in mechanism either for corresponding compounds in the two series or for compounds within a series. Thus, in 50% dioxane-D_2O as the solvent, $k_D^{D_2O}/k_H^{H_2O} > 2.7$ for compounds IV, V, and X-XIII. These values are typical of an A-1 mechanism.[23] The constancy of the ΔS^* term for compounds within a series would certainly lend strong support to the idea that the mechanism is the same for all of them.

Both positive and small negative values of ΔS^* have been obtained for acid-catalyzed hydrolyses of methyl-substituted 1,3-dioxolanes.[24] There would appear to be no reason why either type of value should not be possible for an A-1 reaction but the present data show that an A-1 cleavage of a five-membered ring can have a ΔS^* value from 8 to 10 e.u. more negative than for the exactly analogous open-chain compound.

Acknowledgment.—This work was supported by grants from The National Institutes of Health and the American Cancer Society.

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Reactions of Alkanesulfonyl Chlorides with Ketene N,N- and O,N-Acetals

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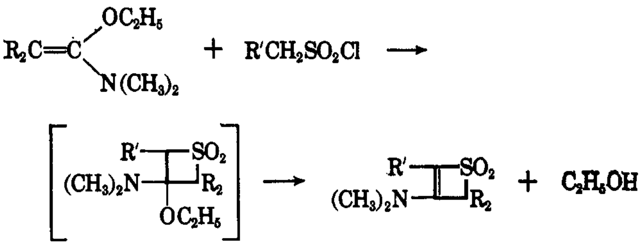
Methanesulfonyl chloride reacts with ketene N,N- and O,N-acetals in the presence of triethylamine in a nonpolar solvent to give 3-(dialkylamino)thiete 1,1-dioxides, but, if polar solvents are used with N,N-acetals, the predominant products are the acyclic sulfonylketene N,N-acetals. Some reactions of the 3-(dialkylamino)-thiete 1,1-dioxides are described.

The reactions of alkanesulfonyl chlorides with compounds containing electron-rich double bonds, such as enamines,[2,3] ketene acetals,[4] ketene O,N-acetals, and ketene N,N-acetals,[5] have been reported recently. This paper is a more detailed account of our earlier work with ketene O,N- and N,N-acetals.

The historical concepts and backgrounds for the production of sulfenes by the action of tertiary amines on alkanesulfonyl chlorides have been thoroughly reviewed by Truce and Norell.[4] The presence of sulfene intermediates in the cycloadditions described in the articles cited previously has been given consideration, but only recently have sulfenes been proved to be intermediates in reactions involving alkanesulfonyl chlorides.[6,7]

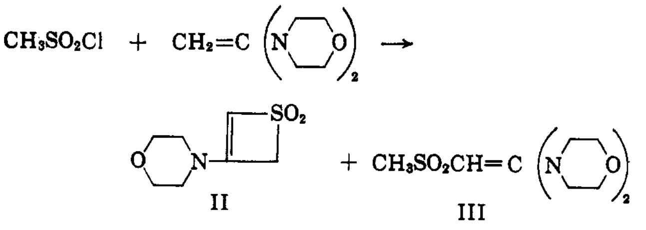
Ketene O,N-acetals, when treated with alkanesulfonyl chlorides in the presence of triethylamine (TEA), yield 3-(dialkylamino)thiete 1,1-dioxides (I). This cycloaddition is similar to the reaction of sulfenes with enamines and ketene acetals because the products are four-membered rings (thietanes) that are formed by 1,2-cycloaddition of a sulfene with a compound containing an electron-rich double bond. The products I, however, are thietes which may have arisen from β-elimination of an alcohol from the intermediate thietane structure.

Ketene N,N-acetals react with alkanesulfonyl chlorides in the presence of triethylamine to give 3-(dialkylamino)thiete 1,1-dioxides and 2-alkylsulfonyl-1,1-bis(dialkylamino)ethylenes. In most cases both types of products are formed, but in widely varying amounts depending upon the polarity of the solvent used and the nature of the alkane group of the sulfonyl chloride.



Ia, R = H; R' = H
b, R = CH_3; R' = H
c, R = CH_3; R' = C_3H_7

Highly polar solvents and higher alkane groups on the sulfonyl chlorides favor the formation of acyclic products, while the use of methanesulfonyl chloride and lower polarity solvents favors cyclic product formation. 4,4'-Vinylidenedimorpholine, methanesulfonyl chloride, and triethylamine in tetrahydrofuran (THF) gave the thiete dioxide II in 79% crude yield. Its infrared spectrum[8] showed that a small amount of the acyclic derivative III was present. II was purified by recrystallization from benzene. Using the same reactants in benzene, II was obtained in 69% crude yield. The use of highly polar solvents favored formation of the acyclic derivative III. When treated in acetonitrile, methanesulfonyl chloride, 4,4'-vinylidenedimorpholine, and triethylamine gave III in 48% yield after purification and in N,N-dimethylformamide gave III in 58% yield after purification. The infrared spectra of the crude reaction mixtures obtained when using highly polar solvents showed the products to be pri-



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[1] To whom all inquiries should be sent.

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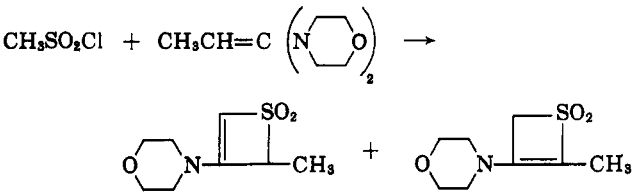
[8] Infrared spectra were determined on a Baird AB-2 instrument.

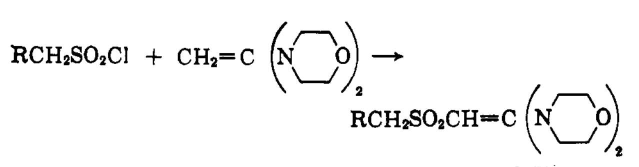
marily acyclic with only a small amount of contamination by the cyclic derivative, whereas the crude products obtained when using lower polarity solvents contained substantial portions of products of both types. The cyclic compounds exhibited characteristic strong infrared absorption bands at 6.2 μ, and the acyclic materials showed bands at 6.5 μ. The compositions of mixtures containing cyclic and acyclic products were estimated from the relative intensities of the absorption bands.

The reaction of methanesulfonyl chloride with 4,4'-propenylidenedimorpholine in the presence of triethylamine using tetrahydrofuran as solvent gave, in 52% yield, a mixture of 4-methyl-3-morpholinothiete 1,1-dioxide (IV) and 2-methyl-3-morpholinothiete 1,1-dioxide (V) in the ratio of 3 to 1. The identities and amounts of IV and V were established from the n.m.r. spectra. The n.m.r. spectrum of V showed an unusual long-range splitting. The methylene group appeared as a quartet at 4.12 p.p.m. (J = 2.1 c.p.s.) and the methyl group as a triplet at 2.00 p.p.m. (J = 2.1 c.p.s.).[9]



IV V

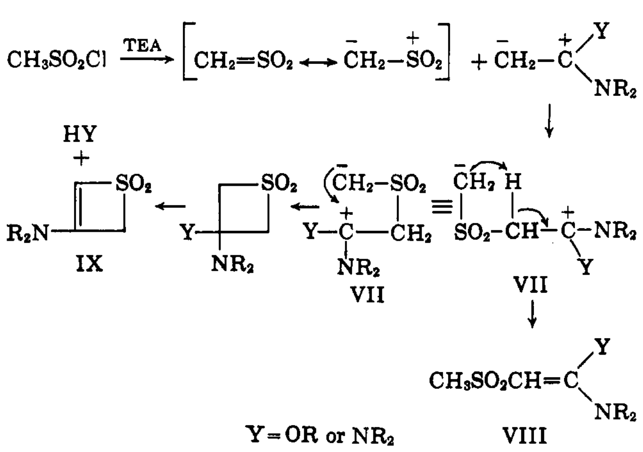
The reaction of 4,4'-vinylidenedimorpholine with 1-butanesulfonyl chloride and α-toluenesulfonyl chloride in the presence of triethylamine in tetrahydrofuran gave only the acyclic products VIa (38%) and VIb (60%).



VIa, R = C_3H_7
b, R = C_6H_5

In toluene, a solvent known to favor the formation of cyclic products with methanesulfonyl chloride, only VIa was obtained with 1-butanesulfonyl chloride.

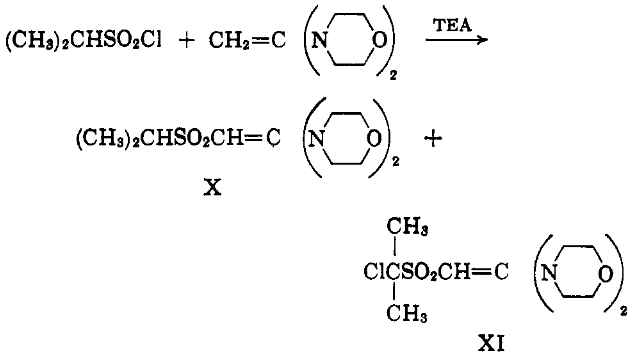
The paths that these reactions follow cannot be stated with certainty, but, in view of recent articles[6,7] demonstrating the existence of sulfene intermediates, we believe the following mechanism is logical. This mechanism is based on the assumption that triethylamine dehydrohalogenates methanesulfonyl chloride to produce sulfene. The sulfene adds to the electron-rich double bond of the ketene O,N- or N,N-acetal to give the intermediate zwitterion VII. The path of collapse of VII determines whether the ultimate product is VIII or IX.



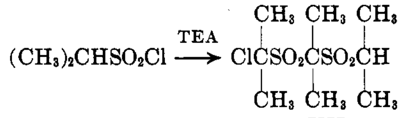
IX NR₂ VII VII VIII

Y = OR or NR₂

The reaction of 2-propanesulfonyl chloride with 4,4'-vinylidenedimorpholine in the presence of triethylamine in tetrahydrofuran gave a 21% yield of a 40:60 mixture of the normal acyclic product X and the unexpected chloroalkyl derivative XI. The composition of this mixture was determined from the n.m.r. spectrum. The less soluble component XI was isolated by crystallization from benzene. Although Fusco, *et al.*,[10] report the formation of a chloroisopropyl derivative XII from 2-propanesulfonyl chloride and triethylamine, their mechanism is inoperative for the formation of XI.



X XI



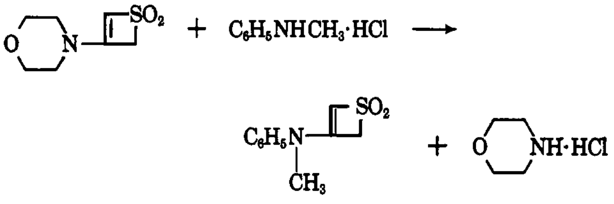
$$(CH_3)_2CHSO_2Cl \xrightarrow{TEA} Cl\underset{CH_3}{\overset{CH_3}{C}}SO_2\underset{CH_3}{\overset{CH_3}{C}}SO_2\underset{CH_3}{\overset{CH_3}{C}}H$$

XII

Benzenesulfonyl chloride and 4,4'-vinylidenedimorpholine in the presence of triethylamine gave 4,4'-(phenylsulfonyl)vinylidenedimorpholine (XIII) in 37% yield.

The 3-(dialkylamino)thiete 1,1-dioxides are crystalline, white, water-soluble solids. Their infrared spectra are characterized by three very strong bands at 6.1–6.2 (olefinic function), and 7.9–8.0 and 9.1 μ (sulfonyl function).

Treatment of Ia with morpholine in refluxing toluene, in an attempt to prepare II by exchange of the amine moiety, showed no reaction. However, II and N-methylaniline hydrochloride in refluxing benzene gave 3-(N-methylanilino)thiete 1,1-dioxide (XIV) in 55% yield. Careful hydrolysis of the 3-(dialkylamino)thiete 1,1-



XIV

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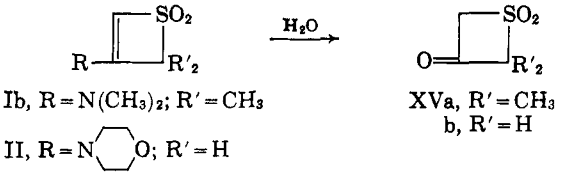
[9] N.m.r. spectra were recorded on a Varian A-60 instrument at 60 Mc. Field position values are referred to tetramethylsilane as an internal standard.

[10] R. Fusco, S. Rossi, and S. Maiorana, *Chim. Ind.* (Milan), **45**, 564 (1963).

dioxides Ib and II using an acidic ion-exchange resin gave the corresponding 3-thietanone 1,1-dioxides XVa and XVb. These cyclic β-keto sulfones were comparable in acidity to carboxylic acids (XVa, pK_a = 4.1, and XVb, pK_a = 4.4). Identifications were made by



Ib, R = $N(CH_3)_2$; R' = CH_3

II, R = N O; R' = H

XVa, R' = CH_3
b, R' = H

elemental analysis and infrared and n.m.r. spectra. No evidence of the enolic forms of these materials was noticed in the infrared or n.m.r. spectra as determined in D_2O, tetrachloroethane, or dimethyl sulfoxide. The reactions of 3-thietanone 1,1-dioxide (XVb) have recently been described by Truce and Norell.[11]

Experimental

Materials.—Methanesulfonyl chloride, 1-butanesulfonyl chloride, and benzenesulfonyl chloride were obtained from Distillation Products Industries. α-Toluenesulfonyl chloride was obtained from Hooker Chemical Corp. 2-Propanesulfonyl chloride[12] [b.p. 62.5–64.5° (7.5 mm.), $n^{20}D$ 1.4529], 4,4'-vinylidenedimorpholine,[13] 4,4'-propenylidenedimorpholine,[13] 1-ethoxy-N,N-dimethylvinylamine,[14] and 1-ethoxy-N,N-dimethylisobutenylamine[15] were prepared by methods described in the literature.

It was observed that the use of good quality, dry reagents and solvents resulted in better yields of product and lessened the formation of intractable dark sirups.

The sulfonyl chlorides were fractionally distilled before use. TEA was distilled from and stored over sodium. THF was a special Du Pont grade containing no more than 5 p.p.m. of water. Acetonitrile was distilled from phosphorus pentoxide. N,N-dimethylformamide was fractionally distilled.

General Procedure for Reaction of Sulfonyl Chlorides with Ketene O,N- and N,N-Acetals.—In order to avoid needless repetition, the experimental conditions for carrying out these reactions have been generalized. A stirred solution of 0.1 mole of the substituted olefin and 0.10–0.11 mole of TEA in 50 ml. of solvent, under a slight pressure of dry nitrogen, was maintained at −5 to +5° while a solution of 0.1 mole of the sulfonyl chloride in 25 ml. of the same solvent was added over a period of 0.5–1 hr. Usually TEA hydrochloride separated immediately. The resulting suspension was allowed to warm slowly to room temperature and was then stirred for about 12 hr. The solid (TEA hydrochloride) was removed by filtration and washed with a small amount of solvent. The filtrate and washings were concentrated under reduced pressure, using a 30 to 40° water bath. The resulting solid was removed from the accompanying viscous sirup by filtration and was washed with a small amount of cold THF and ethyl alcohol.

Infrared spectra of the crude TEA hydrochloride frequently indicated admixture with much additional product. This was separated from the relatively insoluble salt by two or three extractions with acetone at room temperature.

The combined crude product was usually washed with and recrystallized from ethyl alcohol. This solvent was especially advantageous for removing traces of salts and colored sirups.

3-(Dimethylamino)thiete 1,1-Dioxide (Ia).—Under the general procedure with THF as solvent, methanesulfonyl chloride and 1-ethoxy-N,N-dimethylvinylamine gave a 33% yield of Ia, m.p. 120–123°. Infrared absorptions (KBr) were at 6.1, 7.95, and 9.15 μ. The n.m.r. spectrum ($CHCl_3$) showed singlets at 2.90 (dimethylamino group), 4.35 (CH_2), and 5.23 p.p.m. (olefinic proton).

Anal. Calcd. for $C_5H_9NO_2S$: C, 40.8; H, 6.1; N, 9.5; S, 21.7. Found: C, 40.8; H, 6.3; N, 9.4; S, 21.7.

4,4-Dimethyl-3-(dimethylamino)thiete 1,1-Dioxide (Ib).—Under the general procedure with THF as solvent, methanesulfonyl chloride and 1-ethoxy-N,N-dimethylisobutenylamine gave a 69% yield of Ib, m.p. 135–136°. Infrared absorptions (KBr) were at 6.2, 8.0, and 9.2 μ. The n.m.r. spectrum ($CHCl_3$) showed singlets at 1.68 (methyl groups attached to carbon), 2.88 (dimethylamino group), and 5.03 p.p.m. (olefinic proton).

Anal. Calcd. for $C_7H_{13}NO_2S$: C, 48.0; H, 7.5; N, 8.0; S, 18.3. Found: C, 48.2; H, 7.2; N, 7.8; S, 18.1.

4,4-Dimethyl-3-(dimethylamino)-2-propylthiete 1,1-Dioxide (Ic).—Under the general procedure with THF as solvent, 1-butanesulfonyl chloride and 1-ethoxy-N,N-dimethylisobutenylamine gave a viscous product that was purified by molecular distillation followed by recrystallization from butyl ether to give a 22% yield of Ic, m.p. 59–60.5°. Infrared absorptions (KBr) were at 6.15, 8.0, and 9.1 μ. The n.m.r. spectrum (CCl_4) showed a triplet at 0.97 (methyl protons of propyl group), a singlet at 1.57 (*gem*-dimethyl group), a multiplet at 1.62 (CH_2), a triplet at 2.31 ($—CH_2C{=}C$), and a singlet at 2.95 p.p.m. (dimethylamino group).

Anal. Calcd. for $C_{10}H_{19}NO_2S$: C, 55.3; H, 8.8; N, 6.4; S, 15.3. Found: C, 55.3; H, 8.8; N, 6.5; S, 15.0.

3-Morpholinothiete 1,1-Dioxide (II).—Under the general procedure with THF as solvent, methanesulfonyl chloride and 4,4'-vinylidenedimorpholine gave a 79% crude yield of II, m.p. 118–128°. Recrystallization from benzene (10 ml./g.) gave a 29% yield of II, m.p. 138–141°. A sample after recrystallization from ethyl alcohol and sublimation at 117° (0.002 mm.) melted at 140.5–141°. Infrared absorptions (KBr) were at 6.2, 7.9, 8.85, and 9.05 μ. The n.m.r. spectrum ($CHCl_3$) showed triplets at 3.19 and 3.76 (morpholino group), and singlets at 4.38 (CH_2) and 5.30 p.p.m. (olefinic proton).

Anal. Calcd. for $C_7H_{11}NO_3S$: C, 44.4; H, 5.9; N, 7.4; S, 16.9. Found: C, 44.2; H, 6.0; N, 7.2; S, 16.9.

4,4'-(Methylsulfonyl)vinylidenedimorpholine (III).—Under the general procedure with acetonitrile as the solvent, methanesulfonyl chloride and 4,4'-vinylidenedimorpholine gave a 48% yield of III, m.p. 174–176.5°. Infrared absorptions were at 6.5, 7.9, and 9.0 μ. The n.m.r. spectrum ($CHCl_3$) showed a singlet at 2.94 (methyl group), multiplets at 3.10, 3.34, and 3.64 (two morpholine groups), and a singlet at 4.23 p.p.m. (olefinic proton).

Anal. Calcd. for $C_{11}H_{20}N_2O_4S$: C, 47.8; H, 7.3; N, 10.1; S, 11.6. Found: C, 47.9; H, 7.7; N, 10.5; S, 11.2.

4-Methyl-3-morpholinothiete 1,1-Dioxide (IV) **and 2-Methyl-3-morpholinothiete 1,1-Dioxide** (V).—Under the general procedure with THF as solvent, 4,4'-propenylidenedimorpholine and methanesulfonyl chloride gave a 52% yield of a mixture of IV and V, m.p. 136–138° with prior softening at 96°. Infrared absorptions (KBr) were at 6.2, 7.9, and 9.1 μ. The n.m.r. spectrum ($CHCl_3$) indicated a 3:1 ratio of IV and V. The spectrum of IV showed a doublet at 1.19 (methyl group), multiplets at 3.34 and 3.94 (morpholino groups), a quartet at 4.82 (CH), and a singlet at 5.49 p.p.m. (olefinic proton).

Anal. Calcd. for $C_8H_{13}NO_3S$: C, 47.3; H, 6.5; N, 6.9; S, 15.8. Found: C, 47.7; H, 6.8; N, 7.0; S, 16.4.

Recrystallization from benzene gave a fraction rich in V, m.p. 145–145.5°. The n.m.r. spectrum ($CHCl_3$) showed triplets at 2.00 (J = 2.1 c.p.s.) (methyl group), 3.37 and 3.88 (morpholino groups), and a quartet at 4.12 p.p.m. (J = 2.1 c.p.s.) (CH_2).

4,4'-(Butylsulfonyl)vinylidenedimorpholine (VIa).—Under the general procedure with THF as the solvent, 1-butanesulfonyl chloride and 4,4'-vinylidenedimorpholine gave a 38% yield of VIa, m.p. 124–125°. Infrared absorptions (KBr) were at 6.45, 7.9, and 9.0 μ. The n.m.r. spectrum ($CHCl_3$) showed a triplet at 0.93 (methyl group), multiplets at 1.59 (CH_2CH_2), and 3.10 (CH_2SO_2 and CH_2NCH_2 of one morpholino group), a multiplet at 3.34 and an unresolved broad peak at 3.63 (remaining protons of morpholino groups), and a singlet at 4.41 p.p.m. (olefinic proton).

Anal. Calcd. for $C_{14}H_{26}N_2O_4S$: C, 52.8; H, 8.2; N, 8.8; S, 10.1. Found: C, 52.9; H, 8.3; N, 8.7; S, 10.1.

4,4'-(Benzylsulfonyl)vinylidenedimorpholine (VIb).—Under the general procedure with THF as the solvent, α-toluenesulfonyl chloride and 4,4'-vinylidenedimorpholine gave a 60% yield of VIb, m.p. 160–162°. Infrared absorptions (KBr) were at 6.45,

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[11] W. E. Truce and J. R. Norell, *J. Am. Chem. Soc.*, **85**, 3236 (1963).

[12] Made by the action of PCl_5 on sodium 2-propanesulfonate according to the directions of W. Davies and J. H. Dick, *J. Chem. Soc.*, 484 (1932).

[13] H. Baganz and L. Domaschke, *Chem. Ber.*, **95**, 2095 (1962).

[14] H. Meerwin, W. Florian, N. Schön, and G. Stopp, *Ann. Chem.*, **641**, 1 (1961).

[15] K. C. Brannock, R. D. Burpitt, and J. G. Thweatt, *J. Org. Chem.*, **29**, 940 (1964).

7.95, and 9.0 μ. The n.m.r. spectrum (CH_2Cl_2) showed triplets at 3.00 and 3.27 and a quartet at 3.67 (morpholino groups), singlets at 4.02 (olefinic proton) and 4.29 (CH_2), and a multiplet at 7.48 p.p.m. (aromatic protons).

Anal. Calcd. for $C_{17}H_{24}N_2O_4S$: C, 57.9; H, 6.9; N, 8.0; S, 9.1. Found: C, 57.9; H, 6.8; N, 7.6; S, 9.1.

4,4′-(1-Methylethylsulfonyl)vinylidenedimorpholine (X) and 4,4′-(2-Chloro-1-methylethylsulfonyl)vinylidenedimorpholine (XI).—Under the general procedure with THF as solvent, 2-propanesulfonyl chloride and 4,4′-vinylidenedimorpholine gave a 21% yield of a mixture of X and XI, m.p. 136–143°. The n.m.r. spectrum ($CHCl_3$) of the mixture indicated that it was a 40:60 mixture of X and XI. This ratio was determined by comparison of the area under the peaks for the *gem*-dimethyl protons in the spectrum of XI with the area under the peaks for the methyl protons of the isopropyl group in the spectrum of X. Infrared absorptions of the mixture (KBr) were at 6.5, 7.85, and 9.0 μ. The n.m.r. spectra ($CHCl_3$) showed for X, a doublet at 1.33 (methyl protons of isopropyl group), triplets at 3.22 and 3.43, and a multiplet at 3.69 (methylidyne proton of the isopropyl group and protons of morpholino groups), and a singlet at 4.15 p.p.m. (olefinic proton); for XI, a singlet at 1.89 (*gem*-dimethyl group), triplets at 3.22 and 3.43, a multiplet at 3.69 (protons of morpholino groups), and a singlet at 4.15 p.p.m. (olefinic proton).

Anal. Calcd. for 40% X and 60% XI: Cl, 6.3. Found: Cl, 6.3.

Repeated recrystallizations from benzene gave pure XI, m.p. 151–152°. Infrared absorptions (KBr) were at 6.55, 7.8, and 9.0 μ.

Anal. Calcd. for $C_{13}H_{23}ClN_2O_4S$: C, 46.1; H, 6.8; Cl, 10.5; N, 8.3; S, 9.5. Found: C, 46.5; H, 7.0; Cl, 10.3; N, 7.9; S, 9.8.

4,4′-(Phenylsulfonyl)vinylidenedimorpholine (XIII).—Under the general procedure with THF as solvent, benzenesulfonyl chloride and 4,4′-vinylidenedimorpholine gave a 37% yield of XIII, m.p. 162–163°. Infrared absorptions (KBr) were at 6.5, 7.9, and 9.0 μ. The n.m.r. spectrum ($C_2H_2Cl_4$) showed broad unresolved peaks at 3.20 and 3.62 (morpholino groups), a singlet at 4.41 (olefinic proton), and a multiplet at 7.60 p.p.m. (aromatic protons).

Anal. Calcd. for $C_{16}H_{22}N_2O_4S$: C, 56.8; H, 6.6; N, 8.3. Found: C, 56.8; H, 6.4; N, 8.2.

3-(N-Methylanilino)thiete 1,1-Dioxide (XIV).—A mixture of 1.89 g. (0.01 mole) of II and 1.44 g. (0.01 mole) of N-methylaniline hydrochloride in 20 ml. of benzene was refluxed for 1.5 hr. The hot benzene layer was decanted from the solid present. Evaporation of the benzene gave 2.0 g. of solid residue, m.p. 65–70°. One recrystallization from ethyl alcohol gave 1.15 g. (55%) of XIV, m.p. 99–102°. A sample recrystallized again from ethyl alcohol melted at 101.5–103°. Infrared absorptions (KBr) were at 6.25, 6.3, 7.9, 8.25, and 9.1 μ. The n.m.r. spectrum (CH_2Cl_2) showed singlets at 3.24 (methyl group), 4.29 (CH_2), and 5.37 (olefinic proton), and a multiplet at 7.23 p.p.m. (aromatic protons).

Anal. Calcd. for $C_{10}H_{11}NO_2S$: C, 57.4; H, 5.3; N, 6.7; S, 15.3. Found: C, 56.9; H, 5.1; N, 6.3; S, 15.3.

2,2-Dimethyl-3-thietanone 1,1-Dioxide (XVa).—A mixture of 8 g. (0.046 mole) of Ib and 44 g. of the acid form of Amberlite IR-120 ion-exchange resin and 50 ml. of water was stirred for 3 hr. at 25°. After removal of the resin and evaporation of the water *in vacuo*, there was obtained 6.5 g. (95%) of XVa, m.p. 108–110°. A sample after recrystallization from benzene and sublimation at 75° (0.07 mm.) melted at 108.5–110.5°. Infrared absorptions (KBr) were at 3.35 (w), 3.45 (w), 5.6, 5.7, 7.6, 8.4, 8.95, and 9.4 μ. The n.m.r. spectrum ($CHCl_3$) showed singlets at 1.67 (*gem*-dimethyl groups) and 4.91 p.p.m. (CH_2).

Anal. Calcd. for $C_5H_8O_3S$: C, 40.5; H, 5.4; S, 21.6; neut. equiv., 148.2. Found: C, 40.7; H, 5.5; S, 21.3; neut. equiv., 147.2; pK_a (H_2O) = 4.41.

3-Thietanone 1,1-Dioxide (XVb).—A mixture of 168 g. (0.89 mole) of crude II (m.p. 118–128°, contaminated with III), 900 g. of the acid form of Amberlite IR-120 ion-exchange resin and 1.3 l. of water was stirred at room temperature for 3 hr. After removal of the resin and evaporation of the water *in vacuo* at room temperature, there was left a residue of 75.5 g. of crude XVb. Washing with 125 ml. of THF gave 54 g. (51%) of XVb, m.p. 205–211°. A sample after recrystallization from tetrachloroethane and sublimation at 95° (0.05 mm.) melted at 218–223° dec. Infrared absorptions (KBr) were at 3.4 (doublet), 5.5 (w), 5.65, 7.45, 7.6, 8.35, and 8.85 μ. The n.m.r. spectrum ($C_2H_2Cl_4$) showed a single peak at 4.98 p.p.m. (CH_2).

Anal. Calcd. for $C_3H_4O_3S$: C, 30.0; H, 3.4; S, 26.7; neut. equiv., 120.1. Found: C, 29.8; H, 3.8; S, 26.3; neut. equiv., 120.7; pK_a (H_2O) = 4.14.

Sulfonyl Fluorides as Intermediates in Organic Synthesis. II. Synthesis and Alkaline Hydrolysis of 2-(Acylacetyl)aminothiazoles Containing Fluorosulfonyl Substituents

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The synthesis of 2-aminothiazole derivatives, containing 5-fluorosulfonyl or 4-fluorosulfonylphenyl substituents, is described. These compounds can be condensed with β-ketonic esters. The resulting fluorosulfonyl-substituted 2-(acylacetyl)aminothiazoles are converted by alkaline hydrolysis to the corresponding alkali sulfonates. These reactions constitute further examples of the usefulness of fluorosulfonyl-substituted intermediates in the synthesis of sulfonic acid derivatives, which are unaccessible by conventional sulfonation techniques.

The condensation of β-ketonic esters with aminobenzenesulfonyl fluorides and the subsequent alkaline hydrolysis of the resulting N-(acylacetyl)aminobenzenesulfonyl fluorides have been described in a previous paper.[1] This method, which is illustrated by the following reaction, proved to be a generally useful synthetic way to N-(acylacetyl)aminoarylsulfonates (X = aryl). It has now been extended to include fluorosulfonyl derivatives of the 2-aminothiazole series (X = a group containing the thiazole nucleus).

$$RCOCH_2COOC_2H_5 + H_2NXSO_2F \longrightarrow$$

$$RCOCH_2CONHXSO_2F \xrightarrow{NaOH} RCOCH_2CONHXSO_2ONa$$

2-Aminothiazoles with a nuclear fluorosulfonyl substituent could be synthesized according to the reaction sequence shown in Scheme I.

2-Acetylamino-4-methyl-5-chlorosulfonylthiazole (Ia)[2] and the corresponding 4-phenyl derivative (Ib)[3] were converted to the corresponding 5-fluorosulfonyl derivatives IIa and IIb, and subsequently hydro-

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