when 13 was recrystallized from methanol.

Thermolysis of 6. A solution of 0.500 g of 6 in 25 mL of decalin was refluxed for 132 h. The decalin was evaporated and the residue slurried well in 15 mL of Et_2O and filtered. The crude *N*-phenylphthalimide (0.150 g, 56%) melted at 195 °C and was recrystallized from MeOH to give material melting at 202–203 °C. The ether was evaporated and an IR spectrum of the residue was obtained. It showed the peaks common to *N*-phenylphthalimide and also an absorption band of high intensity at 2150 cm^{-1} which is characteristic for a carbodiimide.

Acknowledgment. We thank Dr. William Vanden-Heuvel, Merck Sharp & Dohme Laboratories, Rahway, NJ, for obtaining and commenting on the mass spectra of many of the 2,4-benzodiazepine derivatives.

Registry No. 1a, 66730-24-3; **1b**, 71382-62-2; **1c**, 71382-63-3; **1d**, 71382-64-4; **2b**, 71382-65-5; **2d**, 71382-66-6; **3a**, 71382-67-7; **3b**, 71382-68-8; **3d**, 71382-69-9; **4**, 71382-70-2; **5**, 71382-71-3; **6**, 71382-72-4; **7**, 71382-73-5; **8**, 71382-74-6; **9**, 71382-75-7; **9a**, 71382-76-8; **10**, 5388-42-1; **11**, 622-16-2; **12**, 71382-77-9; **13**, 71382-78-0; *N,N'*-bis(4-bromophenyl)acetamidine, 71382-79-1; *o*-phthaloyl chloride, 88-95-9; *N,N'*-bis(4-ethoxyphenyl)acetamidine, 101-93-9; *N,N'*-diphenyl-α-phenylacetamidine, 19376-79-5; succinyl chloride, 543-20-4; furan-3,4-dicarboxylic acid, 3387-26-6; furan-3,4-dicarbonyl chloride, 52762-41-1; *N,N'*-diphenylacetamidine, 621-09-0; 2,5-dimethyl-1-phenylpyrrole-3,4-dicarboxylic acid, 52175-96-9; 2,5-dimethyl-1-phenylpyrrole-3,4-dicarbonyl chloride, 71411-04-6; 1,2,3-triphenylguanidine, 101-01-9; *o*-chloromethylbenzoyl chloride, 42908-86-1; *p*-nitrobenzoyl chloride, 122-04-3; decalin, 91-17-8; picric acid, 88-89-1; *o*-carbomethoxybenzoyl chloride, 4397-55-1; *N*-phenylphthalimide, 520-03-6.

Chemistry of Ethenesulfonyl Fluoride. Fluorosulfonylethylation of Organic Compounds[1]

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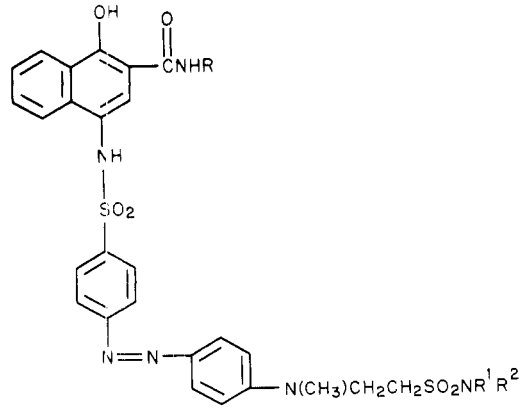
Ethenesulfonyl fluoride (ESF), a stable compound that is readily available from commercial isethionic acid (2-hydroxyethanesulfonic acid) or 2-chloroethanesulfonyl chloride, was shown to be a highly reactive yet selective and versatile intermediate in the synthesis of a wide variety of organosulfur compounds. ESF reacted with active methylene compounds, amines, sulfinates, and thiols to afford 2-fluorosulfonylethyl derivatives in generally excellent yields. The fluorosulfonyl group was stable to most reaction conditions but could be converted by simple, one-step procedures to sulfonamides, sulfonylimidazolides, and sulfonates and to sulfonic acids. ESF reacted with 2-aminoheterocyclic compounds such as 2-aminopyridine to produce fused 1,2,4-thiadiazine 1,1-dioxides, and it reacted with simple enamines to give 2-aminocyclobutanesulfonyl fluorides. Excellent yields resulted from alkylation of 3-amino-2-butenoates with ESF. Both classes of enamine products could be hydrolyzed to give fluorosulfonylated aliphatic and alicyclic ketones and aldehydes. ESF underwent cycloaddition to 2-methoxyfuran to yield 1-methoxy-6-(fluorosulfonyl)-7-oxabicyclo[2.2.1]hept-2-ene, which was hydrolyzed to 2-(fluorosulfonyl)phenol in water. The general utility of ESF in synthesis was demonstrated by its application in the preparation of over 100 otherwise difficultly accessible new compounds.

In the course of work on the design and synthesis of dyes, we required a general and versatile technique for modifying the aqueous solubility of azo dyes by introduction of side-chain sulfonamide groups. For example, introduction of the function $CH_2CH_2SO_2NR^1R^2$ (R^1, R^2 = H or alkyl) into compounds such as



R, R^1, R^2 = H or alkyl

was desired. Since structural modification, or "fine tuning", of this type is essential to many branches of organic chemistry (for example, pharmaceuticals, pesticides, herbicides, and dyes), our findings are presented here regarding the utility of fluorosulfonylethylation reactions of ethenesulfonyl fluoride (**1**, ESF) in this type of organic synthesis. The cycloaddition and heterocyclization chemistry of ESF are also described.

Michael addition of aromatic amines to ethenesulfonamides appeared initially to offer the most direct route to the compounds we sought. Unfortunately, we were unable

$$ArNHR + CH_2{=}CHSO_2NR^1R^2 \rightarrow Ar(R)NCH_2CH_2SO_2NR^1R^2$$

R, R^1, R^2 = H or alkyl

to reproduce the preparation of ethenesulfonamide[2] in sufficient purity and quantity for our purposes. Efforts to prepare sulfonamides from the more readily accessible β-anilinoethanesulfonic acids were also unsuccessful.

$$Ar(R)NCH_2CH_2SO_3H \not\rightarrow Ar(R)NCH_2CH_2SO_2NR^1R^2$$

Goldberg[3] described the stepwise reaction of aniline with 2-chloroethanesulfonyl chloride to give 2-anilinoethanesulfonanilide, but the method did not appear suitable for

$$C_6H_5NH_2 + ClCH_2CH_2SO_2Cl \rightarrow [CH_2{=}CHSO_2NHC_6H_5] \rightarrow C_6H_5NHCH_2CH_2SO_2NHC_6H_5$$

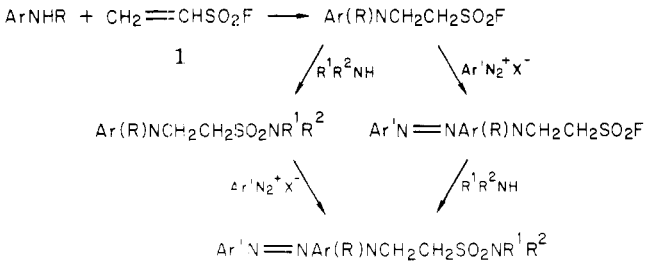
(1) R. D. Burpitt, paper presented in part at the 26th Southeastern Regional Meeting of the American Chemical Society, Oct. 24, 1974; Paper No. 223.

(2) A. S. Matlack, *J. Org. Chem.*, **23**, 729 (1958).

(3) A. A. Goldberg, *J. Chem. Soc.*, 464 (1945).

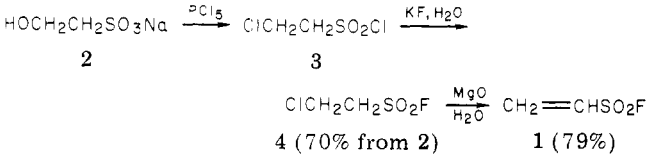
0022-3263/79/1944-3847$01.00/0

Scheme I



R, R^1, R^2 = H or alkyl; Ar = aryl

Scheme II



preparing the corresponding alkyl sulfonamides. Patent literature[4] discloses the reaction of ammonia with 2-chloroalkanesulfonyl fluorides to give either alkenesulfonyl fluorides or 2-aminoalkanesulfonamides.

With this background, we decided that our synthesis objectives might be met by reacting amine-containing diazonium, or coupler, dye components with ethenesulfonyl fluoride (ESF) (1). We expected the resultant 2-(arylamino)ethanesulfonyl fluorides to be convertible to sulfonamides either before or after azo coupling (Scheme I).

Although ESF has been known for a number of years, the chemistry of this interesting difunctional compound has been little investigated. In the course of using ESF in dye chemistry, we have explored its reactivity with nitrogen, sulfur, phosphorus, oxygen, and carbon nucleophiles, with enamines, with dienes, and in preparing various novel heterocycles.

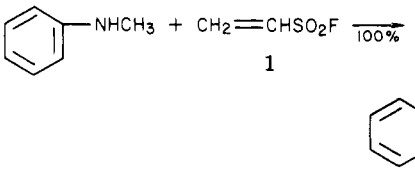
Results and Discussion

Ethenesulfonyl Fluoride (1, ESF). ESF has been prepared chiefly by treating the difficultly accessible and unstable ethenesulfonyl chloride with aqueous KF,[5] by heating 2-chloroethanesulfonyl chloride (3) with dry KF (yield 46%),[6] and by reacting 2-chloroethanesulfonyl fluoride (4) with MgO in water.[7] We found the last route to be the most efficient and used it to prepare 1 in kilogram batches. The overall route from the commercially available isethionic acid sodium salt (2) is given in Scheme II. (See the Experimental Section and supplementary material for precautions regarding the toxic lachrymators 1, 3, and 4.)

The previously reported chemistry of 1 includes chlorination to give 1,2-dichloroethanesulfonyl fluoride,[8] reaction with diazomethane to give (fluorosulfonyl)cyclopropane,[8] reaction with diethylamine to give 2-(diethylamino)ethanesulfonyl fluoride[9] and with ethanethiol to give 2-(ethylthio)ethanesulfonyl fluoride,[9] reaction with diethyl phosphite to give 2-(diethoxyphosphinyl)ethanesulfonyl fluoride,[10] Diels–Alder reaction with cyclopentadiene, cyclohexadiene, and anthracene,[11] and a variety of polymerization and copolymerization processes.[12]

Reaction of ESF with Aromatic Amines. We found that *N*-alkylanilines reacted cleanly with ESF either neat or in solution to afford 2-(*N*-alkylanilino)ethanesulfonyl fluorides in excellent yields.

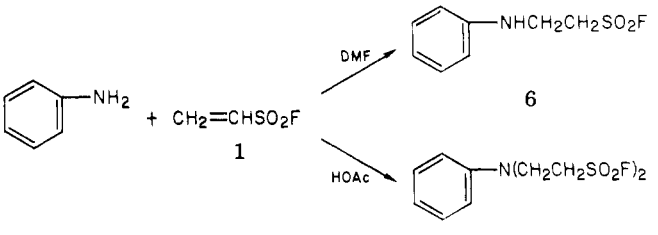
Thus *N*-methylaniline reacted exothermically with ESF to give 5 in quantitative yield. Adduct 5 was also obtained



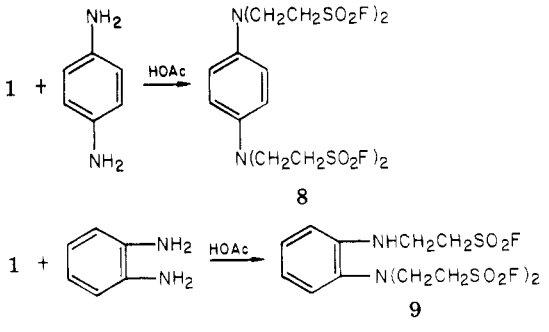
by reacting *N*-methylaniline with 4 in the presence of excess aniline or triethylamine, but the yield was lower (88%) and the workup was complicated by the presence of excess amine. Thus, in general, we found fluorosulfonylethylation using pure ESF superior to that using ESF generated in situ.

The versatility of the fluorosulfonylethylation reaction is shown by the variety of structures listed in Table I.

An interesting solvent effect was seen in the reaction of ESF with aniline. With excess aniline in *N*,*N*-dimethylformamide (DMF) solution, the 1:1 adduct 6 was obtained, whereas in acetic acid the 2:1 adduct 7 was the sole product.



Reaction of *p*-phenylenediamine with 1 gave tetrakis adduct 8, whereas formation of tris product 9 from *o*-phenylenediamine probably reflects steric control.



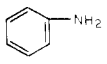
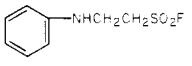
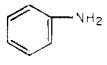
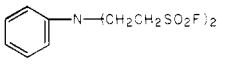
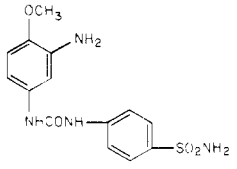
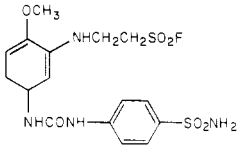
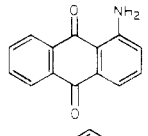
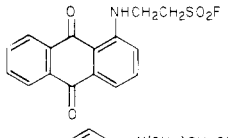
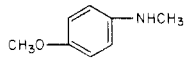
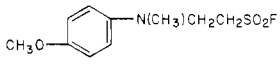
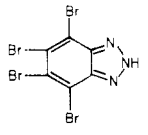
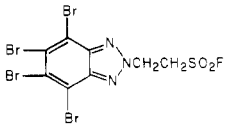
Hydroxy groups did not interfere with the fluorosulfonylethylation of amino groups (see supplementary material and Table I).

Sulfonamides from 2-Aminoethanesulfonyl Fluorides. In no case of the fluorosulfonylethylation

(4) W. Friedlander, U.S. Patent 3 235 593 (1966).
(5) R. M. Hedrick, U.S. Patent 2 653 973 (1953).
(6) (a) O. Scherer and P. Schächer, U.S. Patent 2 783 275 (1957); (b) L. Z. Soborovskii, B. M. Gladshtein, V. N. Chernetskii, and M. I. Kiseleva, *J. Gen. Chem. USSR (Engl. Transl.)*, **28**, 1913 (1958).
(7) O. Scherer and P. Schächer, U.S. Patent 2 884 452.
(8) B. M. Gladshtein, V. N. Chernetskii, M. I. Kiseleva, and L. Z. Soborovskii, *J. Gen. Chem. USSR (Engl. Transl.)*, **28**, 2145 (1958).
(9) B. M. Gladshtein, E. I. Polyanskaya, and L. Z. Soborovskii, *J. Gen. Chem. USSR (Engl. Transl.)*, **31**, 787 (1961).
(10) K. A. Petrov and A. A. Neimysheva, *J. Gen. Chem. USSR (Engl. Transl.)*, **29**, 2991 (1959).
(11) (a) H. Daeniker and J. Druey, *Helv. Chim. Acta*, **45**, 1972 (1962); (b) U.S. Patent 3 136 787.
(12) See, for example: (a) W. Kern, *Makromol. Chem.*, **39**, 1 (1960); (b) *Chem. Abstr.*, **51**, 16003 (1958); (c) **53**, 2694*i* (1959); (d) **55**, 1062 (1961); (e) **72**, 79585 (1970).

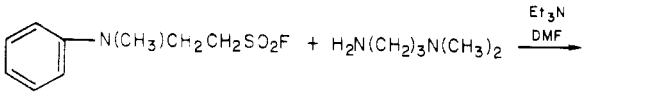
Table I. Fluorosulfonylethylation of Aromatic Amines[a,b]

ArNHR + ESF → Ar(R)NCH$_2$CH$_2$SO$_2$F

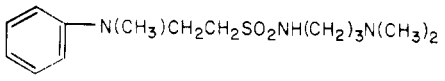
amine	reactn cond[c]	product	text no.	% yield[d]	mp (bp), °C
	DMF, 50 °C		6	86	103-105 (0.5 mm)
	HOAc, 25-32 °C		7	76	86-88
	DMF, 50 °C		10	79	205 dec
	HOAc, 100 °C, 5 h		11[e]	87	203-205
	neat, <100 °C		12	93	52.5-53.5
	pyridine, 100 °C, 1 h		13	77	199-201

[a] All new compounds have IR and NMR spectra consistent with the proposed structures, and elemental analyses (C, H, N, S, F) are within 0.4% of theory. [b] See supplementary material for additional examples of this reaction. [c] Amines were reacted with the calculated amount of ESF under the conditions listed. [d] All yields refer to isolated, purified products. Reactions were generally run at a 0.05-0.5-mol scale. [e] See U.S. Patent 3 952 029 for further examples of [[2-(fluorosulfonyl)ethyl]amino]anthraquinones.

reaction (Table I) did we observe attack of aryl amine on the sulfonyl fluoride group to give sulfonanilides. Indeed, sulfonyl fluoride **12** (see Scheme IV) did not react with excess aniline even at 100 °C. In contrast to this inert behavior with aryl amines, addition of the fluoride to excess aqueous ammonia or alkylamine, either neat or with an inert solvent, gave the corresponding sulfonamides. When an equivalent amount of the amine was used along with triethylamine, triethylenediamine, or 1,8-bis(dimethylamino)naphthalene, the reaction did not go to completion. An equilibrium involving the hydrofluoride salts of both amines was probably responsible. The best yields of sulfonamides were obtained with a two- to fourfold excess of amine; however, a 77% yield of **16** was obtained with **5** and only a 10% excess of *N,N*-dimethylpropanediamine.



5



16

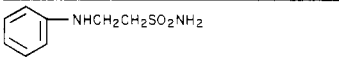
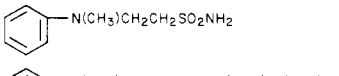
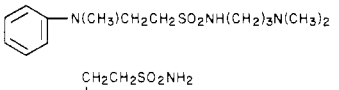
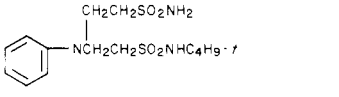
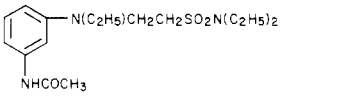
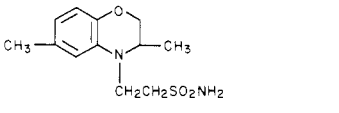
Table II lists representative 2-(arylamino)ethanesulfonamides prepared from the corresponding sulfonyl fluorides.

Of particular interest was the ability of ESF fluorosulfonylethylation chemistry to provide otherwise awkwardly obtained mixed sulfonamides such as **17** (Scheme III).

Early concern regarding the possibility of "reverse-Michael" fragmentation during subsequent manipulation led us to examine the chemistry of ESF–*N*-methyl-*p*-anisidine adduct **12** in more detail (Scheme IV). Reaction of **12** with concentrated aqueous caustic gave sodium sulfonate **21** in good yield, but treatment with sodium methoxide–methanol gave a modest yield of methyl sul-

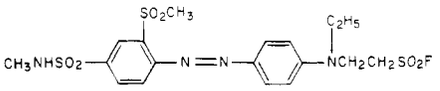
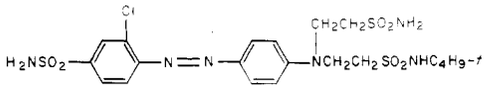
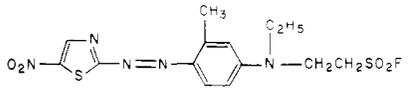
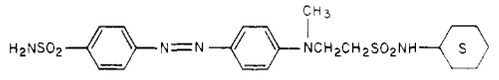
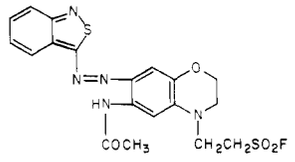
Table II. Sulfonamides from 2-Aminoethanesulfonyl Fluorides[a,b]

Ar(R)NCH$_2$CH$_2$SO$_2$F + HNR^{1}R^2 → Ar(R)NCH$_2$CH$_2$SO$_2$NR^{1}R^2

sulfonamide	text no.	% yield[c,d]	mp, °C
	14	72	77-79
	15	87	88-89
	16	77	syrup
	17	65	156-159
	18	55	syrup
	19	41	126-127

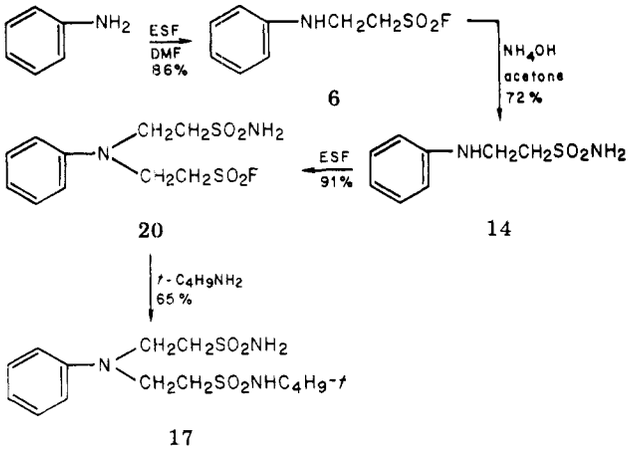
[a] All new compounds have IR and NMR spectra in agreement with proposed structures, and elemental analyses (C, H, N, S) are within 0.4% of theory. [b] See supplementary material for further examples of this reaction. [c] Yields for isolated, purified products are given. [d] See Experimental Section for examples of typical reaction conditions.

Table III. Azo Dyes Prepared via ESF Chemistry[a,b]

text no.	structure	λ_{max} ($10^{-4}\epsilon$)[c]
26		451 (3.05)
27		438 (2.73)
28		564 (4.36)
29		424 (2.87)
30		568 (2.63)

[a] Dyes were prepared from intermediates listed in Table I and II, or in the supplementary material, by standard coupling methodology. See Experimental Section for a typical procedure. [b] All new compounds had IR and NMR spectra in accord with proposed structures, and elemental analyses (C, H, N, S, F) were within 0.4% of theory. [c] In acetone solution.

Scheme III



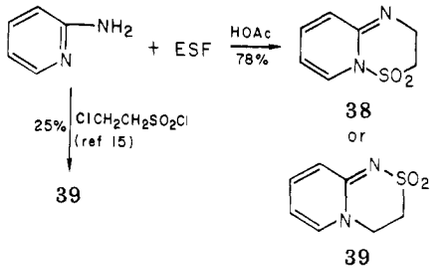
fonate **22** accompanied by a substantial amount of *N*-methyl-*p*-anisidine. Prolonged refluxing of compound **12** with glacial acetic acid resulted in conversion to the anhydrous, readily isolable sulfonic acid **23**; acetyl fluoride was observed as a byproduct. This route allowed "one-pot", water-free preparation of compounds $ArNRCH_2CH_2SO_3H$, since **12** itself was prepared in acetic acid solvent. No reaction between **12** and triethylamine occurred. Sulfonylimidazole **24** was prepared in 67% yield. Finally, we noted that structures of the type **12** oxidized to 2-aminoethenesulfonyl fluorides **25** with active manganese dioxide. The chemistry of these novel, "push–pull" olefins has been described elsewhere.[13]

Fluorosulfonyl and Sulfonamido Azo Dyes. Azo dyes of the type dye-$NRCH_2CH_2SO_2X$ (X = F, OH, NH_2, NHR^1, or NR^1R^2) were, at this point, readily available by way of intermediates of the types given in Tables I and II. Table III lists a representative sample of the extensive series of compounds prepared.

The ESF chemistry developed so far made possible several efficient and flexible approaches to our original objective, compounds of the type **31**. Scheme V illustrates routes to **31** (R = alkyl, R^1 = H, R^2 = C_4H_9-*t*). Diazonium salt **32**, available through conventional chemistry, reacted with sulfonamide **33** to give **31** directly. Alternatively, **32** and **5** were allowed to react to form sulfonyl fluoride **34**, from which **31** was obtained after refluxing in *tert*-butylamine. Synthesis of a series of compounds **31** (R, R^1, R^2 = H or alkyl) was carried out by utilizing both of these routes.

However, routes such as shown in Scheme VI failed due to partial decomposition of the sulfonamide **35** upon attempted conversion to sulfonyl chloride **36**. The success of the routes of Scheme V and the failure of the route of Scheme VI illustrate the versatility of ESF chemistry in avoiding synthesis roadblocks.

Heterocyclic Compounds from ESF Fluorosulfonylethylation. Reaction of ESF with 2-aminopyridine did not give the expected fluorosulfonylethyl derivative. Instead, a compound, $C_7H_8N_2O_2S$, was obtained in 78% yield. Two structures, **38** and **39**, appeared



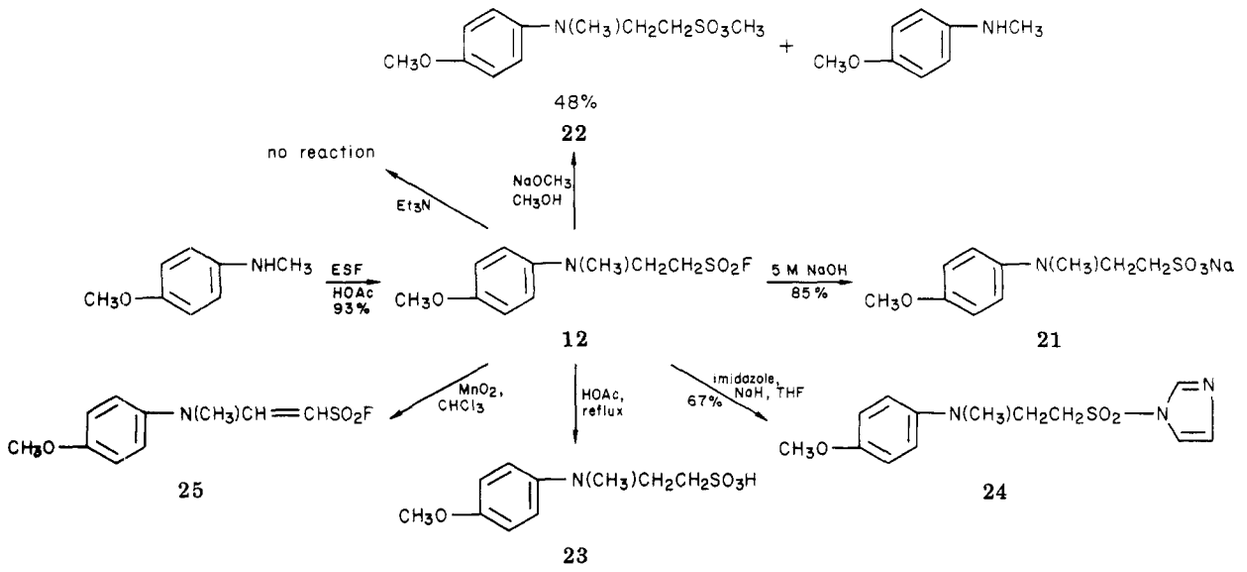
to be possible for this substance. In 1973, Étienne et al.[14] reported the reaction of 2-aminopyridine with 2-chloroethanesulfonyl chloride to give a low yield of **39**, possibly through the intermediacy of ethenesulfonyl chloride. Although our ESF product was identical with that of Étienne, we felt that it would be desirable to establish the structure more rigorously.

Mass, infrared, ^{1}H NMR, and ^{13}C NMR analyses did not allow an unequivocal assignment. Hydrochloric acid treatment only gave the salt, and base hydrolysis afforded only the sodium salt of 2-hydroxypyridine. An approach that did confirm structure **39** is given in Scheme VII.

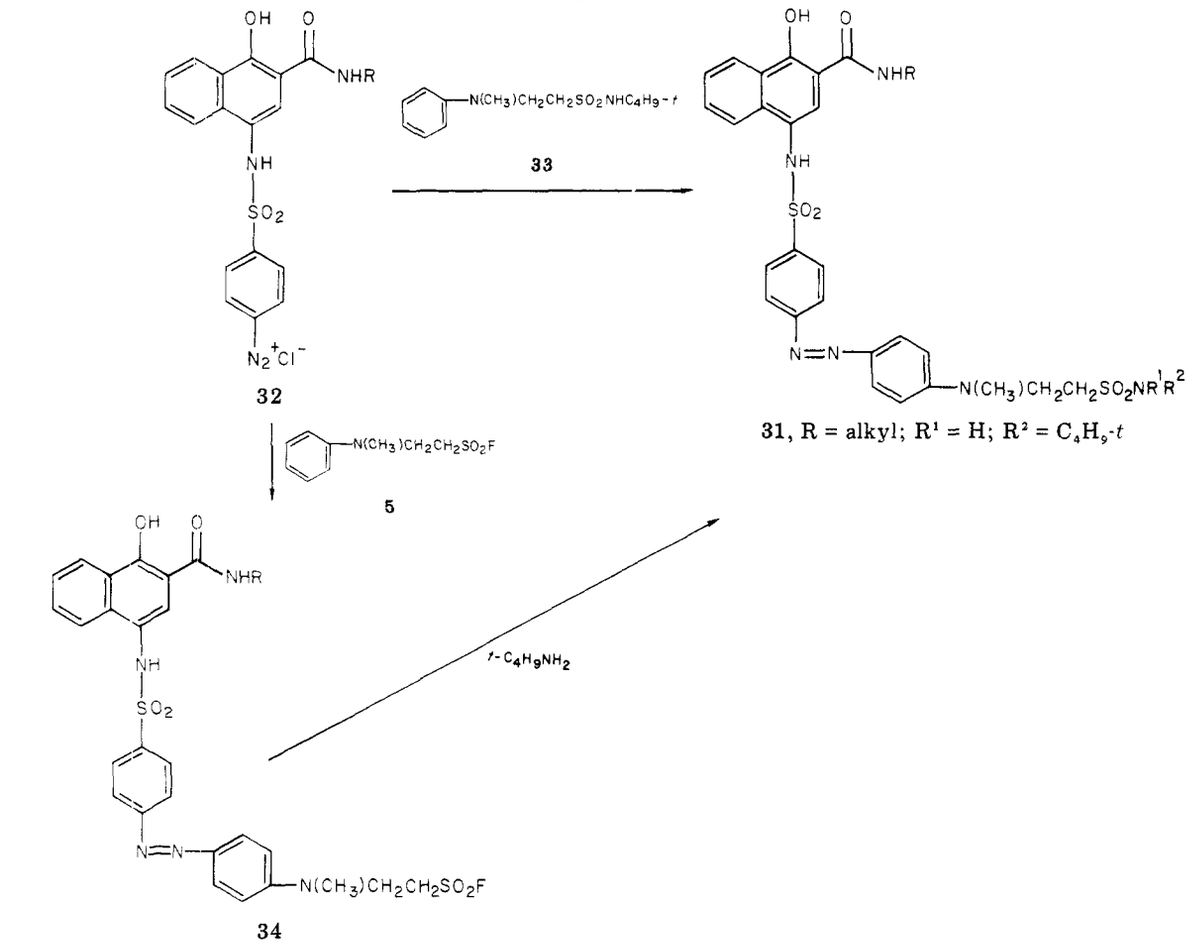
(13) J. A. Hyatt and J. J. Krutak, *J. Org. Chem.*, **42**, 169 (1977).

(14) A. Étienne, A. LeBerre, and J.-P. Giorgetti, *Bull. Soc. Chim. Fr.*, 985 (1973).

Scheme IV

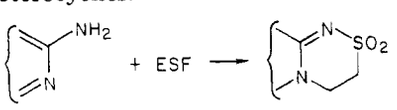


Scheme V



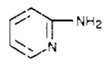
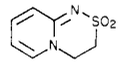
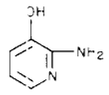
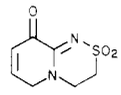
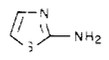
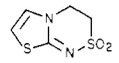
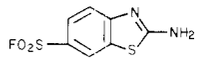
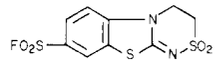
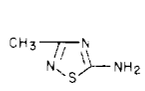
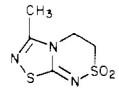
Hydrogenation of the 2-aminopyridine–ESF adduct **39** gave a tetrahydro compound **40**. Reaction of ESF with 2-hydroxypyridine gave sulfonyl fluoride **41** (IR 6.0 μm). This substance was converted to sulfonamide **42** and then hydrogenated to give amide **43**. When heated with phosphorus oxychloride, **43** was converted to the bicyclic sulfonamide **40**, thus establishing the structure by unequivocal synthesis.

The generality of this procedure for synthesis of fused 1,2,4-thiadiazine 1,1-dioxides was established by preparation of the series of examples listed in Table IV. The generally good yields obtained made this route the most attractive for these analogues of known[14,15] diuretic and biocidal heterocyclics.



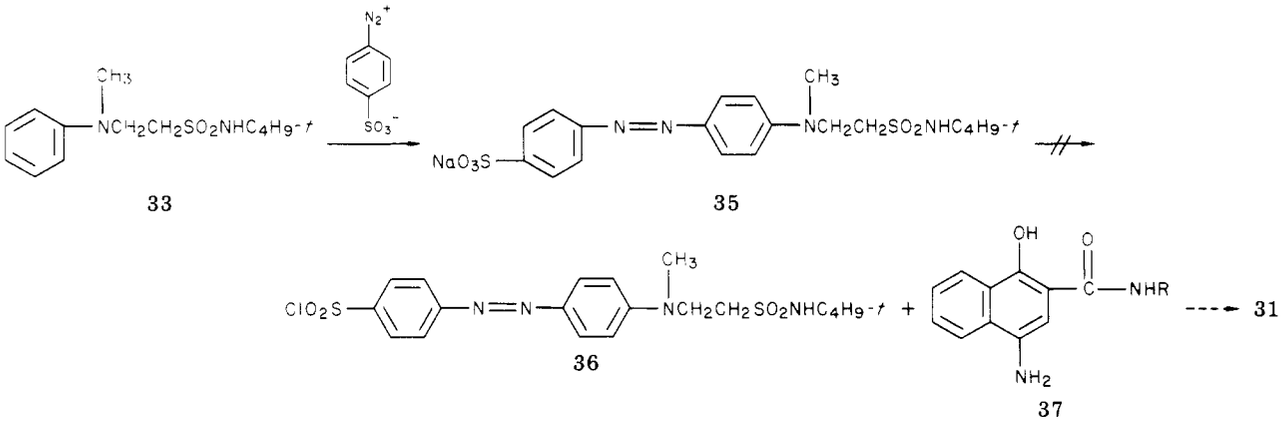
(15) French Patent 1 485 701 (1966).

Table IV. Fused 1,2,4-Thiadiazine 1,1-Dioxides from ESF and Heterocyclic Amines[a,b]

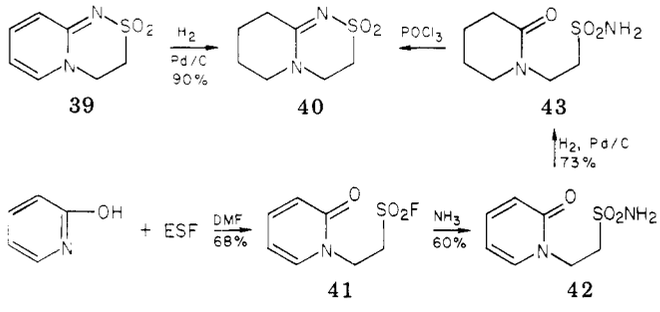
starting amine	product	text no.	% yield[c,d]	mp, °C
		39	78	189-191
		44	40	265 dec
		45	58	191.5-193.5
		46	81	320 dec
		47	74	194.5-196.5

[a] For further examples of compounds in this series, see supplementary material. [b] All new compounds had IR and NMR spectra consistent with the proposed structures, and elemental analyses (C, H, N, S) were within 0.4% theory. [c] Reactions were carried out in acetic acid at 100 °C. [d] Yields are for isolated, purified products.

Scheme VI



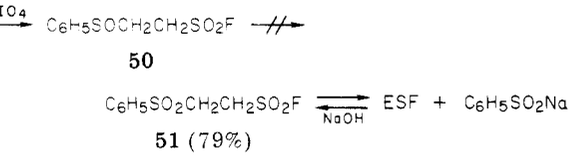
Scheme VII



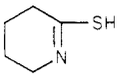
Fluorosulfonylethylation of Thio Compounds. Both alkyl and aryl thiols reacted with ESF to give fluorosulfonylethylated derivatives. The reaction was slow at

$$RSH + ESF \rightarrow RSCH_2CH_2SO_2F$$
$$48,\ R = n\text{-}C_4H_9\ (48\%)$$
$$49,\ R = C_6H_5\ (70\%)$$

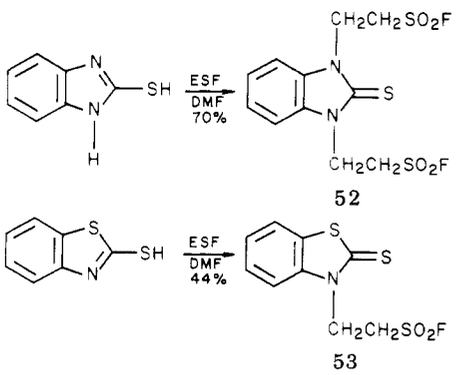
room temperature, but it was accelerated by tributylphosphine catalysis.[16] Compound **49** was smoothly oxidized to the sulfoxide **50** with sodium metaperiodate, and the corresponding sulfone **51** was obtained from ESF and sodium phenylsulfinate. We were unable to convert **50** to **51** directly. Unlike compounds of the type $ArNHCH_2CH_2SO_2F$, sulfone **51** underwent a "reverse-Michael" addition upon treatment with aqueous base. With thiols



of the type



reaction with ESF generally gave the *N*-fluorosulfonylethylated product. Cyclization to give heterocycles was not observed in this series:



(16) D. A. White and M. M. Baizer, *Tetrahedron Lett.*, 3597 (1973).

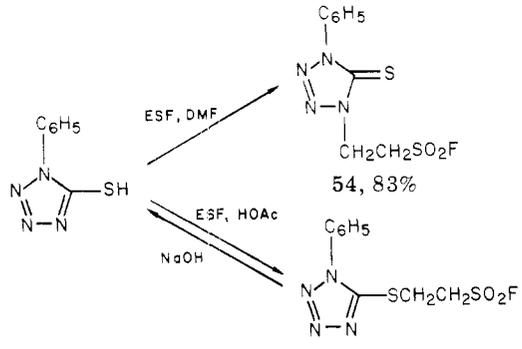
Table V. Fluorosulfonylethylation of Active Methylene Compounds[a,b]

$$XCH_2CN + 2ESF \xrightarrow{Et_3N} FO_2SCH_2CH_2CX(CN)CH_2CH_2SO_2F$$

text no.	X	% yield	mp, °C
56	CO_2CH_3	88	88-89
57	CN	64	120-122
58	$SO_2C_6H_5$	77	182-184
59	$SO_2OC_6H_5$	77	100-102
60	SO_2F	12.5	103-105

[a] Product structures are supported by IR and NMR spectra and elemental analyses (C, H, N, S, ±0.5%). [b] Reactions carried out by addition of Et_3N to a neat mixture of ESF and the active methylene compound. Yields are for recrystallized products.

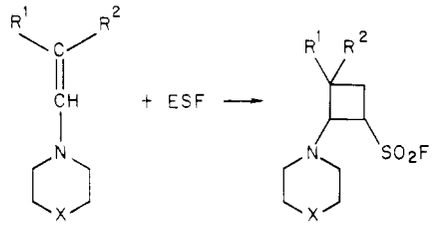
With phenylmercaptotetrazole, a solvent effect was again noted: reaction with ESF in DMF gave thione **54**, whereas in acetic acid **55** was the sole product. Compound **55** reverted to the mercaptotetrazole upon base treatment.



Fluorosulfonylethylation of Active Methylene Compounds. Although ESF failed to react with nitromethane under various conditions, reactions with malonyl derivatives were rapid in the presence of triethylamine, and selective monoalkylation could not be obtained.

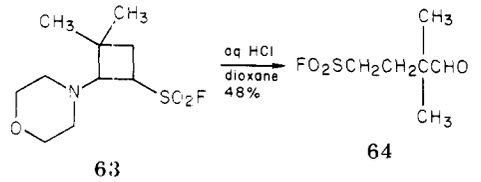
Table V lists several bis(fluorosulfonylethyl) derivatives prepared in this way.

ESF–Enamine Chemistry. ESF reacted with enamines to form cyclobutanes **61–63** in good yields.[17] In



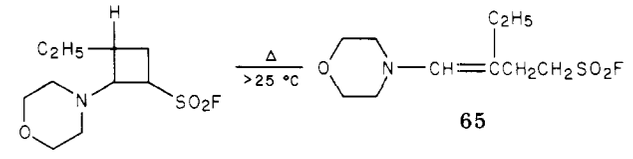
61, X = CH_2; $R^1 = R^2 = CH_3$ (74.5%)
62, X = O; R^1 = H; $R^2 = C_2H_5$ (~65%)
63, X = O; $R^1 = R^2 = CH_3$ (100%)

the case of $R^1 = R^2 = CH_3$, adduct **63** was stable in storage, but it was converted upon treatment with HCl–dioxane–water to 2,2-dimethyl-4-(fluorosulfonyl)butyraldehyde (**64**). Analogous chemistry for alkyl cyclobutyl sulfones is known.[17,18]

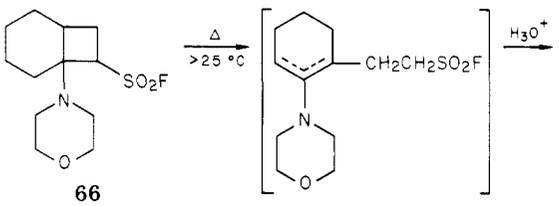


63 64

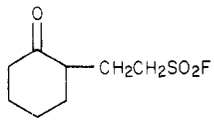
For adducts bearing a β-hydrogen (**62**), the initial cycloadduct was unstable and rearranged rapidly at room temperature to give **65**. This rearrangement also occurred with the *N*-cyclohexenylmorpholine adduct **66**.



62



66



67

(74% from ESF)

Since the fluorosulfonyl group is stable in the presence of aqueous acid, many new compounds containing the sulfonyl fluoride group are thus readily available.

Cycloaddition did not occur when ESF reacted with 3-amino-2-butenoates; carbon alkylation led instead to compounds **68–71**. Acid-catalyzed hydrolysis gave the

$$CH_3C(NHR^1)=CHCO_2R^2 \xrightarrow{ESF} CH_3C(NHR^1)=C(CH_2CH_2SO_2F)CO_2R^2 \xrightarrow{H_3O^+}$$

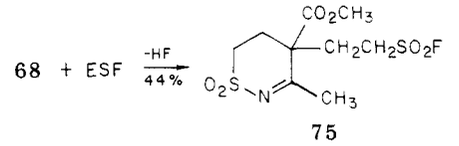
68, R^1 = H; $R^2 = CH_3$ (88%)
69, $R^1 = R^2 = CH_3$ (80%)
70, $R^1 = C_6H_5$; $R^2 = CH_3$ (67%)
71, R^1 = H; $R^2 = C_4H_9$-*t* (78%)

$$CH_3COCHCO_2R^2 \quad (CH_2CH_2SO_2F) \xrightarrow[73,\ 72.5\%]{rI_2SO_4 \text{ in dioxane on}} CH_3COCH_2CH_2CH_2SO_2F$$

74

72, $R^2 = CH_3$ (~80%)
73, $R^2 = C_4H_9$-*t* (88%)

acetoacetates **72** and **73** in good yield. Decarboxylation of **73** gave 5-(fluorosulfonyl)-2-pentanone (**74**) cleanly. Compound **68**, when reacted with a second mole of ESF, lost HF spontaneously and gave **75** in 44% yield.



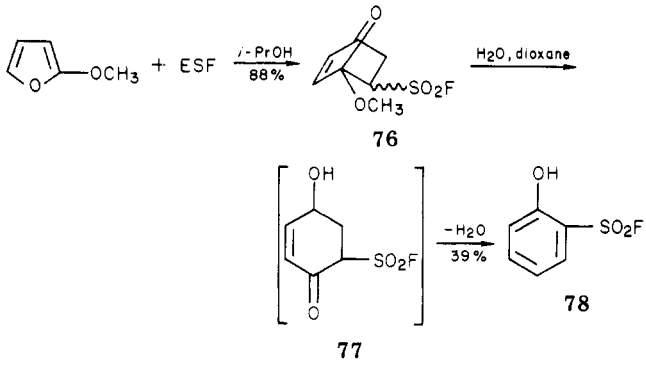
75

Diels–Alder Reactions of ESF. One of the few prior reports of ESF chemistry described cycloaddition to cyclopentadiene and cyclohexadiene.[11] We found that the high reactivity of **1** as a dienophile, coupled with the good stability of the SO_2F group, would allow Diels–Alder synthesis of fluorosulfonylated aromatic systems. Thus room-temperature reaction of **1** with 2-methoxyfuran in 2-propanol gave 1-methoxy-6-(fluorosulfonyl)-7-oxabicyclo[2.2.1]hept-2-ene (**76**) in 88% yield. Treatment of **76**

(17) K. C. Brannock, A. Bell, and R. D. Burpitt, *J. Org. Chem.*, **29**, 801 (1964).

(18) R. Rynbrandt and F. Dutton, *J. Org. Chem.*, **40**, 2282 (1975).

with water–dioxane gave 2-(fluorosulfonyl)phenol (78). The intermediacy of 77 is likely, although this enone could not be isolated.



Conclusion

The ready availability and high reactivity of ESF, coupled with the stability of the fluorosulfonyl group under many reaction conditions, make ESF an unusually attractive and versatile intermediate for the synthesis of a host of new heterocyclic, aromatic, and aliphatic sulfur-containing compounds. Many materials prepared from ESF would otherwise be inaccessible or, at best, available only by difficult manipulations of water-soluble sulfonate compounds. The work presented here should lead to increased utilization of this unique intermediate.

Experimental Section

General Procedures. Melting points were determined in a Thomas-Hoover capillary apparatus and are uncorrected. Boiling points are uncorrected. Infrared spectra were recorded with a Perkin-Elmer Model 137 spectrometer; absorptions are given in microns relative to a polystyrene standard. Nuclear magnetic resonance spectra were obtained with Varian A-60 and JEOL-MH-100 instruments; spectra are reported in δ relative to tetramethylsilane as an internal standard. Visible spectra were recorded with a Perkin-Elmer Model 450 visible–near-infrared spectrometer. Mass spectra were obtained with a Consolidated Electrodynamics Corp. Model 21-110B system. Fluorine microanalysis was performed by Galbraith Laboratories; other analyses were carried out by the Tennessee Eastman Co. analytical laboratories. Solvents were purified or dried according to the methods of Perrin, Armarego, and Perrin.[19]

Caution! 2-Chloroethanesulfonyl chloride (3), 2-chloroethanesulfonyl fluoride (4), and ethenesulfonyl fluoride (1) are severe eye and skin irritants. Systemic toxic effects may result from skin adsorption and exposure to vapors. Exposure to liquid and vapor should be avoided by use of adequate ventilation and appropriate protective clothing. See supplementary material for detailed toxicology of 3, 4, and 1.

2-Chloroethanesulfonyl Chloride (3). This compound was prepared from isethionic acid sodium salt **2** by the method of Goldberg.[3] No difficulty was experienced in producing kilogram batches of **3**, and the crude material was used directly for preparing **4**.

2-Chloroethanesulfonyl Fluoride (4). A solution of potassium fluoride (200 g, 3.44 mol) in water (400 mL) was treated dropwise at 25 °C with a solution of 280 g (1.72 mol) of 2-chloroethanesulfonyl chloride (**3**) in 800 mL of dioxane or tetrahydrofuran. The mixture was stirred for 2 h, and 1 L of water was added. The organic layer was extracted into ether, dried, and distilled to give 172 g (68%) of **4**: bp 93 °C (52 mm) [lit.[4] bp 72–73 °C (18.5 mm)]; IR (neat) 3.35, 7.10, 7.60, 7.72, 8.02, 8.35, 8.72, 8.94, 8.90, 9.70, 10.15, 10.75, 11.2, 12.0, 12.55, 13.95 μm; NMR ($CDCl_3$) δ 3.80 (m). VPC analysis disclosed a single peak (6 ft × $^1/_4$ in., 5% QF-1 on 60–80 A/W DCMS-treated support of Chromosorb P diatomite aggregate, 100–125 °C at 15 °C min^{-1}). This procedure was carried out at a kilogram scale without difficulty.

Anal. Calcd for $C_2H_4ClFO_2S$: Cl, 24.19. Found: Cl, 24.04.

Ethenesulfonyl Fluoride (1). A rapidly stirred mixture of 146 g (1 mol) of **4** and 250 mL of water was treated with 22 g of MgO, added in portions at such a rate that the temperature of the mixture did not exceed 35 °C. Stirring was continued for 2 h after the addition, and the organic layer was separated and dried over $MgSO_4$. Filtration gave 87 g (79%) of ESF with IR and NMR spectra that were indistinguishable from the spectra of distilled material. ESF was also prepared in 41% yield by addition of **4** to triethylamine in Et_2O followed by filtration and distillation. The preferred MgO method was scaled up without difficulty: bp 117–119 °C (1 atm); IR (neat) 3.25, 6.20, 7.96, 8.30, 10.03, 10.47, 12.40, 13.58 μm; NMR ($CDCl_3$) δ 6.70 (m, 2 H), 6.41 (m, 1 H).

Fluorosulfonylethylation of Aromatic Amines (Table I). The following procedures demonstrate the manner in which compounds listed in Table I were prepared.

2-(Phenylamino)ethanesulfonyl Fluoride (6). To a solution of aniline (93 g, 1 mol) in DMF (200 mL) was added a solution of ESF (110 g, 1 mol) in 100 mL of DMF. The temperature of the exothermic reaction was maintained at ≤50 °C. After 1 h the reaction mixture was drowned in water and the crude product (oil phase) was separated, dissolved in diethyl ether, and washed thoroughly with water. Distillation through a 6-in. Vigreux column gave 175 g (86%) of **6**: bp 103–105 °C (0.5 mm); IR (neat) 2.95, 6.25, 6.03, 7.20, 8.30, 13.2 μm; NMR ($CDCl_3$) δ 7.25 (m, 3 H), 6.27 (m, 3 H), 3.62 (s, 4 H).

Anal. Calcd for $C_8H_{10}FNO_2S$: C, 47.27; H, 4.97; N, 6.89; S, 15.77. Found: C, 47.50; H, 4.97; N, 7.03; S, 15.52.

When this preparation was repeated with 2 mol of ESF, compound **6** was obtained in 90% yield.

2,2′-(Phenylimino)bis[ethanesulfonyl fluoride] (7). A solution of aniline (93 g, 1 mol) in acetic acid (300 mL) was stirred at 25 °C and treated with ESF (220 g, 2 mol). The temperature increased to 32 °C, and stirring at ambient temperature was continued for 18 h. The crystalline product that separated was filtered, washed with petroleum ether (bp 30–60 °C), and dried to give 238 g (76%) of **7**. Recrystallization from CCl_4 gave 213 g of **9**: mp 86–88 °C; IR (KBr) 6.30, 6.71, 7.20, 8.10, 8.31, 12.15 (br), 13.25 (br) μm; NMR ($CDCl_3$) δ 7.48 (m, 2 H), 6.97 (m, 3 H), 4.03 (t, 4 H), 3.70 (t, 4 H).

Anal. Calcd for $C_{10}H_{13}F_2NO_4S_2$: C, 38.32; H, 4.15; N, 4.47; S, 20.48; F, 12.14. Found: C, 38.16; H, 4.07; N, 4.48; S, 20.29; F, 12.30.

7 was also prepared as follows. A solution of 2-anilinoethanesulfonyl fluoride (**6**) (2.03 g, 0.01 mol) and ESF (1.1 g, 0.01 mol) in 10 mL of acetic acid was heated on a steam bath for 1 h and drowned in ice–water. The crystalline product that separated was filtered, washed with water, and dried to give 2 g (64%) of **7**, mp 86–88 °C, and shown by NMR and TLC to be identical with an authentic sample.

1-[[2-(Fluorosulfonyl)ethyl]amino]anthraquinone (11). A mixture of 1-aminoanthraquinone (10 g, 0.045 mol) and ethenesulfonyl fluoride (11 g, 0.1 mol) in acetic acid (60 mL) was refluxed for 5 h. The solution was cooled, and the product was collected by filtration and recrystallized from acetic acid to give 13 g (87%) of **11**; mp 203–205 °C; visible spectrum λ_{max} (acetone) 478 nm (ϵ 7000); NMR ($CDCl_3$–Me_2SO-d_6) δ 9.8 (1 H), 8.1 (m, 2 H), 7.7 (m, 2 H), 7.5 (m, 2 H), 7.1 (m, 1 H), 4.0 (m, 4 H); IR (KBr) 2.9, 6.8, 6.85, 6.95, 7.20, 8.30, 8.50, 12.48 μm.

Anal. Calcd for $C_{16}H_{12}FNO_4S$: C, 57.65; H, 3.63; N, 4.21; S, 9.62. Found: C, 57.41; H, 3.60; N, 4.35; S, 9.69.

2-(Methylphenylamino)ethanesulfonyl Fluoride (5). Preparation From ESF. *N*-Methylaniline (107 g, 1 mol) was stirred vigorously and treated with ESF (110 g, 1 mol). The temperature of the exothermic addition reaction was maintained below 100 °C by external cooling. The resultant oil was analyzed by IR, NMR, and TLC and found to be high-purity 2-(*N*-methylanilino)ethanesulfonyl fluoride. The liquid, bp 102–103 °C (0.3 mm), was distilled to give 195 g (90%) of compound **5**: IR (film) 7.15, 8.35 μm; NMR ($CDCl_3$) δ 7.18 (m, 2 H), 6.70 (m, 3 H), 3.77 (m, 2 H), 3.36 (m, 2 H), 2.84 (s, 3 H).

Anal. Calcd for $C_9H_{12}FNO_2S$: C, 49.75; H, 5.58; N, 6.45. Found: C, 49.96; H, 5.61; N, 6.48. This preparation was also carried out by using acetic acid and by using DMF solvent.

(19) D. Perrin, W. Armarego, and D. Perrin, "Purification of Laboratory Chemicals", Pergammon Press, Ltd., Oxford, 1966.

Preparation from 2-Chloroethanesulfonyl Fluoride. A solution of 2-chloroethanesulfonyl fluoride (147 g, 1.0 mol) in benzene (50 mL) was added dropwise with stirring to a solution of *N*-methylaniline (107 g, 1.0 mol) and triethylamine (101 g, 1.0 mol) in benzene (400 mL). The temperature increased to 60 °C during the addition, and the mixture was stirred overnight. Diethyl ether was added, the mixture was washed with water, and the organic layer was dried ($MgSO_4$) and distilled to give, after removal of solvent and 6 g of forerun, 192 g (88%) of **5**.

Sulfonamides (Table II). The following two procedures typify the conversion of fluorosulfonylethyl compounds to the corresponding sulfonamides.

2-(Methylphenylamino)ethanesulfonamide (15). A solution of 2-(methylphenylamino)ethanesulfonyl fluoride (38 g, 0.175 mol) in 100 mL of acetone was added dropwise to a refluxing solution of concentrated ammonium hydroxide (150 mL) and acetone (150 mL). The resultant solution was refluxed for ~0.25 h and the acetone distilled. The residue was cooled and the product collected by filtration and recrystallized from benzene to give 32.6 g (87%) of **15**: mp 88–89 °C; NMR ($CDCl_3$) δ 7.20 (t, 2 H), 6.75 (m, 3 H), 4.9 (m, 2 H), 3.83 (t, 2 H), 3.34 (t, 2 H), 2.96 (s, 3 H).

Anal. Calcd for $C_9H_{14}N_2O_2S$: C, 50.44; H, 6.59. Found: C, 50.56; H, 6.53.

2-[[[2-(*tert*-Butylsulfamoyl)ethyl]phenyl]amino]ethanesulfonamide (17). *tert*-Butylamine (250 mL) was stirred at 25 °C and treated with 2-[phenyl(2-sulfamoylethyl)amino]-ethanesulfonyl fluoride (31 g, 0.10 mol). The solution exothermed to 40 °C and was then stirred at 25 °C for 1.25 h. The mixture was drowned in ice–water (2 L), and acetic acid was added until the pH was about 5.0. The product that separated solidified after several hours and was filtered off, pressed dry on a filter, and recrystallized from 2-propanol (400 mL) to give 29.2 g of **17**. A second recrystallization from ethanol gave 22.1 g of **17**: mp 156–159 °C; IR (KBr) 2.90, 3.03, 6.30, 6.71, 7.40, 7.6–7.7, 7.9, 8.80, 10.0, 13.1 μm; NMR (Me_2SO-d_6) δ 7.25 (m, 2 H), 6.88 (m, 3 H), 6.60 (s, 3 H), 3.82 (m, 4 H), 3.31 (m, 4 H), 1.35 (s, 9 H).

Anal. Calcd for $C_{14}H_{25}N_3O_4S_2$: C, 46.25; H, 6.75; N, 11.56; S, 17.64. Found: C, 46.14; H, 6.88; N, 11.53; S, 17.56.

Sodium 2-[Methyl(*p*-methoxyphenyl)amino]ethanesulfonate (21). A slurry of 2.5 g (0.01 mol) of **12** in 7 mL of 5 M aqueous sodium hydroxide was warmed on a steam bath for 0.5 h, at which time the molten starting material was completely converted to solid product. The reaction mixture was cooled and filtered, and the product was washed with 5 mL of aqueous acetone (1:3) to afford 2.30 g (85%) of white plates, mp >300 °C. A sample was purified by acetone precipitation of an aqueous solution of **21**: IR (KBr) 6.58, 6.90, 7.95, 8.21, 8.39, 8.57, 9.38, 12.05 μm; NMR (D_2O) δ 7.12 (s, 4 H), 3.88 (s, 3 H), 3.75 (m, 2 H), 3.15 (m, 2 H), 2.90 (s, 3 H). The salt did not give reproducible combustion analysis.

Methyl 2-[Methyl(*p*-methoxyphenyl)amino]ethanesulfonate (22). Sodium metal (0.50 g, 0.022 mol) was added to 50 mL of freshly dried and distilled absolute methanol followed by 5.0 g (0.02 mol) of sulfonyl fluoride **12**. The mixture was stirred at reflux under dry argon for 1.5 h, by which time TLC analysis indicated complete consumption of **12** and the formation of some *N*-methyl-*p*-anisidine. The reaction mixture was filtered and stripped in vacuo and produced a gum that crystallized upon aqueous acetone trituration. Filtration afforded 2.53 g (48.5%) of methyl sulfonate **22**: mp 277–280 °C dec; IR (mull) 7.29, 7.92, 8.20, 8.31, 9.61, 11.90, 12.90 μm; NMR (D_2O) δ 7.35 (m, 4 H), 4.18 (m, 2 H), 3.79 (s, 3 H), 3.60 (s, 6 H), 3.07 (m, 2 H).

A sample of the methyl sulfonate **22** was saponified in 1 N NaOH and stripped in vacuo, and the residue was dissolved in D_2O. NMR analysis of this product showed it to be identical with sodium sulfonate **21**.

1-[2-[Methyl(*p*-methoxyphenyl)amino]ethanesulfonyl]-imidazole (24). A solution of 6.8 g (0.11 mol) of imidazole in 200 mL of dry THF was stirred at room temperature under N_2 during the addition of 2.4 g (0.12 mol) of sodium hydride. After 1 h, a solution of 24.7 g (0.10 mol) of **12** in 50 mL of THF was added dropwise. After 1.5 h at room temperature, TLC analysis indicated complete consumption of **12**. The reaction mixture was treated with 5 mL of methanol and filtered through a filtrant of Celite diatomaceous earth, and the filtrate was evaporated to leave an oily product that solidified on standing.

The crude product was recrystallized from ethanol–hexane to afford 19.7 g (66.7%) of white solid: mp 90–92 °C; IR (KBr) 6.60, 7.95, 8.51, 9.36, 12.22, 13.0 μm; NMR ($CDCl_3$) δ 7.98 (m, 1 H), 7.29 (m, 1 H), 7.19 (m, 1 H), 6.72 (m, 4 H), 3.74 (s, 3 H), 3.50 (m, 4 H), 2.78 (s, 3 H).

Anal. Calcd for $C_{13}H_{17}N_3O_3S$: C, 52.88; H, 5.80; N, 14.23; S, 10.84. Found: C, 53.10; H, 5.92; N, 14.24; S, 10.93.

Preparation of Azo Dyes Containing Sulfonyl Fluoride Groups. The dyes shown in Table III are representative of the extensive series of dyes prepared from sulfonyl fluoride and sulfonamide couplers. These dyes were prepared by the usual azo coupling techniques. The aromatic amines were diazotized with either nitrosylsulfuric or nitrous acid and the coupling reactions were conducted at 5–15 °C in an acetic acid/propionic acid mixture buffered at pH 4.5 by sodium acetate as needed. The coupling reactions were stirred for several hours, refrigerated overnight, and subjected to aqueous workup. Crude dyes were generally quite pure, but analytical samples were secured by recrystallization in 2-methoxyethanol solvent. Assigned structures were confirmed by spectral and elemental analyses. The following preparation is typical.

2-[[4-[[2,4-Bis(methylsulfonyl)phenyl]azo]phenyl]-ethylamino]ethanesulfonyl Fluoride (26). Nitrosylsulfuric acid was generated by addition of dry sodium nitrite (0.69 g, 0.01 mol) to 98% sulfuric acid (5 mL) at 25–80 °C and then maintained below 20 °C and treated with 5 mL of propionic acid and 25 mL of acetic acid. The resultant mixture was cooled to 0–5 °C and treated with portions of 2,4-bis(methylsulfonyl)aniline (2.49 g, 0.01 mol). The diazotization continued for 3 h at 0–5 °C. The resultant diazonium salt solution was then added dropwise to a solution of 2-[ethyl(phenyl)amino]ethanesulfonyl fluoride (2.31 g, 0.01 mol) in acetic acid (25 mL) and propionic acid (5 mL) and cooled to 5 °C. After the addition of diazonium salt was completed, the coupling mixture was buffered to pH 4 by adding a sufficient quantity of sodium acetate. After being stirred for 2 h, the reaction mixture was refrigerated at 0 °C overnight. The crude dye was precipitated by addition of 700 mL of ice–water, filtered, and washed thoroughly with water. The air-dried dye cake was shown by TLC to be very pure, yield 4.83 g (98%). The dye cake was dissolved in 50 mL of boiling 2-methoxyethanol, allowed to cool to room temperature, filtered, washed with 2-propanol, and dried. The crystalline dye (**26**) weighed 3.34 g (68%).

Anal. Calcd for $C_{18}H_{22}FN_3O_6S_3$: C, 43.98; H, 4.51; N, 8.55; F, 3.87; S, 19.57. Found: C, 44.16; H, 4.57; N, 8.33; F, 3.70; S, 19.36.

3,4-Dihydropyrido[2,1-*c*][1,2,4]thiadiazine 1,1-Dioxide (39). A solution of 2-aminopyridine (3.96 g, 0.042 mol) and ESF (8.8 g, 0.08 mol) in acetic acid (25 mL) was heated on a steam bath for 1 h. The solvent was stripped in vacuo and the residue triturated with ether to give 6 g (78%) of **39**: mp 189–191 °C; UV λ_{max} (methanol) 248 (ϵ 11 020), 320 nm (ϵ 5078); fluorescence λ_{max} (methanol) 328, 406 nm; NMR (Me_2SO-d_6–pyridine-d_5) δ 7.8 (m, 1), 7.6 (m, 1), 6.16 (m, 2), 4.68 (m, 2), 3.46 (m, 2); mass spectrum m/e 184 (M^+).

Anal. Calcd for $C_7H_8N_2O_2S$: C, 45.64; H, 4.38; N, 15.21; S, 17.41. Found: C, 45.57; H, 4.37; N, 15.47; S, 17.49.

When the reaction was run in ether, a virtually quantitative yield of product separated.

Condensations of ESF with other heterocyclic amines (such as 2-aminopyrimidines, 2-aminopyrazines, 2-aminothiazoles, 2-aminothiadiazoles, and 2-aminobenzothiazoles) were carried out under similar conditions to give the products listed in Table IV. The yields reported were not optimized and reflect the selected method of isolation and recrystallization.

3,4,6,7,8,9-Hexahydropyrido[2,1-*c*][1,2,4]thiadiazine 1,1-Dioxide (40). A solution of 9.2 g (0.05 mol) of **39** in 400 mL of ethanol was hydrogenated at 40 psi of H_2, 40 °C, over 1 g of 5% palladium-on-carbon catalyst until the theoretical quantity of hydrogen was taken up. The catalyst was filtered and the filtrate was evaporated, leaving 8.5 g (90%) of crude product: mp (ethanol) 145–147 °C; NMR ($CDCl_3$–Me_2SO-d_6) δ 3.75 (m, 2), 3.38 (t, 2), 3.25 (t, 2), 2.36 (t, 2), 1.75 (m, 4); IR (mull) 6.36 μm.

Anal. Calcd for $C_7H_{12}N_2O_2S$: C, 44.65; H, 6.44; N, 14.88; S, 17.03. Found: C, 44.78; H, 6.40; N, 14.89; S, 16.94.

Evaporation of a solution of **40** in 10% hydrochloric acid and recrystallization from methanol gave the hydrochloride salt of **40**, mp 195 °C.

Anal. Calcd for $C_7H_{13}ClN_2O_2S$: C, 37.41; H, 5.84; N, 12.47; S, 14.27. Found: C, 37.37; H, 5.76; N, 12.56; S, 14.03.

2-(1,2-Dihydro-2-oxo-1-pyridyl)ethanesulfonyl Fluoride (41). A solution of 9.5 g (0.1 mol) of 2-hydroxypyridine and 11 g (0.1 mol) of ESF in 50 mL of DMF was heated on a steam bath for 5 h. The solvent was stripped in vacuo and left a dark oil that crystallized. Recrystallization of the crude product from isopropyl alcohol gave 14 g (68%) of **41**: mp 111–113 °C; IR (KBr) 6.0, 6.29, 6.48 μm.

Anal. Calcd for $C_7H_8FNO_3S$: C, 40.97; H, 3.94; N, 6.83; S, 15.62. Found: C, 41.04; H, 3.96; N, 6.81; S, 15.63.

2-(1,2-Dihydro-2-oxo-1-pyridyl)ethanesulfonamide (42). A total of 20.5 g (0.1 mol) of 2-(1,2-dihydro-2-oxo-1-pyridyl)-ethanesulfonyl fluoride (**41**) was added in solid portions to about 250 mL of concentrated ammonium hydroxide. The temperature increased to 34 °C, and a solid precipitated that was collected by filtration, washed with water, and dried to give 6.85 g of **42**. The filtrate was evaporated to dryness and the residue recrystallized twice from water to give 5.2 g, mp 197–201 °C. The combined yield was 12 g (60%).

Anal. Calcd for $C_7H_{10}N_2O_3S$: C, 41.57; H, 4.99; N, 13.85; S, 15.85. Found: C, 41.14; H, 4.98; N, 13.80; S, 16.11.

2-(2-Oxo-1-piperidino)ethanesulfonamide (43). A solution of 6.8 g (0.034 mol) of 2-(1,2-dihydro-2-oxo-1-pyridyl)ethanesulfonamide (**42**) in 200 mL of ethanol was hydrogenated over 0.5 g of 5% palladium-on-carbon catalyst until the theoretical quantity of hydrogen was taken up. The catalyst was filtered and the filtrate evaporated on a steam bath. The residue was recrystallized from isopropyl alcohol to give 5.1 g (73%) of **43**, mp 103–106 °C.

Anal. Calcd for $C_7H_{14}N_2O_3S$: C, 40.75; H, 6.85; N, 13.58; S, 15.54. Found: C, 40.67; H, 6.81; N, 13.61; S, 15.57.

Cyclization of 43 to 3,4,6,7,8,9-Hexahydropyrido[2,1-*c*][1,2,4]thiadiazine 1,1-Dioxide (40). A solution of 2 g (0.01 mol) of 2-(2-oxo-1-piperidino)ethanesulfonamide (**43**) in 20 mL of phosphorus oxychloride was refluxed for 4 h. A solid separated on standing and was collected by filtration and dried in vacuo to give 2.1 g of pale tan crystals. The filtrate deposited an additional 0.53 g of product on standing. The NMR and IR spectra indicated this material to be a salt of **40**. A solution of 2 g of this salt in 10 mL of water was allowed to evaporate on a steam bath. The residue was recrystallized from isopropyl alcohol to give 0.84 g of **40** that was identical with the material obtained from 2-aminopyridine.

Reaction of ESF with Thiols. The preparation of **49** given below is typical of the procedures used for compounds **49–55**.

2-(Phenylthio)ethanesulfonyl Fluoride (49). A mixture of ethenesulfonyl fluoride (11 g, 0.1 mol) and benzenethiol (11 g, 0.1 mol) was treated with tributylphosphine (0.5 mL). The temperature of the mixture increased rapidly to 125 °C, and the solution refluxed. After standing overnight, the oil was distilled to give 15.5 g (70%) of **49**, bp 96 °C (0.5 mm).

Anal. Calcd for $C_8H_9FO_2S_2$: C, 43.65; H, 4.08; S, 29.05. Found: C, 43.59; H, 4.30; S, 28.72.

Phenyl 2-(Fluorosulfonyl)ethyl Sulfoxide (50). A solution of 4.39 g (0.0205 mol) of sodium metaperiodate in 30 mL of water was cooled to 5 °C and stirred during the rapid addition of a solution of 3.76 g (0.017 mol) of **49** in 10 mL of methanol. The resultant mixture was stirred at 0–5 °C for 3.5 h, by which time TLC analysis indicated consumption of all sulfide.

The reaction mix, which contained a white solid, was extracted with chloroform, and the dried extract was evaporated to leave an off-white solid product. The crude product was recrystallized from ethanol–hexane to give 2.85 g (70.3%) of pure white needles: mp 105–107 °C; IR (KBr) 7.18, 8.12, 8.48, 9.61, 12.03, 13.28, 14.35 μm; NMR ($CDCl_3$) δ 7.66 (S, 5 H), 2.9–4.1 (m, 4 H).

Anal. Calcd for $C_8H_9FO_3S_2$: C, 40.6; H, 3.84; S, 27.1. Found: C, 40.8; H, 3.89; S, 26.9.

Phenyl 2-(Fluorosulfonyl)ethyl Sulfone (51). To a stirred suspension of 12.0 g (0.06 mol) of sodium benzenesulfinate dihydrate in 50 mL of acetic acid was added 5.5 g (0.05 mol) of ethenesulfonyl fluoride, followed after ~5 min by 5 mL of water. An exotherm to about 40 °C was followed by separation of a white solid; 50 mL of 50% aqueous acetic acid was added to facilitate stirring.

After 4 h, the solid product was filtered and recrystallized from 75 mL of glacial acetic acid to afford 10 g (79.0%) of white needles: mp 177–179 °C; IR (KBr) 7.12, 7.62, 8.32, 8.64, 9.20, 13.40 μm; NMR ($CDCl_3$) δ 8.05 (m, 2 H), 7.80 (m, 3 H), 3.90 (m, 4 H).

Anal. Calcd for $C_8H_9FO_4S_2$: C, 38.0; H, 3.60; S, 25.4. Found: C, 38.1; H, 3.49; S, 25.4.

Bis(fluorosulfonylethylation) of Active Methylene Compounds. The preparation of methyl 2,2-bis[2-(fluorosulfonyl)ethyl]-2-cyanoacetate (**56**) is typical of that of the products in Table V. A mixture of 4.95 g (0.05 mol) of methyl cyanoacetate and 11 g (0.1 mol) of ESF was treated with several drops of triethylamine. The temperature increased spontaneously to 160 °C. A solid mass of crystals resulted on cooling and was recrystallized from ethanol to give 14 g (88%) of **56**, mp (methanol) 88–89 °C.

Anal. Calcd for $C_8H_{11}F_2NO_6S_2$: C, 30.09; H, 3.48; N, 4.39. Found: C, 29.95; H, 3.47; N, 4.17.

ESF–Enamine Chemistry. The following procedures demonstrate the methods used in the series of compounds **61–75**.

3,3-Dimethyl-2-piperidinocyclobutanesulfonyl Fluoride (61). To 13.9 g (0.10 mol) of *N*-isobutenylpiperidine was added dropwise with stirring 11 g (0.10 mol) of ethenesulfonyl fluoride; the temperature of the exothermic reaction was checked at 50 °C by external cooling. After being stirred at 25 °C for 14 h, the dark yellow reaction mixture was distilled to afford 17.8 g (74.5%) of **61**, bp 81–83 °C (1.0 mm), as a clear oil that darkened rapidly upon standing at room temperature: IR (neat) 7.15, 8.37, 11.52, 12.05, 12.52, 12.80, 13.54 μm; NMR ($CDCl_3$) δ 3.90 (apparent q, J = 9.5 Hz, 1 H), 2.92 (d, J = 9.5 Hz, 1 H), 2.32 (m, 4 H), 2.00 (d, J = 9.5 Hz, 2 H), 1.52 (m, 6 H), 1.27 (s, 3 H), 1.20 (s, 3 H).

Anal. Calcd for $C_{11}H_{20}FNO_2S$: C, 52.98; H, 8.10; N, 5.02. Found: C, 52.52; H, 8.02; N, 5.35.

3-Ethyl-2-morpholinocyclobutanesulfonyl Fluoride (62). A solution of ethenesulfonyl fluoride (11 g, 0.1 mol) in ether (25 mL) was added dropwise with stirring to a solution of *N*-(1-butenyl)morpholine (14.1 g, 0.1 mol) in ether (50 mL). The temperature of the reaction mixture was maintained below 30 °C. The solvent was evaporated in a vacuum, and the residue was recrystallized from ether (cold) to give 16 g (65%) of **62**: mp 71–72 °C; NMR ($CDCl_3$) δ 3.93 (m, 1 H), 3.71 (t, 4 H), 3.23 (s, 1 H), 2.5 (m, 6 H), 1.9 (m, 1 H), 1.55 (m, 2 H), 0.9 (t, 3 H).

Anal. Calcd for $C_{10}H_{18}FNO_3S$: C, 47.79; H, 7.22; N, 5.58. Found: C, 47.69; H, 7.14; N, 5.57.

This compound upon standing 48 h at ambient temperature decomposed to an oil.

2-[2-(Fluorosulfonyl)ethyl]cyclohexanone (67). Ethenesulfonyl fluoride (11 g, 0.1 mol) was added dropwise with stirring to a solution of *N*-(1-cyclohexenyl)morpholine (16.7 g, 0.1 mol) in ether (50 mL). The temperature of the mixture was kept below 30 °C by cooling. A white solid separated and was collected by filtration, washed with ether, and dried to give 23 g (83%) of the cycloadduct **66**, mp 69–70 °C. The solid rapidly began to change to an oil with evolution of heat as rearrangement to the thermodynamically more stable monocyclic enamine took place. A solution of **66** (12 g, 0.04 mol) in 5% hydrochloric acid (50 mL) was stirred for 0.25 h. While the oil dissolved rapidly, another oil separated, and it was extracted with ether, washed with water, and dried ($MgSO_4$). Distillation gave 6.7 g (74%) of **67**: bp 131–133 °C (2.1–2.3 mm); IR (film) 5.85 μm; NMR ($CDCl_3$) δ 3.6 (m, 2 H), 2.5 (m, 3 H), 2.2 (m, 2 H), 1.8 (m, 6 H).

Anal. Calcd for $C_8H_{13}FO_3S$: C, 46.14; H, 6.29; S, 15.41. Found: C, 46.38; H, 6.29; S, 15.29.

2,2-Dimethyl-4-(fluorosulfonyl)butyraldehyde (64). A solution of 70.5 g (0.5 mol) of *N*-isobutenylmorpholine in 200 mL of dioxane was stirred at 25 °C and treated dropwise with 55.1 g (0.5 mol) of ESF. External cooling was used to maintain the temperature below 45 °C. After 1.5 h, the solvent could be removed to afford 125.6 g (100%) of **63**. After an additional 1.5 h 50 mL of 5% HCl was added, and the mixture was refluxed 0.5 h. The dioxane was removed in vacuo and the orange residue was diluted with 150 mL of H_2O, extracted with ether (2 × 150 mL), washed with 10% $NaHCO_3$, dried ($MgSO_4$), and distilled through a 12-in. Vigreux column to afford 51.7 g (57%) of **64**, bp 112–125 °C (10 mm). An analytical sample was refractionated:

bp 110–112 °C (9 mm); IR (film) 5.80, 7.15, 8.35 μm; NMR ($CDCl_3$) δ 9.58 (s, 1 H), 3.40 (m, 2 H), 2.10 (m, 2 H), 1.20 (s, 6 H).

Anal. Calcd for $C_6H_{11}FO_3S$: C, 39.55; H, 6.16; S, 17.60. Found: C, 39.60; H, 6.06; S, 17.41.

Methyl 3-Amino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (68). Ethenesulfonyl fluoride (5.5 g, 0.05 mol) was added to a solution of methyl 3-amino-2-butenoate (6.35 g, 0.055 mol) in ether (30 mL). The temperature increased to 30 °C, and a white solid that separated was collected by filtration. An additional 3.7 g was obtained by evaporation of the filtrate and trituration of the residue with benzene to give a total of 9.9 g (88%) of **68**: mp 118–119 °C; IR (mull) 6.19 μm; NMR ($CDCl_3$) δ about 6.5 (2 H), 3.7 (s, 3 H), 3.47 (m, 2 H), 2.86 (m, 2 H), 2.05 (s, 3 H).

Anal. Calcd for $C_7H_{12}FNO_4S$: C, 37.33; H, 5.38; N, 6.22; S, 14.24. Found: C, 37.35; H, 5.12; N, 6.05; S, 14.13.

Methyl 3-Oxo-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (72). A solution of methyl 3-amino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (6.35 g, 0.55 mol) in warm methanol (75 mL) was treated with 10% hydrochloric acid (150 mL). An oil that separated was extracted with ether, washed with water, and dried ($MgSO_4$). The solvent was evaporated and the residue distilled to give 20.7 g (80%) of **72**: bp 92–95 °C (0.1 mm); IR (neat) 5.75, 5.83 μm; NMR ($CDCl_3$) δ 3.80 (s and t, 4 H), 3.53 (m, 2 H), 2.45 (q, 2 H), 2.31 (s, 3 H).

Anal. Calcd for $C_7H_{11}FO_5S$: C, 37.17; H, 4.91; S, 14.18. Found: C, 37.58; H, 4.96; S, 13.79.

Methyl 4-[2-(Fluorosulfonyl)ethyl]-5,6-dihydro-3-methyl-1,1-dioxo-4*H*-1,2-thiazine-4-carboxylate (75). A solution of ethenesulfonyl fluoride (2.2 g, 0.02 mol) and methyl 3-amino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (**68**) (2.25 g, 0.01 mol) in acetic acid (15 mL) was allowed to stand for 15 h at room temperature. The precipitated product was collected by filtration and dried to give 1.4 g (44%) of **75**: mp 175–176 °C; NMR ($CDCl_3$) δ 3.92 (m, 2 H), 3.84 (s, 3 H), 3.4 (m, 2 H), 2.5 (m, 4 H), 2.24 (s, 3 H).

Anal. Calcd for $C_9H_{14}FNO_6S_2$: C, 34.28; H, 4.48; N, 4.45; S, 20.34. Found: C, 34.38; H, 4.45; N, 4.40; S, 20.43.

Methyl 3-Anilino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (70). A solution of ethenesulfonyl fluoride (3.3 g, 0.03 mol) and methyl 3-anilino-2-butenoate (5.79 g, 0.03 mol) in ether (25 mL) was allowed to stand 15 h at ambient temperature. The ether was evaporated and the residue recrystallized from methanol to give 6 g (67%) of **70**: mp 102–103 °C; NMR ($CDCl_3$) δ about 11.2 (1 H), 7.26 (m, 3 H), 7.03 (m, 2 H), 3.77 (s, 3 H), 3.47 (m, 2 H), 2.95 (m, 2 H), 2.05 (s, 3 H).

Anal. Calcd for $C_{13}H_{16}FNO_4S$: C, 51.82; H, 5.36; N, 4.65; S, 10.64. Found: C, 51.99; H, 5.13; N, 4.67; S, 10.83.

***tert*-Butyl 3-Amino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (71).** A solution of 16.0 g (0.10 mol) of *tert*-butyl 3-amino-2-butenoate in 125 mL of dry ether was stirred at room temperature during the dropwise addition of 11.0 g (0.10 mol) of ethenesulfonyl fluoride. After the initial mild exotherm (to 30 °C), the mixture was let stand at 25 °C for 14 h and evaporated under reduced pressure. The solid residue was recrystallized from aqueous methanol to afford **71**: 21.0 g (78%); mp 71–73 °C; IR (mull) 2.92, 3.05, 6.10, 7.20, 8.37, 8.70, 12.0, 12.4 μm; NMR ($CDCl_3$) δ 7.50 (br s, 2 H), 3.60 (m, 2 H), 2.78 (m, 2 H), 2.02 (s, 3 H), 1.48 (s, 9 H).

Anal. Calcd for $C_{10}H_8FNO_4S$: C, 44.9; H, 6.80; N, 5.23; S, 11.9. Found: C, 45.0; H, 6.51; N, 5.15; S, 12.26.

***tert*-Butyl 2-Acetyl-4-(fluorosulfonyl)butanoate (73).** A solution of 13.4 g (0.05 mol) of *tert*-butyl 3-amino-2-[2-(fluorosulfonyl)ethyl]-2-butenoate (**71**) in 125 mL of methanol was stirred at room temperature during the addition of 75 mL of 10% aqueous HCl. After a mildly exothermic reaction, a light yellow oily product separated and was isolated by ether extraction. The yield of crude **73**, pure by TLC and NMR analysis, was 11.8 g (88.0%): IR (neat) 5.76, 5.81, 7.15, 8.75 μm; NMR ($CDCl_3$) δ 3.55 (m, 3 H), 2.6–1.8 (m, 2 H), 2.34 (s, 3 H), 1.58 (s, 9 H). This material was not purified further but was used as obtained for the preparation of 4-oxopentanesulfonyl fluoride.

4-Oxopentanesulfonyl Fluoride (74). A solution of 2.68 g (0.01 mol) of keto ester **73** in 25 mL of *p*-dioxane was treated with 3 drops of concentrated sulfuric acid and refluxed gently for 60 h. The reaction mixture was then evaporated in vacuo to about 5 mL, diluted with 50 mL of ether, washed with aqueous $NaHCO_3$ and water, dried, and evaporated to afford 1.22 g (72.5%) of **74** as a yellow liquid that was homogeneous by NMR and TLC analysis. An analytical sample was prepared by short-path distillation: bp 64–65 °C (1.0 mm); IR (neat) 5.81, 7.13, 8.32, 12.57 μm; NMR ($CDCl_3$) δ 3.58 (m, 2 H), 2.77 (t, J = 7 Hz, 2 H), 2.20 (s, 3 H), 2.20 (m, 2 H).

Anal. Calcd for $C_5H_9FO_3S$: C, 35.69; H, 5.39; S, 19.07. Found: C, 36.12; H, 5.37; S, 19.15.

1-Methoxy-7-oxabicyclo[2.2.1]hept-5-ene-2-sulfonyl Fluoride (76). A solution of 9.8 g (0.1 mol) of 2-methoxyfuran in 25 mL of 2-propanol was treated dropwise with 11 g (0.1 mol) of ESF, and the resultant exotherm was checked at 30 °C. After 2 h, a white solid product precipitated and was filtered to afford 18.5 g (89%) of **76**: mp 79–82 °C, 86–87 °C after 2-propanol recrystallization. The compound was unstable in air but could be stored for several days in vacuo at 25 °C: IR (KBr) 6.30, 7.15, 8.35, 10.29, 11.32, 12.65, 13.20 μm; NMR ($CDCl_3$) δ 6.78 (d of d, J = 2, J = 6 Hz, 1 H), 6.48 (d, J = 6 Hz, 1 H), 5.02 (d of d, J = 2, J = 5 Hz, 1 H), 3.90 (d of d, J = 4.5, J = 10 Hz, 1 H), 3.65 (s, 3 H), 2.70 (m, 1 H), 1.88 (d of d, 1 H).

Anal. Calcd for $C_7H_9FO_4S$: C, 40.38; H, 4.36; S, 15.40. Found: C, 40.38; H, 4.28; S, 15.26.

2-Hydroxybenzenesulfonyl Fluoride (78). A solution of 8.32 g (0.04 mol) of 1-methoxy-7-oxabicyclo[2.2.1]hept-5-ene-2-sulfonyl fluoride was dissolved in 50 mL of dioxane, and 0.9 mL water was added. The mixture was stirred at 25 °C for 8 h and evaporated in vacuo to afford a clear syrup: IR (neat) 2.94, 5.95, 7.14 μm. The syrup was distilled in vacuo to afford 2.35 g (39%) of 2-(fluorosulfonyl)phenol (**78**): bp 65–70 °C (0.6–0.7 mm); IR (neat) 2.92, 6.30, 6.82, 6.92, 7.21, 8.32, 11.85, 12.60, 13.18, 14.30 μm; NMR ($CDCl_3$) δ 7.85 (m, 2 H), 7.52 (s, 1 H), 7.22 (m, 2 H).

Anal. Calcd for $C_6H_5FO_3S$: C, 40.90; H, 2.87. Found: C, 40.86; H, 3.22.

2-(1,2-Dihydro-2-oxo-1-pyridyl)ethanesulfonic Acid. Solvolysis of Sulfonyl Fluoride (41). A mixture of 20.9 g (0.1 mol) of 2-(1,2-dihydro-2-oxo-1-pyridyl)ethanesulfonyl fluoride (**41**) and 50 mL of acetic acid was refluxed overnight, cooled to room temperature, and filtered to give 16 g (79%) of the sulfonic acid, mp 256–259 °C after recrystallization from DMF.

Anal. Calcd for $C_7H_9NO_4S$: C, 41.37; H, 4.47; N, 6.89; S, 15.78. Found: C, 41.40; H, 4.48; N, 6.96; S, 15.37.

Registry No. **1**, 677-25-8; **2**, 1562-00-1; **3**, 1622-32-8; **4**, 762-70-9; **5**, 60353-82-4; **6**, 60353-00-6; **7**, 60353-09-5; **8**, 71517-21-0; **9**, 71517-22-1; **10**, 60353-07-3; **11**, 59385-75-0; **12**, 71517-23-2; **13**, 71517-24-3; **14**, 60353-10-8; **15**, 26841-25-8; **16**, 60353-16-4; **17**, 71517-25-4; **18**, 71517-26-5; **19**, 71517-27-6; **20**, 60353-01-7; **21**, 71517-28-7; **22**, 71517-29-8; **23**, 71517-30-1; **24**, 71517-31-2; **25**, 71517-32-3; **26**, 60353-83-5; **27**, 66756-24-9; **28**, 60353-29-9; **29**, 71517-33-4; **30**, 60353-45-9; **39**, 39270-66-1; **40**, 33260-62-7; **40**·HCl, 33260-68-3; **41**, 71517-34-5; **42**, 71517-35-6; **43**, 71517-36-7; **44**, 71517-37-8; **45**, 71517-38-9; **46**, 71517-39-0; **47**, 71517-40-3; **48**, 71517-41-4; **49**, 71517-42-5; **50**, 71517-43-6; **51**, 71517-44-7; **52**, 71517-45-8; **53**, 71517-46-9; **54**, 71517-47-0; **55**, 71549-39-8; **56**, 71517-48-1; **57**, 71517-49-2; **58**, 71517-50-5; **59**, 71517-51-6; **60**, 71517-52-7; **61**, 71517-53-8; **62**, 71517-54-9; **63**, 71517-55-0; **64**, 71517-56-1; **65**, 71517-57-2; **66**, 71517-58-3; **67**, 71517-59-4; **68**, 71517-60-7; **69**, 71517-61-8; **70**, 71517-62-9; **71**, 71517-63-0; **72**, 71517-64-1; **73**, 71517-65-2; **74**, 71517-66-3; **75**, 71517-67-4; **76**, 71517-68-5; **78**, 71517-69-6; aniline, 62-53-3; *N*-methylaniline, 100-61-8; *p*-phenylenediamine, 106-50-3; *o*-phenylenediamine, 95-54-5; 4-[*N*-(3-amino-4-methoxyphenyl)ureido]benzenesulfonamide, 71517-70-9; 1-aminoanthraquinone, 82-45-1; 4-methoxy-*N*-methylbenzenamine, 5961-59-1; 4,5,6,7-tetrabromo-2*H*-benzotriazole, 71549-41-2; 2-[(3-acetamidophenyl)ethylamino]ethanesulfonyl fluoride, 60353-02-8; 2-(3,6-dimethyl-4*H*-1,4-benzoxazin-4-yl)ethanesulfonyl fluoride, 71517-71-0; ammonium hydroxide, 1336-21-6; *N*,*N*-dimethylpropanediamine, 109-55-7; *tert*-butylamine, 75-64-9; diethylamine, 109-89-7; imidazole, 288-32-4; 2,4-bis(methylsulfonyl)aniline, 42986-91-4; 2-[ethyl(phenyl)amino]ethanesulfonyl fluoride, 60353-81-3; 2-aminopyridine, 504-29-0; 2-hydroxypyridine, 142-08-5; 2-amino-3-hydroxypyridine, 16867-03-1; 2-aminothiazole, 96-50-4; 2-amino-5-(fluorosulfonyl)benzothiazole, 1643-64-7; 5-amino-3-methyl-1,2,4-thiadiazole, 17467-35-5; benzenethiol, 108-98-5; sodium benzenesulfinate, 873-55-2; benzimidazolethiol, 583-39-1; benzothiazolethiol, 149-30-4; phenylmercaptotetrazole, 86-93-1; methyl cyanoacetate, 105-34-0; propanedinitrile, 109-77-3; (phenylsulfonyl)acetonitrile, 7605-28-9; (phenoxysulfonyl)acetonitrile, 71517-72-1; (fluorosulfonyl)acetonitrile, 50408-65-6; *N*-isobutenylpiperidine, 673-33-6;

N-(1-butenyl)morpholine, 15431-03-5; *N*-isobutenylmorpholine, 2403-55-6; *N*-(1-cyclohexenyl)morpholine, 670-80-4; methyl 3-amino-2-butenoate, 14205-39-1; methyl 3-(methylamino)-2-butenoate, 13412-12-9; methyl 3-(phenylamino)-2-butenoate, 40801-08-9; *tert*-butyl 3-amino-2-butenoate, 14205-43-7; 2-methoxyfuran, 25414-22-6; 2-(1,2-dihydro-2-oxo-1-pyridyl)ethanesulfonic acid, 71517-73-2; 2,2′-(4-hydroxyphenylimino)bis[ethanesulfonyl fluoride], 71517-74-3; 2-(1-naphthalenylamino)ethanesulfonyl fluoride, 60353-08-4; 2,2′-[(3-trifluoromethylphenyl)imino]bis[ethanesulfonyl fluoride], 71517-75-4; 2-[(3-(methoxycarbonyl)-5-phenylthiophen-2-yl)-amino]ethanesulfonyl fluoride, 71517-76-5; 2-[(5-acetamido-2-methylphenyl)amino]ethanesulfonyl fluoride, 71517-77-6; *N,N′*-bis[(2-fluorosulfonyl)ethyl]benzenediamine, 71549-36-5; 4-aminophenol, 123-30-8; 1-naphthalenamine, 134-32-7; 3-(trifluoromethyl)benzenamine, 98-16-8; 3-(methoxycarbonyl)-5-phenylthiophene-2-amine, 61325-02-8; 5-acetamido-2-methylbenzenamine, 6375-16-2; 1-[[2-(fluorosulfonyl)ethyl]amino]-4-(methylamino)anthraquinone, 59385-74-9; 1,4-bis[[2-(fluorosulfonyl)ethyl]amino]anthraquinone, 59385-80-7; 1,5-bis[[2-(fluorosulfonyl)ethyl]amino]anthraquinone, 59385-77-2; 1,4-bis[[2-(fluorosulfonyl)ethyl]amino]-2-methoxyanthraquinone, 59385-78-3; 1-benzamido-4-[[2-(fluorosulfonyl)-ethyl]amino]anthraquinone, 59385-79-4; 1-amino-4-(methylamino)anthraquinone, 1220-94-6; 1,4-diaminoanthraquinone, 128-95-0; 1,5-diaminoanthraquinone, 129-44-2; 1,4-diamino-2-methoxyanthraquinone, 2872-48-2; 1-amino-4-benzamidoanthraquinone, 81-46-9; 2-(ethylphenylamino)ethanesulfonyl fluoride, 60353-81-3; 2-[ethyl(3-methylphenyl)amino]ethanesulfonyl fluoride, 60353-04-0; 2-[(3-chlorophenyl)ethylamino]ethanesulfonyl fluoride, 60353-05-1; 2-[(5-acetamido-2-methoxyphenyl)ethylamino]ethanesulfonyl fluoride, 60353-06-2; 2-[(2,2,2-trifluoroethyl)phenylamino]ethanesulfonyl fluoride, 71517-78-7; *N*-ethylbenzenamine, 103-69-5; *N*-acetyl-*N′*-ethyl-*m*-phenylenediamine, 41378-27-2; *N*-ethyl-3-methylbenzenamine, 102-27-2; 3-chloro-*N*-ethylbenzenamine, 15258-44-3; 5-acetamido-*N*-ethyl-2-methoxybenzenamine, 57039-61-9; *N*-(2,2,2-trifluoroethyl)benzenamine, 351-61-1; 2-(2,3-dihydro-6-nitro-4*H*-1,4-benzoxazin-4-yl)ethanesulfonyl fluoride, 71517-79-8; 2-(6-acetamido-2,3-dihydro-4*H*-1,4-benzoxazin-4-yl)ethanesulfonyl fluoride, 71517-80-1; 2-indolin-1-ylethanesulfonyl fluoride, 71517-81-2; 2-1*H*-benzotriazol-1-ylethanesulfonyl fluoride, 71517-82-3; 2-1*H*-1,2,4-triazol-1-ylethanesulfonyl fluoride, 71517-83-4; 2-imidazol-1-ylethanesulfonyl fluoride, 71517-84-5; 3,4-dihydro-6-nitro-2*H*-1,4-benzoxazine, 28226-22-4; 6-acetamido-3,4-dihydro-1*H*-1,4-benzoxazine, 71517-85-6; 2,3-dihydro-1*H*-indole, 496-15-1; 1*H*-benzotriazole, 95-14-7; 1*H*-1,-2,4-triazole, 288-88-0; *N*-butyl-2-(methylphenylamino)ethanesulfonamide, 60353-13-1; 2-(benzylphenylamino)ethanesulfonamide, 60353-15-3; 2,2′-(phenylimino)bis[ethanesulfonamide], 60353-17-5; 2-[(3-acetamidophenyl)ethylamino]ethanesulfonamide, 60353-18-6; *N*-butyl-2-(ethylphenylamino)ethanesulfonamide, 60353-14-2; *N*-*tert*-butyl-2-(methylphenylamino)ethanesulfonamide, 71517-86-7; 2-[(ethyl(3-methylphenyl)amino]ethanesulfonamide, 71517-87-8; 2-[(3-acetamidophenyl)ethylamino]-*N*-ethylethanesulfonamide, 71517-88-9; 2-(benzylphenylamino)ethanesulfonyl fluoride, 71517-89-0; 2-[(5-acetamido-2-methylphenyl)amino]ethanesulfonamide, 71517-90-3; *N*-ethyl-2-[(5-acetamido-2-methylphenyl)amino]ethanesulfonamide, 71517-91-4; *N,N*-diethyl-2-[(5-acetamido-2-methylphenyl)amino]-ethanesulfonamide, 71517-92-5; 2-[ethyl[4-[(4-sulfamoylphenyl)-azo]phenyl]amino]ethanesulfonyl fluoride, 60353-19-7; 2-[[4-[[2,4-bis(methylsulfonyl)-3-methylphenyl]azo]phenyl]ethylamino]-ethanesulfonyl fluoride, 60353-22-2; 2-[[3-acetamido-4-[(2,4-bis-(methylsulfonyl)phenyl]azo]phenyl]ethylamino]ethanesulfonyl fluoride, 71517-93-6; 2-[[5-acetamido-2-methoxy-4-[[3-(methoxycarbonyl)-4-methyl-5-nitro-2-thienyl]azo]phenyl]ethylamino]-ethanesulfonyl fluoride, 60353-32-4; 2,2′-[[4-[(2-chloro-4-sulfamoylphenyl)azo]phenyl]imino]bis[*N*-*tert*-butylethanesulfonamide], 66756-25-0; *N*-butyl-2-[[4-[(2-chloro-5-sulfamoylphenyl)azo]-phenyl]methylamino]ethanesulfonamide, 66756-16-9; 2-[[4-[(2-methoxy-5-sulfamoylphenyl)azo]phenyl]methylamino]ethanesulfonamide, 66756-26-1; 2-[[4-[[2-chloro-5-(methylsulfonyl)-phenyl]azo]phenyl]amino]ethanesulfonamide, 71517-94-7; 2-[[4-[(2-chloro-5-sulfamoylphenyl)azo]phenyl](2,2,2-trifluoroethyl)-amino]ethanesulfonamide, 71517-95-8; 4-sulfamoylaniline, 63-74-1; 5-nitro-2-thiazolamine, 121-66-4; methyl 2-amino-4-methyl-5-nitro-3-thiophenecarboxylate, 71517-96-9; 2-chloro-4-sulfamoylaniline, 53297-68-0; 2-chloro-5-sulfamoylaniline, 29092-34-0; 2-methoxy-5-sulfamoylaniline, 6973-08-6; 2,1-benzisothiazol-3-amine, 2400-12-6; phenyliminobis[*N*-*tert*-butylethanesulfonamide], 71517-97-0; 2-[phenyl(2,2,2-trifluoroethyl)amino]ethanesulfonamide, 71517-98-1; 3,4-dihydro-9-methylpyrido[2,1-*c*][1,2,4]thiadiazine 2,2-dioxide, 71517-99-2; 3,4-dihydropyrimido[2,1-*c*][1,2,4]thiadiazine 2,2-dioxide, 71518-00-8; 3,4-dihydro-6-methylpyrimido[2,1-*c*][1,2,4]thiadiazin-8(9*H*)-one 2,2-dioxide, 71518-01-9; 3,4-dihydro-6-methylthiazolo-[2,3-*c*][1,2,4]thiadiazine-7-sulfonyl fluoride 2,2-dioxide, 71518-02-0; 3,4-dihydro-7-[(4-methoxyphenyl)azo]-6-methylthiazolo[2,3-*c*][1,-2,4]thiadiazine 2,2-dioxide, 71518-03-1; 3,4-dihydro-8-(methylsulfonyl)[1,2,4]thiadiazino[3,4-*b*]benzothiazole 2,2-dioxide, 71518-04-2; 3,4-dihydro[1,2,4]thiadiazino[3,4-*b*]benzothiazole 2,2-dioxide, 71518-05-3; 3-methyl-2-pyridinamine, 1603-40-3; 2-pyrimidinamine, 109-12-6; 2-amino-6-methyl-4-pyrimidinol, 3977-29-5; 5-(fluorosulfonyl)-4-methyl-2-thiazolamine, 2196-72-7; 5-[(4-methoxyphenyl)azo]-4-methyl-2-thiazolamine, 71549-34-3; 2-benzothiazolamine, 136-95-8; 6-(methylsulfonyl)-2-benzothiazolamine, 17557-67-4; 7-cyclohexyl-3,4-dihydro[1,3,4]thiadiazolo[2,3-*c*][1,2,4]thiadiazine 2,2-dioxide, 71518-06-4; 3,4-dihydro[1,3,4]thiadiazolo[2,3-*c*][1,2,4]-thiadiazin-7-amine 2,2-dioxide, 71518-07-5; 5-cyclohexyl-1,3,4-thiadiazol-2-amine, 56882-77-0; 1,3,4-thiadiazole-2,5-diamine, 2937-81-7.

Supplementary Material Available: Further examples of reactions covered in Tables I–IV and toxicological data on compounds **3**, **4**, and **1** (12 pages). Ordering information is given on any current masthead page.

Reactions of Isocyanates with 1-Cyanothioformanilide

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The triethylamine-catalyzed reaction of 1-cyanothioformanilide (**2**) with isocyanates forms 1-substituted 5-imino-3-phenyl-4-thioxo-2-imidazolidinones **5** in excellent yield. Compounds **5** are converted by aqueous acid into 3-phenyl-4-thioxo-2,5-imidazolidinediones **6** and are oxidized by H_2O_2 in HOAc to 3-phenylimidazolidinetriones **4**. Condensation of **5** with *o*-phenylenediamine yields 1*H*-imidazo[4,5-*b*]quinoxalin-2(3*H*)-ones **8**. Upon being heated **2** reacts with 2 equiv of isocyanate to form 5-carbamoylimino-3-phenyl-4-thioxo-2-imidazolidinones **7**.

Nitriles containing an appropriately located nucleophilic group have been reported to undergo cyclization reactions with isocyanates to form imino or (if the possibility for tautomerism exists) amino heterocycles. Typical examples are the formation of aminooxazoles from α-aminonitriles,[1] iminotetrahydroquinazolines from anthranilonitrile,[2] iminooxazolidinones from cyanohydrins,[3] and iminoimidazolidinones from iminodiacetonitrile.[4] The work described in this paper was undertaken to investigate the expected analogous behavior toward isocyanates of 1-

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