Table III. 2,5-Dialkoxy-2,3,5-triarylthiazolidin-4-ones (5)

compd, R =	mp	% yield	formula[b]
5a, Me	168	45	$C_{23}H_{21}NO_3S$
5a, Et	121-140[a]	49	$C_{25}H_{25}NO_3S$
5a, *n*-Pr	138	41	$C_{27}H_{29}NO_3S$
5b, Me	145	42	$C_{23}H_{20}ClNO_3S$
5c, Me	174	43	$C_{23}H_{20}ClNO_3S$
5c, Et	48-80[a]	43	$C_{25}H_{24}ClNO_3S$
5d, Me	149	47	$C_{23}H_{20}ClNO_3S$

[a] Mixture of stereoisomers. [b] Satisfactory analytical values (±0.3% for C, H, N, Cl) were reported for all compounds in the table.

mp 168 °C. Further elution with chloroform gave first benzanilide (94 mg, 24%), followed by an acidic fraction, mainly *m*-chlorobenzoic acid.

In an alternative procedure, the evaporation residue was dissolved in chloroform (50 mL), washed with saturated $NaHCO_3$ solution (3 × 150 mL), dried, and evaporated. Crystallization of the residue gave directly compound **5** (350 mg). Chromatography of the mother liquor gave **6** and **7**.

Other oxidations of compounds **1** in alcohols were carried out similarly. Data of compounds **5** obtained are listed in Table III.

3,4-Dimethoxy-1,3,4-triphenylazetidin-2-one (15). Raney nickel (3 g) was added to a solution of **5a** (R = Me, 375 mg) in ethanol (50 mL). After being stirred at room temperature for 20 min the mixture was filtered and evaporated and the residue was crystallized from ethanol to give 88 mg (31%) of **15**: mp 163 °C; IR ν_{max} 1750 cm^{-1} (C=O); NMR δ 3.50, 3.84 (s, 3 H each, OCH_3), 7.1-7.8 (m, 15 H, Ph); mass spectrum, *m/e* (relative intensity) 359 (4, M^+), 240 (3, PhC(OMe)=C(OMe)Ph), 211 (40, PhN=C(OMe)Ph), 119 (6, PhNCO), 105 (100, PhCO).

Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C, 76.46; H, 6.00; N, 3.66.

Oxidation of 2. To a solution of anhydro-5-hydroxy-3-methyl-2-phenylthiazolium hydroxide (**2**, 382 mg, 2 mmol) in ethanol (150 mL) was added *m*-chloroperbenzoic acid (2 mmol). After being stirred for 5 min the solution was evaporated and the residue chromatographed on silica gel. Elution with benzene gave 110 mg (28%) of *N*-formyl-*N*-methylthiobenzanilide (**9**), mp 70-71 °C (see text for spectral properties).

Anal. Calcd for C_9H_9NOS: C, 60.33; H, 5.06; N, 7.82; S, 17.86. Found: C, 60.11; H, 5.14; N, 7.66; S, 17.62.

Further elution with benzene gave 83 mg (25%) of *N*-methylthiobenzamide (**10**), mp 77 °C (lit.[18] mp 79 °C). Elution with chloroform gave 144 mg (33%) of 3-methyl-2-phenylthiazolidine-4,5-dione (**8**), mp 155 °C (from ethanol) (see text for spectral properties).

Anal. Calcd for $C_{10}H_9NO_2S$: C, 57.97; H, 4.38; N, 6.76; S, 15.45. Found: C, 58.27; H, 4.48; N, 6.53; S, 15.23.

Reaction of 8 with Primary Amines. A solution of **8** (60 mg) and benzylamine (40 mg) in benzene (10 mL) was refluxed for 2 min and evaporated. Crystallization of the residue from ethanol afforded 53 mg (85%) of *N*-benzyl-*N*-methyloxamide, mp 185 °C (lit.[19] mp 184-185 °C).

In the same manner the reaction with cyclohexylamine gave 90% *N*-cyclohexyl-*N*-methyloxamide, mp 214 °C.

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.20. Found: C, 58.75; H, 8.61; N, 15.10.

Registry No. 1a, 18100-80-6; **1b**, 68236-17-9; **1c**, 73308-33-5; **1d**, 59208-06-9; **2**, 1280-28-0; **5a** (R = Me), 75111-01-2; **5a** (R = Et), isomer 1, 75102-33-9; **5a** (R = Et), isomer 2, 75102-34-0; **5a** (R = *n*-Pr), 75102-35-1; **5b** (R = Me), 75102-36-2; **5c** (R = Me), 75102-37-3; **5c** (R = Et), isomer 1, 75102-38-4; **5c** (R = Et), isomer 2, 75102-39-5; **5d** (R = Me), 75102-40-8; **5d** (R = Et), isomer 1, 75102-41-9; **5d** (R = Et), isomer 2, 75102-42-0; **6a**, 17570-85-3; **7a**, 93-98-1; **8**, 75102-43-1; **9**, 75102-44-2; **10**, 5310-14-5; **15**, 75102-45-3; **18** (R = CH_2Ph), 7666-51-5; **18** (R = cyclohexyl), 75102-46-4; benzylamine, 100-46-9; cyclohexylamine, 108-91-8.

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Reactions of 2-Fluoro-2-nitro-1,3-propanediol. Trifluoromethanesulfonates and 3-Fluoro-3-nitrooxetane[1]

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The reaction of diethyl fluoronitromalonate with base and formaldehyde provided a convenient synthesis of 2-fluoro-2-nitro-1,3-propanediol. This diol reacted with triflic anhydride to give 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate and 2-fluoro-2-nitro-1,3-propylene ditriflate. The monotriflate reacted with base to give 3-fluoro-3-nitrooxetane. The ditriflate underwent displacement reactions with sodium azide, 2-fluoro-2,2-dinitroethanol, and methanol. Reactions of 3-fluoro-3-nitrooxetane with strong acids resulted in ring opening to give 3-substituted 2-fluoro-2-nitropropanols. The oxetane was polymerized with phosphorus pentafluoride. Triflates derived from 2,2-dinitro-1,3-propanediol and 2-(hydroxymethyl)-2-nitro-1,3-propanediol did not cyclize.

Primary 2-nitro and 2,2-dinitro alcohols readily undergo the reverse Henry reaction under basic conditions to give nitronate salts and formaldehyde.[2] This reaction is markedly inhibited by a fluorine α to nitro as a manifestation of the "fluorine effect" or the destabilization of a nitronate salt by an α fluorine.[3] Thus, 2-fluoro-2,2-dinitroethanol can be alkylated under basic conditions,[4-6] and 2-fluoro-2-nitro-1,3-propanediol has even been reported to give a stable dialkoxide salt. In order to explore further the chemistry of 2-fluoro-2-nitro-1,3-propanediol, we have developed an improved method for its preparation, and the present paper describes reactions of its trifluoromethanesulfonates (triflates).

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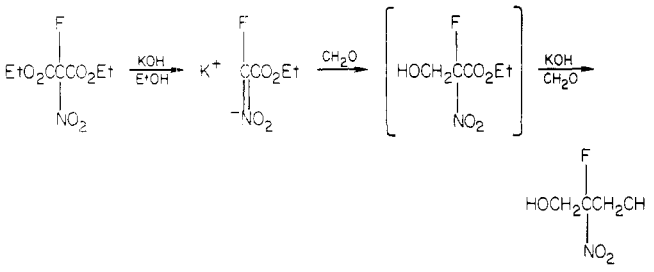
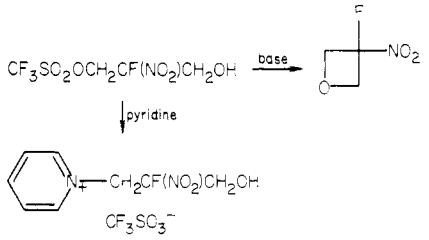
Scheme I



Scheme II



Triflates have been used previously[7] to alkylate polynitro alcohols that could not be alkylated by other reagents. One objective of this work was to utilize both the stability of 2-fluoro-2-nitro alcohols under basic conditions and the high reactivity of triflates in displacement reactions to synthesize 3-fluoro-3-nitrooxetane. Two nitrooxetanes were reported previously, and only one had a nitro group on the ring; the reaction of 2-(hydroxymethyl)-2-nitro-1,3-propanediol with phosphorus pentachloride was reported to give 3-(chloromethyl)-3-nitrooxetane[8] as a minor byproduct. The other reported nitrooxetane, 3,3-bis(nitromethyl)oxetane was obtained from 3,3-bis(iodomethyl)oxetane and silver nitrite.[9]

2-Fluoro-2-nitro-1,3-propanediol was first synthesized by fluorination of the nitronate salt of 2,2-dimethyl-5-nitro-1,3-dioxane and subsequent acid hydrolysis of the dioxane.[10] The fluorination of the nitronate salt of 2-nitro-1,3-propanediol was also reported to afford 2-fluoro-2-nitro-1,3-propanediol, but a dilute (1:50) fluorine–nitrogen mixture and prolonged reaction times were used.[11] We were unable to carry out this fluorination on a useful scale because of ignition at the fluorine inlet.

A much more facile direct fluorination gives diethyl fluoronitromalonate from diethyl nitromalonate in high yield, and hydrolysis of this product has been shown to give ethyl fluoronitroacetate.[12] These reactions provide the basis for a convenient preparative route to 2-fluoro-2-nitro-1,3-propanediol. A solution of diethyl fluoronitromalonate in ethanol was treated with 1 equiv of potassium hydroxide below −10 °C and then with 2 equiv of aqueous formaldehyde. Hydrolysis, decarboxylation, and formylation took place in situ to give 2-fluoro-2-nitro-1,3-propanediol. The crude diol could not be recrystallized easily, and the high pot temperatures needed for distillation resulted in some decomposition. However, silylation of the crude diol enabled convenient purification by distillation, and the silyl groups were readily removed with refluxing methanol. A 71% yield of 2-fluoro-2-nitro-1,3-propanediol was obtained in this way from diethyl fluoronitromalonate (Scheme I).

The desired triflates were prepared from the above alcohol by conventional procedures, with the predominant product determined by the stoichiometry. A twofold excess of 2-fluoro-2-nitro-1,3-propanediol reacted with triflic anhydride and pyridine to give a 79% yield of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate and a 9% yield of 2-fluoro-2-nitro-1,3-propylene ditriflate. When only 1 equiv of the diol was used, the yields of monotriflate and ditriflate were 52% and 28%, respectively. Reaction of the diol with 2 equiv of both triflic anhydride and pyridine afforded the ditriflate in 76% yield (eq 1).

$$HOCH_2CF(NO_2)_2CH_2OH \xrightarrow[\text{pyridine}]{(CF_3SO_2)_2O} CF_3SO_2OCH_2CF(NO_2)CH_2OH + CF_3SO_2OCH_2CF(NO_2)CH_2OSO_2CF_3 \quad (1)$$

The cyclization of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate proved to be a surprisingly facile reaction and gave 3-fluoro-3-nitrooxetane, the first fully characterized oxetane with a nitro group on the ring. Thus the use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base, in methylene chloride solution at room temperature, provided a 62% isolated yield of 3-fluoro-3-nitrooxetane. Similar yields (NMR) were obtained with potassium hydroxide or potassium carbonate in aqueous dioxane, with triethylamine in chloroform, and with potassium methoxide in methanol. The latter reaction gave no evidence of methoxide displacement of the triflate group. Pyridine, however, did not effect cyclization, but underwent N-alkylation to give 2-fluoro-3-hydroxy-2-nitro-1-propylpyridinium triflate (Scheme II).

Displacement reactions of 2-fluoro-2-nitro-1,3-propylene ditriflate were also studied. Sodium azide in dimethyl sulfoxide at room temperature gave a quantitative yield of 1,3-diazido-2-fluoro-2-nitropropane, identified spectrally and by conversion to the bis(triazole) derivative with propiolic acid (eq 2). Similarly, the reaction of the ditriflate with 2-fluoro-2,2-dinitroethanol in dioxane–formalin afforded a 22% yield of 1,3-bis(2-fluoro-2,2-dinitroethoxy)-2-fluoro-2-nitropropane (eq 3). The ditriflate underwent rapid decomposition with methanolic potassium methoxide at room temperature, but with refluxing methanol containing suspended sodium sulfate, a 32% yield of 1,3-dimethoxy-2-fluoro-2-nitropropane and a 16% yield of 2-fluoro-3-methoxy-2-nitro-1-propyl triflate were obtained. Sodium sulfate has been used previously as a mild acid scavenger in triflate reactions[7] (eq 4).

$$CF_3SO_2OCH_2CF(NO_2)CH_2OSO_2CF_3 \xrightarrow[Me_2SO]{NaN_3} N_3CH_2CF(NO_2)CH_2N_3 \quad (2)$$

$$CF_3SO_2OCH_2CF(NO_2)CH_2OSO_2CF_3 + FC(NO_2)_2CH_2OH \xrightarrow[CH_2O]{KOH} FC(NO_2)_2CH_2OCH_2CF(NO_2)CH_2OCH_2CF(NO_2)_2 \quad (3)$$

$$CF_3SO_2OCH_2CF(NO_2)CH_2OSO_2CF_3 \xrightarrow[Na_2SO_4]{CH_3OH} CH_3OCH_2CF(NO_2)CH_2OCH_3 + CF_3SO_2OCH_2CF(NO_2)CH_2OCH_3 \quad (4)$$

Ring opening of 3-fluoro-3-nitrooxetane occurred with strong acids. Concentrated hydrochloric acid, hydrobromic acid, and anhydrous triflic acid gave 3-chloro-2-fluoro-2-nitro-1-propanol, 3-bromo-2-fluoro-2-nitro-1-propanol, and

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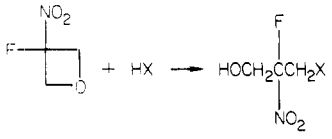
2-fluoro-3-hydroxy-2-nitro-1-propyl triflate, respectively (eq 5). With 50% aqueous sulfuric acid, 2-fluoro-2-

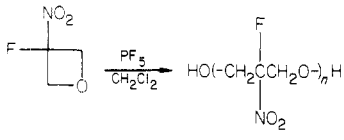


(5)

X = Cl, Br, CF_3SO_3

nitro-1,3-propanediol was obtained. The oxetane did not react, however, with glacial acetic acid at 80 °C, with triflic anhydride in ether at room temperature, or with methanolic strong acids.

Cationic polymerizations of oxetanes are inhibited by electron-withdrawing substituents,[13] and polymerizations of examples with substituents comparable to those of 3-fluoro-3-nitrooxetane have not been reported. An effective catalyst for oxetane polymerizations has been reported to be phosphorus pentafluoride.[14] Reaction of an excess of this catalyst with 3-fluoro-3-nitrooxetane in methylene chloride at room temperature resulted in rapid polymerization (eq 6). A polymeric diol precipitated, which had



(6)

a molecular weight of 2500 (vapor-phase osmometer).

The importance of fluorine in the cyclization of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate to give 3-fluoro-3-nitrooxetane was shown by reactions of nonfluorine-containing analogues. The reaction of 2,2-dinitro-1,3-propanediol with equimolar amounts of pyridine and triflic anhydride in ether gave a 47% yield of 2,2-dinitro-3-hydroxy-1-propyl triflate and a 14% yield of 2,2-dinitro-1,3-propylene ditriflate. Similarly, 2-(hydroxymethyl)-2-nitro-1,3-propanediol gave 3-hydroxy-2-(hydroxymethyl)-2-nitro-1-propyl triflate and 2-(hydroxymethyl)-2-nitro-1,3-propylene ditriflate. Both 2,2-dinitro-3-hydroxy-1-propyl triflate and 3-hydroxy-2-(hydroxymethyl)-2-nitro-1-propyl triflate underwent decomposition with potassium carbonate or triethylamine under the conditions that were used to prepare 3-fluoro-3-nitrooxetane. Aqueous sodium bicarbonate and 2,2-dinitro-3-hydroxy-1-propyl triflate gave 2,2-dinitro-1,3-propanediol.

Experimental Section

NMR and IR spectra were recorded with a Varian T-60 spectrometer and a Perkin-Elmer 700 spectrometer, respectively. A Varian 920 gas chromatograph was used for GLC separations, and a Mechrolab 301A vapor osmometer was used for molecular weight determinations. Previously described safety precautions for nitro compounds[15,16] were observed.

2-Fluoro-2-nitro-1,3-propanediol. A solution of 3.3 g (0.05 mol) of 85% potassium hydroxide in 35 mL of ethanol was added over 15 min to a solution of 11.3 g (0.05 mol) of diethyl fluoronitromalonate[12] in 35 mL of ethanol at −12 to −27 °C. After 30 min, 8.5 mL (0.11 mol) of formalin (37%) was added. The reaction mixture was allowed to warm to room temperature over 1 h and was stirred an additional 2 h. The starting material was consumed completely on the basis of NMR spectra. The reaction mixture was then filtered and the solvent was removed in vacuo. To the residue were added 100 mL of ether and 15 mL (0.15 mol) of pyridine. The ether solution was then decanted, and the remaining orange gum was extracted with 50 mL of acetonitrile. To the combined acetonitrile and ether solutions was added 25 mL (0.15 mol) of trimethylsilyl chloride, and the reaction mixture was then refluxed for 5.5 h and stirred overnight at room temperature. Distillation of the solution gave 10.07 g (70.7%) of 1,3-bis(trimethylsiloxy)-2-fluoro-2-nitropropane: bp 82–83 °C (0.1 mm); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 18 H, $SiMe_3$), 3.85 and 4.13 (s and AB q pattern, 4 H, CH_2); ^{19}F NMR ($CDCl_3$) φ 141.2 (quintet, J = 16 Hz); IR (CH_2Cl_2) 1575, 1360 (NO_2), 1130, 860 ($SiMe_3$), 1090 cm^{-1} (CF). Anal. Calcd for $C_9H_{22}NFSi_2O_4$: C, 38.13; H, 7.82. Found: C, 37.74; H, 7.87.

A solution of the above compound in 100 mL of methanol was refluxed for 4 h and solvent was then removed in vacuo to afford 4.91 g (70.6%) of 2-fluoro-2-nitro-1,3-propanediol: mp 86–87 °C (lit.[11] mp 86–87 °C); ^{1}H NMR (acetone d_6) δ 3.95 (s), 4.23 (AB quartet), 4.80 (t, J = 6 Hz, 2 H, OH); ^{19}F NMR (acetone-d_6) φ 145.6 (quintet, J = 16 Hz); IR (CH_2Cl_2) 3620 (OH), 1575, 1335 (NO_2), 1040 cm^{-1} (CF). An AB quartet and a singlet have been observed previously for CH_2CFNO_2 in the ^{1}H NMR spectrum.[17]

2-Fluoro-3-hydroxy-2-nitro-1-propyl Triflate. A solution of 10.9 mL (0.065 mol) of triflic anhydride in 210 mL of ether was added dropwise to a solution of 17.4 g (0.124 mol) of 2-fluoro-2-nitro-1,3-propanediol and 6.0 mL (0.074 mol) of pyridine in 210 mL of ether. The reaction temperature was kept below 26 °C. After the reaction mixture was stirred for 16 h, the precipitate that formed was filtered and washed with ether (2 × 40 mL). Removal of the ether in vacuo left 26.2 g of a white solid, which was partitioned between 300 mL of methylene chloride and 60 mL of water. The methylene chloride solution was washed with 30 mL of water, dried over sodium sulfate, and chromatographed on a 125-g silica gel column (methylene chloride). Elution with a total of 500 mL of methylene chloride gave 2.2 g (8.9%) of ditriflate. Further elution with 500 mL of 9:1 methylene chloride–ethyl acetate afforded 13.26 g (78.9%) of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate. Recrystallization from methylene chloride–petroleum ether at −10 °C gave an analytical sample: colorless hygroscopic solid; mp 29–30 °C; ^{1}H NMR ($CDCl_3$) δ 2.65 (br s, 1 H, OH), 4.10 (d, J = 14 Hz, 2 H, CH_2OH), 5.07 (AB q, J = 14 Hz, 2 H, $CH_2OSO_2CF_3$); ^{19}F NMR ($CDCl_3$) φ 72.0 (s, 3 F, SO_2CF_3), 139.4 (quintet, J = 14 Hz, 1 F, O_2NCF); IR (CH_2Cl_2) 3625 (OH), 1580, 1350 (NO_2), 1420, 1220, 1140, 900 (SO_2CF_3), 1000 cm^{-1} (CF).

Anal. Calcd for $C_4H_5F_4NSO_6$: C, 17.22; H, 1.86; N, 5.17. Found: C, 17.82; H, 1.75; N, 5.31.

The combined aqueous layers were extracted with ethyl acetate (3 × 100 mL) to give 8.70 g of 2-fluoro-2-nitro-1,3-propanediol.

2-Fluoro-2-nitro-1,3-propylene Ditriflate. A solution of 1.39 g (0.010 mol) of 2-fluoro-2-nitro-1,3-propanediol and 1.8 mL (0.022 mol) of pyridine in 10 mL of chloroform was added dropwise at 0–5 °C to a solution of 5.8 g (0.02 mol) of triflic anhydride in 10 mL of chloroform. After 3 h, the reaction mixture was washed with ice–water (2 × 10 mL) and the chloroform solution was dried over sodium sulfate. The solvent was removed in vacuo, and the residue was chromatographed on a 64-g silica gel column (methylene chloride). Elution with a total of 300 mL of methylene chloride afforded 2.80 g (75.5%) of 2-fluoro-2-nitro-1,3-propylene ditriflate. Recrystallization from methylene chloride–petroleum ether gave an analytical sample: mp 57–58 °C; ^{1}H NMR ($CDCl_3$) δ 4.93 (d, J = 14 Hz); ^{19}F NMR ($CDCl_3$) φ 71.8 (s, 6 F, SO_2CF_3), 136.7 (quintet, J = 14 Hz, 1 F, O_2NCF); IR (CH_2Cl_2) 1595, 1320 (NO_2), 1420, 1220, 1140, 900 (OSO_2CF_3), 1005 cm^{-1} (CF).

Anal. Calcd for $C_5H_4F_7NS_2O_8$: C, 14.90; H, 1.00; N, 3.47. Found: C, 15.30; H, 0.91; N, 3.61.

3-Fluoro-3-nitrooxetane. A solution of 3.1 mL (0.0207 mol) of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in 18 mL of methylene chloride was added dropwise to a solution of 5.42 g (0.020 mol) of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate in 36 mL of methylene chloride. After 75 min, the reaction mixture was chromatographed on a 30-g silica gel column (methylene chloride) to give 2 g of crude product. Vacuum distillation afforded 1.486 g (61.4%) of 3-fluoro-3-nitrooxetane. An analytical sample was obtained by preparative GC (12% QF-1 on Chromasorb W, 100 °C): bp 31 °C (1.5 mm); ^{1}H NMR ($CDCl_3$) δ 4.97 (sextet); ^{19}F NMR ($CDCl_3$) φ 127.7 (quintet, J = 14 Hz); IR (CH_2Cl_2) 1575, 1345 (NO_2), 1000 cm^{-1} (CF); $n_D^{24.5}$ 1.4281.

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Anal. Calcd for $C_3H_4FNO_3$: C, 29.76; H, 3.33; N, 11.58. Found: C, 30.13; H, 3.35; N, 12.07.

The use of the silica gel column for the removal of the DBU triflic acid salt was employed as the salt was not easily extracted from methylene chloride by water. The refractive index of the distilled oxetane was the same as that of the sample isolated by GC.

1,3-Bis(2-fluoro-2,2-dinitroethoxy)-2-fluoro-2-nitropropane. To a solution of 1.545 g (10.0 mmol) of 2-fluoro-2,2-dinitroethanol (FDNE) in 15 mL of 2:1 dioxane–formalin was added 0.665 g (10.0 mmol) of potassium hydroxide (85%). The yellow solution was cooled with an ice bath to 22 °C, and 1.013 g (2.5 mmol) of 2-fluoro-2-nitro-1,3-propylene ditriflate was then added. The temperature of the reaction mixture rose to 32 °C over 6 min, and the pH dropped from 11 to 8. After 1 h the solvent was removed in vacuo, and to the residue were added 5 mL of water and 25 mL of 1:1 carbon tetrachloride-methylene chloride. The water layer was extracted with two 12-mL portions of this solvent, and the combined organic solution was then washed with water (4 × 25 mL), and dried over sodium sulfate. Removal of solvent in vacuo gave 0.64 g of a 3:1 mixture of the di- and monoethers (^{19}F NMR). Chromatography on 25 g of silica gel (2:1 methylene chloride–petroleum ether) gave 0.222 g (21.6%) of 1,3-bis(2-fluoro-2,2-dinitroethoxy)-2-fluoro-2-nitropropane; crystallization from methylene chloride–petroleum ether afforded an analytical sample: mp 52 °C; ^1H NMR (9:1 $CDCl_3$–acetone-d_6) δ 4.2 (d, J = 16 Hz, 4 H, $CH_2CFNO_2CH_2$), 4.70 (d, J = 16 Hz, 4 H, $CH_2CF(NO_2)_2$); ^{19}F NMR (9:1 $CDCl_3$–acetone-d_6) ϕ 109.4 (br m, 2 F, $CF(NO_2)_2$), 138.7 (quintet, J = 16 Hz, 1 F, $CFNO_2$); IR (CH_2Cl_2) 1600, 1320 cm^{-1} (NO_2); d_{25} 1.709.

Anal. Calcd for $C_7H_8F_3N_5O_{12}$: C, 20.45; H, 1.96; N, 17.03. Found: C, 20.47; H, 1.90; N, 16.70.

1,3-Diazido-2-fluoro-2-nitropropane. A solution of 0.407 g (1.0 mmol) of 2-fluoro-2-nitro-1,3-propylene ditriflate in 5.5 mL of dimethyl sulfoxide was stirred at room temperature for 22 h with 0.225 g (3.3 mmol) of sodium azide. The reaction mixture was then diluted with 50 mL of water and extracted with methylene chloride (3 × 17 mL). The methylene chloride solution was washed with water (5 × 25 mL) and dried over sodium sulfate. Removal of the methylene chloride in vacuo afforded 0.195 g (100%) of 1,3-diazido-2-fluoro-2-nitropropane: ^1H NMR ($CDCl_3$) δ 3.87 (d, J = 16 Hz); ^{19}F NMR ($CDCl_3$) ϕ 133.8 (quintet, J = 16 Hz); IR ($CDCl_3$) 2150 (N_3), 1580, 1320 (NO_2) cm^{-1}.

A solution of 0.184 g of 1,3-diazido-2-fluoro-2-nitropropane and 0.159 g (2.27 mmol) of propiolic acid in 1.0 mL of chloroform was allowed to stand at room temperature for 54 h. The resulting precipitate was washed with chloroform to give 0.234 g of 1,3-bis[1-(4-(or 5-)-carboxy-1,2,3-triazolo)]-2-fluoro-2-nitropropane. An analytical sample was crystallized from acetone–carbon tetrachloride: mp 163–170 °C; ^1H NMR (acetone-d_6) δ 5.77 (m, 4 H, CH_2), 7.73 (s, 2 H, CO_2H) and 8.57 (s, 2 H, Ar); ^{19}F NMR (acetone-d_6) ϕ 134.0 (quintet, J = 16 Hz).

Anal. Calcd for $C_9H_8FN_7O_6$: C, 32.84; H, 2.45; N, 29.78. Found: C, 32.44; H, 2.65; N, 29.21.

1,3-Dimethoxy-2-fluoro-2-nitropropane. A mixture of 1.55 g (3.8 mmol) of 2-fluoro-2-nitro-1,3-propylene ditriflate, 31 mL of methanol, and 3.1 g of sodium sulfate was refluxed for 24 h. The reaction mixture was filtered and solvent was removed in vacuo to give 0.649 g of a yellow liquid. Chromatography on silica gel (1:1 methylene chloride–hexane) afforded 0.169 g (15.5%) of 2-fluoro-3-methoxy-2-nitro-1-propyl triflate: ^1H NMR ($CDCl_3$) δ 3.42 (s, 3 H, OCH_3), 3.92 (d, J = 15 Hz, 2 H, CH_2OCH_3), 4.95 (d, J = 15 Hz, 2 H, $CH_2OSO_2CF_3$); ^{19}F NMR ($CDCl_3$) ϕ 72.9 (s, 3 F, SO_2CF_3), 138.0 (quintet, J = 15 Hz, 1 F, $CFNO_2$). A 0.203-g (32.1%) sample of 1,3-dimethoxy-2-fluoro-2-nitropropane was also obtained: ^1H NMR ($CDCl_3$) δ 3.40 (s, 6 H, OCH_3), 3.73 and 4.03 (s and AB q pattern, 4 H, CH_2); ^{19}F NMR ($CDCl_3$) ϕ 138.6 (quintet, J = 16 Hz); IR (CH_2Cl_2) 1580, 1360 cm^{-1} (NO_2).

Anal. Calcd for $C_5H_{10}FNO_4$: C, 35.93; H, 6.03; N, 8.38. Found: C, 36.22; H, 6.24; N, 8.34.

2-Fluoro-3-hydroxy-2-nitro-1-propylpyridinium Triflate. To a solution of 0.271 g (1.0 mmol) of 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate in 2.7 mL of ether was added 0.081 mL (1.0 mmol) of pyridine. After the reaction mixture was stirred for 8 days at room temperature, ^{19}F NMR of the ether solution indicated that a small amount of the original monotriflate still remained. The ether was decanted from the viscous oil that had precipitated. The oil was washed with 2 mL of ether and with 20 mL of methylene chloride, leaving 0.316 g (90.3%) of 2-fluoro-3-hydroxy-2-nitro-1-propylpyridinium triflate: ^1H NMR (acetone-d_6) δ 4.33 (d, J = 16 Hz, 2 H, CH_2OH), 5.35 (1 H, OH), 5.75 (d, J = 16 Hz, 2 H, $CH_2NC_5H_5$); ^{19}F NMR (acetone-d_6) ϕ 78.0 (s, 3 F, SO_2CF_3), 137.5 (quintet, J = 16 Hz, 1 F, $FCNO_2$).

3-Chloro-2-fluoro-2-nitro-1-propanol. To 0.242 g (2.0 mmol) of 3-fluoro-3-nitrooxetane was added 1.0 mL (12 mmol) of concentrated HCl. After being allowed to stand for 30 min at room temperature, the reaction mixture was diluted with 4 mL of water and extracted with ethyl acetate (3 × 5 mL). The ethyl acetate solution was dried over potassium carbonate, and the solvent was then removed in vacuo to give 0.304 g (96.5%) of 3-chloro-2-fluoro-2-nitro-1-propanol. Chromatography on silica gel (9:1 methylene chloride–ethyl acetate) afforded an analytical sample: ^1H NMR ($CDCl_3$) δ 3.08 (br s, 1 H, OH), 4.05 (d, J = 16 Hz, 2 H, $CH_2OH(Cl)$), 4.12 (d, J = 16 Hz, 2 H, $CH_2Cl(OH)$); ^{19}F NMR ($CDCl_3$) ϕ 137.4 (quintet, J = 16 Hz); IR (CH_2Cl_2) 3630 (OH), 1580, 1360 cm^{-1} (NO_2).

Anal. Calcd for $C_3H_5NFClO_3$: C, 22.87; H, 3.20; N, 8.89. Found: C, 22.59; H, 3.41; N, 8.70.

3-Bromo-2-fluoro-2-nitro-1-propanol. To 0.363 g (3.0 mmol) of 3-fluoro-3-nitrooxetane was added 1.5 mL (13.5 mmol) of 48% HBr. After 1 h at room temperature, the reaction mixture was extracted with ether (3 × 10 mL). The ether extract was dried over sodium sulfate and potassium carbonate, and solvent was then removed in vacuo to give 0.564 g (93.1%) of 3-bromo-2-fluoro-2-nitro-1-propanol. Chromatography on silica gel (9:1 methylene chloride–ethyl acetate) afforded an analytical sample: ^1H NMR ($CDCl_3$) δ 3.25 (br t, 1 H, OH), 3.85 (d, J = 16 Hz, 2 H, CH_2Br), 3.92 (AB q, J = 16 Hz, 2 H, CH_2OH); ^{19}F NMR ($CDCl_3$) ϕ 134.0 (quintet, J = 16 Hz); IR (CH_2Cl_2) 3630 (OH), 1580, 1360 cm^{-1} (NO_2).

Anal. Calcd for $C_3H_5NFBrO_3$: C, 17.84; H, 2.50; N, 6.93. Found: C, 17.70; H, 2.53; N, 6.98.

Polymerization of 3-Fluoro-3-nitrooxetane. Phosphorus pentafluoride was bubbled into a solution of 0.121 g (1.0 mmol) of 3-fluoro-3-nitrooxetane in 1.2 mL of methylene chloride. Within a few minutes a solid had precipitated. The addition of PF_5 was stopped, and 0.2 mL of methanol was added. The solid was then filtered, washed well with methylene chloride, and air-dried to afford 0.100 g (82.6%) of poly(3-fluoro-3-nitrotrimethylene ether): mp 233–235 °C; ^1H NMR (Me_2SO-d_6) δ 4.03 (AB q, J = 16 Hz); ^{19}F NMR (Me_2SO-d_6) ϕ 139.8 (m); mol wt (vapor-phase osmometer, DMF, 60 °C) 2500.

2,2-Dinitro-3-hydroxy-1-propyl Triflate and 2,2-Dinitro-1,3-propylene Ditriflate. A solution of 1.7 mL (0.010 mol) of triflic anhydride in 15 mL of ether was added dropwise over a 9-min period at 12–18 °C to a solution of 1.66 g (0.010 mol) of 2,2-dinitro-1,3-propanediol and 0.81 mL (0.010 mol) of pyridine in 15 mL of ether. The mixture was stirred for 2 h at room temperature, and the resulting precipitate was filtered and washed with ether. Removal of ether in vacuo gave 3.0 g of a yellow liquid, which was dissolved in 20 mL of methylene chloride, washed with water, dried over sodium sulfate, and stripped of solvent. The residue was chromatographed on 60 g of silica gel. Elution with 100 mL of methylene chloride and 50 mL of 95:5 methylene chloride–ethyl acetate gave 0.607 g (14.0%) of 2,2-dinitro-1,3-propylene ditriflate. Crystallization from methylene chloride–petroleum ether gave an analytical sample: mp 54–55 °C; ^1H NMR ($CDCl_3$) δ 5.26 (s); ^{19}F NMR ($CDCl_3$) ϕ 72.0 (s); IR (CH_2Cl_2) 1590, 1305 (NO_2), 1425, 1220, 1140, 930 (OSO_2CF_3), 1000 cm^{-1} (CF).

Anal. Calcd for $C_5H_4N_2F_6S_2O_{10}$: C, 13.96; H, 0.94; N, 6.51. Found: C, 14.00; H, 1.02; N, 6.29.

Further elution with 9:1 methylene chloride–ethyl acetate afforded 1.4 g (46.8%) of 2,2-dinitro-3-hydroxy-1-propyl triflate. Crystallization from methylene chloride–petroleum ether gave an analytical sample: mp 43–44 °C; ^1H NMR ($CDCl_3$) δ 2.76 (br s, 1 H, OH), 4.52 (s, 2 H, CH_2OH), 5.21 (s, 2 H, $CH_2OSO_2CF_3$); ^{19}F NMR ($CDCl_3$) ϕ 72.4 (s); IR (CH_2Cl_2) 3620 (OH), 1585, 1320 (NO_2), 1420, 1220, 1140, 840 (OSO_2CF_3), 995 cm^{-1} (CF).

Anal. Calcd for $C_4H_5N_2F_3SO_8$: C, 16.11; H, 1.69; N, 9.40. Found: C, 16.27; H, 1.68; N, 9.67.

3-Hydroxy-2-(hydroxymethyl)-2-nitro-1-propyl Triflate and 2-(Hydroxymethyl)-2-nitro-1,3-propylene Ditriflate. A

solution of 1.9 mL (11.0 mmol) of triflic anhydride in 15 mL of 9:1 ether–ethyl acetate was added dropwise over 15 min at 18–21 °C with ice-bath cooling to a solution of 1.51 g (10.0 mmol) of 2-(hydroxymethyl)-2-nitro-1,3-propanediol and 0.90 mL (11.0 mmol) of pyridine in 30 mL of 1:1 ether–ethyl acetate. The mixture was stirred at room temperature for 1 h, and the resulting precipitate was filtered and washed with ether. Sovent was removed, and the residue wash chromatographed on 111 g of silica gel (4:1 methylene chloride–ethyl acetate) to give 0.671 g (16.2%) of 2-(hydroxymethyl)-2-nitro-1,3-propylene ditriflate. Crystallization from methylene chloride–petroleum ether gave an analytical sample: mp 56–57 °C; ^{1}H NMR ($CDCl_3$) δ 2.70 (br s, 1 H, OH), 4.05 (s, 2 H, CH_2OH), 4.90 (s, 4 H, $CH_2OSO_2CF_3$); ^{19}F NMR ($CDCl_3$) ϕ 72.4 (s); IR (CH_2Cl_2) 3600 (OH), 1570, 1355 (NO_2), 1420, 1220, 1150, 830 (OSO_2CF_3), 980 cm^{-1} (CF).

Anal. Calcd for $C_6H_6F_6NSO_9$: C, 17.36; H, 1.70; N, 3.37. Found: C, 18.59; H, 1.75; N, 3.64.

Continued elution afforded 1.258 g (44.4%) of 3-hydroxy-2-(hydroxymethyl)-2-nitro-1-propyl triflate. Crystallization from methylene chloride–petroleum ether gave an analytical sample: mp 72–73 °C; ^{1}H NMR (acetone-d_6) δ 4.03 (s, 4 H, CH_2OH), 4.47 (s, 2 H, OH), 5.10 (s, 2 H, $CH_2OSO_2CF_3$); ^{19}F NMR (acetone-d_6) ϕ 74.8 (s); IR ($CDCl_3$) 3610, 3380 (OH), 1560, 1360 (NO_2), 1420, 1225, 1150, 870, (OSO_2CF_3), 980 cm^{-1} (CF).

Anal. Calcd for $C_5H_8F_3NSO_7$: C, 21.21; H, 2.85; N, 4.95. Found: C, 21.02; H, 2.81; N, 4.76.

Registry No. 2-Fluoro-2-nitro-1,3-propanediol, 4776-99-2; 2-fluoro-3-hydroxy-2-nitro-1-propyl triflate, 70187-43-8; 2-fluoro-2-nitro-1,3-propylene ditriflate, 75233-63-5; 3-fluoro-3-nitrooxetane, 70187-44-9; 1,3-bis(2-fluoro-2,2-dinitroethoxy)-2-fluoro-2-nitropropane, 75233-64-6; 1,3-diazido-2-fluoro-2-nitropropene, 75233-65-7; 1,3-dimethoxy-2-fluoro-2-nitropropane, 75233-66-8; 2-fluoro-3-hydroxy-2-nitro-1-propylpyridinime triflate, 75233-68-0; 3-chloro-2-fluoro-2-nitro-1-propanol, 75233-69-1; 3-bromo-2-fluoro-2-nitro-1-propanol, 75233-70-4; poly(3-fluoro-3-nitromethylene ether), 75232-62-1; 2,2-dinitro-3-hydroxy-1-propyl triflate, 75233-71-5; 2,2-dinitro-1,3-propylene ditriflate, 75233-72-6; 3-hydroxy-2-(hydroxymethyl)-2-nitro-1-propyl triflate, 75233-73-7; 2-(hydroxymethyl)-2-nitro-1,3-propylene ditriflate, 75247-60-8; diethyl fluoronitromalonate, 680-42-2; 1,3-bis(trimethylsiloxy)-2-fluoro-2-nitropropane, 75233-74-8; triflic anhydride, 358-23-6; FDNE, 17003-75-7; propiolic acid, 471-25-0; 1,3-bis[1-(4-(or 5-)-carboxy-1,2,3-triazolo)]-2-fluoro-2-nitropropane, 75232-63-2; 2-fluoro-3-methoxy-2-nitro-1-propyl triflate, 75233-75-9; 2-(hydroxymethyl)-2-nitro-1,3-propanediol, 126-11-4.

New Synthesis of Isoxazoles and Isothiazoles. A Convenient Synthesis of Thioenaminones from Enaminones

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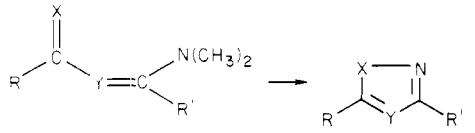
The reaction of 1-aryl-3-(dimethylamino)-2-propen-1-ones (enaminones) and 1-aryl-3-(dimethylamino)-2-propene-1-thiones (thioenaminones) with hydroxylamine-*O*-sulfonic acid gave, respectively, isoxazoles in 76–84% yields and isothiazoles in 60–65% yields. The reaction of enaminones with phosphorus oxychloride, followed by treatment with sodium perchlorate and reaction with sodium sulfide, gave thioenaminones in 40–73% yields.

Recently, we described a general method[1] for the synthesis of 1,2,4-thiadiazoles **4** in which the (dimethylamino)alkylidene moiety was utilized as a masked acyl function.[1-5] This method involved the reaction of *N'*-(thioaroyl)-*N,N*-dimethylamidines **1** with an aminating agent such as *O*-mesitylenesulfonylhydroxylamine (MSH) or hydroxylamine-*O*-sulfonic acid (HSA) to give 1,2,4-thiadiazoles **4** in excellent yields.



1, X = S; Y = N
2, X = O; Y = CH
3, X = S; Y = CH

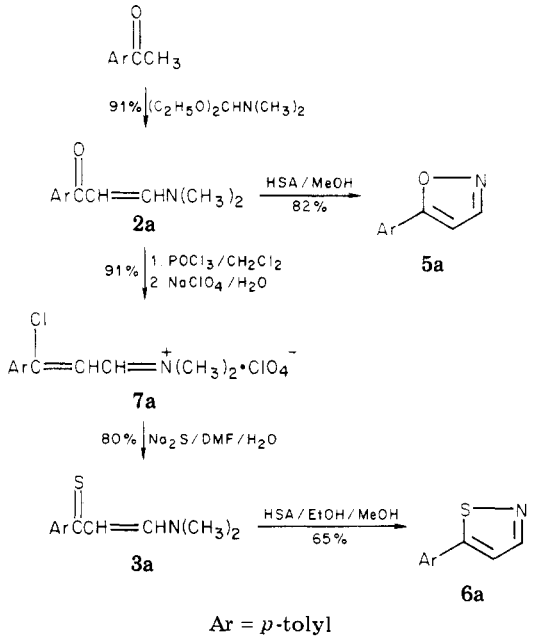
4, X = S; Y = N
5, X = O; Y = CH
6, X = S; Y = CH

We now report the extension of the method to the synthesis of isoxazoles **5** and isothiazoles **6** by the reaction of enaminones **2** and thioenaminones **3** with HSA. We also report a convenient synthesis of thioenaminones **3** from enaminones **2**.

Results and Discussion

Enaminones **2** were prepared in 87–93% yields by the reaction of acetophenones with *N,N*-dimethylalkanamide diethyl acetal or dimethyl acetal.[3,6-8] Thioenaminones **3** were prepared in 40–73% yields by the reaction of the

Scheme I



Ar = *p*-tolyl

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