Organic Chemistry

Geminal (difluoroamino)nitro compounds

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A novel preparative method for the synthesis of geminal (difluoroamino)nitro compounds was developed. The method involves the reaction of *N,N*-difluoro-*O*-fluorosulfonylhydroxylamine with the corresponding salts of nitro compounds. Dependences of the yields of (difluoroamino)nitro compounds on the reaction conditions, the nature of the cation in the salts, and the properties of solvents were studied.

Key words: synthesis, geminal (difluoroamino)nitro compounds, cation, solvents and solvent mixtures.

Previously we have shown that treatment of sodium derivatives of diethyl malonate or malodinitrile or some salts of dinitro compounds with *N,N*-difluoro-*O*-fluorosulfonylhydroxylamine (**1**) affords the corresponding fluoroimino[1] and difluoroamino[2] derivatives. The possibility of using compound **1** in syntheses of this type has also been reported by other researchers.[3]

In the present work we have continued our study of the reactions of compound **1** with salts of nitro compounds and have shown that the results depend to a large extent on the reaction conditions and, most of all, on the type of solvent used.

For example, alkyl dinitroacetates, nitromalonates, and nitrocyanoacetates are successfully difluoroaminated in MeCN (Scheme 1).

The highest yields of the difluoroamino derivatives (**3a—f**) are achieved when X = Li; for X = Na, the yields are somewhat lower and for X = K, they are even lower (Table 1).

In addition, when the K-salts were used, the degree of disproportionation of compound **1** to give FNO and

Scheme 1

$$\underset{\mathbf{1}}{F_2NOSO_2F} + \underset{\mathbf{2a-f}}{XC(NO_2)RCOOR'} \rightarrow \underset{\mathbf{3a-f}}{F_2NC(NO_2)RCOOR'}$$

X = Li, Na or K

	a	**b**	**c**	**d**	**e**	**f**
R	NO_2	NO_2	COOMe	COOEt	CN	CN
R′	Me	Et	Me	Et	Me	Et

Table 1. Dependence of the yield of (difluoroamino)nitro compounds **3** on the nature of the cation

Compound	Yield (%)		
	Li	Na	K
3a	—	51.9	—
3b	—	50.2	32.2
3c	75.6	—	—
3d	91.4	—	39.5
3e	67.4	—	—
3f	72.8	—	36.3

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SO_2F_2 was always larger than with X = Na and Li. However, high yields of difluoroamino derivatives were achieved only for compounds **3a—f**, in which the initial anion is stabilized by an alkoxycarbonyl and/or by a cyano group. The attempts to difluoroaminate bromodinitromethane or 1,1,3,3-tetranitropropane salts in MeCN led only to the complete decomposition of the reactants accompanied by the evolution of nitrogen oxides and intense fluorination of the glass apparatus.

According to the generally accepted opinion,[4—6] in the case of ambident anions, the highest yield of stable $C-NF_2$ derivatives and, correspondingly, the lowest yield of the unstable $O-NF_2$ derivatives is achieved either in a heterogeneous process or in a process involving weakly polar solvents. However, the contact of compound **1** with solid nitroethane and dinitroethane salts at temperatures from 20 to −15 °C resulted inevitably in an explosion. The reaction in question could not be accomplished in CH_2Cl_2, even if it involved the highly stable sodium salt of dinitroacetonitrile.[2]

In view of the foregoing, it was of interest to carry out this reaction in a solvent having an intermediate polarity between MeCN (ε = 37.5)[6] and CH_2Cl_2 (ε = 8.9).[6] We suggested that in this case, conditions would be more favorable for a thermodynamically controlled reaction and for high aggregation of salts of the nitro derivatives than in MeCN. We tested the following solvents: Me_2CO (ε 20.7),[6] $MeCO_2Et$ (ε 6.0),[6] diglyme (ε 7.5),[7] and the following solvent mixtures (v/v): sulfolane—CH_2Cl_2 (1 : 2), MeCN—CH_2Cl_2 (1 : 1, 1 : 2 and 1 : 3), whose ε values are 24.7, 26.1, 21.2, and 19.9, respectively.* Vigorous destruction of the reactants was observed only in diglyme. In all the other experiments carried out at −20 to −40 °C, compound **1** was gradually consumed almost completely (GLC) and the initial salt (**4a**) dissolved; however, the products (**5a** and then **5b—e**) could be isolated in reasonable yields only in 1 : 2 and 1 : 3 acetonitrile—CH_2Cl_2 mixtures.

$$\underset{\mathbf{1}}{F_2NOSO_2F} + \underset{\mathbf{4a-e}}{XC(NO_2)_2R''} \rightarrow \underset{\mathbf{5a-e}}{F_2NC(NO_2)_2R'''}$$

X = Li, Na

	R''	R'''
a	$CH_2C(NO_2)_2X$	$CH_2C(NO_2)_2NF_2$
b	$C(NO_2)_2X$	$C(NO_2)_2NF_2$
c	Br	Br
d	CH_2OH	CH_2OH
e	$CH_2C(NO_2)_2CH_2OH$	$CH_2C(NO_2)_2CH_2OH$

Unlike the above-considered interaction of **1** with the salts of nitro compounds in acetonitrile, in which the transformation was almost completed immediately after mixing the reactants, completion of the reaction of **1** with **4a** (X = Li) in a solvent mixture required that the reactants be kept at a temperature from −30 to −10 °C for no less than 5—6 h. Products **5a,d,e** were obtained in 65, 41, and 25% yields, respectively. The yield of **5b** did not exceed 5—7%, which may have been due to the high degree of swelling of **4b** (X = Li or Na)* in acetontrile and in its mixtures with CH_2Cl_2. The yield of **5c** was 11%, possibly due to the side formation of dibromodinitromethane.

Subsequently, we were able to synthesize compounds **5e** and even **5a** (although, as a mixture with **5e**) by treatment of 2,2,4,4-tetranitropentane-1,5-diol (**6**) with MgO in an aqueous medium:

$$\underset{\mathbf{1}}{F_2NOSO_2F} + \underset{\mathbf{6}}{HOCH_2C(NO_2)_2CH_2C(NO_2)_2CH_2OH} \xrightarrow[H_2O]{MgO}$$

$$\longrightarrow \underset{\mathbf{5a}}{F_2NC(NO_2)_2CH_2C(NO_2)_2NF_2} + \underset{\mathbf{5e}}{F_2NC(NO_2)_2CH_2C(NO_2)_2CH_2OH}$$

Methacrylate **7** was obtained from alcohol **5d** in the presence of pyridine *N*-oxide:

$$CH_2{=}CMeC(O)Cl + \underset{\mathbf{5d}}{HOCH_2C(NO_2)_2NF_2} \xrightarrow{C_5H_5N\rightarrow O} \underset{\mathbf{7}}{CH_2{=}CMeCOOCH_2C(NO_2)_2NF_2}$$

The properties of the compounds obtained are listed in Table 2.

Experimental

Warning. Compounds **3a—f**, **5a******—e**, and **7** are highly sensitive and explode upon impact, friction, heating, or contact with an open flame. Therefore, all operations with these compounds require that the corresponding precautions are taken.

Methyl *N,N*-difluoroaminodinitroacetate (3a). At −25 to −20 °C, a suspension (9 g, 0.0483 mol) of sodium methyl dinitroacetate in 20 mL of acetonitrile was added portionwise under N_2 to a solution of *N,N*-difluoro-*O*-fluorosulfonylhydroxylamine (**1**) (7.5 g, 0.05 mol) in 30 mL of acetonitrile. The mixture was kept at this temperature for 2 h, slowly heated to ~20 °C, purged with N_2, and treated with 100 mL of ice water. The oil was separated, and the aqueous layer was treated with CH_2Cl_2 (2 × 20 mL) to extract the product. The combined organic phase was washed with an equal amount of ice water and dried with $MgSO_4$. Fractionation gave 5.4 g (51.9%) of a colorless liquid, b.p. 58 °C (8 Torr). Ethyl *N,N*-difluoroaminodinitroacetate (**3b**), dimethyl (**3c**) and diethyl (**3d**) *N,N*-difluoroaminonitromalonate, and methyl (**3e**)

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* The data obtained by S. F. Belov, M. V. Lomonosov Institute of Fine Chemical Technology.

* Diammonium salt **4b** is swollen to a markedly lesser degree, but its use did not lead to an increase in the yield of **5b**.

** When HMDS was added to a ~20% solution of **5a** in CCl_4 in a tube for recording of ^1H NMR spectra, the solution exploded.

Table 2. Characteristics of the compounds synthesized

Compound	B.p./°C (p/Torr) [M.p./°C]	n_D^{20}	d_4^{20}	Molecular formula	Found/Calculated (%)				IR spectrum, ν/cm^{-1}	^{19}F NMR spectrum, ppm (CF_3COOH as the external standard)
					C	H	F	N		
3a	58 (8)	1.4041	1.531	$C_3H_3F_2N_3O_6$	16.52 16.74	1.47 1.35	17.73 17.65	19.85 19.59	1789 (CO), 1602, 1340 (NO_2)	−118.5
3b	58—59 (4)	1.4100	1.448	$C_4H_5F_2N_3O_6$	20.25 20.96	2.02 2.18	16.49 16.59	18.27 18.34	1782 (CO), 1585, 1343 (NO_2), 965 912, 843 (NF)	−120
3c	81—82 (2.5)	1.4117	1.420	$C_5H_6F_2N_2O_6$	26.73 26.31	2.59 2.63	17.02 16.66	12.31 12.29	1787 (CO), 1605, 1348 (NO_2), 1100, 1050, 935, 905 (NF)	−120
3d	60 (1)	1.4120	1.356	$C_7H_{10}F_2N_2O_6$	32.47 32.81	3.87 3.91	15.28 14.84	10.87 10.94	1775 (CO), 1593, 1340 (NO_2), 1095, 957, 901 (NF)	−40[a]
3e	59—60 (8)	1.4008	1.393	$C_4H_3F_2N_3O_4$	24.15 24.61	1.35 1.54	19.90 19.49	21.17 21.51	2266 (C≡N), 1796, (CO), 1613, 1331 (NO_2), 1050, 956, 905 (NF)	−123.9
3f	54—55 (5)	1.4009	1.371	$C_5H_5F_2N_3O_4$	28.66 28.71	2.74 2.39	18.57 18.18	20.36 20.10	2268 (C≡N), 1792, (CO), 1617, 1330 (NO_2), 1007, 950, 905 (NF)	−45[a]
5a[b]	50 (0.01) [−3÷−5]	1.4425	1.735	$C_3H_2F_4N_6O_4$	11.25 11.04	0.60 0.61	22.83 23.31	26.13 25.77	3000, 2960 (CH_2), 1592, 1282 (NO_2), 1000, 911, 846 (NF)	−118
5b	[75]	—	—	$C_2F_4N_6O_8$	7.33 7.69	—	23.61 24.36	26.65 26.92	1610, 1270 (NO_2), 930, 900 (NF)	−123
5c[c]	65 (95)	1.4617	2.056	$CBrF_2N_3O_4$	4.71 5.09	—	16.57 16.10	17.97 17.80	1605, 1299 (NO_2), 950, 900, 865 (NF)	
5d	[48—49]	—	—	$C_2H_3F_2N_3O_5$	12.41 12.83	1.59 1.60	19.97 20.32	22.33 22.46	—	−110
5e[d]	[57—59]	—	—	$C_4H_5F_2N_5O_9$	15.47 15.74	1.75 1.64	12.11 12.46	23.13 22.95	—	−118.2
7	50—52 (1)	1.4427	1.389	$C_6H_7F_2N_3O_6$	27.91 28.24	2.50 2.75	14.47 14.90	16.43 16.47	1752 (CO), 1637 (C=C), 1600, 1300 (NO_2) 950, 918, 865 (NF)	−36[a]

[a] $CFCl_3$ as the external standard. [b] ^{1}H NMR, δ (HMDS): 4.56 (CH_2). [c] Found (%): Br 34.25. Calculated (%): Br 33.89. [d] ^{1}H NMR, δ (HMDS): 4.52 (CH_2), 4.70 (CH_2OH), 2.87 (OH).

and ethyl (3f) *N,N*-difluoroaminonitrocyanoacetate were prepared in a similar way.

1,3-Bis(*N,N*-difluoroaminodinitro)propane (5a). At −30 °C, 2.7 g of **1** was condensed, and, simultaneously, a suspension of the dilithium salt of 1,1,3,3-tetranitropropane (3 g, 0.0126 mol) in 25 mL of a mixture of anhydrous acetonitrile and CH_2Cl_2 (1 : 2 v/v) was added portionwise under N_2 and with intense stirring to a solution of *N,N*-difluoro-*O*-fluorosulfonylhydroxylamine (**1**) (2.6 g) in 20 mL of the same solvent mixture (the total amount of **1** was 5.3 g (0.0351 mol)). The addition was carried out at such a rate as to maintain the temperature below −27 °C. The mixture was kept for 1.5 h at −25 to −30 °C, for 1 h at −15 to −20 °C, and for 2.5 h at −10 to −15 °C. Then the mixture was slowly heated to 5 °C, purged with N_2, and treated with 500 mL of ice water. The organic layer was separated and the aqueous layer was treated with CH_2Cl_2 (3 × 50 mL) for extraction. The combined extracts were washed with 100 mL of a 1% aqueous solution of $NaHCO_3$ and with ice water (5 × 100 mL), and dried with $MgSO_4$. Then the solvent was evaporated *in vacuo*. Fractionation gave 2.7 g (65%) of a slightly yellowish viscous liquid, b.p. 50 °C (0.01 Torr). 1,2-Bis(*N,N*-Difluoroamino)tetranitroethane (**5b**), *N,N*-difluoroaminobromodinitromethane (**5c**), 2-*N,N*-difluoroamino-2,2-dinitroethanol (**5d**), and 4-*N,N*-difluoroamino-2,2,4,4-tetranitrobutan-1-ol (**5e**) were prepared under similar conditions.

4-*N,N*-Difluoroamino-2,2,4,4-tetranitrobutan-1-ol (5e). A mixture of 2,2,4,4-tetranitropentane-1,5-diol (**6**) (5 g, 0.0175 mol), MgO (0.7 g, 0.0175 mol), *N,N*-difluoro-*O*-fluorosulfonylhydroxylamine (**1**) (6 g, 0.0397 mol), and 60 mL of water was stirred for 5.5 h under N_2 in a reactor equipped with a reflux condenser filled with solid carbon dioxide. Then the mixture was purged with N_2, the product was extracted with CH_2Cl_2 (3 × 25 mL), and the extract was washed with ice water (3 × 100 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The residue was crystallized from hexane with freezing down to −60 to −70 °C, and the precipitate was separated to give 0.9 g (16.8%) of colorless crystals with m.p. 56—57 °C.

A similar experiment involving 6.7 g (0.0234 mol) of compound **6** and the addition of CH_2Cl_2 to the reaction mixture gave 2.5 g of a viscous liquid, b.p. 85 °C (0.009 Torr), n_D^{20} 1.4762, d_4^{20} 1.715. The liquid consisted of 64% **5a** and 36% **5e** (GLC).

2-(*N,N*-Difluoroamino)-2,2-dinitroethyl methacrylate (7). A solution of methacryloyl chloride (2.2 g, 0.0214 mol) in 30 mL of chloroform and then a solution of pyridine *N*-oxide (2 g, 0.0214 mol) in 20 mL of chloroform were added to a solution of 2-*N,N*-difluoroamino-2,2-dinitroethanol (14 g, 0.0214 mol) in 30 mL of dry chloroform. The mixture was kept for 24 h at 20 °C and treated with 300 mL of ice water. The oil was separated, washed with water (3 × 100 mL), dried with $MgSO_4$, and concentrated *in vacuo*. Rectification gave 3.7 g (67.6%) of a colorless liquid, b.p. 50—52 °C (1 Torr).

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