2,4-Diaryl-3-dimethylaminothietane 1,1-Dioxides. Synthesis, Configuration, and Stability[1]

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Reaction of *trans*-β-dimethylaminostyrene (**2**) with phenylsulfene gave the thietane 1,1-dioxide isomers **3a** and **4a**, and the acyclic isomer **5a**. Configurations were assigned to **3a** and **4a** on the basis of their NMR spectra and relative stabilities. Isomer **4a** was unstable and isomerized to a mixture of **3a** and **5a** on treatment with triethylamine. When heated in ethanol, **4a** gave a number of decomposition products the nature of which confirmed the reversibility of the cycloaddition reaction. The isomer ratios for cyclic products were sensitive to solvent change and supported a dipolar intermediate for the cyclization. Reaction of **2** with *p*-chlorophenylsulfene gave only two cycloadducts (**3b** and **4b**) which indicated that the configuration of **2** was maintained during cyclization. A substituent effect is evident in the cyclization with *p*-nitrophenylsulfene and in the stability of the cyclic product.

As part of an investigation of thietane 1,1-dioxide derivatives for analgetic activity, certain intermediary 2,4-diaryl-3-dimethylaminothietane 1,1-dioxides (**3** and **4**) were prepared. We now wish to report on the chemistry of these intermediates.

It is well established that sulfenes,[2] generated by base-induced dehydrohalogenation of sulfonyl halides, react with enamines to afford 3-aminothietane 1,1-dioxides and, in some instances, acyclic substitution products.[3] In the present work, the reaction of phenylmethanesulfonyl chloride (**1a**) with *trans*-β-dimethylaminostyrene (**2**) in the presence of triethylamine gave a mixture of the thietane 1,1-dioxide isomers **3a** and **4a**, and the acyclic species **5a** in high yield (Scheme I). The ratio of the three isomers in the crude product was conveniently determined from the integrals for the *N*-methyl protons in the NMR spectrum. Isomer separation was achieved by fractional crystallization.

Isomer **3a** was assigned a cis configuration (phenyls cis to each other and trans to the dimethylamino group) on the basis of its NMR spectrum which showed H_a and H_b as a doublet, and H_c as a triplet (J = 9 Hz). The magnitude of the coupling constant was explicable in terms of a folded thietane 1,1-dioxide ring[5] on which all three ring substituents occupy pseudoequatorial positions and thus axial–axial coupling of vicinal H. That isomer **4a** possessed a trans configuration was evident from the magnetic nonequivalence of H_a and H_b which were seen as a pair of doublets in the 100-MHz spectrum. The doublets were further split as a consequence of ^4J coupling (J_{ab} = 1 Hz).[5e] The shift to lower field (H_b) is consistent with the observation that equatorial protons of 2-halogeno-3-morpholinothietane 1,1-dioxides always appear at lower field than axial protons.[6a] A nonambigous assignment of conformation to **4a** using NMR spectroscopy was not possible because of the equivalency of the vicinal coupling constants $J_{ac} = J_{bc}$ = 9.4 Hz).[5d] However, it is likely that the conformation shown in Scheme I is preferred since inversion gives a species in which both a phenyl ring and the dimethylamino group are pseudoaxial. Models indicate that severe nonbonded interactions between the dimethylamino group and sulfonyl oxygen would ensue in the inverted conformation. The trans phenyl configuration assigned to **4a** was further supported by the upfield shift of the *N*-methyl protons (δ 1.93 vs. δ 2.10 in **3a**) which is attributed to the shielding of these protons by the phenyl ring cis to the dimethylamino group.

The NMR data for the cyclic isomers (**3b, 4b**) obtained from the reaction of *p*-chlorophenylmethanesulfonyl chloride and **2** correlates well with that of **3a** and **4a** and readily allows determination of configuration. That only two cyclic isomers were formed in the reaction of **2** and *p*-chlorophenylsulfene was in agreement with the few reports in the literature to the effect that the configuration of trans acyclic enamines is maintained in the sulfene cycloadducts.[6a,11,12] It followed therefore that the *p*-chlorophenyl group in **4b** was cis to the dimethylamino moiety. Chemical evidence supporting this configurational assignment was obtained by examination of the thiete products obtained from the amine oxide elimination reaction on cyclic isomers **3b** and **4b**.[13]

In the case of *p*-nitrophenylsulfene cyclization with enamine (**2**) where only one cyclic product was obtained, a cis pseudoequatorial arrangement of aromatic groups was assigned. Considering the instability of the trans isomers **4a** and **4b** together with solvent effects on isomer ratios (see below) the most stable isomer **3c** is expected. In the NMR spectrum the *N*-methyl protons of **3c** appear at δ 2.14 in accord with values observed for cis isomers **3a** and **3b**. H_a and H_b in **3c** although formally nonequivalent surprisingly appear as a doublet.

Scheme I

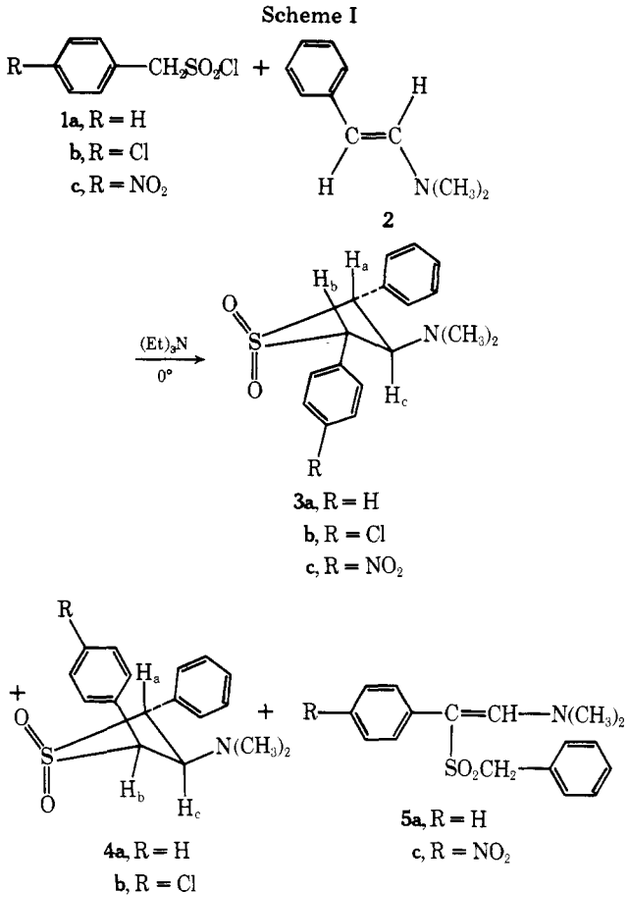


Table I. Effect of Solvent on the Composition of Isomers from the Reaction of *trans*-β-Dimethylaminostyrene with Sulfenes Derived from Sulfonyl Chlorides (1a,b,c)

	Ratio, %							
	(R = H)[a,b]			(R = Cl)			(R = NO_2)[a]	
Solvent	*c*	*t*	Acyclic	*c*	*t*	Acyclic	*c*	acyclic
Et_2O–THF	15	82	3				98	2
$CHCl_3$	19	74	7	20	70	10	89	11
CH_3CN	35	60	5	40	55	5	72	28
CH_3CN–H_2O[c]	36	47	17				67	33

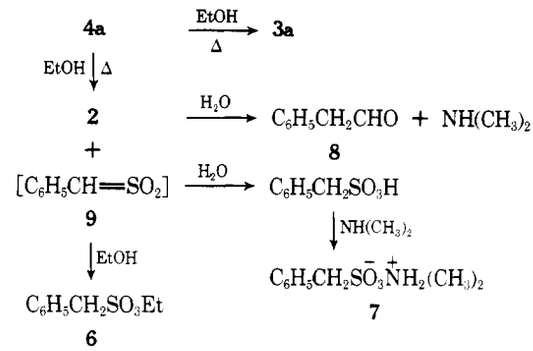
[a] Reactions run under identical conditions using the same quantities of reactants. [b] Essentially identical results were obtained when the reaction was repeated. [c] H_2O at twice the molar equivalent of enamine was added to flask just prior to initiating the addition of sulfonyl chloride.

Acyclic isomer **5a** was readily identified from IR and NMR spectra. Spectroscopic evidence was obtained for an acyclic isomer analogous to **5a** from the reaction of enamine and *p*-chlorophenylsulfene but the compound was not isolated. The corresponding acyclic isomer **5c** is bright yellow. Comparison of the UV spectrum of **5c** (λ_{max} 250 (ε 18 700) and 271 nm (ε 19 700) with that of **5a** (λ_{max} 253 nm (ε 15 800)) indicated that the nitro group was attached to the styryl chromophore in **5c.** This required that **5c** arise from a cycloadduct rather than by direct sulfonylation of **2.**

The observation that considerable decomposition occurred when the crude product was crystallized from hot hexane–ethanol prompted an investigation of the relative stability of **3a** and **4a.** After refluxing a sample of pure cis isomer **3a** in ethanol for 1 h, 81% remained unchanged. When trans isomer **4a** was treated in the same manner, complete decomposition occurred. NMR analysis revealed that approximately 57% of the decomposition products from **4a** consisted of **2** (28%), **3a** (11%), and ethyl phenylmethanesulfonate (**6,** 61%). Part of the remaining 43% was apparently composed of sulfonic acid salts. NMR analysis of the water soluble products obtained by refluxing a sample of **4a** in ethanol for 12 h showed that 67% of the trans isomer had been converted to dimethylammonium phenylmethanesulfonate (**7**). When an ethanol solution of **4a** was analyzed by VPC with the injection port at 280 °C, peaks attributable to **2** and **6** and a peak having the same retention time as phenylacetaldehyde (**8**) were observed. Under the same conditions, **3a** gave only minor, unidentified peaks. These results confirm the reversibility of the cycloaddition reaction. The cycloaddends, **2** and **9,** are regenerated depending on the relative stability of the cycloadduct (Scheme II). Reaction of **9** with ethanol accounted for the sulfonate ester **6,** and reaction with water present in the ethanol to give a sulfonic acid and subsequent protonation of dimethylamine liberated by hydrolysis of **2** explained the formation of **7.** Hamid and Trippett[7] have also presented evidence that the cycloaddition of sulfenes to enamines is, in some cases at least, reversible.

To further study the relative stability of **3a** and **4a,** a solution of crude material in acetonitrile (consisting of 19% **3a,** 74% **4a,** and 7% **5a**) and an equimolar amount of triethylamine hydrochloride was treated with triethylamine at room temperature for 4 days. NMR analysis of the product indicated that 92% of the starting material was accounted for and of this 64% was **3a,** 8% **4a,** and 28% **5a.** The decisive conversion of **4a** to **3a** is somewhat analogous to the base-induced epimerization of *trans*-2,4-diphenylthietane 1,1-dioxide to the cis isomer reported by Dodson and co-workers[5b] and confirms the configurational assignments made for **3a** and **4a.** Truce reported a slow isomerization of the least stable isomer of 2,2-dimethyl-3-dimethylamino-4-phenylthietane 1,1-dioxide in acetonitrile containing triethylamine to the more stable trans isomer (phenyl trans to amino moiety).[6b] It was also apparent from the present results that some cyclic material underwent

Scheme II



ring opening to give **5a.** Alkali hydroxide-catalyzed cleavage of thietane 1,1-dioxides to the corresponding acyclic isomers is known[4,8,9] and certain 2-halogeno-3-morpholinothietane 1,1-dioxides ring cleave to acyclics with refluxing dioxane and triethylamine.[6c]

The relative stabilities of the cyclic isomers of 2-(4-chlorophenyl)-3-dimethylamino-4-phenylthietane 1,1-dioxide are quite evident. The trans (**4b**) decomposed on attempted recrystallizations from hot solvent while cis isomer (**3b**) could be readily crystallized. This apparent substituent effect on stability is even more evident with the single cis *p*-nitro analogue. Pure **3c** dissolved in acetonitrile isomerized spontaneously at room temperature to give **5c.** Adding triethylamine to a solution of **3c** results in the immediate formation of a dark reddish color. In addition to the formation of **5c** some crude water-soluble product could be recovered which from the IR was apparently salts of *p*-nitrophenylsulfonic acid.

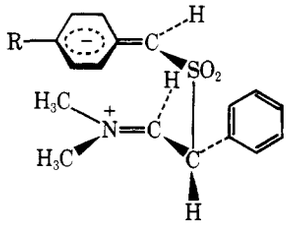
The ratio of isomers in the products from these cyclizations was found to vary with the solvent used and a brief study of these effects was undertaken. In most instances the yields were high (>90%). Isomer compositions of the crude products were determined by NMR. Solvents employed and the results are recorded in Table I.

The predominant formation of the least stable trans isomers in the cyclizations of phenyl- and *p*-chlorophenyl sulfenes is not unusual. Similar findings for sulfene–enamine reactions have been reported.[6a,b] As solvent polarity is increased the more stable cis isomers were formed in increasing amounts suggesting a dipolar intermediate may be involved in these cyclizations.[6d]

Before considering this possibility it was important to determine whether solvent effects were reaction mode related or simply a result of isomerization and ring opening of lesser stable trans products which could increase with rising solvent polarity.[10] In the instance of phenylsulfene cyclization with β-dimethylaminostyrene this is not the case and several experiments illustrated this. Using acetonitrile as solvent the relative composition of isomers **3a, 4a,** and **5a** was the same whether reactants were dumped together with workup in 15

min or if sulfonyl chloride was added during 1 h and the reaction stirred a further 15 h (ice–H_2O conditions). If post-isomerization were operative the longer addition and reaction time should result in greater proportions of cis and perhaps acyclic isomer since trans encounters excess triethylamine. Pure trans isomer was subjected to Et_3N and Et_3N·HCl under the usual reaction conditions in the solvents THF–Et_2O and acetonitrile. Upon workup (98% recoveries) no cis or acyclic isomer could be detected in the NMR of either of the crude products. Finally pure trans isomer (half the molar equivalent of reactants in a typical reaction) was dissolved in CH_3CN–H_2O (see Table I) and the usual cyclization carried out using half the normal quantities of reactants. NMR analysis of the product (18% **3a**, 75% **4a**, 7% **5a**) showed that added trans isomer acted as a simple diluent with no degradation.

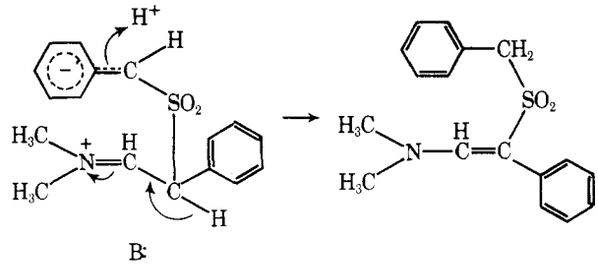
Mechanistic possibilities for the cyclization of a variety of sulfenes to enamines have recently been discussed in the literature.[6b] Both concerted and stepwise processes were considered but experimental data do not as yet provide the answer concerning a definitive mechanism. Our own data tend to support the zwitterionic intermediate concept at least for the sulfene-enamine cyclizations reported here. Electrostatic attractions of the delocalized charges in the intermediate favor the formation of the trans product as observed when R = H



or Cl. As solvent polarity increases a tighter solvation effect on the dipolar species would allow greater product discrimination. Hence the formation of the more thermodynamically stable cis isomer is increased in the polar acetonitrile solvent.

The formation of a single cis isomer when R = NO_2 (*p*-nitrophenyl trans to amino moiety) has similarily been observed by Truce and Rach.[6b] They suggested a possible substituent effect which through greater carbanion stabilization or more efficient charge dispersal, decreasing electrostatic attractions would lead to the more stable cyclic product. Rapid isomerization of least stable isomer under reaction conditions could not be discounted and in our example may well be true considering the low stability of even the cis isomer (**3c**). It is surprising, however, that no trans was detected in the Et_2O–THF reaction (Table I). The yield was high with little formation of acyclic isomer partly because of the low solubility of **3c** which precipitates readily once formed. Considering the physical properties of the trans isomers **4a** and **4b** (decreased solubilities compared to cis isomers) at least some trans isomer corresponding to **3c** was expected particularly if it was the preferred isomer. We therefore tend to interpret the results of the *p*-nitrosulfene reaction as a substituent effect with respect to a zwitterionic mechanism.

The existence of a zwitterionic intermediate in these cycloadditions suggests the possibility of increased formation of acyclic product as solvent polarity increases.[3a] This was not observed (Table I, R = H, Cl) in our study and is consistent with previous reports for sulfene–enamine cycloadditions.[3a] The addition of a small amount of H_2O to acetonitrile was an attempt to trap intermediate by providing a ready proton source. The overall yield of products (**3a, 4a, 5a**) was slightly reduced since the H_2O present can compete for reaction with the sulfene. The proportion of acyclic isomer **5a** was found to be significantly increased (Table I). While apparently successful, this unfortunately represents only one example.



B:

It was thought that *p*-nitrophenylsulfene cyclization should have given further evidence of this nature. A substituent effect, if operative, by stabilizing or prolonging the lifetime of the intermediate would enhance acyclic isomer formation. When the reaction was run in CH_3CN–H_2O no evidence for any acyclic isomer other than **5c** (formed from ring opening of cyclic isomer) could be detected. Adding pure **3c** to CH_3CN–H_2O under the reaction conditions gave the same proportion of acyclic (**5c**) as obtained in the normal cycloaddition reaction.

Experimental Section

Melting points were determined with a Thomas–Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded with a Beckman IR-10 spectrophotometer using potassium bromide wafers unless otherwise stated. Ultraviolet spectra were determined in acetonitrile with a Bausch and Lomb Model 505 spectrophotometer. Nuclear magnetic resonance spectra were obtained on a Varian A-60, T-60 or XL-100 spectrometer, using tetramethylsilane as the internal standard; unless otherwise stated, the solvent was deuteriochloroform and the concentration of solutions was ca. 10%. Vapor phase chromatography was carried out on a Micro-Tek gas chromatograph Model MT-200 with flame ionization detector using a 6 ft × 5/32 in. (i.d.) stainless steel column packed with 5% SE-30 on Chromport (70–80 mesh); conditions are specified. Microanalyses were performed by Alfred Bernhardt Mikronanalytisches Laboratorium, 5251 Elbach uber Engelskirchen, Fritz-Pregl-Strasse 14-16, West Germany.

Materials. Commercial anhydrous diethyl ether was dried using sodium wire. Dry acetonitrile was obtained by distilling reagent grade solvent from phosphorus pentoxide. Anhydrous tetrahydrofuran was prepared by distilling solvent of low peroxide content from lithium aluminum hydride. Dry, ethanol-free chloroform was prepared according to the sulfuric acid procedure of Vogel.[14]

The preparation of β-dimethylaminostyrene (**2**) has previously been described.[4] The NMR spectra of solution and neat samples showed the presence of only one geometric isomer which was assigned a trans configuration on the basis of the magnitude of the coupling constant for the vinyl protons (J = 14 Hz). This was in agreement with the assignment made by Caserio and co-workers.[15] VPC analysis of an acetone solution of **2** with the nitrogen flow at 54 mL/min and the injection port, oven, and detector at 255, 150, and 243 °C, respectively, gave one peak, retention time 2.5 min.

Phenylmethanesulfonyl chlorides were prepared according to literature methods.[16,17] Triethylamine was distilled from KOH pellets and stored over the same.

General Procedure for the Reaction of *trans*-β-Dimethylaminostyrene (2) with Arylmethanesulfonyl Chlorides. A stirred solution of 1.0 equiv of **2** and 1.0 equiv of triethylamine in solvent was cooled in ice water. A dry nitrogen atmosphere was provided and the system was protected from moisture. Arylmethanesulfonyl chloride (1.0 equiv) dissolved in solvent was added dropwise over a period of 15 min. After stirring for an additional 45 min the reaction mixture was evaporated under vacuum with the aid of a lukewarm water bath. The resulting residue was dissolved in $CHCl_3$ and extracted with several equal portions of water to remove the triethylamine hydrochloride. Evaporation of the dried (Na_2SO_4) organic layer under reduced pressure gave the crude product.

***cis*-2,4-Diphenyl-3-dimethylaminothietane 1,1-Dioxide (3a).** Under the general conditions of the reaction, using 100 mL of acetonitrile as solvent, **1a** (12.95 g, 0.069 mol) and **2** (10.00 g, 0.068 mol) afforded 20.19 g (98.6%) of crude solid.[18] Crystallization from hexane–ethanol followed by three recrystallizations from hexane–methyl ethyl ketone gave **3a** as transparent plates, mp 137–138 °C dec; IR 1320, 1133 cm^{-1} (sulfone); NMR δ 7.70–7.23 (m, 10, phenyls), 5.28 (d, 2, J = 9 Hz, H_a and H_b), 3.68 (t, 1, J = 9 Hz, H_c), and 2.10 (s, 6, N-methyls).

Anal. Calcd for $C_{17}H_{19}NO_2S$ (301.41): C, 67.74; H, 6.35, N, 4.65. Found: C, 67.91; H, 6.46; N, 4.64.

***trans*-2,4-Diphenyl-3-dimethylaminothietane 1,1-Dioxide (4a).**[4] Under the general conditions, 12.95 g (0.069 mol) of **1a** dissolved in 126 mL of 1:1 THF–Et_2O was reacted with 10.00 g (0.068 mol) of **2** in 100 mL of Et_2O to give 19.80 g (96.7%) of crude yellow solid.[18] Crystallization from hexane–methyl ethyl ketone gave **4a** as white, fluffy needles, mp 112–113 °C dec. After two recrystallizations, the mp was 114.5–115.5 °C dec (lit.[4] 109 °C); IR 1320, 1160 cm^{-1} (sulfone); NMR (agreed with lit.[4]) δ 7.68–7.22 (m, 10, phenyls), 5.43 (broad t, 2, H_a and H_b), 3.68 (t, 1, J = 9 Hz, H_c), and 1.93 (s, 5, N-methyls); NMR (100 MHz) δ 5.494 (m, 1, J_{bc} = 9.4 Hz, J_{ba} = 1 Hz, H_b), 5.304 (m, 1, J_{ac} = 9.4 Hz, J_{ab} = 1 Hz, H_a).

Benzyl 1-Phenyl-2-dimethylaminoethenyl Sulfone (5a). The first mother liquor from the isolation of **3a** was cooled in a dry ice box overnight which caused an off-white solid to precipitate. Evaporation of the supernatant gave a brown oil which was heated with hexane and dissolved with a minimum amount of ethanol. Cooling the solution in a refrigerator gave **5a** as colorless crystals which were recrystallized from methyl ethyl ketone to give transparent plates, mp 130–131 °C; IR 1630 (enamine), 1276, 1125 cm^{-1} (sulfone); NMR δ 7.41 (d, 10, phenyls), 7.00 (s, 1, vinyl), 4.05 (s, 2, benzyl), and 2.60 (s, 6, N-methyls); UV_{max} 253 nm (ϵ 15 800).

Anal. Calcd for $C_{17}H_{19}NO_2S$ (301.41): C, 67.74; H, 6.35; N, 4.65. Found: C, 67.78; H, 6.34; N, 4.76.

Decomposition of *trans*-2,4-Diphenyl-3-dimethylaminothietane 1,1-Dioxide (4a) in Ethanol. A solution of 233 mg of pure **4a** in 50 mL of ethanol was heated at reflux for 1 h. Evaporation under reduced pressure gave a yellow, mobile oil which possessed an odor similar to that of **2**. A strong band at 1640 cm^{-1} in the IR spectrum (neat) supported the presence of **2** and strong bands at 1350, 1170, and 920 cm^{-1} suggested the presence of a sulfonic acid ester. In the NMR spectrum signals attributable to **2**, **3a**, and ethyl phenylmethanesulfonate (**6**) were apparent by comparison with spectra of authentic samples. No absorption due to the starting material **4a** was observed. The three compounds accounted for approximately 57% of the oil of which 28% was **2**, 11% **3a** and 61% **6**. A major peak at δ 2.28 was unassigned.

A solution of 467 mg (1.55 mmol) of pure **4a** in 100 mL of ethanol was heated at reflux for 12 h. Evaporation under reduced pressure gave a viscous oil with an aldehydic odor. The oil was dissolved in 30 mL of $CHCl_3$ and extracted with three 20-mL portions of water. Evaporation of the pooled aqueous extracts in vacuo afforded 300 mg of white, gummy solid. NMR analysis indicated that 75% of this material (225 mg, 1.04 mmol) was dimethylammonium phenylmethanesulfonate (**7**). Three crystallizations from hexane–acetone gave transparent needles, mp 116–118 °C. A mixture melting point with an authentic sample of **7** was not depressed and the IR spectra were superimposable.

VPC analysis of an ethanol solution of pure **4a** with the nitrogen flow at 55 mL/min, and the injection port, oven, and detector at 280, 140, and 250 °C, respectively, gave four peaks excluding that of the solvent. Three of the peaks were identified by coinjection with authentic samples as phenylacetaldehyde **8** (1.4 min), **2** (4.4 min) and **6** (7.8 min).

Ethyl Phenylmethanesulfonate (6).[19] To a refluxed solution of 5.06 g (0.050 mol) of triethylamine in 100 mL of absolute ethanol was added 9.53 g (0.050 mol) of **1a** dissolved in 30 mL of CH_3CN dropwise over a period of 1 h. The system was protected from moisture with a drying tube. After refluxing for another 2 h the reaction was evaporated under reduced pressure. The resulting residue was dissolved in 50 mL of $CHCl_3$ and extracted with three 50-mL portions of water. Evaporation of the dried ($MgSO_4$) organic layer gave 4.29 g (50%) of crude product (**6**) as a pale yellow oil. Double distillation afforded an analytical sample of **6** as a colorless liquid, bp 87 °C (0.02 mm) (lit.[19] 129–130 °C (0.04 mm)); IR (neat) 1350, 1170, 920 cm^{-1} (sulfonic acid ester); NMR δ 7.32 (s, 5, phenyl), 4.32 (s, 2, benzyl), 4.11 (q, 2, J = 7 Hz, methylene), and 1.25 (t, 3, J = 7 Hz, methyl).

Anal. Calcd for $C_9H_{12}O_3S$ (200.26): C, 53.98; H, 6.04; S, 16.01. Found: C, 53.88; H, 6.15; S, 16.16.

Dimethylammonium Phenylmethanesulfonate (7). Phenylmethanesulfonyl chloride (**1a**) (2.0 g, 0.011 mol) was heated in 150 mL of boiling water for 30 min to give a homogeneous solution (acid to indicator paper). The solution was reduced to a volume of about 30 mL by evaporation under vacuum and then treated with excess dimethylamine. The remaining water was evaporated to give a pale yellow oil which solidified when washed with acetone. Three crystallizations from hexane–acetone gave 1.1 g (46%) of **7** as transparent needles, mp 116–118 °C; IR 3180–2820, 2475 (ammonium band), 1210, 1052 cm^{-1} (sulfonic acid); NMR δ 8.37–7.72 (band, 2, NH_2), 7.52–7.20 (m, 5, phenyl), 4.05 (s, 2, benzyl), and 2.26 (t, 6, J = 5.5 Hz, N-methyls).

Anal. Calcd for $C_9H_{15}NO_3S$ (217.28): C, 49.75; H, 6.96; N, 6.45. Found: C, 49.68; H, 7.38; N, 6.39.

Isomerization of *trans*-2,4-Diphenyl-3-dimethylaminothietane 1,1-Dioxide (4a). Crude product which was essentially pure in the three isomers and consisted of 19% **3a**, 74% **4a**, and 7% **5a** (NMR analysis) was used. To a stirred solution of 3.01 g (0.010 mol) of crude product and 1.38 g (0.010 mol) of triethylamine hydrochloride in 20 mL of dry CH_3CN and 10 mL of dry $CHCl_3$ which was protected from moisture were added two drops of triethylamine. The isomerization was followed by removing samples at intervals and observing the increase in intensity of the enamine band (1630 cm^{-1}) of **5a**. The greatest increase occurred during the first day and no change was detectable at the end of the third day. The solution was allowed to sit for another 24 h and then evaporated in vacuo to give a residue which was dissolved in 20 mL of $CHCl_3$ and extracted with three 20-mL portions of water. Evaporation of the dried (Na_2SO_4) organic layer under reduced pressure gave a yellow solid. NMR analysis of this material indicated that 92% was accounted for by the three isomers of which 64% was **3a**, 8% **4a**, and 28% **5a**.

***trans*-2-(4-Chlorophenyl)-3-dimethylamino-4-phenylthietane 1,1-Dioxide (4b).** Under the conditions of the general reaction, 4.50 g (0.020 mol) of **1b** in 38 mL of $CHCl_3$ was added dropwise over a period of 0.5 h to 2.94 g (0.02 mole) of **2** and 2.02 g (0.020 mole) of triethylamine in 30 mL of $CHCl_3$. After 8 h, the white precipitate (**4b**, 3.79 g, 56%) was collected by suction filtration and washed with $CHCl_3$. Extensive decomposition occurred when crystallization of crude **4b** was attempted. Washing several times with $CHCl_3$ gave an analytical sample, mp 154 °C dec;[20] IR 1323, 1164 cm^{-1} (sulfone); NMR (≈2%) δ 7.69–7.40 (m, 9, aromatics), 5.49 (d, 1, J = 9.5 Hz, H_b), 5.31 (d, 1, J = 9.5 Hz, H_a), 3.69 (t, 1, J = 9.5 Hz, H_c), and 1.96 (s, 5, N-methyls).

Anal. Calcd for $C_{17}H_{18}ClNO_2S$ (335.85): C, 60.80; H, 5.40; N, 4.17. Found: C, 60.63; H, 5.20; N, 4.18.

***cis*-2-(4-Chlorophenyl)-3-dimethylamino-4-phenylthietane 1,1-Dioxide (3b).** Evaporation under reduced pressure of the filtrate from the reaction described for **4b** gave a residue which was redissolved in 25 mL of $CHCl_3$ and extracted with four 10-mL portions of water. Evaporation of the dried (Na_2SO_4) organic layer followed by washing of the resulting residue with Et_2O yielded a yellow solid (0.82 g, 12%) which consisted of 35% **3b** and 65% **4b** (NMR analysis[21]). Evaporation of the Et_2O washings followed by washing of the residue with Et_2O afforded 0.30 g (4%) of yellow solid. Crystallization of this latter material from hexane–ethanol gave the cis isomer as white needles, mp 145–146 °C dec; IR 1333, 1164 cm^{-1} (sulfone); NMR δ 7.63–7.26 (m, 9, aromatics), 5.25 (d, 1, J = 9 Hz, H_a[22]), 5.22 (d, 1, J = 9 Hz, H_b), 3.57 (t, 1, J = 9 Hz, H_c), and 2.08 (s, 6, N-methyls).

Anal. Calcd for $C_{17}H_{18}ClNO_2S$ (335.85): C, 60.80; H, 5.40; N, 4.17. Found: C, 60.88; H, 5.34; N, 4.20.

***cis*-2-(4-Nitrophenyl)-3-dimethylamino-4-phenylthietane 1,1-Dioxide (3c).** Under the general reaction conditions *p*-nitrophenylmethanesulfonyl chloride 2.36 g (0.01 M) in 25 mL of CH_3CN was added to 1.47 g (0.01 M) of **2** and 1.01 g (0.01 M) of Et_3N in 25 mL of CH_3CN. Cold ether (200 mL) is added to precipitate Et_3N·HCl. After filtration the filtrate was evaporated to give an orangish residue. Addition of ether causes product to precipitate. Upon filtering and evaporation further product is obtained on treating oily residue with ether and hexane.[18] Crystallization from hexane–methyl ethyl ketone gave **3c** as pale yellow prisms, mp 130–131 °C dec; IR 1524, 1354 (nitro group), 1336, 1324, 1160, 1138 cm^{-1} (sulfone); NMR δ 8.47–8.20 (m, 2, protons ortho to nitro group), 7.87–7.60 (m, 2, protons meta to nitro group), 7.60–7.33 (m, 5, phenyl), 5.36 (d, 2, J = 9 Hz, H_a and H_b), 3.70 (t, 1, J = 9 Hz, H_c), and 2.14 (s, 6, N-methyls).

Anal. Calcd for $C_{17}H_{18}N_2O_4S$ (346.40): C, 58.95; H, 5.24; N, 8.09. Found: C, 60.14; H, 5.12; N, 7.99.

Although the analysis was not satisfactory for carbon, the results of the analyses performed on the thiete 1,1-dioxide derived from **3c** were satisfactory.[13]

With Et_2O–THF as solvent further addition of Et_2O when reaction is complete results in precipitation of most of the product.[18] Et_3N·HCl is removed by triturating solid with H_2O. With $CHCl_3$ as solvent Et_3N·HCl is removed by extracting $CHCl_3$ with H_2O. Evaporation of the dried (Na_2SO_4) $CHCl_3$ leaves a dark orange-red oil which on ether treatment provides solid crude product.[18]

After sitting at room temperature for 2 h, a solution of 100 mg of **3c** in 5 mL of CH_3CN had turned bright orange. NMR analysis of the oil obtained by evaporating the solution under reduced pressure after 43 h indicated that 87% was accounted for by the isomers **3c** and **5c** of which 34% was **3c** and 76% **5c**.

Benzyl 1-(4-Nitrophenyl)-2-dimethylaminoethenyl Sulfone (5c). A reddish-black oil was obtained when the Et_2O filtrate from the synthesis of **3c** was evaporated under reduced pressure. Washing the oil with Et_2O caused 1.7 g (6.5%) of yellow solid to separate which was found to consist of 36% **3c** and 61% **5c** (NMR analysis). Two crystallizations from 1-butanol gave **5c** as bright yellow, flat needles, mp 165.5–166.5°; IR 1625 (enamine), 1530, 1355 (nitro group), 1297, 1135, 1115 cm^{-1} (sulfone); NMR δ 8.30–8.03 (m, 2, protons ortho to nitro group), 7.60–7.30 (m, 7, protons meta to nitro group and phenyl protons), 7.11 (s, 1, vinyl), 4.13 (s, 2, benzyl), and 2.67 (s, 6, N-methyls); UV_{max} 250 (ϵ 18 700) and 271 nm (ϵ 19 700).

Anal. Calcd for $C_{17}H_{18}N_2O_4S$ (346.40): C, 58.95; H, 5.24; N, 8.09. Found: C, 58.99; H, 5.09; N, 8.22.

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Registry No.—**1a,** 1939-99-7; **1b,** 6966-45-6; **1c,** 4025-75-6; **2,** 14846-39-0; **3a,** 63268-45-1; **3b,** 63231-37-8; **3c,** 63231-38-9; **4a,** 63268-46-2; **4b,** 63268-47-3; **5a,** 63231-34-5; **5c,** 63231-35-6; **6,** 42454-54-6; **7,** 63231-36-7.

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2,4-Diarylthiete 1,1-Dioxides. Synthesis, Thermolysis Studies, and Addition Reactions

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Several 2,4-diarylthiete 1,1-dioxides were prepared by amine oxide elimination of the corresponding 2,4-diaryl-3-dimethylaminothietane 1,1-dioxides. The thiete 1,1-dioxides were readily thermolyzed to chalcones and evidence was obtained which supports the involvement of a vinylsulfene intermediate in the thermolytic transformation. A ketonic sulfone was isolated and identified from thermolytic degradation of **4.** Addition of hydrogen cyanide or nitroethane to the thiete 1,1-dioxides followed by reduction to the primary amines and subsequent dimethylation gave 2,4-diaryl-3-dimethylaminomethylthietane 1,1-dioxides. 3-Cyanothietane 1,1-dioxide (**7c**) on treatment with base eliminates SO_2 to form olefins. The utility of thiete 1,1-dioxides to add HCN provides a synthetic route to a number of 3-substituted thietane 1,1-dioxides.

2-Aryl-3-dimethylaminomethylthietane 1,1-dioxides are of interest as conformationally restricted analogues of diphenylpropylamine-type analgetics. In order to synthesize the title compounds it was felt that appropriate thiete 1,1-dioxides would prove to be ideal intermediates. The reactivity of thiete 1,1-dioxides to nucleophilic addition is known,[1c,d] and it appeared feasible to utilize this property in the preparation of 3-cyano- and 3-nitroalkylthietane 1,1-dioxides which could be reduced to the 3-aminomethyl functional group. During the course of this work the amine oxide elimination reaction proved useful in confirming the conformation of the starting thietane 1,1-dioxides. Thermolysis studies of the thiete 1,1-dioxides were initiated to obtain chemical evidence as to the position of the double bond relative to differing aryl substituents.

2,4-Diarylthiete 1,1-dioxides (**4, 5, 6**) were obtained by the amine oxide elimination reaction of 3-dimethylaminothietane 1,1-dioxides (**1, 2, 3**)[1b] (Scheme I). Treatment of either a mixture of the cis and trans isomers (**1a, 1b**)[2] or the cis isomer alone with peracetic acid gave 2,4-diphenylthiete 1,1-dioxide (**4**)[3] in good yield. Because of the intramolecular nature of the amine oxide elimination reaction,[5] its application to the isomers **2a** and **b** provided a means of verifying their assigned configurations. In **2a** both H-2 and H-4 are cis to the dimethylamino group and, therefore, according to the intramolecular mechanism of the elimination this isomer should have given a mixture of thiete 1,1-dioxide isomers **5a** and **b.** On the other hand, as only H-4 in **2b** is cis to the basic group, this isomer should have afforded **5b.** When a dilute tetrahydrofuran solution of **2a** was treated with peracetic acid the