidation of 3,3-difluoro-1,4-pentadiene (*7*), the oxidation of perfluoro-1,4,7-octatriene (*8*), and the oxidation of perfluoro-1,4-cyclohexadiene (*9*). Initially, the hydrolysis of 2,2-dichloro-1,1,2-trifluoropropionic acid was selected for study. However, only very low yields of 10 were obtained by this method. The remaining reported syntheses (*7-9*) involved multistep reactions of difficult to synthesize intermediates. To overcome these difficulties, a simple two-step reaction was developed for the synthesis of 10. Following the procedure of Hasek et al. (*9*), 2,3,5,6-tetrachloro-1,1,4,4 tetrafluoro-2,5-cyclohexadiene, 12, was prepared in 77% yield by the reaction of chloranil, 11, and sulfur tetrafluoride. Oxidation of 12 with potassium per-

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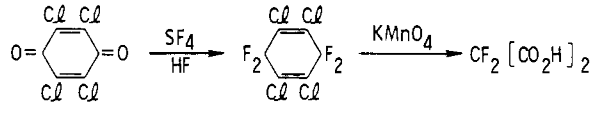
Table I. Dinitrofluoroethyl Amines and Carbamates[a]

Compound	Yield, %	Mp, °C	Bp, °C/mm	n_D^{25}
$CH_3N(CN)CH_2C(NO_2)_2F$	44.0		93-94/0.01	1.4560
$CF_3CH_2N(NO_2)CH_2C(NO_2)_2F$	45.2	60-61		
$[CH_2N(NO_2)CH_2C(NO_2)_2F]_2$	86.7	147-148		
$CH_3NHCO_2CH_2C(NO_2)_2F$	93.0		84-86/1.0	1.5530
$C_6H_5NHCO_2CH_2C(NO_2)_2F$	95.2	68-70		
$CH_2[NHCO_2CH_2C(NO_2)_2F]_2$	55.0	129-130		
$CH_3N(NO_2)CO_2CH_2C(NO_2)_2F$	84.5		111-113/0.015	1.4689

[a] Elemental analyses for C, H, and N have been reviewed and are in accord with theory.

manganate gave the desired 10 in 57.5% yield. Esterification of 10 with 1 gave bis(2,2-dinitro-2-fluoroethyl)difluoromalonate, 13, in 46.5% yield. The reaction was carried out without catalysis using benzene solvent to distill azeotropically off the water formed during the esterification. Similarly, bis(2,2-dinitro-2-fluoroethyl)tetrafluorosuccinate, 14, was prepared by the esterification of tetrafluorosuccinic acid with 1.



11 12 10

In the aromatic series, 2′,2′-dinitro-2′-fluoroethyl-2,4,6-trinitrobenzoate (15) and bis(2′,2′-dinitro-2′-fluoroethyl)-2,4,6-trinitrotrimesoate, 16, were prepared. 2,4,6-Tris(2′,2′-dinitro-2′-fluoroethoxy)-*s*-triazine, 17, and tris(2′,2′-dinitro-2′-fluoroethyl)-*s*-triazine-2,4,6-tricarboxylate, 18, were synthesized in the heterocyclic series. A miscellaneous ester prepared included 2,2-dinitro-2-fluoroethoxy trimethyl silane, 19. The method of preparation and properties of the 2,2-dinitro-2-fluoroethyl esters are summarized in Table II.

Infrared spectra of the 2,2-dinitro-2-fluoroethyl esters showed carbonyl absorptions at 5.7 μ and *gem*-dinitro absorptions at 6.2 μ and 7.6 μ.

EXPERIMENTAL

General (Caution!). Most of the starting materials and products described herein are explosives of moderate to considerable sensitivity to initiation by impact, shock, friction, and other means and should be handled with care. Many dinitrofluoromethyl compounds also show varying degrees of toxicity. Particularly 2,2-dinitro-2-fluoroethanol may cause painful burns when brought into contact with the skin.

Microanalyses were by Victor Dayan and Steve Gird of this laboratory. Melting and boiling points are uncorrected. Infrared spectra were run on a Perkin-Elmer 137 Infracord spectrophotometer. Typical procedures are given for the preparation of the dinitrofluoromethyl compounds.

1,1,8,8-Tetranitro-1,8-difluoro-3,6-diazaoctane, 2c. A solution of 2.0 grams (0.05 mole) of sodium hydroxide in 10 ml of water was added dropwise to a solution of 7.7 grams (0.05 mole) of 2,2-dinitro-2-fluoroethanol (*10*), 3.35 grams (0.025 mole) of ethylenediamine dihydrochloride, and 25 ml of water. An oil separated. After the addition was complete, the mixture was stirred for an additional 30 min. The mixture was extracted with 3 × 20-ml portions of methylene chloride. The combined methylene chloride extracts were washed several times with water, dried, and concentrated in vacuo leaving 6.7 grams (80.7%) of amber oil.

1,1,3,6,8,8-Hexanitro-1,8-difluoro-3,6-diazaoctane, 3c. One gram (0.003 mole) of 2c was added at 0° to 10° C to a solution of 5 ml of 99% nitric acid and 5 ml of 96% sulfuric acid. The mixture was heated at 45-50° C for 1 hr, cooled, and poured on ice. The white solid was collected, washed with water, and dried in vacuo over potassium hydroxide. The yield was 1.1 grams (86.7%) mp 145-8° C. Recrystallization from ethylene dichloride gave the product with the properties described in Table I.

1,1-Dinitro-1-fluoro-3-cyano-3-azabutane, 3a. To a solution of 4.44 grams (0.027 mole) of 2a in 25 ml of chloroform was added 2.7 grams (0.027 mole) of cyanogen bromide in 25 ml of chloroform. The resulting solution was refluxed overnight. A white solid was in evidence at this point; it was filtered and identified as the hydrobromide salt of 2a. The filtrate was washed several times with cold 5% hydrochloric acid and finally with water. It was then dried over magnesium sulfate, and the solvent was removed under reduced pressure to give 2.33 grams (44%) of liquid, n_D^{25} 1.4564. Distillation through a small molecular still gave a product with the properties described in Table I. The infrared spectrum was consistent with the assigned structure (N—CN absorption, 4.55 μ; C—NO_2 absorption 6.3 μ).

***N*-Methyl 2,2-dinitro-2-fluoroethyl Carbamate, 4a.** A mixture of 4.24 grams (0.0275 mole) of 2,2-dinitro-2-fluoroethanol 4.24 grams (0.0275 mole), methyl isocyanate 1.57 grams (0.0275 mole), and 20 ml ethylene dichloride was placed in a 50-ml flask fitted with magnetic stirrer and reflux condenser. A catalytic amount of ferric acetonyl acetonate (0.01 gram) was added to the solution which caused a slight warming. The mixture was then refluxed for 2 hr and then allowed to cool before the ethylene dichloride solvent was removed under reduced pressure. The remaining liquid was distilled through a short path column to give 5.38 grams (93% yield) of colorless liquid with the properties described in Table I.

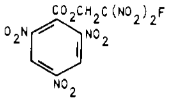
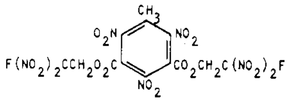
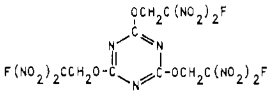
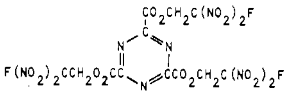
***N*-methyl *N*-nitro-2,2-dinitro-2-fluoroethyl Carbamate, 5a.** A solution of 5.02 grams (0.0238 mole) of 4a in 35 ml acetic anhydride was added dropwise into 35 ml of stirred absolute nitric acid which was held at 5-10° C by means of an ice bath. Stirring was continued for 1 hr after addition was completed. The mixture was quenched over 40 grams of ice, and the aqueous mixture was extracted with three 50-ml portions of methylene chloride. The combined methylene chloride extracts were washed three times with water, twice with 5% sodium bicarbonate, and twice with water. The final water wash proved to be neutral. The methylene chloride extract was dried over magnesium sulfate and the methylene chloride removed under reduced pressure. The remaining liquid was distilled through a short path column to give 5.15 grams (84.5%) of product with the product with the properties described in Table I.

Bis(2,2-dinitro-2-fluoroethyl)oxalate, 7a, from Oxalyl Chloride, Method A. A mixture of 17.7 grams (0.14 mole) of oxalyl chloride, 43.0 grams (0.28 mole) of 2,2-dinitro-2-fluoroethanol, 2.0 grams anhydrous aluminum chloride, and 200-ml ethylene dichloride was refluxed for 18 hr. Evolution of hydrogen chloride had ceased at this time. The hot solution was treated with decolorizing carbon and filtered using Celite filter aid. The solid from the cooled solution was collected and recrystallized from ethylene dichloride. The yield of white solid was 27.5 grams (56%), with the properties given in Table II.

From Reaction of 2,2-Dinitro-2-fluoroethanol with Diethylnitrofluoromalonate. A mixture of 33.4 grams (0.15 mole) of diethylfluoronitromalonate (*5*) and 46.0 grams (0.30 mole) of 2,2-dinitro-2-fluoroethanol was cooled to 0° in an ice bath. While stirring, 120 ml of an ice-cold mixture of 1:1 96% H_2SO_4:33% fuming H_2SO_4 was added slowly. The reaction mixture was allowed to come to ambient temperature and was stirred for 10 days. Considerable gassing and etching of the flask were noted after approximately three days, and continued throughout the 10 days. The reaction mixture was cooled to 0° C and poured over 500 grams of ice. The white solid precipitate was filtered and washed with water. Yield of crude dry product was 16.7 grams (30.9%), mp 89–93° C. Recrystallization from $CHCl_3$ raised the melting point to 101–2° C. A mixed mp with 7a as obtained above was undepressed.

Tris(2,2-dinitro-2-fluoroethyl)-*s*-triazine-2,4,6-tricarboxylate, 18, Method B. A solution of 2.69 grams (0.01 mole) of *s*-triazine-2,4,6-tricarbonic acid chloride (*11*) in 20 ml of ethylene dichloride was added dropwise over a 15-min period to a solution of 4.85 grams (0.03 mole) of 2,2-dinitro-2-fluoroethanol, 248 grams (0.03 mole) of pyridine, and 20 ml of ethylene dichloride cooled in an ice bath. After a half hour, the ice bath was removed and the solution refluxed for 2 hr. The mixture was cooled to 0° C, and the resulting slurry was dissolved in a mixture of methylene chloride and 4% aqueous hydrochloric acid. The organic layer was washed with two 40-ml portions each of 4% hydrochloric acid, 5% sodium bicarbonate, and water, and dried ($MgSO_4$). The drying agent was filtered off and the solvent removed under reduced pressure to yield 4.9 grams (79%) of white solid, mp 100–101° C. Recrystallization from chloroform gave a product with the properties listed in Table II.

Table II. Dinitrofluoroethyl Esters[a]

Compound	Esterfication method[b], % yield	Mp, ° C
$[CO_2CH_2C(NO_2)_2F]_2$	A (56)	101–102
$CF_2[CO_2CH_2C(NO_2)_2F]_2$	D (46.5)	[c]
$[CF_2CO_2CH_2C(NO_2)_2F]_2$	D (12.0)	46–47[d]
$CH_3SiOCH_2C(NO_2)_2F$	B (79.5)	[e]
	B (71.3)	107–108
	C (22.3)	135–137
	B (70)	76–77
	B (79)	104–106

[a] Elemental analyses for C, H, N have been reviewed and are in accord with theory. [b] Esterification method: A. Acid Chloride-Ethylene Dichloride-Aluminum Chloride. B. Acid Chloride-Methylene Dichloride-Pyridine. C. Acid Chloride-Methylene Dichloride-Potassium Carbonate. D. Acid-Benzene. [c] Bp 131.5–132.5°/0.5 mm, n_D^{23} 1.4308. [d] Bp 112–114°/0.005 mm. [e] Bp 30°/0.3 mm, n_D^{25} 1.4100.

Bis(2,2-dinitro-2-fluoroethyl)difluoromalonate, 13, Method D. A mixture of 130 grams (0.83 mole) of potassium permanganate, 42.1 grams (0.15 mole) of 2,3,4,5-tetrachloro-1,1,4,4-tetrafluoro-1,5-cyclohexadiene, 9, and 400-ml water was refluxed with stirring for 12 hr. The unreacted hexadiene (20.0 grams, 0.009 mole) was then co-distilled with water from the reaction mixture. The remaining aqueous solution was acidified with 50% sulfuric acid and filtered to remove the solid manganese dioxide. The filtrate was extracted continuously with ether for 27 hr. The ether extract was dried ($MgSO_4$) and the ether removed under vacuum to yield a thick viscous liquid. The liquid was taken up in a minimum amount of hot benzene, which yielded 12.3 grams (57.5%) of difluoromalonic acid upon cooling, mp 112–115° [lit. value (6) 117–18°].

A mixture of 11.9 grams (0.085 mole) of difluoromalonic acid, 28.5 grams (0.19 mole) of 2,2-dinitro-2-fluoroethanol, and 150 ml of benzene was placed in a 500-ml flask fitted with magnetic stirrer, Dean-Stark Trap, and reflux condenser protected by a "Drierite" drying tube. The mixture was stirred and refluxed for 124 hr during which time approximately 1.8 ml of water was collected in the Dean-Stark trap. The mixture was then treated with decolorizing carbon and allowed to cool. The solution was filtered and the benzene solvent removed under reduced pressure. The residual liquid was distilled twice through a 6-in. Vigreaux column to yield 16.31 grams (46.5%) of a colorless liquid with the properties given in Table II.

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