Thietane 1,1-Dioxides[1]

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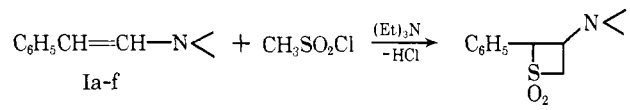
Cyclization of methanesulfonyl chloride with the appropriate enamine in the presence of triethylamine gave 3-alkylamino-2-phenylthietane 1,1-dioxides (IIa–e). In addition to cyclic products the acyclic derivatives, 2-dimethylamino- and 2-pyrrolidino-1-methanesulfonyl-1-phenylethylene (III and IV) were isolated. Some properties and chemistry are discussed. Reduction of the thietane 1,1-dioxides to the corresponding thietanes was unsuccessful. The thietane 1,1-dioxides were of interest as possible MAO inhibitors. None of the compounds tested showed significant *in vitro* MAO inhibitory activity.

It has been postulated that the potent monoamine oxidase (MAO) inhibitory activity exhibited by 2-phenylcyclopropylamine might be explained in terms of the electronic and steric properties of the cyclopropane ring system.[2] Cyclobutyl and larger cycloalkyl analogs of 2-phenylcyclopropylamine are much less active MAO inhibitors presumably for steric reasons and because of a change of electronic properties of the ring system. For a review of structure–activity relationships of MAO inhibitors in the phenycyclopropylamine series see Zirkle and Kaiser.[3] Heterocyclic analogs of cyclopropane have also shown MAO inhibition activity *in vitro*. Paget and Davis[4] reported activity of phenyldiaziridines and more recently Shirodkar[5] found 1-phenethyl- and 1-isopropyl-2-phenylaziridine to be potent *in vitro* MAO inhibitors. These compounds are unique in that the amine nitrogen is an integral part of the ring system and may lend further support to the theory that a small, electron-dense ring system serves as a point of attachment or attraction to the enzyme, MAO. In order to further investigate this theory it appeared that heterocyclic analogs of 2-phenylcycloalkylamines in which the hetero atom could provide the electron density would merit study for MAO inhibitory activity. During the course of pursuing thietane derivatives for MAO inhibition studies a number of 3-dialkylamino-2-phenylthietane 1,1-dioxides (IIa–e) were synthesized and the chemistry and properties of these derivatives are reported here. Since these compounds are heterocyclic analogs of 2-phenylcyclobutylamine, they appeared worthy of a screen for *in vitro* MAO inhibition activity.

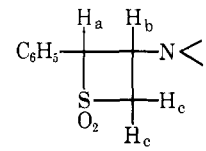
Methanesulfonyl chloride was cyclized with the appropriate enamine (Ia–f) in the presence of triethylamine to give the corresponding thietane 1,1-dioxide (IIa–e) (Chart I). This cyclization is considered to occur *via* a sulfene intermediate.[6,7]

The cyclization reactions were performed in anhydrous ether under the general reaction conditions described for these reactions.[7] The thietane 1,1-dioxides (IIa–e) were obtained as white, crystalline, water-insoluble solids. None of the compounds rapidly decolorized 1% $KMnO_4$ solution. Infrared spectra showed no olefinic absorption. Strong sulfone bands occured at 7.6 and 8.9 μ with a third strong band around 8.4 μ (possible contribution by C–N stretch). Nmr spectra were in accord with the ring structure, all compounds showing a signal for the benzylic proton (H_a) at δ 5.3 (doublet), ring methylene protons (H_c) at 4.05 (multiplet with the appearance of a triplet), and the remaining ring proton (H_b) at 3.35 (quartet). The causative agent for the unusual triplet for the ring methylene protons (H_c) is not known.

CHART I



	-N<	% yield of IIa–f, Et2O	% yield of IIa–f, CH3CN
a,	$N(CH_3)_2$	47	75
b,	N⟨ ⟩	35	75
c,	N⟨ ⟩O	51	55
d,	N⟨ ⟩	24	..
e,	N⟨ ⟩NCH_3	36	..
f,	$N(C_2H_5)_2$	Nil	..



A similar observation has been reported.[8] The thietane 1,1-dioxides (IIa–e) are soluble in dilute acids and are readily precipitated from solution by the addition of base, a useful procedure for the isolation and purification of these derivatives from the crude oils or resinous solids often obtained in the cyclization reactions.

In the cyclization reactions for the dimethylamino (IIa) and pyrrolidino (IIb) derivatives, the acyclic products, 2-dimethylamino-1-methanesulfonyl-1-phenethylene (III) and 2-pyrrolidino-1-methanesulfonyl-1-

(1) (a) The support of this work by a research grant from the Purdue Research Foundation is gratefully acknowledged. (b) From the Ph.D. Thesis of F. S. Abbott, Purdue University.

(2) (a) B. Belleau and J. Moran, *J. Med. Pharm. Chem.*, **5**, 215 (1962); (b) *Ann. N. Y. Acad. Sci.*, **107**, 822 (1963).

(3) C. L. Zirkle and C. Kaiser in "Psychopharmacological Agents," Vol. I, M. Gordon, Ed., Academic Press Inc., New York, N. Y., 1964, p 445.

(4) C. J. Paget and C. S. Davis, *J. Med. Chem.*, **7**, 626 (1964).

(5) J. N. Wells, A. V. Shirodkar, and A. M. Knevel, *J. Med. Chem.*, **9**, 195 (1966).

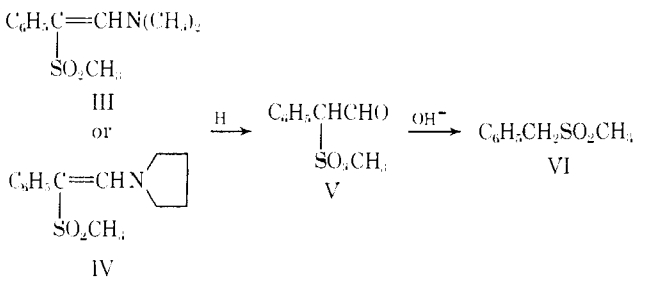
(6) R. H. Hasek, R. H. Meen, and J. C. Martin, *J. Org. Chem.*, **30**, 1495 (1965).

(7) G. Opitz, H. Schempp, and H. Adolph, *Ann. Chem.*, **684**, 92 (1965).

(8) L. A. Paquette, *J. Org. Chem.*, **29**, 2854 (1964).

phenethylene (IV), respectively, were isolated in addition to the cyclic products. These compounds (III and IV) rapidly decolorized 1% $KMnO_4$ solution and showed strong olefinic absorption in the infrared at 6.1–6.2 μ. Strong sulfone bands appeared at 7.9 and 9.0 μ. Ultraviolet and nmr spectra were in accord with structures III and IV. The acyclic products appeared slightly less soluble in 1 *N* HCl than their cyclic counterparts (IIa and b), but upon dissolving in acid were not recoverable since hydrolysis to α-methanesulfonylphenylacetaldehyde (V) (identified as the 2,4-dinitrophenylhydrazone) readily occurs. When either III or IV was dissolved in dilute acid followed by adjustment of the pH to 12 with NaOH, benzyl methyl sulfone (VI) slowly crystallized from the solution (Chart II). This

CHART II

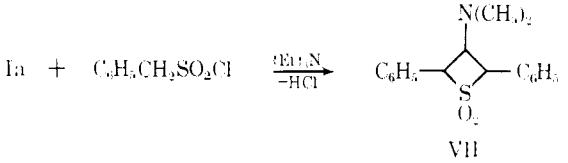


conversion of an α-alkanesulfonylaldehyde to the sulfone with loss of formate under the influence of base has been described as analogous to a reverse aldol condensation.[9] A second product was isolated in small quantity from the cyclization reaction in the synthesis of 3-morpholino-2-phenylthietane 1,1-dioxide (IIc). This solid rapidly decolorized 1% $KMnO_4$ solution and ultraviolet and infrared spectra were similar to those for III and IV; however, attempts to hydrolyze this material to the aldehyde V were unsuccessful and the identity of this compound remains unknown.

It cannot be stated with certainty that acyclic products were not formed in the other cyclization reactions since they may have been lost or undetected during work-up of the reaction. Infrared spectroscopy was not suitable for detection of traces of acyclic product in the crude reaction mixtures because the olefinic absorptions of the starting enamines and acyclic compounds appear at the same frequency. The yields of III (6%) and IV (4%) were the maximum isolated from the cyclization reactions. When the cyclization reactions for IIa and IIb were performed in the polar solvent, acetonitrile, none of the acyclic products (III or IV, respectively) were isolated, although the yields of IIa and IIb were improved relative to those when ether was utilized as solvent; polar solvents such as acetonitrile have been reported to enhance the yield of acyclic relative to cyclic products in the reaction of alkanesulfonyl chlorides with ketene N,N-acetals.[6]

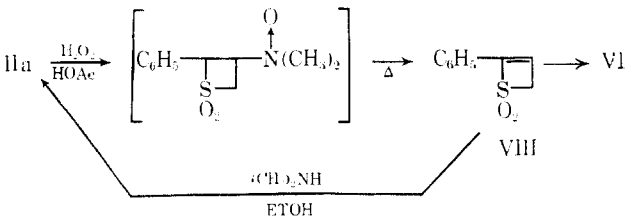
The reaction of methanesulfonyl chloride with β-diethylaminostyrene (If) in the presence of triethylamine in anhydrous ether gave only a dark viscous oil. Neither cyclic nor acyclic products were isolated or detected.

Phenylmethanesulfonyl chloride was cyclized with β-dimethylaminostyrene in the presence of triethylamine to give 2,4-diphenyl-3-dimethylaminothietane 1,1-dioxide (VII) in 43% yield.



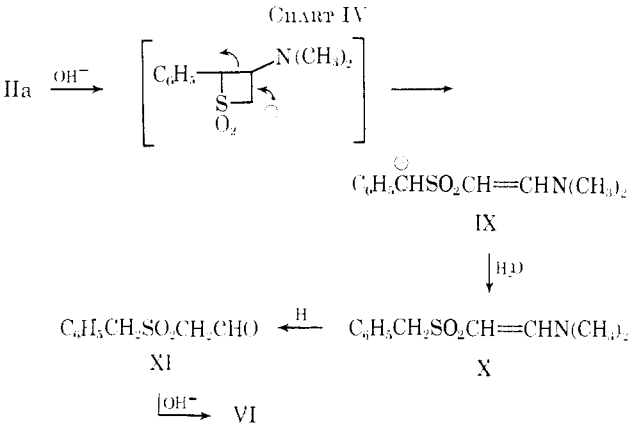
Pyrolysis of the N-oxide of 3-dimethylamino-2-phenylthietane 1,1-dioxide (IIa) gave 2-phenylthiete 1,1-dioxide (VIII) (Chart III). IIa could be recovered from treatment of VIII with an ethanolic solution of dimethylamine. The reaction of VIII with 5% NaOH in aqueous methanol gave benzyl methyl sulfone (VI). The reaction pathway may be the same as that proposed for the action of aqueous base on thiete 1,1-dioxide.[9]

CHART III



Ring opening of 3-dimethylamino-2-phenylthietane 1,1-dioxide (IIa) occurred under the influence of aqueous base to give 2-dimethylamino-1-phenymethanesulfonylethylene (X) (Chart IV). Acid hydrolysis

CHART IV



of X gave phenylmethanesulfonylacetaldehyde (XI), identified as the 2,4-dinitrophenyhydrazone, while acid hydrolysis of X followed by the addition of excess base gave benzyl methyl sulfone (VI). The formation of the stable anion IX may provide the driving force to account for this type of ring opening.

Reductions of IIa and IIc with lithium aluminum hydride ($LiAlH_4$) to the corresponding thietanes were unsuccessful. Basic work-up of the reaction mixtures gave small amounts of dark yellow oils having mercaptan odors and with IIc morpholine was isolated. Vapor phase chromatography of the oils indicated at least 5 components present, none of which were identified. These results indicate that under the conditions of the $LiAlH_4$ reduction, ring cleavage of the phenyl-sub-

(9) D. C. Dittmer and M. E. Christy, *J. Am. Chem. Soc.*, **84**, 399 (1962).

stituted thietane 1,1-dioxides occurs with a variety of products possible. $LiAlH_4$ reduction of 3,3-diethoxy-2-phenylthietane 1,1-dioxide has been reported to give a product resulting from a cleavage of the ring.[10]

Biological Studies.—Compounds IIa, IIb, IIc, and X were screened for MAO inhibitory activity using an *in vitro* assay for MAO activity as described by Wurtman and Axelrod.[11] Rat liver homogenate (2 mg of tissue/ml) was used as the enzyme source. Inhibitor concentrations in the incubation mixtures were 5×10^{-4} *M*. Iproniazid served as the standard inhibitor (5×10^{-4} *M* iproniazid inhibits the enzyme substrate reaction by approximately 85%). Solutions of IIa, b, and c in water were prepared using the hydrochloride salts. X was dissolved as the free base. None of the compounds showed significant activity at 5×10^{-4} *M*. At 2.5×10^{-4} *M*, IIa did exhibit comparable activity to 5×10^{-4} *M* iproniazid, but the inhibition is not significant in terms of potent MAO inhibition.

Experimental Section

Melting points were determined on a Büchi apparatus with open capillary tubes and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 21 spectrometer, using potassium bromide wafers unless otherwise stated. Ultraviolet spectra were determined in 95% ethanol with a Bausch and Lomb Model 505 spectrophotometer. Nmr spectra were determined in $CDCl_3$ with a Varian A-60 spectrometer at 60 Mc and tetramethylsilane as the internal standard. An Aerograph gas chromatograph, Model A-90-S, was utilized for vapor phase chromatography (particulars are specified). Elemental analyses were performed by Galbraith Laboratories Inc., Knoxville 21, Tenn.

Materials.—Methanesulfonyl chloride (Eastman, White Label) was redistilled prior to use. Phenylmethanesulfonyl chloride was prepared as described in the literature.[12] Triethylamine was distilled and stored over NaOH. β-Morpholinostyrene[13] and β-piperidinostyrene[14] were prepared as described in the literature. β-Dimethylaminostyrene[15] was prepared from phenylacetaldehyde and anhydrous dimethylamine over anhydrous K_2CO_3 in 57% yield [bp 110–115° (20 mm)] by the procedure of Mannich and Davidsen.[16] Molecular sieve (Fisher no. 5a) may be substituted for the K_2CO_3.

β-Pyrrolidinostyrene was prepared from phenylacetaldehyde and pyrrolidine by the benzene azeotrope method[17] to give a yellow liquid, bp 98–103° (0.1 mm), in 68% yield. β-(4-Methylpiperazino)styrene was similarly prepared. The product was obtained as slightly yellow crystals, mp 57–59° (from petroleum ether), in 69% yield. All of the enamines show strong absorptions in the infrared at 6.1, 6.25, and 10.7 μ.

General Procedure for the Reaction of Methanesulfonyl Chloride with Enamines.—Enamine (0.1 mole) and triethylamine (0.11 mole) were added to 250 ml of anhydrous ether and the mixture was cooled in ice water. Dry nitrogen atmosphere was provided and the system was protected from moisture. Methanesulfonyl chloride (0.1 mole) was added to the stirred reaction mixture during 1 hr and the reaction mixture was stirred for 12 hr at room temperature. The triethylamine hydrochloride fraction was removed by filtration and washed with small portions of ether. The filtrate and washings were concentrated under reduced pressure. The solid obtained was purified by recrystallization from ethanol or combinations of hexane and ethanol. In several instances a portion of the product had precipitated and was removed with the triethylamine hydrochloride fraction. This was recovered by dissolving the hydrochloride in water and collecting the insoluble product by filtration or by eluting the product with acetone. Anhydrous THF may be used in the cyclization reaction and is a better solvent for the sulfone products. When acetonitrile was used as solvent the experimental conditions were as described in the literature.[6]

3-Dimethylamino-2-phenylthietane 1,1-Dioxide (IIa).—Under the general reaction conditions methanesulfonyl chloride (11.4 g, 0.1 mole) and β-dimethylaminostyrene (14.0 g, 0.1 mole) gave a crude yellow solid. This material was dissolved in 1 *N* HCl with gentle heating. Upon cooling and making the aqueous solution basic (NaOH) a white precipitate formed. The solid was collected by filtration and recrystallized to give 10 g (47%) of IIa as colorless needles, mp 116–117°.

Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71. Found: C, 58.44; H, 6.67.

The hydrochloride salt, recrystallized from ethanol–ether, melted at 173–175° dec.

Using acetonitrile as solvent 0.1 mole of methanesulfonyl chloride and 0.1 mole of β-dimethylaminostyrene gave 16.9 g (75%) of IIa.

2-Dimethylamino-1-methanesulfonyl-1-phenylethylene (III).—The synthesis of IIa was performed in ether as described above except instead of adding the crude solid to 1 *N* HCl, fractional crystallization using hexane–ethanol was employed to isolate 1.5 g (6.6%) of pure III as colorless plates, mp 103–105° (III is slightly more soluble in ether and ethanol than IIa). Infrared analysis gave strong broad absorptions at 6.2, 7.9, and 9.0 μ. The ultraviolet spectrum gave λ_{max}^{EtOH} 243 mμ (ε 14,600). The nmr spectrum showed signals at δ 7.42 (singlet, phenyl and one vinyl proton, 6) and 2.71 and 2.69 (9 methyl protons) integrating as one signal.

Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71. Found: C, 58.65; H, 6.75.

A portion of III was dissolved in a minimum of 2 *N* HCl with heating. The cold acidic mixture was saturated with NaCl and extracted with chloroform. The $CHCl_3$ was dried (Na_2SO_4) and removed under reduced pressure to give a small quantity of viscous colorless oil. Treatment of this oil with 2,4-dinitrophenylhydrazine reagent gave a yellow 2,4-dinitrophenylhydrazone. Recrystallization of this derivative from methanol–acetone gave fine yellow crystals, mp 193–195°. The compound was found to be the 2,4-dinitrophenylhydrazone of α-methanesulfonylphenylacetaldehyde (V).

Anal. Calcd for $C_{15}H_{14}N_4O_6S$: C, 47.52; H, 3.72. Found: C, 47.40; H, 3.72.

Upon repeating the hydrolysis of III in 1 *N* HCl followed by adjustment of the solution to pH 12 with NaOH, white needles slowly crystallized from the solution at room temperature. Recrystallization of this solid from hexane–ethanol gave benzyl methyl sulfone (VI), mp 126–127°. Infrared analysis gave strong absorptions at 7.65 and 8.95 μ (sulfone). A mixture melting point with benzyl methyl sulfone prepared by the oxidation of benzyl methyl sulfide[18] was not depressed and the infrared spectra were superimposable.

3-Pyrrolidino-2-phenylthiethane 1,1-Dioxide (IIb) and 2-Pyrrolidino-1-methanesulfonyl-1-phenylethylene (IV).—Under the general conditions of the reaction β-pyrrolidinostyrene (13 g, 0.075 mole), triethylamine (8.3 g, 0.08 mole), and methanesulfonyl chloride (8.6 g, 0.075 mole) gave after recrystallization, 6.6 g (35%) of IIb as white crystals, mp 115–116°.

Anal. Calcd for $C_{13}H_{17}NO_2S$ (IIb): C, 62.12; H, 6.81. Found: C, 62.23; H, 6.92.

The hydrochloride salt was prepared and recrystallized from ethanol–ether to give white crystals, mp 176–177° dec.

Using acetonitrile as solvent, 0.1 mole of β-pyrrolidinostyrene and 0.1 mole of methanesulfonyl chloride gave 18.8 g (75%) of recrystallized IIb.

Under the general reaction conditions used to prepare IIb a second product was isolated either by recrystallization of the semisolid obtained by evaporation of the ether filtrate after most of IIb had been removed, or by dissolving crude IIb obtained by complete evaporation of the solvent in cool 1 *N* HCl and collecting the less soluble second product by filtration. Recrystallization of this second product from hexane–ethanol gave 1.0 g (4.0%) of faintly yellow crystalline plates, mp 145°. Infrared absorptions occurred at 6.2 (olefin) and 7.9 and 9.0 μ (sulfone). The ultraviolet spectrum gave λ_{max}^{EtOH} 249 mμ (ε

(10) W. E. Truce and J. R. Norell, *J. Am. Chem. Soc.*, **85**, 3236 (1963).
(11) R. J. Wurtman and J. Axelrod, *Biochem. Pharmacol.*, **12**, 1439 (1963).
(12) J. M. Sprague and T. B. Johnson, *J. Am. Chem. Soc.*, **59**, 1837 (1937).
(13) W. Ziegenbein and W. Franks, *Chem. Ber.*, **90**, 2291 (1957).
(14) R. Dulou, E. Elkik, and A. Veillard, *Bull. Soc. Chim. France*, 967 (1960).
(15) J. R. Geigy, British Patent 832,078 (April 6, 1960); *Chem. Abstr.*, **54**, 20877*g* (1960).
(16) C. Mannich and H. Davidsen, *Chem. Ber.*, **69B**, 2106 (1936).
(17) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).
(18) F. G. Bordwell, and B. M. Pitt, *ibid.*, **77**, 572 (1955).

12,300). The nmr spectrum showed signals at δ 7.55 (singlet, vinyl proton, 1), 7.35 (singlet, phenyl, 5), 3.05 (multiplet, CH_2-NCH_2, 4), 2.75 (singlet, SO_2CH_3, 3), and 1.75 (multiplet, remaining pyrrolidine protons, 4). The compound was hydrolyzed in 2 *N* HCl as described for III and the 2,4-dinitrophenylhydrazone of α-methanesulfonylphenylacetaldehyde (V) was obtained (identified by mixture melting point).

Anal. Calcd for $C_{18}H_{17}NO_2S$ (IV): C, 62.12; H, 6.81. Found: C, 62.20; H, 6.94.

3-Morpholino-2-phenylthietane 1,1-Dioxide (IIc).—Under the general conditions of the reaction, β-morpholinostyrene (11.0 g, 0.058 mole), triethylamine (6.48 g, 0.064 mole), and methanesulfonyl chloride (6.64 g, 0.058 mole) gave a crude yellow solid which was purified by dissolving in 1 *N* HCl, filtering the solution and precipitating the product by the addition of NaOH. Recrystallization gave 8.0 g (51%) of white crystalline material, mp 145°. The hydrochloride salt, recrystallized from ethanol–ether, melted at 189–190° dec.

Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.40. Found: C, 58.17; H, 6.17.

The reaction was performed using acetonitrile as solvent to give 8.5 g (55%) of recrystallized product (IIc).

3-Piperidino-2-phenylthietane 1,1-Dioxide (IId).—Under the general conditions of the reaction, β-piperidinostyrene (9.3 g, 0.05 mole), triethylamine (5.6 g, 0.06 mole), and methanesulfonyl chloride (5.72 g, 0.05 mole) gave a dark viscous oil on work-up. The oil was added to 100 ml of 1 *N* HCl and warmed gently. When cool, the acidic aqueous layer was extracted with 50 ml of chloroform. After being dried (Na_2SO_4) the $CHCl_3$ was evaporated to give a polymeric solid. This material did not give a 2,4-dinitrophenylhydrazone derivative. The acidic aqueous layer was made basic with NaOH to give a white solid which upon recrystallization gave 3.5 g (24%) of colorless plates, mp 85°.

Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.21. Found: C, 63.27; H, 7.06.

3-(4-Methylpiperazino)-2-phenylthietane 1,1-Dioxide (IIe).—Under the general reaction conditions, β-(4-methylpiperazino)-styrene (10.1 g, 0.05 mole), triethylamine (5.6 g, 0.06 mole), and methanesulfonyl chloride (5.73 g, 0.05 mole) gave a brown gummy residue. The residue was added to 50 ml of 1 *N* HCl and gently heated. Extraction of this mixture with chloroform and evaporation of the $CHCl_3$ gave an oily residue which did not give a 2,4-dinitrophenylhydrazone. The acidic aqueous layer was made basic with NaOH to give an oil which was extracted with $CHCl_3$. The $CHCl_3$ layer was dried (Na_2SO_4) and the solvent was removed by evaporation to give, after recrystallization, 5.0 g (36%) of colorless crystalline solid, mp 115–116°. A further 1 g of product was obtained from the triethylamine hydrochloride fraction by adding the salts to strong NaOH solution and extracting the insoluble sulfone-free base with $CHCl_3$.

Anal. Calcd for $C_{14}H_{20}N_2O_2S$: C, 59.97; H, 7.19. Found: C, 60.10; H, 7.30.

2,4-Diphenyl-3-dimethylaminothietane 1,1-Dioxide (VII).—Under the general reaction conditions, β-dimethylaminostyrene (7.3 g, 0.05 mole), triethylamine (5.0 g, 0.05 mole), and phenylmethanesulfonyl chloride (9.5 g, 0.05 mole) dissolved in 50 ml of 1:1 anhydrous ether and THF for the addition, gave after recrystallization 6.5 g (43%) of product as feathery white crystals, mp 109°. The nmr spectrum gave signals at δ 7.5 (singlet, phenyls, 10), 5.4 (triplet, benzylic protons, 2), 3.65 (triplet, remaining ring proton, 1), and 1.89 (singlet, N-methyls, 6).

Anal. Caled for $C_{17}H_{19}NO_2S$: C, 67.74; H, 6.35. Found: C, 67.59; H, 6.19.

3-Phenylthiete 1,1-Dioxide (VIII).—3-Dimethylamino-2-phenylthietane 1,1-dioxide (2.25 g, 0.01 mole) was dissolved in a mixture of 5 ml of glacial acetic acid and 5 ml of acetic anhydride contained in a 50-ml erlenmeyer flask and the solution was cooled to 0° in an ice–salt–water bath. To this was added dropwise with stirring 2.3 g of 30% H_2O_2 solution. The reaction mixture was stirred an additional 12 hr at 25°, again cooled in ice, and neutralized with concentrated NaOH. The mixture was heated in a water bath with stirring under reduced pressure (water pump) for 1-2 hr or until practically dry. Water (20 ml) was added and the mixture was extracted with two 20-ml portions of chloroform. The $CHCl_3$ extracts were dried (Na_2CO_3) and evaporated *in vacuo* to give 1.5 g (83%) of white solid (VIII). Recrystallization from hexane–ethanol gave white needles, mp 96°. The infrared spectrum showed strong absorptions at 7.65, 8.5, 8.8 (sulfone), and a strong band at 12.2 μ (olefin). The ultraviolet spectrum gave λ_{max}^{EtOH} 253 mμ (ε 14,000). The nmr spectrum showed signals at δ 7.48 (singlet, phenyl, 5), 7.0 (triplet, olefinic proton, 1) (J = 2 cps), and 4.54 (doublet, methylene protons, 2) (J = 2 cps).

Anal. Calcd for $C_9H_8O_2S$: C, 59.98; H, 4.47. Found: C, 59.95; H, 4.47.

A solution of VIII (0.5 g) in 60 ml of 5% NaOH in equal parts of methanol–water was heated on a steam bath until most of methanol had evaporated. The mixture was cooled and 0.275 g of white solid was collected by filtration. Recrystallization from hexane–ethanol gave white needles, mp 126–126.5°. A mixture melting point with benzyl methyl sulfone was not depressed. A solution of VIII (1.0 g) in 100 ml of ethanol saturated with dimethylamine was allowed to stand for 5 days. The ethanol was evaporated and the resulting solid was extracted with 1 *N* HCl. The insoluble portion was removed by filtration and the filtrate made basic with NaOH to give a white precipitate which after recrystallization from hexane–ethanol gave 0.7 g (57%) of 3-dimethylamino-2-phenylthietane 1,1-dioxide, mp 116–117° (no depression of mixture melting point with IIa).

2-Dimethylamino-1-phenylmethanesulfonylethylene (X).—A solution of IIa (2.25 g, 0.01 mole) in 50 ml of methanol containing 0.56 g (0.02 mole) of $NaBH_4$ (or 1 g of NaOH) was refluxed 6 hr, 50 ml of water was added, and the solution was heated on a steam bath until most of the methanol had evaporated. The aqueous solution was cooled in a freezer and filtered to give 1.8 g of white solid, mp 80 ± 3°. The solid was readily soluble in dilute HCl and rapidly decolorized 1% $KMnO_4$ solution. Several recrystallizations from ether–petroleum ether gave white crystalline X, mp 85–86°. Infrared analysis showed strong absorptions at 6.15 (olefin), 7.7–7.9, and 9.2 μ (sulfone). The ultraviolet spectrum gave λ_{max}^{EtOH} 251 mμ (ε 22,600). The nmr spectrum showed signals at δ 7.45 (singlet, phenyl, 5), 6.95 (doublet, vinyl proton, 1) (J = 13 cps), 4.68 (doublet, vinyl proton, 1) (J = 13 cps), 4.24 (singlet, methylene, 2), and 2.83 (singlet, N-methyls, 6).

Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71. Found: C, 58.81; H, 6.83.

A solution of 0.25 g of X in 10 ml of 1 *N* HCl was heated for several minutes. When cool the solution was saturated with NaCl and extracted with two 10-ml portions of chloroform. The $CHCl_3$ extract was dried (Na_2SO_4) and evaporated to give a few drops of colorless oil. Treatment of the oil with 2,4-dinitrophenylhydrazine reagent gave an orange 2,4-dinitrophenylhydrazone. Recrystallization from ethyl acetate gave orange crystals, mp 199–200°. A sample analyzed as the 2,4-dinitrophenylhydrazone of phenylmethanesulfonylacetaldehyde (XI).

Anal. Calcd for $C_{15}H_{14}N_4O_6S$: C, 47.52; H, 3.72. Found: C, 47.29; H, 3.78.

Hydrolysis of X in 1 *N* HCl followed by adjustment of the pH to 12 with NaOH gave white needles, mp 125–127°, identified as benzyl methyl sulfone by mixture melting point and comparison of infrared spectra.

Lithium Aluminum Hydride Reduction of IIa and IIc.—IIa (9.0 g, 0.04 mole) dissolved in 60 ml of anhydrous THF was added dropwise to 4.5 g (0.12 mole) of powdered $LiAlH_4$ stirring in 120 ml of anhydrous THF at 0°. The reaction mixture was stirred at 4° for 8 hr, 25° for 12 hr, and finally refluxed for 1 hr. Amine was evolved. The reaction mixture was decomposed by the dropwise addition of 4.5 ml of H_2O, 3.4 ml of 20% NaOH, and 15.7 ml of water, in that order. The crystalline salts were removed by filtration and washed with ether, and the ether filtrate and washings were evaporated to give a small amount of dark oil. Vapor phase chromatography of the oil utilizing 182.9 × 0.64 cm copper column of 10% FFAP on firebrick at 150° and 50 cc/min of helium indicated at least five components. Distillation of the oil gave crude material (bp ~210°). The infrared spectrum of this material showed strong bands at 3.0 and 9.5 μ suggesting an alcohol as the main component. The material was not identified. When acid work-up was employed for the $LiAlH_4$ reaction, a dark oil was obtained which decomposed violently on attempted distillation (H_2S odor was prominent.)

The reaction of IIc (0.01 mole) with $LiAlH_4$ (0.03 mole) gave results similar to those for IIa except morpholine could be isolated by distillation of the crude reaction products.

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