5 ml of chloroform. After 10 min the solvent was removed, and the solid residue was washed well with water and crystallized from ether–petroleum ether (bp 30–60°), giving 66 mg (0.283 mmol, 88%) of **4a**: mp 66–67° dec; λ_{max} (MeCN) (10^{-3} ϵ) 298 nm (2.35), 290 (2.46), and 239 (28.2); ^{1}H NMR ($CDCl_3$) δ 7.95–7.8 (m, 2 H, aromatic), 7.3 (m, 6 H, aromatic), and 1.5 (s, 1 H, NH). The NH band was at 3200 cm^{-1}.

Anal. Calcd for $C_{12}H_9NOS \cdot H_2O$: C, 61.8; H, 4.75; N, 6.00; S, 13.7. Found: C, 61.9; H, 4.81; N, 5.86; S, 13.8.

B. Compound **4a** was also obtained by adding 10% sodium hydroxide solution to a suspension of **2** in ethanol and working up as before.

Methylation of 4a. Formation of 5,5-Dihydro-5-(methylimino)phenoxathiin Iodide (5). To a solution of 110 mg (0.511 mmol) of **4a** in ether was added 2 ml of methyl iodide. Pale yellow crystals of **5** deposited during 15 min of stirring, giving 149 mg (0.42 mmol, 81.5%), mp 121–122° dec.

Conversion of 5 into 5,5-Dihydro-5-(methylimino)phenoxathiin Perchlorate (6). An excess of silver perchlorate was added to a stirred solution of 100 mg (0.28 mmol) of **5** in acetonitrile. After 10 min the precipitated silver iodide was filtered, the solution was evaporated, and the residue was washed with water and crystallized from aqueous methanol, giving 88 mg (0.27 mmol, 96%) of **6**, mp 160–162° dec, mmp with authentic **6** (see below) 159–160° dec.

Reaction of 1 with Methylamine. Formation of 6. A suspension of 1.02 g (3.41 mmol) of **1** in acetonitrile was stirred for 10 min and methylamine gas was bubbled in until the purple color disappeared. Reaction was slower than with ammonia. Work-up and chromatography, as earlier, gave 457 mg (2.28 mmol, 67%) of phenoxathiin, 31 mg (0.144 mmol, 4%) of phenoxathiin 5-oxide, and 143 mg (0.433 mmol, 13%) of **6**, mp 158–159° dec, from aqueous acetone: λ_{max} (MeCN) (10^{-3} ϵ) 302 nm (5.43), 280 (3.54), and 233 (20.0); ^{1}H NMR (Me_2SO-d_6) δ 8.0–8.2 (m, 2 H, aromatic), 7.7 (m, 6 H, aromatic), and 2.2 (s, 3 H, Me). The NH proton could not be detected in Me_2SO solvent, presumably because of exchange, but gave rise to a 3280-cm^{-1} band in the infrared.

Anal. Calcd for $C_{13}H_{12}NSClO_5$: C, 47.3; H, 3.67; N, 4.25; S, 9.72; Cl, 10.7. Found: C, 47.3; H, 3.42; N, 4.39; S, 9.92; Cl, 10.7.

Reaction of 4a with Tosyl Chloride. Formation of *N*-Tosyl Phenoxathiin Sulfilimine (7). A suspension of 53 mg (0.17 mmol) of **2** in ether was deprotonated by addition of 1 ml of pyridine. Tosyl chloride (42 mg, 0.22 mmol) was added, and after 1 hr of stirring the solvent was removed. The residue was washed well with water and crystallized from aqueous ethanol to give 26 mg (0.07 mmol, 41%) of **7**, mp 166–168°, infrared identical with that of an authentic sample, mp 168–170°, made by reaction of phenoxathiin with chloramine-T according to method B of Tsujihara et al.[15]

Reaction of 1 with 4a. Preparation of 3a. A suspension of 139 mg (0.463 mmol) of **1** in 10 ml of acetonitrile was stirred for 10 min and a solution of 51 mg (0.237 mmol) of **4a** in 3 ml of acetronitrile was added. The disappearance of the color of **1** was quite slow. After 20 min the pale purple color was discharged by adding 1 drop of water. The solution was stirred with a small amount of sodium carbonate (to neutralize perchloric acid) and evaporated. Column chromatography gave 47.6 mg (0.237 mmol, 51%) of phenoxathiin (benzene), 19 mg (0.09 mmol) of phenoxathiin 5-oxide (chloroform), and 101 mg (0.196 mmol, 42%) of **3a** (acetone), mp 236–238° dec, from aqueous methanol.

Reaction of 4a with Thianthrene Cation Radical Perchlorate (8). Formation of 5,5-Dihydro-5-(5-thianthreniumylimino)phenoxathiin Perchlorate (9). Reaction was carried out as with the reaction of **4a** with **1**, using 52 mg (0.165 mmol) of **8** and 19.5 mg (0.091 mmol) of **4a**. After stirring with sodium carbonate the solution was poured into water and the precipitate was taken up in acetone and precipitated with ether. Crystallization from aqueous methanol gave 41 mg (0.077 mmol, 47%) of **9**, mp 208–210° dec.

Anal. Calcd for $C_{24}H_{16}NS_3ClO_5$: C, 54.4; H, 3.04; N, 2.64; S, 18.2; Cl, 6.69. Found: C, 54.1; H, 3.02; N, 2.47; S, 18.4; Cl, 6.56.

The acetone–ether filtrate from the precipitation of **9** was evaporated, and the residue was taken up in chloroform and subjected to TLC on silica gel with benzene development, giving 19.5 mg (0.09 mmol, 55%) of thianthrene and 7 mg (0.03 mmol) of thianthrene 5-oxide.

Registry No.—**1**, 55975-63-8; **2**, 55975-55-8; **3a**, 55975-57-0; **4a**, 54002-03-8; **5**, 55975-58-1; **6**, 55975-60-5; **7**, 54462-91-8; **8**, 35787-71-4; **9**, 55975-62-7; phenoxathiin, 262-20-4; methyl iodide, 74-88-4; silver perchlorate, 7783-93-9; methylamine, 74-89-5; tosyl chloride, 98-59-9.

References and Notes

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Dimethyl Sulfoxide–Trifluoroacetic Anhydride. A New and Efficient Reagent for the Preparation of Iminosulfuranes[1]

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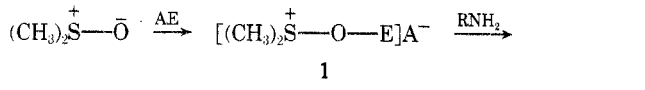
The scope and limitations are described of the recently reported dimethyl sulfoxide–trifluoroacetic anhydride (DMSO–TFAA) reagent for the preparation of iminosulfuranes. Yields range from 40 to 90% with aryl amines, including ortho-substituted ones, aryl amides, aryl sulfonamides, and urea. Previously uncharacterized iminosulfuranes have been prepared from sulfanilamide (mono- and diylides) and sulfadiazine. Relatively basic amines (cyclohexylamine, benzylamine), *o*- and *p*-diaminobenzenes, anthranilamide, ansidine, and 2- and 4-aminopyridines failed to yield isolable iminosulfuranes.

This paper defines the scope and limitations of the recently reported dimethyl sulfoxide–trifluoroacetic anhydride (DMSO–TFAA) reagent for the efficient preparation of iminosulfuranes (sulfilimines) and compares the reagent's utility with that of other "activated" DMSO reagents. In our preliminary communications[1a] only a few iminosulfuranes were reported and no information was then available on the limitations of the new reagent.

The activation of DMSO by a number of electrophiles is well documented, typically chlorine,[2] acetic anhydride,[3] toluenesulfonic anhydride,[4] methanesulfonic anhydride,[4] alkyl chloroformates,[5] toluenesulfonyl chloride,[4] cyanuric chloride,[4] sulfur trioxide,[1b,6,7] phosphorus pentoxide,[6,8,9] and dicyclohexylcarbodiimide.[10,11] All of these electrophiles have been used to activate DMSO for the oxidation of alcohols but only the last three electrophiles (AE) and acetic anhydride have also been used for the preparation of iminosulfuranes (2) (eq 1). Preparation of 2 in good yield requires an intermediate (1) containing a good leaving group (OE^-) readily displaced by the nucleophilic nitrogen compounds.[12]



$$(CH_3)_2\overset{+}{S}\text{—}\bar{O} \xrightarrow{AE} [(CH_3)_2\overset{+}{S}\text{—}O\text{—}E]A^- \xrightarrow{RNH_2}$$

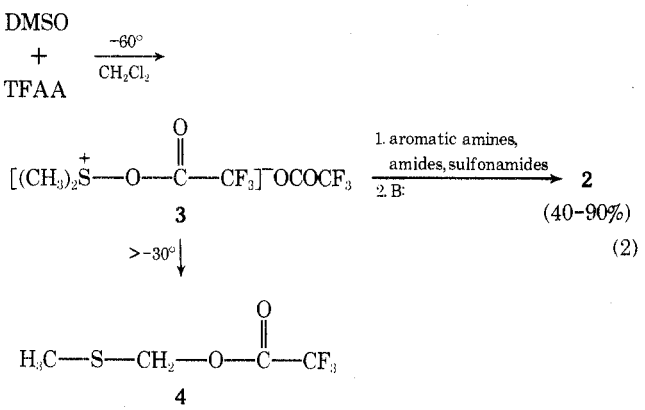
1

$$[(CH_3)_2\overset{+}{S}\text{—}NH\text{—}R]A^- \xrightarrow{B:} (CH_3)_2\overset{+}{S}\text{—}\bar{N}\text{—}R \quad (1)$$

2

Results and Discussion

Scope. Activation of DMSO with acyl halides and certain anhydrides at room temperature, particularly in the absence of a moderating solvent, can and does proceed explosively. TFAA falls into that category, but we correctly concluded that it should be possible to moderate its reaction with DMSO by working at low temperature in an unreactive solvent. Even under those conditions, DMSO and TFAA react almost instantly and exothermically at −60° in methylene chloride to produce a white precipitate which, for convenience, is written as 3 (eq 2). This precipitate is stable below −30° but on warming the system it becomes homogeneous, and the Pummerer rearrangement product (4) forms; it is readily observed by NMR (δ 5.35, 2 H, s; 2.28, 3 H, s).



DMSO + TFAA $\xrightarrow[CH_2Cl_2]{-60°}$

$$[(CH_3)_2\overset{+}{S}\text{—}O\text{—}\overset{O}{\overset{\|}{C}}\text{—}CF_3]^-OCOCF_3$$

3

$\xrightarrow{>-30°}$

$$H_3C\text{—}S\text{—}CH_2\text{—}O\text{—}\overset{O}{\overset{\|}{C}}\text{—}CF_3$$

4

$\xrightarrow[2.\ B:]{1.\ \text{aromatic amines, amides, sulfonamides}}$ 2 (40–90%) (2)

We have no direct evidence for the structure of 3, as we have failed in all attempts to isolate it. We can intercept and trap 3, however, with a wide range of nitrogen-containing nucleophiles, such as certain aromatic amines, amides, and sulfonamides (eq 2). These nucleophiles react rapidly and cleanly. Crude 2, after basification (when required) with triethylamine or 5–10% aqueous sodium hydroxide, is obtained in 40–90% yields in almost analytical purity without further purification (Table I).[17] With many aromatic amines, the reactions are complete within a few minutes after all the amine has been added (TLC); with sulfonamides reaction takes about 30–60 min and with amides up to 240 min is required. In contrast, DMSO activated by sulfur trioxide or phosphorus pentoxide requires considerably longer reaction times (ca. 20 times longer).[1b]

Table I lists the iminosulfuranes (2) (or their salts) prepared and also yields, melting points, NMR, and elemental analyses. In one case (6), both the ylide (y) and its picrate (p) were isolated. In three other cases (5, 7, 8) only the picrate was stable enough for characterization. In one case (15) only the trifluoroacetate could be obtained. All compounds had the predicted NMR spectra. Compounds that had been previously reported by us and/or others (5, 7, 9, 11, 13, 14, 16, 17) were additionally characterized by melting point and ir comparison with authentic samples and, in several cases, by mixture melting point as well. New compounds were characterized spectrally and by elemental analyses. Thin layer chromatography was a useful monitor of purity.

One noteworthy feature of the DMSO–TFAA reagent is is reactivity even with aromatic amines containing certain ortho substituents (CH_3, NO_2). Such amines could not be converted to *N*-aryliminosulfuranes by our earlier procedure in which DMSO is activated by SO_3.[1b] For completeness, *o*-fluoroaniline was also converted to the *N*-aryliminosulfurane (Table I, 8).

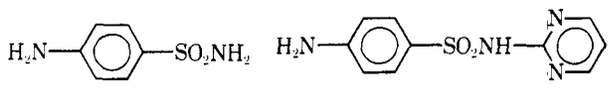
Amides (benzamide, *p*-nitrobenzamide, and urea) readily form *N*-acyliminosulfuranes (Table I, 13, 14, 15) in excellent yield with the DMSO–TFAA reagent. Reaction times (90–240 min, as derived from TLC data) are longer than with aromatic amines and a small excess of the reagent (3) is required to obtain optimum yields. With benzamide, addition of base is essential to obtain the ylide (13) but with *p*-nitrobenzamide, the ylide 14 precipitates during the reaction and does not require basification to obtain at least a 90% yield of almost pure product. The additional acidity of the NH proton resulting from the *p*-nitro group coupled with the low solubility of the product (14) shifts the equilibrium cleanly and almost quantitatively from salt to ylide.

Urea, an amide with two identical nucleophilic sites, can in principle form a mono- and diylide as well as the corresponding salts. A pure dylide or disalt could not be obtained even with a large excess of the reagent (3); a complex mixture of products was shown by TLC. However, when equimolar quantities of urea and the reagent (3) were used, an excellent yield (80%) of the monotrifluoroacetate salt of the monoylide (Table I, 15) was obtained.

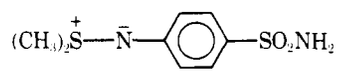
The reaction of sulfonamides (benzene- and *p*-nitrophenylsulfonamide) with the reagent (3) turned out to be two to four times more rapid than that with amides, even though sulfonamides are poorer nucleophiles. Sulfonamides, however, are considerably stronger acids than amides and may exist in equilibrium with their conjugate base, the sulfonamido anions. Although only small quantities of these anions are likely to be present, they should be superior nucleophiles to free amides and, if the equilibrium is rapidly restored, the overall reaction rate should be higher with sulfonamides. This argument is supported by our work with *p*-aminobenzenesulfonamide (PABS) described below. With sulfonamides basification is not required as the NH proton is readily lost and the ylides precipitate from the reaction mixture.

Sulfanilamide (18) poses an intriguing synthetic challenge as it can, in prinicple, form two monoiminosulfuranes, one with the ylide function on the amino side (20) and the other with the ylide function on the sulfonamido side (21), and one diiminosulfurane (22). Sulfadiazine (19) can yield only one iminosulfurane, the monoylide (23).

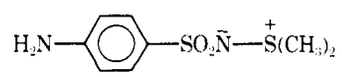
The diylide 22 (eq 3) appeared to be the easiest of the group to prepare as we had already established that both the amino and sulfonamido functions react cleanly and rapidly with the reagent 3. When 18 was allowed to react with an excess of 3 in methylene chloride below −40° (usually −50 to −60°) for about 2 hr followed by customary addition of triethylamine (TEA) to the reaction solution, a



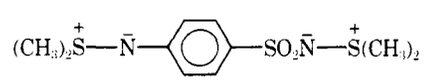
18 19



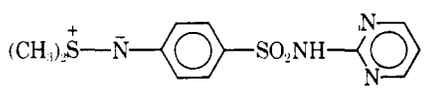
20



21

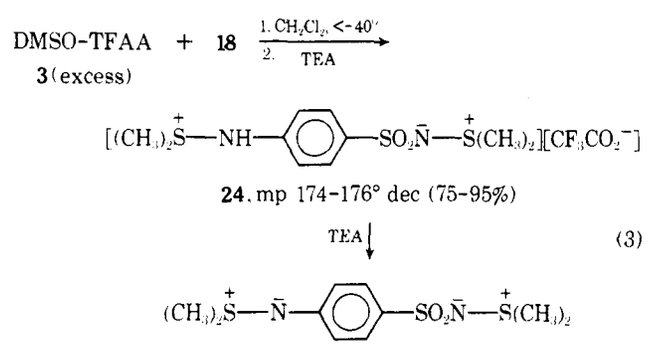


22



23

75–95% yield of **24**, mp 174–176° dec, the monotrifluoroacetate salt of **22** rather than **22**, was unexpectedly formed. To obtain **22** it was necessary to react **24** with virtually neat TEA (some methylene chloride was needed to enhance the solubility of **24**) in a separate step.



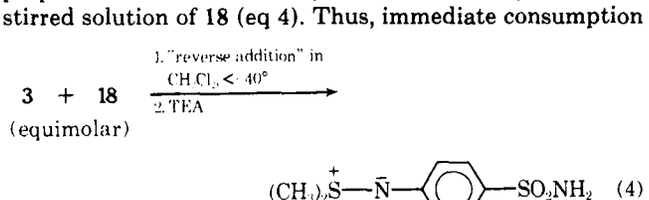
24, mp 174–176° dec (75–95%)

(3)

22, mp 179–182° dec (59%)

To prepare **20** (iminosulfurane on the amino group of **18**) it was planned to take advantage of the known higher rate of reaction of an amino group, relative to sulfonamido, with reagent **3**. However, when an equimolar quantity of sulfanilamide (**18**) was added to **3** at low temperatures both functional groups reacted and selective reaction could not be achieved. Based on our earlier work with various para-substituted aromatic amines,[6] we conclude that the electron-withdrawing sulfonamido group must be reducing the nucleophilicity of the amino group to the point where both functional groups in **18** react at similar although probably not identical rates.

It was possible to obtain the desired monoylide (**20**), however, by a "reverse addition" technique, using a specially designed all-glass apparatus, in which the reagent **3**, prepared at or below −40°, was added slowly to a cold stirred solution of **18** (eq 4). Thus, immediate consumption



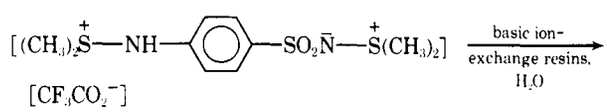
(4)

20, mp 135–137° dec (50%)

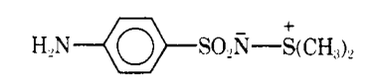
of **3** was assured and at no time was it present in excess (as is the case when **18** is added to **3**). The exclusive product isolated in the "reverse addition" method was **20** obtained in about 50% yield after addition of TEA to deprotonate the intermediate sulfonium salt. Compound **20**, mp 135–137° dec, gives a negative ninhydrin test and fails to form an azo dye with β-naphthol (free amino group absent) and it is soluble in aqueous base (free sulfonamido group present).[18] Spectra and elemental analysis confirmed its structure.

The direct preparation of **21** (iminosulfurane on the sulfonamido group) from **18** and **3** was expected to be difficult, if not impossible, because of the intrinsically lower nucleophilicity of the sulfonamido group. Even in cases where we attempted to reduce the nucleophilicity of the amino group markedly be making the trifluoroacetate salt of **18**, we were not successful in the direct selective reaction of the sulfonamido group.

Compound **21** was obtained unexpectedly, however, in about 30% yield when we attempted to convert **24**, the monotrifluoroacetate salt (eq 3), to the diiminosulfurane (**22**) by treatment with basic ion-exchange resins in an aqueous system (eq 5). Treatment of **24** with Amberlite



24

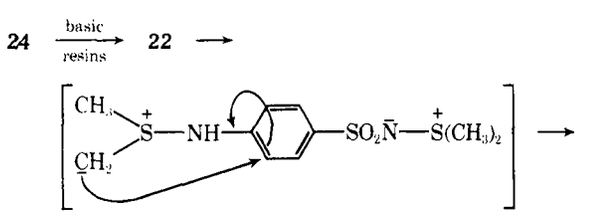


(5)

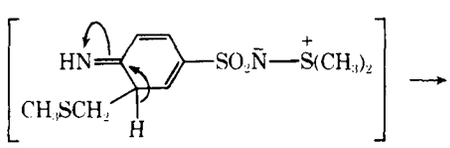
21, mp 190–193° dec (30%)

IR-45 (IRA-400 or IRC-50) at room temperature caused selective hydrolysis on the amino side; **21**, mp 190–193° dec, was obtained in 30% yield after recrystallization from isopropyl alcohol or purification by column chromatography on silica gel. Compound **21** gives a positive ninhydrin test and is insoluble in dilute aqueous base, as would be expected. Spectral properties and elemental analysis confirmed the structure. Independent synthetic studies, to be described below, distinguished unequivocally between **20** and **21**.

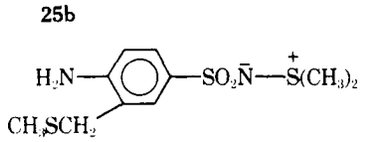
Prior to purification, **21** was shown by TLC to be contaminated by another compound with a higher R_f value. Chromatography yielded a compound, mp 158–159°, whose NMR spectrum suggested that it contained the $-CH_2SCH_3$ group. On the basis of spectral data, elemental analysis, mechanistic considerations, and literature reports,[19] the contaminant in crude **21** was deduced to be a new compound **25** formed by a Sommelet–Hauser type of reaction.



25a



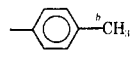
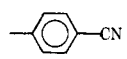
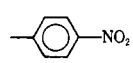
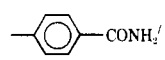
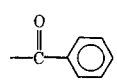
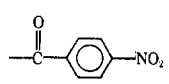
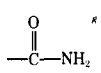
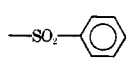
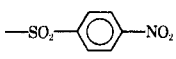
25b



(6)

25, mp 162–163°

Table I
Iminosulfuranes (2) from DMSO–TFAA Reagent and Nitrogen Compounds

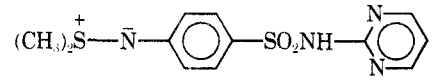
R in $(CH_3)_2S^+$-N^--R	Yield, %	Mp, °C Found	Mp, °C Lit.	Elemental analysis and NMR data[a]
 5	60	130–130.5 dec	128–130[13]	Calcd for $C_{14}H_{14}N_4O_7S$: C, 44.0; H, 3.70; N, 14.8; S, 8.37. Found: C, 44.4; H, 4.11; N, 15.1; S, 8.18. NMR 3.3, 6 H, s; 7.3, 5 H, m; 8.6, 2 H, s
 6	40 (y)[d] 75 (p)	132–132.5 dec 165–168 dec[e]	RT[14]	NMR (y) 2.4, 3 H, s; 3.6, 6 H, s; 7.1, 4 H, m. Calcd for $C_{15}H_{16}N_4O_7S$ (p): C, 45.5; H, 4.07; N, 14.1; S, 8.07. Found: C, 45.3; H, 4.03; N, 14.0; S, 8.07. NMR (p) 2.4, 3 H, s; 3.4, 6 H, s; 7.1, 4 H, m; 8.6, 2 H, s
 7	60	165–166 dec	165–167[13]	NMR 2.2, 3 H, s; 3.2, 6 H, s; 7.0, 4 H, m, 8.6, 2 H, s
 8	85	140–141 dec[e]		Calcd for $C_{14}H_{13}FN_4O_7S$: C, 42.0; H, 3.25; N, 14.0; S, 8.00. Found: C, 41.9; H, 3.12· N, 13.9; S, 7.73. NMR 3.3, 6 H, s; 7.2, 4 H, m; 8.6, 2 H, s
 9	65	108–109 dec	111–112[1b] 108–112[13]	NMR 2.8, 6 H, s; 7.1, 2 H, d; 7.7, 3 H, d
 10	60	73–74[e]		Calcd for $C_8H_{10}N_2O_2S$: C, 48.5; H, 5.05; N, 14.1. Found: C, 48.2; H, 5.17; N, 13.9. NMR 2.6, 6 H, s; 7.50, 1 H, m; 7.90, 1 H, m; 8.16, 1 H, m; 8.56, 1 H, m
 11	65	166–167 dec	172–174[1b] 164–166[10]	NMR 2.8, 6 H, s; 7.6, 2 H, d; 8.3, 2 H, d
 12	55	90		NMR 2.6, 6 H, s; 6.7, 2 H, d; 7.7, 2 H, d
 13	60	108–110	106–108[15]	NMR 2.8, 6 H, s; 7.3, 3 H, m; 8.0, 2 H, m
 14	90	217–218 dec	220–222[1b]	
 15	80	136–137[e]		Calcd for $C_5H_9F_3N_2O_3S$: C, 25.6; H, 3.87; F, 24.4; N, 12.0; S, 13.7. Found: C, 26.0; H, 3.84; F, 24.2; N, 11.7; S, 13.4. NMR 3.2, 6 H, s; 7.0, 3 H, s (broad)
 16	80	129–131	128–130.5[1b] 131[16]	NMR 2.7, 6 H, s; 7.35, 3 H, m; 7.85, 2 H, m
 17	85	184–185	183–185[1b] 186[10]	NMR 2.8, 6 H, s; 8.0, 2 H, m; 8.4, 2 H, m

[a] $CDCl_3$ or DMSO-d_6 solution; XL-100 NMR spectrometer; δ values (Me_4Si = 0). [b] Isolated as picrate only. [c] Both ylide and picrate isolated; y = ylide and p = picrate. [d] The free ylide is unstable; an elemental analysis was not obtained. [e] New compounds. [f] This compound was not completely characterized and its structure is still uncertain. [g] Isolated as trifluoroacetate only.

The sequence that best explains the formation of **25** from **24** via **25a** and **25b** in the presence of basic ion-exchange resins is shown in eq 6.

Sulfadiazine (**19**) readily forms an iminosulfurane (**23**), sodium salt (dihydrate), mp 265–268° dec, in 70% yield from reagent **3** and **19** (eq 7). In contrast to **19**, **23** is readily

3 + 19 $\xrightarrow[2.\ 10\%\ NaOH]{1.\ CH_2Cl_2,\ <-40^\circ}$



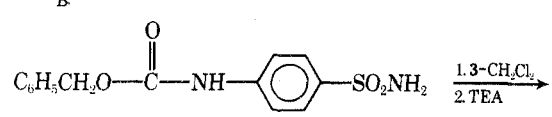
(Na salt dihydrate) (7)

23, mp 265–268° dec (70%)

soluble in water, producing a slightly alkaline solution (pH 9). Compound **23** undergoes the Sommelet–Hauser type of rearrangement in aqueous solution at room temperature ($t_{1/2} \simeq 24$ hr) (determined by NMR) but it appears to be stable in the solid state.

Independent Synthesis. Monoylides **20** and **21** are isomeric and have similar NMR spectra. Although **20** gives a negative ninhydrin test and is soluble in aqueous base and **21** gives a positive ninhydrin test and is insoluble in aqueous base, such structure proof is inadequate. The structure of **21** was demonstrated by the synthetic sequence shown in eq 8a and 8b. To block the free amino group, sulfanilamide (**18**) was treated with benzyl chloroformate in acetone in the presence of sodium bicarbonate thereby forming **26**, mp 192–193° (80%) (eq 8a). Compound **26** (free amino group blocked) was then converted to the iminosulfurane (**27**) (ylide on the sulfonamido side), mp 148–149° (50%), by reaction with the DMSO–TFAA reagent (**3**) followed by deprotonation with TEA. The same compound was formed by reaction of **21** with benzyl chloroformate (eq 8b); it was

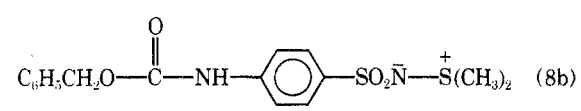
18 $\xrightarrow[B:]{C_6H_5CH_2OCCl}$



26, mp 192–193° (80%)

27, mp 148–149° (50%) (8a)

21 $\xrightarrow[B:]{C_6H_5CH_2OCCl}$



(8b)

27

identical with **27** in every way (NMR, ir, uv, melting point, mixture melting point). It can therefore be concluded that **21** is the monoylide with a free amino group (ylide on the sulfonamide side) and **20** must be its isomer with a free sulfonamido group (ylide on the amino side). Both **26** and **27** give negative ninhydrin tests, as would be expected as neither compound contains a free amino group.

We have also tried to remove the benzyloxycarbonyl group selectively from **27** to re-form **21** using either hydrogenolysis in methanol with 5% Pd/C catalyst at 60 psi or the more recently reported reagent, boron trifluoroacetate in trifluoroacetic acid.[20] Hydrogenolysis yielded a mixture of sulfanilamide (**18**) and **26** but not **21**. We believe this is the first reported hydrogenolytic cleavage of the S–N bond in iminosulfuranes. The results indicate that hydrogenolysis of the S–N bond is more rapid than cleavage of the benzyloxycarbonyl group. The boron trifluoroacetate reagent cleaved both the benzyloxycarbonyl and ylide groups (no selectivity was noted); **18** was isolated in good yield.

Limitations. Cyclohexylamine and benzylamine did not yield ylides or their salts on reaction with the reagent (**3**); under a variety of conditions the trifluoroacetates of the amines were obtained instead. These amines are considerably more basic than aromatic amines and, rather than perform a nucleophilic displacement reaction on the sulfur atom of the reagent, they may abstract a proton from the dimethylsulfonium moiety instead. No success was obtained with *o*- and *p*-diaminobenzene or anthranilamide for reasons that are not evident. With *p*-anisidine attempts were made to isolate the picrate of the ylide but the reaction products decomposed. 2- and 4-aminopyridine yielded picrates of the amines and not of the ylides.

Experimental Section[21]

General Procedures. Compounds 16 and 17 (Table I). DMSO (1.45 ml, 0.02 mol) was dissolved in CH_2Cl_2 (10 ml) in a three-neck flask with a magnetic stirrer, thermometer, nitrogen inlet, and drying tube. Dry nitrogen was passed through the stirred solution cooled to −60° and TFAA (2.8 ml, 0.02 mol) was added slowly while maintaining the temperature below −50°. The reaction was exothermic and a white precipitate of **3** formed immediately. (Similar results have been obtained using a 2:1 molar ratio of DMSO to TFAA and 5 ml of CH_2Cl_2).

p-Nitrobenzenesulfonamide (2.0 g, 0.01 mol) was slowly added as a slurry in DMSO–CH_2Cl_2 (10 ml of 4:1 v/v) at or below −50°. (TLC was not useful in monitoring this reaction owing to interference by DMSO.) After 1 hr the stirred reaction mixture was allowed to warm to room temperature and the precipitate was filtered, washed with 5% aqueous NaOH to remove any residual starting material, then with water, and dried. Pure **17**, mp 184–185° (2.34 g, 88%), was obtained without further work-up. Compound **16**, mp 129–131°, was similarly prepared (80%).

Compounds 13, 14, 15 (Table I). In the preparation of **13**, all the benzamide was consumed in 1 hr (TLC) below −35°. The reaction mixture was diluted to 50 ml with CH_2Cl_2 and excess 10% aqueous sodium hydroxide was added. The organic layer was washed with water (2 × 10 ml), dried over $MgSO_4$, filtered, and evaporated to dryness. The residue, obtained in 100% yield, consisted of **13** contaminated with a small quantity of DMSO. It was washed several times with ether to yield pure **13**, mp 108–110° (60% yield). Omission of the base in the work-up gave a mixture of products in the initial residue; **13** was one of them but it could not be obtained in a pure state unless the residue was washed with aqueous base.

A variation in procedure was used in preparing **14**. A stirred slurry of *p*-nitrobenzamide (2.4 g, 0.015 mol) in DMSO (1.45 ml, 0.02 mol) and CH_2Cl_2 (15 ml) was cooled to −60° and TFAA (2.8 ml, 0.02 mol) was added slowly while maintaining the temperature below −50°. After 2.5 hr all of the amide was consumed (TLC) and the reaction mixture was allowed to warm to room temperature. Ether (30 ml) was added and the precipitate was filtered, washed with ether, and dried, mp 217–218° (2.96 g, 92%). A single crystallization from methanol yielded product of mp 220–222°.[1b]

To prepare **15**, a slurry of urea (1.2 g, 0.02 mol) in DMSO–CH_2Cl_2 (4 ml of 1:1 v/v) was added to the reagent (**3**) prepared from equimolar quantities (0.02 mol) of DMSO and TFAA in CH_2Cl_2 (10 ml) at −50°. After 3 hr the reaction mixture was allowed to warm to room temperature and the precipitate was filtered and dried; mp 136–135° (80%). Recrystallization from ethanol–ether (1:3) did not raise the melting point. Analysis showed that **15** was the trifluoroacetate of the monoylide.

Use of 0.03 mol of reagent (**3**) to 0.01 mol of urea yielded a mixture of products one of which corresponded to **15** (TLC). No further examination was made of this reaction.

Compounds 5–11. The reagent (**3**) was prepared from DMSO (0.018 mol) and TFAA (0.01 mol) in CH_2Cl_2 (5 ml) at −60°. *p*-Nitroaniline (0.01 mol dissolved in 5 ml of CH_2Cl_2 + 3 ml of DMSO) was slowly added while maintaining the temperature below −40° during the addition. By the time all the amine had been added, the precipitate of **3** had disappeared. Aqueous 10% sodium hydroxide solution (5 ml) was added and the stirred reaction mixture was allowed to warm to room temperature. The solution was extracted with CH_2Cl_2 (2 × 20 ml) and the combined CH_2Cl_2 extracts were washed with water (2 × 10 ml) and dried over anhydrous $MgSO_4$. Evaporation of the filtrate to dryness under vacuum yielded a brown residue in quantitative yield. Recrystallization from CH_2Cl_2–ether using decolorizing carbon yielded pure **11**, mp 166–167° dec (65%) (melting point, NMR, ir, TLC identical with those of an authentic sample[1b]).

Compound **10** was similarly prepared but reaction time was 1 hr. The crude product was a reddish oil whose NMR and ir indicated

that it was mainly **10**. Recrystallization from CH_2Cl_2–ether (1:5) yielded orange needles: mp 73–74° (60%); ir 3010, 2920, 1600, 1510, 1350, 1270, 1170, 910, 840, 750, 670 cm^{-1}.

The ylide from *o*-fluoroaniline was obtained as an oil that could not be crystallized; its NMR spectrum was consistent with the proposed structure. The picrate salt of the ylide (compound **8**) was prepared from **3** (0.02 mol) and *o*-fluoroaniline (0.01 mol) in CH_2Cl_2 (10 ml) at −50° followed by addition of a methanol solution of picric acid at −20°. The yellow precipitate was filtered, washed with cold solvent, and dried. Analysis and NMR confirmed its structure as the picrate salt of **8**, mp 140–141° dec (85%).

Compounds **5**, **6** and **7** were also isolated as picrates, essentially as just described; their melting points with decomposition are 130–130.5°, 165–168°, and 165–166°, respectively. The ylide **6**, mp 132° dec, could be prepared also but it was too unstable to obtain an elemental analysis; its NMR was consistent with the ylide structure. During the determination of its melting point it blackened.

Preparation of 24 and 22. To a stirred slurry of **3** (0.03 mol) at −60° a solution of sulfanilamide (**18**, 1.72 g, 0.01 mol) in DMSO (4.5 ml) or DMSO–CH_2Cl_2 (10 ml of 1:1 v/v) was added dropwise. After about 1–2 hr TEA (0.02 mol) was added and the stirred reaction mixture was allowed to warm to room temperature. Ether (20–100 ml) was added and the white precipitate (3.5–4.5 g) was separated by filtration. Recrystallization either from methanol, methanol–acetone, or methanol–methylene chloride yielded pure **24** (75–95%): mp 174–176° dec; NMR (Me_4Si 0) [DMSO-d_6–D_2O (1:1)] δ 2.8 s, 6 H; 3.36, s, 6 H; 7.3, dd, 2 H; 7.8, dd, 2 H; ir 1250 (SO_2 asymmetrical), 1120 (SO_2 symmetrical), 1690 cm^{-1} (C=O). Anal. Calcd for $C_{12}H_{17}F_3N_2O_4S_3$: C, 35.5; H, 4.20; F, 14.0; N, 6.89; S, 23.6. Found: C, 35.8; H, 4.19; F, 13.8; N, 6.9; S, 23.4.

Compound **24** (0.41 g, 0.001 mol) was stirred for 1 hr at room temperature with excess TEA (2.5 ml) and CH_2Cl_2 (2 ml). Solution was not obtained; the solid (0.170 g, 59%), mp 179–182° dec, was filtered, washed, and dried under vacuum. It was shown to be pure **22** by spectral measurements and elemental analysis: NMR (DMSO-d_6) δ 2.65, 2, 6 H; 2.8, s, 6 H; 6.8, dd, 2 H; 7.5, dd, 2 H. Anal. Calcd for $C_{10}H_{16}N_2O_2S_3$: C, 41.4; H, 5.47; N, 9.58; S, 32.9. Found: C, 41.2; H, 5.28; N, 9.37; S, 32.6.

The conversion of **24** to **22** was also conducted in D_2O–NaOH solution in an NMR tube. Compound **24** (27 mg) was dissolved in D_2O (1 ml) in an NMR tube and its spectrum was recorded. A few drops of 50% aqueous NaOH solution was added and the NMR spectrum was immediately rerecorded: NMR (D_2O δ 5) **24**, 3.1, s, 6 H; 3.6, s, 6 H; 7.6, dd, 2 H; 8.2, dd, 2 H; **22**, 2.7, s, 12 H; 6.8, dd, 2 H; 7.5, dd, 2 H.

Preparation of 20. A. Unsuccessful Preparation. Sulfanilamide (**18**, 0.01 mol) in DMSO–CH_2Cl_2 (7 ml of 1:1 v/v) was added to **3** (0.01 mol) at −50° with stirring, followed after 5 min by the addition of TEA (0.02 mol). The reaction mixture was allowed to warm to room temperature. An oil separated from which the supernatant solvent layer was decanted. The residual oil was washed with CH_2Cl_2–diethyl ether (1:1), leaving a sticky solid residue (2.2 g). Its NMR spectrum indicated that it was mainly the diiminosulfurane monosalt, **24**. TLC showed three spots corresponding to **24** and **18** (major products) and a minor unidentified species.

B. Successful Preparation. In a specially constructed apparatus consisting of two three-neck flasks vertically arranged and interconnected by means of a stopcock between the upper and lower flasks (both of which could be independently cooled), reagent **3** (0.02 mol) was prepared in the upper flask, the contents of which were mechanically stirred at −50°. The intermediate was then added dropwise to the lower flask which contained **18** (0.02 mol) in DMSO–CH_2Cl_2 (10 ml of 1:1 v/v) at −50°, magnetically stirred. The addition required about 30 min. Stirring was continued at −50° for an additional 15 min and the lower flask was allowed to warm to room temperature. TEA (8 ml) was added and the white precipitate that formed was filtered, washed successively with cold CH_2Cl_2 and diethyl ether, and dried; compound **20** (2.3 g, 50%), mp 135–137° dec, was thus obtained in analytical purity. It gave a negative ninhydrin test and did not form an azo dye with β-naphthol. It was insoluble in water but soluble in aqueous base (sulfonamide group present): NMR (DMSO-d_6 + D_2O) (D_2O δ 4.0) 2.7, s, 6 H; 6.7, dd, 2 H; 7.5, dd, 2 H. Anal. Calcd for $C_8H_{12}N_2O_2S_2$: C, 41.4; H, 5.20; N, 12.1; S, 27.6. Found: C, 41.3; H, 5.14; N, 12.0; S, 27.4.

Preparation of 21. A. Compound **24** (1.2 g, 0.003 mol) was dissolved in water (40 ml) and prewashed Amberlite IR-45 ion-exchange resin (10 ml of aqueous slurry) was added. After overnight stirring, the mixture was filtered and the filtrate was freeze dried. The precipitate was recrystallized from *i*-PrOH, yielding **21** (0.200 g, 30%), mp 190–193° (positive ninhydrin test).

B. A. 7.2 × 2.5 cm column was packed with 60 ml of a slurry of Amberlite IRA-400 (Cl^-) ion-exchange resin. A 5% NaOH solution (120 ml) was passed through the column to convert the resin to the hydroxide form. The column was then washed thoroughly with distilled water (ca. 500 ml) until the pH of the effluent was 7. The monotrifluoroacetate **24** (4.8 g) was dissolved in H_2O–MeOH (35 ml of 85:15 v/v) and the solution was added to the column. The column was eluted with H_2O–MeOH (300 ml of 95:5 v/v adjusted to pH 9) and the eluate was evaporated to dryness at 30° under high vacuum. The residual solid was triturated with *i*-PrOH to yield an insoluble white solid (2.7 g). TLC showed the presence of three components, one major and two minor. Ir and NMR indicated that trifluoroacetic acid had been completely removed. Column chromatography on silica gel (80 g) and elution with MeOH–$CHCl_3$ (5:95) yielded **25** (600 mg), mp 162–163°, and **21** (1.2 g), mp 190–193°. Anal. Calcd for $C_{10}H_{16}N_2O_2S_3$ (**25**): C, 41.4; H, 5.20; N, 12.1; S, 27.6; *m/e* 292. Found: C, 41.2; H, 5.47; N, 9.46; S, 32.8; *m/e* 292. Anal. Calcd for $C_8H_{12}N_2O_2S_2$ (**21**): C, 41.4; H, 5.20; N, 12.1; S, 27.6. Found: C, 41.4; H, 5.18; N, 11.9; S, 27.5. NMR spectra (DMSO-d_6) (Me_4Si 0) **21**, δ 6.6–7.4, dd, 4 H; 5.68, broad s, 2 H (signal disappears on addition of D_2O); 2.65, s, 6 H; **25**, 7.4, s, 1 H, 6.7–7.4, dd, 2 H; 5.60, broad s, 2 H (signal disappears on addition of D_2O); 3.62, s, 2 H; 2.64, s, 6 H; 1.98, s, 3 H. Ir (Nujol mull) **21**, 3440, 3330, 1248, 1125, 1090, 950, 840, 772 cm^{-1}; **25**, 3440, 3330, 3250, 1253, 1117, 1094, 958, 769 cm^{-1}; uv λ_{max} (EtOH) **21**, 211 nm (ε 16,300), 265 (24,500); **25**, 216 nm (ε 382), 267 (361).

Preparation of 23. To a stirred slurry of **3** (0.02 mol) in DMSO–CH_2Cl_2 (12 ml of 1:1 v/v) at −60°, *N'*-2-pyrimidinylsulfanilamide (sulfadiazine, **19**) in DMSO–CH_2Cl_2 (35 ml) was added while maintaining the temperature at or below −45°. After 30 min 10% NaOH (25 ml) was slowly added and the reaction mixture was stirred for an additional 30 min at −45°. After warming to room temperature, the reaction mixture was filtered yielding crude **23** (4.4 g, 70%). It was dissolved in a minimum quantity of water without heating, *i*-PrOH was added to the cloud point, and the mixture was cooled to 0–5° to yield **23** as the sodium salt (dihydrate): mp 265–268°; NMR (D_2O) δ 2.68, s, 6 H; 6.65, t, 1 H; 6.85, d, 2 H; 7.75, d, 2 H; 8.25, d, 2 H. Compound **23** is unstable in water and undergoes a Sommelet–Hauser type of rearrangement ($t_{1/2} \simeq$ 24 hr at room temperature): ir (Nujol mull) 1405, 1210, 1115, 815 cm^{-1}; uv λ_{max} (EtOH) 285 nm (ε 17,400). Anal. Calcd for $C_{12}H_{13}N_4O_2S_2Na \cdot 2H_2O$: C, 39.1; H, 4.64; N, 15.2; S, 17.4; Na, 6.24. Found: C, 39.5; H, 4.64; N, 15.19; S, 17.4; Na, 6.30.

Independent Syntheses. 26. Sulfanilamide (**18**, 1.72 g, 0.01 mol) was dissolved in acetone (20 ml) followed by addition to the stirred solution of aqueous sodium bicarbonate (1.26 g, 0.015 mol in 5 ml of H_2O) and then benzyl chloroformate (2.5 ml, ca. 0.02 mol). After 18 hr, the reaction mixture was evaporated to dryness at 40°. The white residue was triturated with H_2O and filtered. The dried precipitate was washed with cold methylene chloride and ether. The residue was crystallized from *i*-PrOH to yield **26**, mp 192–193° (negative ninhydrin test). TLC (10% MeOH–$CHCl_3$ development) gave a single spot (R_f 0.5).

Compound 27. The DMSO–TFAA complex was prepared at −45° from DMSO (1.9 ml) dissolved in CH_2Cl_2 (5 ml) and TFAA (1.5 ml, 0.01 mol). To the resulting stirred suspension, **26** (2.5 g, 0.008 mol) dissolved in DMSO–CH_2Cl_2 (15 ml of 1:2 v/v) was added at −45° or below. After 10 min, TEA (1.7 ml) was added and the reaction mixture was allowed to warm to room temperature. After concentration to a small volume at 45° under vacuum, *i*-PrOH–Et_2O (1:1) was added to remove soluble impurities (mainly DMSO). The white solid residue (1.5 g, 50%) was crystallized from *i*-PrOH to yield **27**: mp 148–149°; NMR (DMSO-d_6) (Me_4Si 0) **26**, δ 5.20, s, 2 H; 7.20, broad s, 2 H; 7.40, s, 5 H; 7.62–7.80, dd, 4 H; **27**, 2.65, s, 6 H; 5.18, s, 2 H; 7.40, s, 5 H; 7.60, s, 4 H.

Conversion of 21 to 27. To a stirred solution of **21** (0.1 g) in acetone (3 ml), aqueous $NaHCO_3$ (0.2 g in 2 ml of H_2O) was added followed by benzyl chloroformate (1 ml). After 3 hr the reaction mixture was evaporated to dryness and worked up as above. The product obtained was identical in every way with **27** (NMR, ir, uv, melting point, mixture melting point).

Attempted Debenzylation of 27. Attempted reconversion of **27** to **21** by hydrogenolysis in methanol with 5% Pd/C catalyst at 60 psi or with boron trifluoroacetate in trifluoroacetic acid was unsuccessful. Hydrogenolysis yielded a mixture of **18** and **26** and the boron reagent yielded only **18**.

Acknowledgment. We thank the National Cancer Institute of the U.S. Public Health Service (CA-07803 and

122273) and the Samuel S. Fels Fund for partial support of this research.

Registry No.—**5** picrate, 55975-86-5; **6**, 27691-49-2; **6** picrate, 55871-34-6; **7** picrate, 55871-35-7; **8** picrate, 55871-37-9; **9**, 39159-87-0; **10**, 55871-38-0; **11**, 27691-52-7; **13**, 19397-91-2; **14**, 55259-85-5; **15** trifluoroacetate, 55871-40-4; **16**, 19871-30-8; **17**, 18922-58-2; **18**, 63-74-1; **19**, 68-35-9; **20**, 55871-41-5; **21**, 24194-22-7; **22**, 55871-42-6; **23**, 55871-43-7; **24**, 55871-44-8; **25**, 55871-45-9; **26**, 55871-46-0; **27**, 55871-47-1; DMSO, 67-68-5; TFAA, 407-25-0; *p*-nitrobenzenesulfonamide, 6325-93-5; benzamide, 55-21-0; *p*-nitrobenzamide, 619-80-7; urea, 57-13-6; *p*-nitroaniline, 100-01-6; *o*-fluoroaniline, 348-54-9; benzyl chloroformate, 501-53-1.

References and Notes

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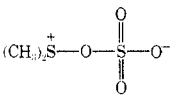
(12) "Activation" of DMSO by sulfur trioxide or phosphorus pentoxide yields a "zwitterionic" intermediate **1**, with a good leaving group. With sulfur trioxide, for example, **1** can be written as A; NMR evidence supports such a formulation.[1b]



A

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(18) Sulfanilamide (**18**) gives a positive ninhydrin test and is soluble in aqueous base.
(19) P. Gassman and G. Gruetzmacher, *J. Am. Chem. Soc.*, **96**, 5487 (1974), and following papers.
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(21) Infrared spectra were recorded on a Perkin-Elmer 137B or Pye Unicam SP-1000. NMR spectra (hydrogen only) were obtained on Varian Models A-60A or XL-100 with Me_4Si as internal standard. Melting points (uncorrected) were obtained using a Thomas-Hoover capillary apparatus. TLC was conducted on Eastman silica gel chromatograms or coated microscope slides with fluorescent indicator; visualization was effected either with uv light or by development in a chamber containing iodine crystals. All reactants were the purest obtainable; in all cases purity exceeded 97%. Solvents were the best commercial grades and were used as received, except methylene chloride, which was dried and fractionally distilled. DMSO was distilled under reduced pressure from calcium hydride and stored in a nitrogen atmosphere over Linde molecular sieve 4A. Trifluoroacetic anhydride was obtained from various chemical supply houses and was used as received; it contained less than 0.1% free acid. Sulfanilamide and sulfadiazine were the purest grades and were used as received.

Acid-Catalyzed Reactions of Epoxides with Dimethyl Sulfoxide[1a]

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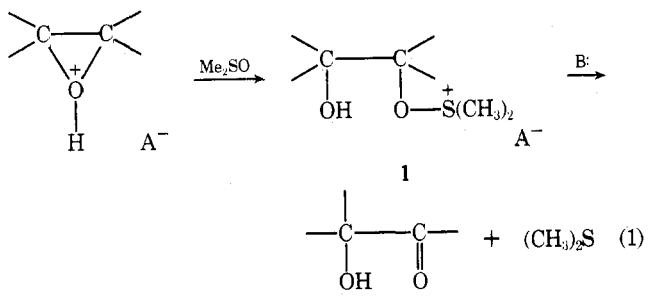
Ring-opening reactions of styrene oxide, *p*-nitrostyrene oxide, cyclopentene, cyclohexene, and cycloheptene oxides, and *cis*- and *trans*-9,10-epoxystearic acids with Me_2SO in the presence of strong acids have been studied both by NMR and preparatively. In most instances, initial products are vicinal hydroxyalkoxysulfonium salts. Regiospecificity of ring opening is observed with styrene oxide and *p*-nitrostyrene oxide; stereospecificity is observed with cyclohexene oxide and *cis*- and *trans*-9,10-epoxystearic acids. Treatment of selected salts with bases yields mixtures of 1,2-ketols and glycols even in the absence of water, with glycols usually predominating. In contrast with cyclohexene oxide, which reportedly gives fair to good yields of adipoin on treatment with boron fluoride etherate followed by base, cyclopentene and cylcoheptene oxides isomerize largely to the corresponding ketones.

In an earlier study[2] we showed that 2,4,6-trinitrobenzenesulfonic acid is a useful strong acid catalyst for the regio- and stereospecific preparation of crystalline vicinally substituted hydroxyalkoxysulfonium salts (**1**, eq 1) from Me_2SO and epoxides.



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To assess the generality of the acid-catalyzed Me_2SO ring-opening reaction, we had been concurrently exploring other strong acid catalysts (boron trifluoride, fluoroboric, trifluoroacetic, methanesulfonic, sulfuric, and nitric acids) which also provide anions of low nucleophilicity; this paper describes the results of that investigation. Although crystalline salts (**1**) were usually not obtained with the latter group of acids, the course of the reactions and the initial products were readily monitored by NMR. In addition we are reporting (a) the overall oxidation of epoxides to α-hydroxy ketones (ketols) (**2**) via the intermediate salts (**1**) upon treatment with base, (b) the stereospecific conversion of epoxides to 1,2-glycols by hydrolysis of **1** or its attack by nucleophiles, and (c) some miscellaneous reactions of the epoxides and salts (**1**).

The regiospecificity of attack of many nucleophiles on unsymmetrical epoxides under acid conditions has been