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.

Acknowledgments. This work was supported in part by Medical Research Council of Canada Grant MA-3044.

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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(3) For reviews see: (a) G. Opitz, *Angew. Chem. Int. Ed. Engl.*, **6,** 107 (1967); (b) W. E. Truce and L. K. Liu, *Mech. React. Sulfur Compd.*, **4,** 145 (1969).
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(19) Although a boiling point for **6** has been reported (W. E. Truce and D. J. Vrencur, *Can. J. Chem.*, **47,** 860 (1969)), no other details appear to have been published.
(20) Melting point bath was preheated to 150 °C and heating rate was ca. 1 °C/min.
(21) Because of the relatively low solubility of **4b** in $CDCl_3$, the mixture was converted to the HCl salts and analyzed as a solution in Me_2SO-d_6.
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2,4-Diarylthiete 1,1-Dioxides. Synthesis, Thermolysis Studies, and Addition Reactions

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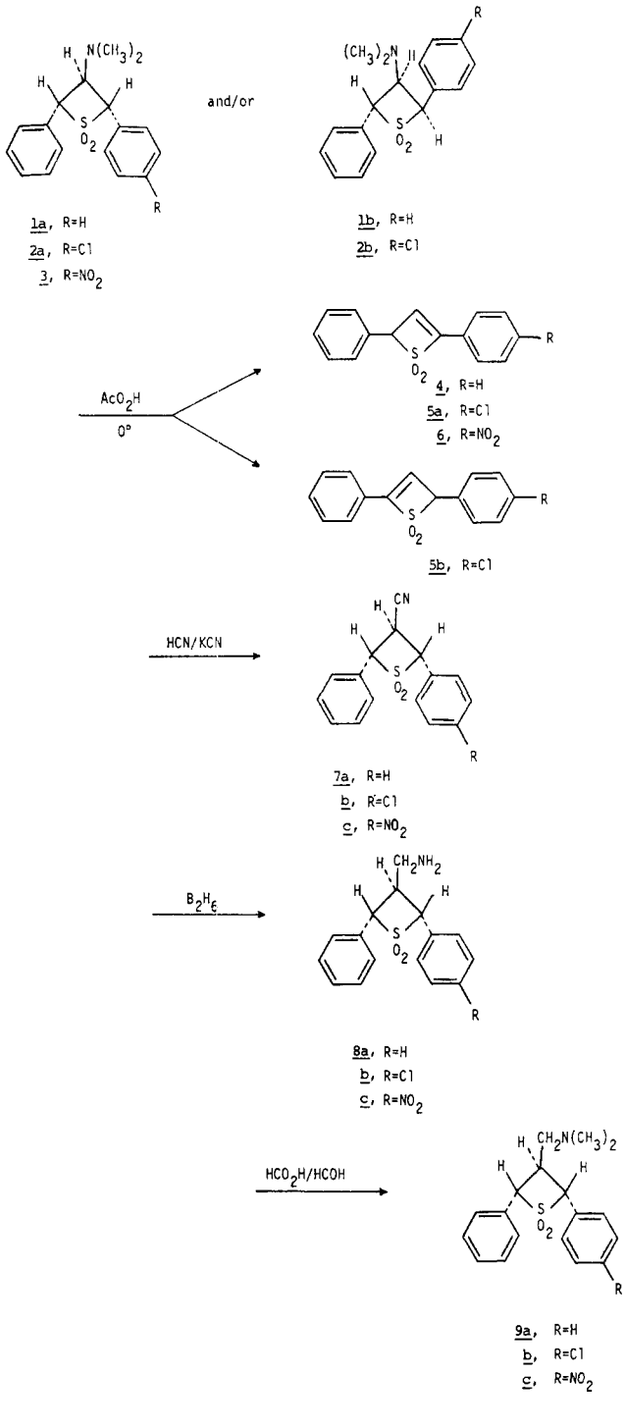
Several 2,4-diarylthiete 1,1-dioxides were prepared by amine oxide elimination of the corresponding 2,4-diaryl-3-dimethylaminothietane 1,1-dioxides. The thiete 1,1-dioxides were readily thermolyzed to chalcones and evidence was obtained which supports the involvement of a vinylsulfene intermediate in 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.

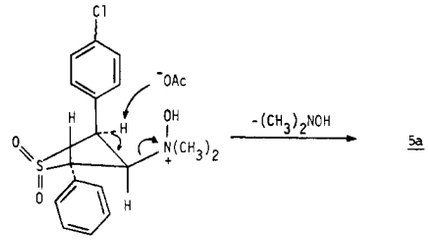
2,4-Diarylthiete 1,1-dioxides (**4, 5, 6**) were obtained by the amine oxide elimination reaction of 3-dimethylaminothietane 1,1-dioxides (**1, 2, 3**)[1b] (Scheme I). Treatment of either a mixture of the cis and trans isomers (**1a, 1b**)[2] or the cis isomer alone with peracetic acid gave 2,4-diphenylthiete 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

Scheme I



product obtained was found by NMR analysis to consist of 65% **5a** and 35% **5b**. The preferential formation of **5a** is attributable, at least in part, to the acidifying effect of the *p*-chloro substituent on H-2. Repeating the reaction in tetrahydrofuran with isomer **2b** gave 18% **5a** and 82% **5b**. Thus, the results were consistent with the configurations previously assigned to **2a** and **b**.[1b] In contrast, the elimination reaction of **2b** in glacial acetic acid gave a product composed of 95% **5a** and 5% **5b**. A plausible explanation for this result is that under acidic conditions, an intermolecular (E2) mechanism is operative. Attack of acetate ion at the pseudoequatorial proton (H-2) which is sterically less hindered (as well as more acidic) than the pseudoaxial proton (H-4) in the protonated *N*-oxide form **10** of **2b** would favor formation of **5a**.

The UV spectrum of **5a** showed a maximum at 262 nm (ε 26 300) and that of **5b** possessed a shoulder at 230 nm (ε

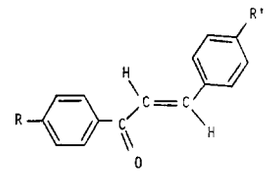


10

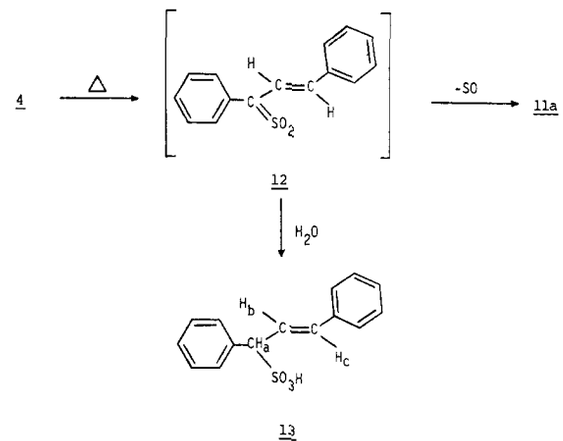
20 300) and a maximum at 256 nm (ε 22 600). The bathochromic shift observed in the spectrum of **5a** was attributed to the conjugation of the *p*-chlorophenyl ring with the heterocyclic double bond. The wavelength maximum in the spectrum of **5b** was similar to that observed in the spectrum of **4** (λ_{max} 255 nm, ε 19 600) and it was reasonable, therefore, that the *p*-chlorophenyl ring in **5b** was unconjugated. These configurational assignments were further supported by the NMR spectra which showed H-4 in **5a** at lower field (λ 5.91) than H-4 in **5b** (δ 5.85). It has been reported that the benzylic proton of 2-phenylthietane occurs at lower field than that of 2-(4-chlorophenyl)thietane.[6]

NMR analysis of the crude product from the reaction of **3** with peracetic acid in glacial acetic revealed the presence of only one thiete 1,1-dioxide, **6**. The bathochromic shift evident in the UV spectrum of **6** (λ_{max} 288 nm, ε 19 000) when compared to the spectrum of **4** indicated that the *p*-nitrophenyl ring in **6** was conjugated with the heterocyclic double bond. The greater acidity of H-2 relative to that of H-4 in **3** probably accounts for the exclusive formation of **6**. Downfield shifts of protons H-3 and H-4 in the NMR of **6** as compared to **4** and **5** were observed and attributed to substituent and solvent effects.

Thermolytic Reactions. It had been observed that 2,4-diphenylthiete 1,1-dioxide (**4**) at its melting point decomposed with vigorous evolution of gas. An IR spectrum of the melt was almost identical with *trans*-benzylideneacetophenone (*trans*-chalcone, **11a**). Heating a sample of **4** at 166 °C for 3



11a, R=R'=H
b, R=Cl; R'=H
c, R=H; R'=Cl



min gave **11a** to the extent of 92% as well as a small, undetermined amount of the cis isomer as measured by GC. King and co-workers have proposed that thermolytic conversion of

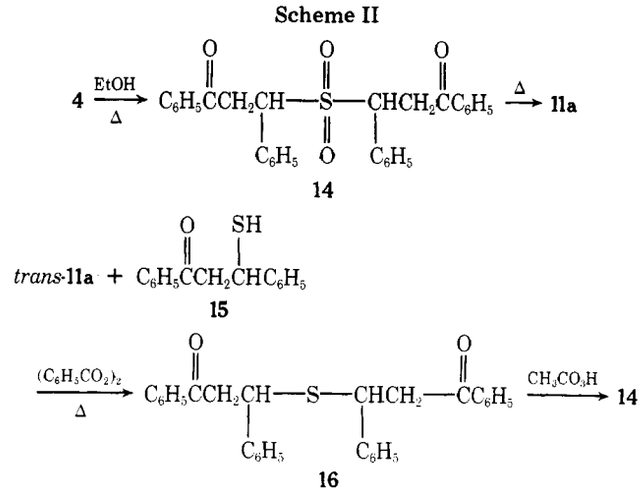
thiete 1,1-dioxides to α,β-unsaturated carbonyl compounds involves electrocyclic opening of the heterocycle to give a vinyl sulfene intermediate which then undergoes desulfinylation.[7] According to this mechanism, the formation of **11a** would occur via the intermediate **12**.[8] A previous attempt to trap the vinyl sulfene intermediate derived from thiete 1,1-dioxide met limited success.[9] It was considered of interest, therefore, to investigate the possible trapping of **12**. Water was used as the trapping agent since it is known that sulfenes react readily with water to give sulfonic acids. Refluxing a solution of **4** in aqueous tetrahydrofuran gave the predicted sulfonic acid **13** in 71% crude yield as well as a small amount of **11a** and a ketonic sulfone, **14**. The UV spectrum of **13** (λ_{max} 253 (ϵ 21 600), 282.5 (ϵ 2740) and 292 nm (ϵ 1450)) was quite similar to that reported[12] for the carboxylic analogue of **13**, 2,4-diphenyl-3-butenoic acid (λ_{max} 252 (ϵ 22 490), 283.5 (ϵ 2080), and 292.5 nm (ϵ 1320)). Although the configuration of the carboxylic acid was not assigned, from a consideration of the procedure whereby the acid was synthesized,[11] it was most certainly trans. The same configuration was, therefore, assigned to **13**.[12] As the free sulfonic acid was unstable, it was further characterized as the stable dimethylamine salt. In the NMR spectrum of the salt, the protons (H_a, H_b, and H_c) appeared as an ABX system with coupling constants J_{bc} = 15.0 Hz, J_{ab} = 9.0 Hz and J_{ac} = −1 Hz. The magnitude of the couplings was in accord with structure **13**.[13]

Thermolysis of **5a** and **b** provided further evidence for the double bond positions in the two isomers. According to the proposed mechanism,[7] isomer **5a** should have given benzylidene-*p*-chloroacetophenone (**11b**) whereas **5b** should have yielded *p*-chlorobenzylideneacetophenone (**11c**). Indeed, heating **5a** at 164 °C for 3 min afforded **11b** in 80% yield and no **11c** (GC analysis). When **5b** was treated in the same manner, an 85% yield of **11c** was obtained and no **11b**. Heating the *p*-nitro derivative **6** at 166 °C for 3 min gave one major product (GC) which possessed characteristic chalcone bands in the infrared, but the predicted product was not isolated.

Some decomposition of **4** occurred upon recrystallization from hot solvents and particularly so when the solvent was ethanol. Mother liquors contained **11a** plus a small amount of white solid which was identified as a ketonic sulfone from IR spectra. Refluxing **4** in ethanol allowed isolation of 17% of the ketonic sulfone **14** (Scheme II). Fractional crystallization of the crude sulfone gave white needles (mp 184–185 °C) and transparent plates (mp 196–197 °C) which are considered to be diastereoisomers of bis(1,3-diphenyl-3-oxopropyl) sulfone (**14**) based on the spectroscopic and synthetic evidence. Besides absorption characteristics of a sulfone, bands at 1683 and 1241 cm^{-1} in the IR spectrum of the low melting isomer indicated the presence of a benzoyl functionality. Comparison of its UV spectrum (λ_{max} 244 nm, ϵ 25 000) with that of acetophenone[13b] (λ_{max} 240 nm, ϵ 13 000) suggested two benzoyl groups per molecule. The NMR spectrum was in agreement with structure **14** and showed the nonaromatic protons as an ABX pattern. From the 100-MHz spectrum, the chemical shift of protons A was calculated[14] to be δ 3.72 (J_{AX} = 2.8 Hz) and that of protons B to be δ 3.93 (J_{BX} = 10.2 Hz) with J_{AB} = 17.5 Hz. The IR spectrum of the high melting isomer was quite similar but not identical with that of the low melting material, whereas the NMR spectra were superimposable.

To confirm the assigned structure, an unequivocal synthesis of **14** was carried out (Scheme II). Heating β-mercapto-β-phenylpropiophenone (**15**) with *trans*-**11a** in the presence of benzoyl peroxide gave the sulfide **16**.[15] The sulfide **16** was not purified but was oxidized directly to give **14**. Fractional crystallization gave white needles, the IR, UV, and NMR spectra of which were identical with those of the low melting ketonic sulfone derived from **4**. A mixture melting point of the two was not depressed. Because of the synthetic procedure

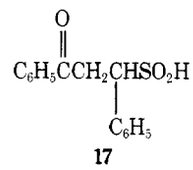
Scheme II



used, both diastereoisomeric forms of **14** (*dl* and *meso*) should have been formed. A second substance was obtained as transparent plates, the melting point and IR spectrum of which were identical with those of the high melting isomer from the decomposition of **4**.

When either diastereoisomeric form of **14** was heated at its melting point it decomposed with vigorous evolution of a gas to give **11a** (IR analysis). The thermolysate from the low melting isomer was found by GC to consist of a mixture of *trans*- and *cis*-**11a**, respectively. A possible mechanism is desulfonylation[17] of **14** followed by loss of a hydrogen atom from each of the intermediate radical fragments to give **11a**.

Compound **14** is formally derived from two molecules of **4** by the loss of sulfur monoxide and the addition of water. Since sulfinic acids are known to readily add to α,β-unsaturated carbonyl compounds to give sulfones[18] and since **11a** is formed along with **14** in the decomposition of **4** in hot ethanol, it is tempting to implicate the sulfinic acid **17** in the formation of



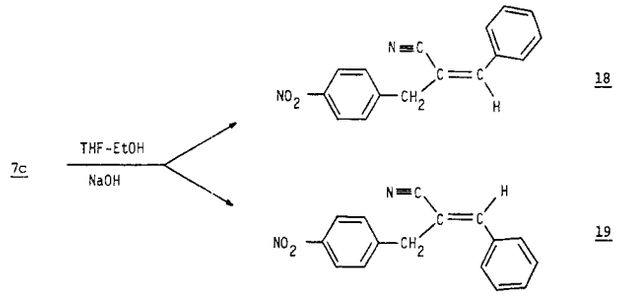
17

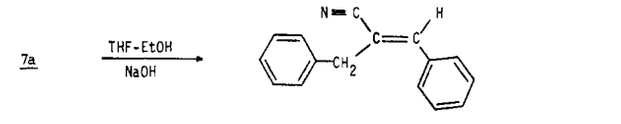
14. Although several mechanisms can be evoked whereby **17** is formed from **4** in the presence of water, no direct experimental evidence has been obtained so far for its formation. Attempts to generate **17** by treating the sulfone (**14**) with alcoholic KOH or dimethylamine in chloroform were unsuccessful. Chalcone forms immediately under these conditions as expected.[18] Perhaps the sulfinic acid if formed also readily decomposes to chalcone.

Addition Reactions. The addition of HCN to thiete (**4**) gave *cis*-2,4-diphenyl-3-cyanothietane 1,1-dioxide (**7a**). The reaction proceeds best using a solution of HCN in ethanol, catalyzed by a small amount of KCN. An excess of KCN or other base can lead to intractable black tars. The cis configuration of the phenyl rings was apparent from the equivalence of the benzylic protons and the magnitude of the vicinal coupling constant (10.5 Hz) in the NMR spectrum. The absence of trans isomer was not unexpected considering the instability of *trans*-2,4-diphenyl-3-dimethylaminothietane 1,1-dioxide (**1b**) relative to the cis isomer **1a**.[1b] The course of the addition may be rationalized in terms of approach of cyanide ion from the least hindered side of the thiete (**4**), i.e., side opposite the phenyl group at C-4, to generate an intermediate carbanion. Protonation of the carbanion then occurs to give the more stable cis isomer. Even if some trans isomer were

initially formed, epimerization to **7a** could occur under the basic conditions (KCN) of the reaction.

By analogy, the hydrogen cyanide adduct **7b** from a mixture of **5a** and **5b** was assigned a cis configuration as was the adduct **7c** obtained from **6**. The sensitivity of these cyano compounds to basic conditions was readily apparent in the case of **7c**. Column chromatographic work-up of the reaction residue after isolation of **7c** gave two additional compounds which from the IR appeared to be conjugated nitriles. Sulfone bands were absent. Elemental analyses were in agreement with the geometric isomers **18** and **19**.





20

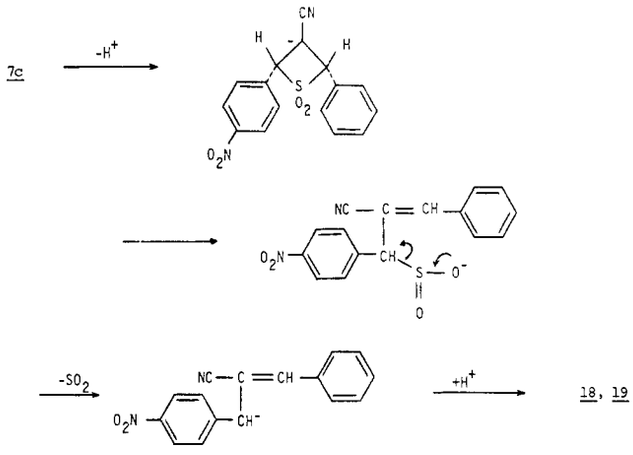
To confirm that the conjugated nitriles isolated from the HCN addition reaction were derived from cyclic product, **7c** was treated with base and gave a 2.5:1 mixture of **18** and **19** as estimated by NMR and GC. Similar treatment of **7a** gave a small quantity of conjugated nitrile, **20**, and considerable polymerized solids.

Irradiation of a methanol solution of the isomers (2.5:1/18:19) reversed the ratio to give a mixture of 1:2.5 of **18** and **19** at equilibrium. The possibility that **18** and **19** were positional rather than geometric isomers is thus ruled unlikely. Isomer **18**, λ_{max} 278 nm (ϵ 26 700), was assigned the (*Z*) configuration and **19**, λ_{max} 270 nm (ϵ 39 000), assigned (*E*). These values are comparable to the reported values of (*Z*) and (*E*) isomers of cinnamic acid nitrile, 273 (16 596) and 272 (39 500), respectively.[13c] In the NMR spectrum of **19** the benzylic and vinylic protons are shifted downfield compared to **18** and may be the result of a greater degree of deshielding of these protons by the cyano group and aromatic ring, respectively, in isomer **19**. The conjugated nitrile, **20**, was assigned the (*E*) configuration based on the UV spectral data, λ_{max} 278 nm (ϵ 42 000). The λ_{max} observed for **20** also supports the assigned structures of **18** and **19**. Had the *p*-nitrophenyl group been conjugated with the nitrile a bathochromic shift of λ_{max} for **18** and **19** would have been expected (consider the trans isomers of cinnamic and 4-nitrocinnamic acid (λ_{max} 273 nm and 300 nm, respectively).[13c]

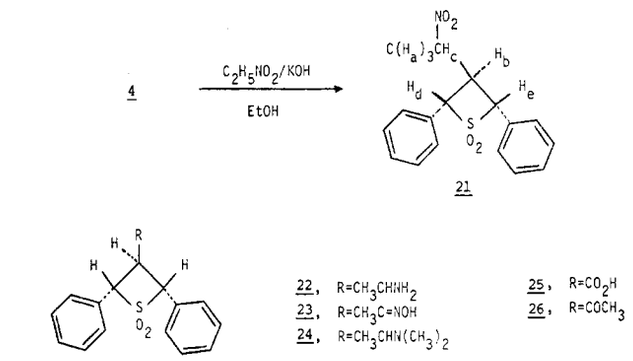
A possible mechanism for a base catalyzed elimination to form conjugated nitriles is outlined in Scheme III. Ring opening to give the allylic carbanion shown is perhaps preferred because of the inductive nature of the *p*-nitro substituent.

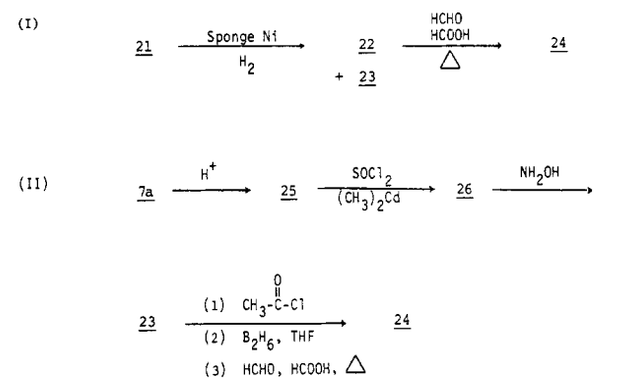
Reduction of the 3-cyano compounds with diborane followed by dimethylation of the resulting primary amines **8a, b,** and **c** afforded the final compounds **9a, b** and **c**. Although a derivative of **9c** suitable for elemental analysis could not be prepared, its IR and NMR spectra were in agreement with the assigned structure.

Scheme III



Scheme IV





cis-2,4-Diphenyl-3-(1-dimethylaminomethyl)thietane 1,1-dioxide (**24**) was prepared by two routes (Scheme IV). The more efficient method involved Michael addition of nitroethane to **4** to give **21**. Crystals of this adduct obtained from hexane–benzene contained one molecule of benzene for every two molecules of **21** (NMR and GC). In the NMR spectrum H_d and H_e were nonequivalent and appeared as overlapping doublets. It was reasonable to assume that nitroethane, in the same manner as HCN, added to **4** to give a thietane 1,1-dioxide derivative with the phenyl rings cis. Therefore, the nonequivalence of the benzylic protons was attributable to the asymmetry of the 1-nitroethyl substituent at C-3. Catalytic reduction of **21** gave a mixture of the primary amine **22** and the oxime **23**. Elemental analyses were not obtained for **22** and **23** but spectroscopic data and two different reaction schemes involving these compounds were considered sufficient criteria for identification. The equivalence of the benzylic protons and the magnitude of the vicinal coupling constant (10 Hz) in the NMR spectrum of **23** indicated that this compound possessed

a cis configuration. Assuming that no epimerization occurred during the hydrogenation procedure, this observation supported the assignment of a cis configuration to **21.** Dimethylation of **22** gave the desired product **24.** Compounds **22** and **24** were considered to possess the same configuration as **21.**

A second approach to **24** utilized the 3-cyano compound **7a.** Acid hydrolysis of the nitrile gave *cis*-2,4-diphenyl-3-carboxythietane 1,1-dioxide (**25**) in 89% yield. Treatment of the acid chloride of **25** with dimethylcadmium afforded the ketone **26.** No product could be isolated when attempts were made to prepare **26** directly by reacting **7a** with methyllithium or methylmagnesium bromide. Attempts to synthesize **22** or **24** from **26** by application of the Leuckart reaction[19] were unsuccessful. The ketone decomposed under the reaction conditions of prolonged heating. It has been reported that oxime acetates are reduced to primary amines by diborane.[20] Preparation of **24** via this procedure was investigated in a preliminary fashion. Ketone **26** was converted to the oxime **23** which was acetylated and then treated with diborane. Dimethylation of the crude product gave **24** in low yield.

The analgetic activities of the thietane 1,1-dioxide derivatives described in this paper will be reported elsewhere.

Experimental Section

The instrumentation was as previously described.[1b] Columns used for gas–liquid chromatography (GC) were 6 ft × $^5/_{32}$ in. (i.d.) silanized glass. Packings were 5% SE-30 on Chromport (70–80 mesh), 3% QF-1 on Gas-Chrom Q (100–120 mesh), and 3% OV-225 on Gas Chrom Q (100/120). GC/MS data of the unsaturated nitrile isomers were obtained using a Varian Mat 111 spectrometer at 70 eV. An AEI MS9 with computer interface (courtesy of UBC Chemistry) was used for accurate mass determinations.

The GC calibration curves referred to below were prepared using authentic samples of chalcones which were synthesized according to literature procedures and crystallized from hexane–ethanol: *trans*-benzylideneacetophenone (**11a**),[22] mp 55–56 °C (lit.[22] 55–57 °C); *trans*-benzylidene-*p*-chloroacetophenone (**11b**),[23b] mp 96.5–98 °C (lit.[24] 94–96 °C); and *trans*-*p*-chlorobenzylideneacetophenone (**11c**),[23a] mp 112–113.5 °C (lit.[23a] 114.5 °C). The hydrogen cyanide solution used in the synthesis of the 3-cyano adducts **7a, b** and **c** was prepared by mixing 80 mL of liquefied HCN[25a] with 2 L of ice-cold 100% ethanol.

2,4-Diphenylthiete 1,1-Dioxide (4). To a slurry of 14.5 g (0.048 mol) of **1a** in 14.5 mL of glacial acetic acid cooled in an ice–water bath was added 43.5 mL of 40% peracetic acid dropwise over a period of 45 min. After stirring for 17 h the reaction mixture was neutralized with a saturated solution of Na_2CO_3 and then extracted with 300 mL of $CHCl_3$. The $CHCl_3$ layer was washed with 10% HCl and then dried over $MgSO_4$. Evaporation under reduced pressure with the aid of a lukewarm water bath gave 10.5 g (85%) of beige solid. Crystallization from hexane–benzene afforded 9.3 g (76%) of **4** as white, fluffy needles, mp 137–138 °C dec (lit.[3] 133–134 °C); IR 1303, 1150 cm^{-1} (sulfone); NMR δ 7.77–7.27 (m, 10, phenyls), 7.03 (d, 1, J = 2 Hz, H-3), and 5.92 (d, 1, J = 2 Hz, H-4); UV_{max} 255 (CH_3CN) nm (ϵ 19 600) (lit.[3] (EtOH) 257 nm (ϵ 17 400)). Essentially the same yield of product was obtained when the starting material was a mixture of **1a** and **b.**

Anal. Calcd for $C_{15}H_{12}O_2S$ (256.32): C, 70.29; H, 4.72. Found: C, 69.93; H, 4.92.

2-(4-Chlorophenyl)-4-phenylthiete 1,1-Dioxide (5a). In the same manner as described above, 27.0 g (0.080 mol) of **2b** in 27 mL of glacial acetic acid was reacted with 80 mL of 40% peracetic acid. Work-up afforded a yellow solid which upon crystallization from EtOH gave 13.7 g (59%) of **5a** as white needles, mp 128–129 °C dec; IR 1302, 1160 cm^{-1} (sulfone); NMR δ 7.67–7.25 (m, 9, aromatics), 7.02 (d, 1, J = 2 Hz, H-3), and 5.91 (d, 1, J = 2 Hz, H-4); UV_{max} 262 (ϵ 26 300) and 294 nm (shoulder) (ϵ 1400).

Anal. Calcd for $C_{15}H_{11}ClO_2S$ (290.77): C, 61.96; H, 3.81; Cl, 12.19. Found: C, 61.93; H, 4.25; Cl, 12.31.

2-Phenyl-4-(4-chlorophenyl)thiete 1,1-Dioxide (5b). In the same manner as described above, 35.4 g (0.0105 mol) of **2a** in 35 mL of glacial acetic acid was reacted with 106 mL of peracetic acid. Crystallization of the product from EtOH gave 13.2 g (43.2%) of white solid which was found to be a mixture of **5a** and **b** by IR analysis. Evaporation of the mother liquor and crystallization of the residue from EtOH gave a further 4.1 g (13.4%) of isomer mixture enriched in **5b.** Repeated recrystallization of the latter solid from EtOH gave pure **5b** as white, shiny leaflets, mp 130–131 °C dec; IR 1310, 1160 cm^{-1} (sulfone); NMR δ 7.70–7.08 (m, 9, aromatics), 6.98 (d, 1, J = 2 Hz, H-3); and 5.85 (d, 1, J = 2 Hz, H-4); UV_{max} 230 (shoulder) (ϵ 20 300), 256 (ϵ 22 600), and 290 nm (shoulder) (ϵ 800).

Anal. Calcd for $C_{15}H_{11}ClO_2S$ (290.77): C, 61.96; H, 3.81; Cl, 12.19. Found: C, 61.72; H, 4.12: Cl, 12.10.

Effect of Starting Material Configuration on the 5a:5b Product Ratio. To a stirred solution of 0.50 g (1.5 mmol) of **2a** in 45 mL of THF was added 3.0 mL of 40% peracetic acid dropwise over a period of 2 min. The reaction temperature was maintained at 27 ± 1 °C by cooling the reaction flask in an ice–water bath when necessary. After stirring for 5 h, the solution was evaporated under reduced pressure to a volume of about 10 mL. Upon adding 40 mL of distilled water a white solid precipitated. The mixture was carefully neutralized with a saturated Na_2CO_3 solution and the solid was collected and dried, yield 0.40 g (92%). The IR spectrum indicated a mixture of **5a** and **b** free of starting material. In the 100 MHz spectrum H-3 and H-4 of **5a** appeared as doublets at δ 7.017 and 5.904 and the corresponding protons of **5b** appeared as doublets at δ 6.980 and 5.858. From the doublet integrals the product compostion was determined to be 65% **5a** and 35% **5b.**

When an identical reaction in THF was run using 0.5 g of **2b,** the product (0.37 g, 85%) was found by 100 MHz NMR to consist of 18% **5a** and 82% **5b.**

In the same manner as described for the preparation of **4,** 1.90 g (5.7 mmol) of **2b** in 2.0 mL of glacial acetic acid was reacted with 6.0 mL of 40% peracetic acid for 20 h. The reaction mixture was then diluted with water until precipitation of solid was no longer evident. After collecting and drying, the solid weighed 1.46 g (89%). NMR analysis gave the composition as 95% **5a** and 5% **5b.**

2-(4-Nitrophenyl)-4-phenylthiete 1,1-Dioxide (6). Because of the instability of **3** to crystallization, crude material containing approximately 12% acyclic isomer[1b] as impurity was used. In the same manner as described for the preparation of **4,** 20.3 g of starting material in 20 mL of glacial acetic acid was reacted with 61 mL of 40% peracetic acid. After stirring for 2 h, the reaction was worked up to give 15.0 g (96%) of crude product, mp 139–142 °C. Crystallization from EtOH gave **6** as pale yellow leaflets, mp 147–148 °C dec; IR 1520, 1320 (nitro group), 1300, 1155 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 8.57–8.30, 8.07–7.83 (m, 4, AA′BB′ pattern due to *p*-nitrophenyl), 8.18 (d, 1, J = 2 Hz, H-3), 7.50 (s, 5, phenyl), and 6.49 (d, 1, J = 2 Hz, H-4); UV_{max} 288 nm (ϵ 19 000).

Anal. Calcd for $C_{15}H_{11}NO_4S$ (301.32): C, 59.79; H, 3.68; N, 4.65. Found: C, 59.83; H, 3.75; N, 4.79.

Thermolysis of 4. A stoppered 8 × 70 mm test tube containing 30.0 mg (0.117 mmol) of **4** was placed in a 166 °C oil bath for 3.0 min. During the first minute the solid melted and a gas was rapidly evolved from the melt. Upon cooling, the brownish-yellow residue was dissolved in sufficient $CHCl_3$ to give 10 mL of solution which was immediately analyzed for *trans*-benzylideneacetophenone (**11a**) by GC using the 3% QF-1 column with the injection port, oven and detector at 240, 170, and 270 °C, respectively, and the nitrogen flow at 67 mL/min. By reference to a straight-line calibration curve (peak area vs. concentration) the total amount of **11a** (retention time 6.3 min) in the solution was determined to be 22 mg (92%). A second minor peak in the chromatogram possessed the same retention time (3.2 min) as *cis*-benzylideneacetophenone.[21] The IR spectrum (neat) of another thermolysate obtained in the same manner was essentially identical with that of an authentic sample of **11a.**

Thermolysis of 5a. In the same manner as described for the thermolysis of **4,** 30.0 mg (0.103 mmol) of **5a** was heated in a 164 °C bath for 3 min. Upon cooling, the orange solid was dissolved in $CHCl_3$ with 0.1% benzil as internal standard and immediately analyzed for *trans*-benzylidine-*p*-chloroacetophenone (**11b**) using the 3% QF-1 column with the injection port, oven and detector at 240, 200, and 270 °C, respectively, and the nitrogen flow at 67 mL/min. By reference to a straight-line calibration curve (peak height **11b**/peak height internal standard vs. conc. **11b**) the total amount of **11b** (retention time 3.6 min) was determined to be 20 mg (80%). A minor peak at 1.9 min was attributed to *cis*-benzylidene-*p*-chloroacetophenone.[21] The IR spectrum of a second thermolysate showed only slight discrepancies from that of an authentic sample of **11b.**

Thermolysis of 5b. In a manner identical with that described for the thermolysis of **5a, 5b** was thermolyzed to give 21 mg (85%) of *trans*-*p*-chlorobenzylideneacetophenone (**11c**) (retention time 3.9 min). A minor peak at 2.2 min in the chromatogram was attributed to *cis*-*p*-chlorobenzylideneacetophenone.[21] The IR spectrum of the solid product obtained in a second thermolysis was almost identical with that of authentic **11c.**

Decomposition of 4 in Aqueous Tetrahydrofuran. ***trans***-

1,3-Diphenylpropene-3-sulfonic Acid (13). A solution of 2.56 g (0.01 mol) of **4** in a mixture of 40 mL of THF and 10 mL of water was refluxed for 41 h. Evaporation in vacuo gave a viscous, yellow oil which was dissolved in 20 mL of $CHCl_3$ and extracted with 40 mL of water. The aqueous layer (acidic to indicator paper) was evaporated under vacuum to give a pale yellow, crystalline solid (1.95 g, 71%). Crystallization from hexane–$CHCl_3$ afforded **13** as fine, off-white needles, mp 97–102 °C dec; IR 3700–2400, 1225, 1050 cm^{-1} (sulfonic acid); UV_{max} (H_2O) 253 (ε 21 600), 282.5 (shoulder) (ε 2740) and 292 (ε 1450). The free acid was unstable and slowly decomposed during a period of a week. Evaporation of a $CHCl_3$ solution of **13** which had been treated with excess dimethylamine afforded the salt as a white solid. Crystallization from hexane–benzene gave white needles, mp 169–170 °C; IR 3040–2480 (ammonium band), 1250, 1225, 1160, 1027 cm^{-1} (sulfonic acid salt); NMR δ 7.91–7.10 (m, 12, phenyls and NH_2), 7.01–6.30 (m, AB portion of ABX, 2, vinylic protons), 4.72–4.85 (m, X portion of ABX, 1, benzylic). Compound **13** was submitted for analysis as its dimethylamine salt.

Anal. Calcd for $C_{17}H_{21}NO_3S$ (319.42): C, 63.92; H, 6.63. Found: C, 63.93; H, 6.53.

Evaporation of the dried (Na_2SO_4) $CHCl_3$ layer from the extraction of **13** gave a brown oil, the IR spectrum (neat) of which indicated the presence of **11a**. The chalcone was extracted with two 20-mL portions of hot hexane and then quantitated by GC (3% QF-1 column), yield 0.15 g (7%).

Decomposition of 4 in Ethanol. Bis(1,3-diphenyl-3-oxopropyl) Sulfone (14). A solution of 2.56 g (0.010 mol) of **4** in 250 mL of 95% ethanol was heated at reflux for 2 h and then evaporated under reduced pressure to give a yellow oil. When a solution of the oil in 20 mL of hot ethanol was allowed to cool a white solid precipitated. The solid was collected and the filtrate was evaporated and treated again with ethanol to give additional solid. Repeating the process twice gave a total of 0.41 g (17%) of **14**. The product was fractionated by heating it in ethanol or hexane–methyl ethyl ketone and then filtering to remove material that was reluctant to dissolve. Upon cooling, the filtrate gave white needles, mp 184–185 °C dec; IR 1683, 1241 (benzoyl group), 1307, 1138 cm^{-1} (sulfone); UV_{max} (CH_3OH) 244 nm (ε 25 000); NMR δ 7.93–7.67 (m, 4, ortho protons of benzoyl groups), 7.53–7.23 (m, 16, phenyls and remaining protons of benzoyl groups), 4.70 (m, X portion of ABX pattern, 2, benzylic H) and 4.20–3.39 (m, AB portion of ABX pattern, 4, methylenes).

Anal. Calcd for $C_{30}H_{26}O_4S$ (482.60): C, 74.66; H, 5.43; O, 13.26; S, 6.64. Found: C, 74.21; H, 5.66; O, 13.62; S, 7.00.

Crystallization of the less soluble portions of the product from ethanol or hexane–methyl ethyl ketone gave transparent plates, mp 196–197 °C dec; IR 1683, 1241 (benzoyl group), 1310, 1292, 1138 cm^{-1} (sulfone).

Evaporation of the final filtrate from the isolation of the ketonic sulfone gave a brownish-yellow oil. The IR spectrum (neat) of this material showed strong bands at 1665 and 1600 cm^{-1} attributable to **11a**. Vacuum distillation afforded 0.2 g (10%) of crude **11a** as a yellow, viscous liquid which solidified upon collection, bp 120–130 °C (0.1 mm) [lit.[26] 208 °C (25 mm)]. Crystallization from petroleum ether (bp 60–80 °C) gave *trans*-**11a** as pale yellow prisms, mp 54–55 °C (lit.[26] 57–58 °C). The infrared spectrum was superimposable with that of an authentic sample. Coinjection with authentic *trans*-**11a** on a 5% SE-30 column with the injection port, oven and detector at 282, 193, and 253 °C, respectively, and the nitrogen flow at 80 mL/min gave one peak, retention time 5.1 min.

Synthesis of Bis(1,3-diphenyl-3-oxopropyl) Sulfone (14). A mixture of 2.08 g (0.010 mol) of *trans*-**11a**,[27] 2.42 g (0.010 mol) of **15**[28] and 20 mg of benzoyl peroxide was heated on a steam bath for 6 h. Mixing the product with Et_2O caused a white solid (1.86 g) to separate which was collected and tentatively identified as an α-hydroxy sulfide.[16] Evaporation of the supernatant gave 2.64 g of yellow oil (**16**). In the IR spectrum (neat) S–H stretching absorption was absent and a strong aromatic ketone band appeared at 1680 cm^{-1}. To a cooled solution of the oil in 10 mL of $CHCl_3$ and 10 mL of glacial acetic acid was added 4.6 mL of 40% peracetic acid dropwise over a period of 5 min. After 20 h, evaporation of the $CHCl_3$ under reduced pressure caused a white solid (**14**) to precipitate. Dilution of the supernatant with water and extraction with $CHCl_3$ followed by evaporation of the dried (Na_2SO_4) organic layer gave a yellow oil from which additional solid product was isolated by warming with ethanol. The total yield of **14** was 1.70 g (60%, based on weight of **16**). Fractional crystallization from hexane–methyl ethyl ketone gave white needles and transparent plates which were identical with the low and high melting isomers of **14**, respectively.

Thermolysis of 14. A sample of **14** (low melting diastereoisomer) in a stoppered 8 × 70 mm test tube was placed in a 160 ° C oil bath which was then rapidly heated to 200 °C. When the evolution of gas from the melt had subsided (2 min), the tube was removed. The IR spectrum (neat) of the resulting yellow syrup was very similar to that of *trans*-**11a**. Analysis by GC using a 3% QF-1 column with the injection port, oven and detector at 240, 170, and 270 °C, respectively, and the nitrogen flow at 67 mL/min gave two peaks which corresponded to *cis*-**11a** (3.2 min) and *trans*-**11a** (6.3 min). The ratio of cis to trans based on peak area was 1:4.

***cis*-2,4-Diphenyl-3-cyanothietane 1,1-Dioxide (7a).** A solution of 10.00 g (0.039 mol) of **4** in 250 mL of $CHCl_3$ was diluted with 500 mL of EtOH (100%) and 250 mL of HCN solution. Addition of 575 mg of powdered KCN caused the reaction to turn bright yellow. After stirring for 18 h a precipitate was present which was collected and washed with 400 mL of water. Air drying gave 8.57 g (77.6%) of pale yellow powder, mp 235–237 °C. Crystallization from *n*-butyl alcohol afforded **7a** as white, feather-shaped crystals, mp 236–237 °C; IR 2245 (nitrile), 1338, 1178, 1138 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 7.81–7.33 (m, 10, phenyls), 6.34 (d, 2, J = 10.5 Hz, H-2 and H-4), and 4.77 (t, 1, J = 10.5 Hz, H-3).

Anal. Calcd for $C_{16}H_{13}NO_2S$ (283.35): C, 67.82; H, 4.63; N, 4.94. Found: C, 67.80; H, 4.73; N, 4.84.

***cis*-2-(4-Chlorophenyl)-3-cyano-4-phenylthietane 1,1-Dioxide (7b).** In a manner identical with that described for the preparation of **7a**, 15.00 g (0.0516 mol) of a mixture of **5a** and **b** was reacted to give 6.80 g (42.0%) of **7b** as a white crystalline solid, mp 198–199 °C. Evaporation of the filtrate and fractional crystallization of the resulting yellow solid from EtOH afforded 2.26 g (14.0%) of additional product and 2.07 g (13.8%) of starting material. Crystallization from EtOH gave **7b** as fine, white needles, mp 199–200 °C; IR 2280 (nitrile), 1333, 1180, 1148 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 7.89–7.43 (m, 9, aromatics), 6.39 (d, 2, J = 11 Hz, H-2 and H-4), and 4.76 (t, J = 11 Hz, H-3).

Anal. Calcd for $C_{16}H_{12}ClNO_2S$ (317.79): C, 60.47; H, 3.81; Cl, 11.16. Found: C, 60.26; H, 3.82; Cl, 11.18.

***cis*-2-(4-Nitrophenyl)-3-cyano-4-phenylthietane 1,1-Dioxide (7c).** The procedure was similar to that described for the preparation of **7a**. A solution of 10.26 g (0.0341 mol) of **6** in 308 mL of THF was diluted with 256 mL of HCN solution and 590 mg of powdered KCN was added. After stirring for 5 h, the reaction solution was evaporated under reduced pressure to give an orange-brown oil. Washing the oil with EtOH caused a solid to separate. The supernatant was evaporated and the resulting oil was again treated with EtOH. Repeating the process several times gave a total of 7.52 g (67%) of pale yellow solid. Crystallization from hexane–$CHCl_3$ afforded **7c** in two polymorphic forms: white needles, mp 164–165 °C, and pale yellow rosettes, mp 152–153 °C; IR 2275 (nitrile), 1530, 1353 (nitro group), 1334, 1177, 1145 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 8.57–8.28, 8.15–7.91 (m, 4, AA'BB' pattern due to *p*-nitrophenyl), 7.88–7.40 (m, 5, phenyl), 6.56 (d, 1, J = 10.5 Hz, H-2), 6.48 (d, 1, J = 10.5 Hz, H-4), and 4.92 (t, 1, J = 10.5 Hz, H-3). Compound **7c** was submitted for analysis as the low melting polymorph.

Anal. Calcd for $C_{16}H_{12}N_2O_4S$ (328.34): C, 58.53; H, 3.68, N, 8.53. Found: C, 58.65; H, 3.75; N, 8.58.

Isolation of Unsaturated Nitriles (18, 19, 20). The final filtrate from the work-up of **7** (4.5 g of orange-brown oil) was heated in 20 mL of benzene and filtered. The filtrate was applied to a 2.5 × 60 cm column of 95 g of silica gel and developed with benzene. Fractions 1 and 2 were a mixture of **18** and **19** and **7c**, respectively. Two other fractions contained small amounts of unidentified substances. Fraction 1 was recrystallized with hexane–benzene and the resulting needles and plates separated by hand. Further recrystalllization of the plates gave **18**, mp 100–101 °C; IR (KBr) 2220 (α,β-unsaturated nitrile), 1626 (conjugated double bond), 1520, 1348 cm^{-1} (nitro); NMR ($CDCl_3$) δ 8.37–8.07 (m, 2, H ortho to nitro), 7.97–7.27 (m, 7, H meta to nitro and remaining phenyl), 7.08 (s, 1, vinylic), and 3.83 (s, 2, benzylic); UV_{max} (CH_3CN), 278 nm (ε 26 700); GC/MS *m/e* 264 (M^+, 71) 247 (42), 218 (29), 217 (100), 140 (34), 109 (41), 106 (30), 91 (39).

Further recrystallization of the needles gave **19**, mp 132–133 °C; IR (KBr) 2225, 1625, 1516 and 1348 cm^{-1}; NMR ($CDCl_3$) δ 8.36–8.09 (m, 2, H ortho to nitro), 7.61–7.28 (m, 8, remaining phenyl plus vinylic), and 3.93 (s, 2, benzylic); UV_{max} (CH_3CN) 270 nm (ε 39 000); GC/MS, *m/e* 264 (M^+, 70), 247 (41), 218 (29), 217 (100), 140 (34), 109 (42), 106 (26), 91 (35).

Anal. Calcd for $C_{16}H_{12}N_2O_2$ (264.28): C, 72.72; H, 4.58. Found **18**: C, 72.58; H, 4.66. Found **19**: C, 72.53; H, 4.48.

Treatment of 0.33 g of **7c** in 10 mL of THF and 50 mL of EtOH with dropwise addition of 2 mL of 1 N NaOH caused a deep magenta color to form which gradually disappeared. After 30 min 2 mL of glacial acetic was added and the solution evaporated to an orange solid. The

solid was dissolved in $CHCl_3$ and extracted several times with H_2O. The $CHCl_3$ layer dried (Na_2SO_4) and the $CHCl_3$ removed gave 0.26 g of orange solid. The NMR indicated a mixture of **18** and **19** which approximately accounts for 90% of the crude solid. Impurities were also present; δ 4.31, 2.4, and 1.25. GC analysis (3% QF-1, oven 210 °C, N_2 65 mL/min) gave peaks with identical retention times to **18** and **19** previously isolated (R_t = 14.3 and 13.1 min, respectively). Irradiation of a 1% solution of the isomers in methanol (450-W Hanovia arc lamp at room temperature through Pyrex) for 2 h gave an equilibrium mixture of 1:2.5 of **18** and **19**, respectively. Further irradiation or prolonged refluxing in benzene did not change this equilibrium.

Treatment of 2.0 g of **7a** dissolved in 160 mL of THF–EtOH (50:50) with 18 mL of 1 N NaOH while heating at 60–70 °C resulted in the precipitation of a white solid (polymer). Glacial acetic acid (20 mL) was added and the solution evaporated to dryness. The residue was extracted with benzene and chromatographed on a column as described for the isolation of **18** and **19**. A white solid (0.6 g) **20** was isolated which after recrystallization from EtOH gave fine colorless needles, mp 212–213 °C, IR (KBr) 2225, 1395, 695 cm^{-1}; NMR ($CDCl_3$) δ 7.18–7.48 (m, 11, aromatic plus vinylic proton), 4.53 (s, 2, benzylic); UV_{max} (CH_3CN) 278 nm (ϵ 42 000); GC/MS *m/e* 219 (M^+, 12), 218 (50), 140 (100); accurate mass measurement, calculated/observed, 219.1047/219.1022 ($C_{16}H_{13}N$), 218.0969/218.0968 ($C_{16}H_{12}N$).

***cis*-2,4-Diphenyl-3-aminomethylthietane 1,1-Dioxide (8a).** To a slurry of 14.15 g (0.050 mol) of finely powdered **7a** in 125 mL of dry THF was added 250 mL of a 0.3 M solution of diborane[29] in THF dropwise over a period of 1.5 h. The system was protected from moisture. After stirring for 13 h, the excess diborane was decomposed by the dropwise addition of EtOH followed by refluxing for 1 h. Upon cooling, the solution was treated with HCl gas until it turned a slight yellow. Evaporation in vacuo gave a pale yellow syrup which was dissolved in 100 mL of water and suction filtered. The filtrate was basified with 18 N NaOH and extracted with 250 mL of $CHCl_3$. The $CHCl_3$ layer was washed with 10% NaCl and dried over Na_2SO_4. Evaporation under reduced pressure gave 7.20 g (50%) of pale yellow solid. Crystallization from water–EtOH afforded **8a** as large transparent prisms, mp 110–113 °C; IR 3425, 3365 (NH_2 group), 1310, 1165, 1150 cm^{-1} (sulfone); NMR δ 7.61–7.23 (m, 10, phenyls), 5.21 (d, 2, J = 10 Hz, H-2 and H-4), 3.38–2.80)m, 3, H-3 and CH_2), and 1.60–1.15 (band, 2, NH_2).

Anal. Calcd for $C_{16}H_{17}NO_2S$ (287.38): C, 66.87; H, 5.96; S, 11.16. Found: C, 67.03; H, 6.32; S, 11.33.

***cis*-2-(4-Chlorophenyl)-3-aminomethyl-4-phenylthietane 1,1-Dioxide (8b).** In a manner identical with that described for the preparation of **8a**, 12.9 g (9.041 mol) of **7b** in 101 mL of dry THF was reacted with 203 mL of 0.3 M diborane in THF to give 9.8 g (75%) of **8b** as a white solid, mp 39–45 °C; IR 3500–3300 (NH_2 group), 1320, 1150 cm^{-1} (sulfone); NMR δ 7.60–7.30 (m, 9, aromatics), 5.23 (d, 1, J = 10 Hz, H-4), 5.20 (d, 1, J = 10 Hz, H-2), 3.33–2.80 (m 3, H-3 and CH_2), and 1.18 (s, 2, NH_2). Compound **8b** was analyzed as the picric acid salt, mp 249–250 °C dec (from 10% acetic acid).

Anal. Calcd for $C_{22}H_{19}ClN_4O_9S$ (550.93): C, 47.96; H, 3.48; N, 10.17. Found: C, 48.31; H, 3.36; N, 10.03.

***cis*-2-(4-Nitrophenyl)-3-aminomethyl-4-phenylthietane 1,1-Dioxide (8c).** In the same manner as described for the preparation of **8a**, 9.0 g (0.027 mol) of **7c** dissolved in 73 mL of dry THF was reacted with 146 mL of 0.3 M diborane in THF. Work-up gave a yellow syrup which was dissolved in 20 mL of $CHCl_3$–EtOH (9:1) and chromatographed in two equal portions on 60 × 2.5 cm silica gel columns (60–200 mesh, 94 g per column), using $CHCl_3$–EtOH (9:1) as the developing solvent. Two main fractions were obtained from each column. The second fractions were pooled and evaporated under vacuum to give 5.9 g (66%) of pale yellow, viscous oil which did not solidify when triturated with various solvents. The oil appeared to be the desired product **8c** according to its spectroscopic properties: IR (neat) 3400, 3340 (NH_2 group), 1515, 1350 (nitro group), 1310, 1150 cm^{-1} (sulfone); NMR δ 8.41–8.13, 7.85–7.55 (m, 4, AA'BB' pattern due to *p*-nitrophenyl), 7.55–7.32 (m, 5, phenyl), 5.37 (d, 1, J = 10 Hz, H-2), 5.31 (d, 1, J = 10 Hz, H-4), 3.41–2.88 (m, 3, H-3 and CH_2), and 1.20 (s, 2, NH_2). Minor impurity signals in the NMR spectrum occurred at δ 1.07 and 0.98. The intention was to submit **8c** for elemental analysis as its dimethylated derivative **9c**.

***cis*-2,4-Diphenyl-3-dimethylaminomethylthietane 1,1-Dioxide (9a).** The procedure was adopted from the literature.[30] A mixture of 1.77 g (6.2 mmol) of **8a**, 3.2 g of 90.7% formic acid and 2.9 mL of 37% formaldehyde solution was heated at 93± 1 °C in an oil bath for 18 h. A pale yellow solution was rapidly obtained and during the first 0.5 h a vigorous evolution of gas occurred. The solution was mixed with 6.5 mL of 4 N HCl and evaporated under vacuum to give a viscous oil. A solution of the oil in 60 mL of water was basified with 10 N NaOH and extracted with 60 mL of $CHCl_3$. The $CHCl_3$ layer was washed with H_2O and dried over Na_2SO_4. Evaporation under reduced pressure gave 1.67 g (86%) of pale yellow solid. Crystallization from hexane–ethanol with charcoal treatment afforded **9a** as fine, white needles, mp 123–124 °C; IR 1315, 1154 cm^{-1} (sulfone); NMR δ 7.63–7.27 (m, 10, phenyls), 5.13 (d, 2, J = 10 Hz, H-2 and H-4), 3.45–2.83 (m, 1, H-3), 2.62 (d, 2, J = 6 Hz, CH_2), and 2.06 (s, 6, *N*-methyls).

Anal. Calcd for $C_{18}H_{21}NO_2S$ (315.44): C, 68.54; H, 6.71; N, 4.44. Found: C, 68.74; H, 6.65; N, 4.58.

***cis*-2-(4-Chlorophenyl)-3-dimethylaminomethyl-4-phenylthietane 1,1-Dioxide (9b).** In a manner similar to that described for the preparation of **9a**, 9.0 g (0.028 mol) of **8b** was reacted with 40 mL of 90.7% formic acid and 37 mL of 37% formaldehyde solution for 19 h. Work-up gave 9.6 (98%) of pale yellow solid. Crystallization from hexane–ethanol with charcoal treatment afforded **9b** as short, white needles, mp 124–125 °C; IR 1325, 1155 cm^{-1} (sulfone); NMR δ 7.48 (s, 9, aromatics), 5.13 (d, 1, J = 10 Hz, H-4), 5.09 (d, 1, J = 10 Hz, H-2), 3.39–2.75 (m, 1, H-3), 2.60 (d, 2, J = 6 Hz, CH_2), and 2.06 (s, 6, N-methyl).

Anal. Calcd for $C_{18}H_{20}ClNO_2S$ (349.88): C, 61.79; H, 5.76; N, 4.00. Found: C, 61.64; H, 5.81; N, 3.91.

***cis*-2-(4-Nitrophenyl)-3-dimethylaminomethyl)-4-phenylthietane 1,1-Dioxide (9c).** In a similar manner as described for the preparation of **9a**, 4.8 g (0.015 mol) of **8c** was reacted with 23 mL of 90.7% formic acid and 20 mL of 37% formaldehyde solution for 11 h. Work-up gave 3.5 g of straw-colored syrup. The syrup was dissolved in 150 mL of anhydrous Et_2O and treated with anhydrous HCl gas. The resulting white precipitate was collected and dissolved in 50 mL of water. Neutralization with a saturated solution of Na_2CO_3 gave a copious white precipitate which upon collection reverted to a straw-colored oil. While sitting for 2 weeks the oil changed to a glass, mp 39–43 °C; IR 1520, 1350 (nitro group), 1320, 1155 cm^{-1} (sulfone); NMR δ 8.44–8.19, 7.87–7.58 (m, 4, AA'BB' pattern due to *p*-nitrophenyl), 7.50 (s, 5, phenyl), 5.23 (d, 1, J = 10 Hz, H-2), 5.17 (d, 1, J = 10 Hz, H-4), 3.35–2.83 (m, 1, H-3), 2.64 (d, 2, J = 6 Hz, CH_2), and 2.10 (s, 6, *N*-methyls). Attempts to crystallize the HCl and picric acid derivatives of **9c** were unsuccessful.

***cis*-2,4-Diphenyl-3-carboxythietane 1,1-Dioxide (25).** A mixture of 10.00 g (0.0353 mol) of **7a** and 70 mL of Me_2SO was heated to give a solution to which was added 50 mL of 50% H_2SO_4. The resulting mixture was heated at reflux for 3 h. Upon cooling, the solution was poured onto 200 g of crushed ice with stirring and the mixture was diluted with 500 mL of water. An off-white precipitate was collected and dried. Crystallization from 1,2-dichloroethane gave 9.45 g (89%) of **25** as white, fluffy needles, mp 223–224 °C; IR 3270, 1730 (carboxylic acid), 1305, 1172, 1130 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 7.83–7.33 (m, 10, phenyl), 5.90 (d, 2, J = 10 Hz, H-2 and H-4), and 4.15 (t, 1, J = 10 Hz, H-3).

Anal. Calcd for $C_{16}H_{14}SO_4$ (302.35): C, 63.56; H, 4.67; S, 10.60. Found: C, 63.40; H, 4.79; S, 10.54.

***cis*-2,4-Diphenyl-3-acetylthietane 1,1-Dioxide (26).** A mixture of 40.00 g (0.132 mol) of **25** and 400 mL of freshly distilled thionyl chloride was heated at reflux for 5 h. The system was protected from moisture. Evaporation of the excess thionyl chloride under reduced pressure gave the acid chloride as a cream-colored solid, mp 140–141 °C; IR 1780 (acid chloride), 1333, 1180, 1137 cm^{-1} (sulfone); carboxylic acid bands at 3270 and 1730 cm^{-1} were absent. A solution of the unpurified acid chloride in 140 mL of dry THF was drained into a vigorously stirred organocadium reagent which was cooled in an ice–water bath. The reagent was prepared just prior to the reaction by reacting 4.01 g (0.165 mol) of Mg turnings in 40 mL of dry THF and then adding 15.13 g (0.0825 mol) of anhydrous $CdCl_2$ according to a method adopted from the literature.[25] When the addition of the acid chloride was complete, the ice–water bath was removed and the reaction was stirred at room temperature for 8 h. Approximately 180 mL of THF was evaporated under reduced pressure. The gray suspension was poured onto a mixture of 200 g of crushed ice and 100 mL of dilute H_2SO_4. The mixture was then extracted with a total of 350 mL of $CHCl_3$. The combined $CHCl_3$ extracts were evaporated under reduced pressure to a volume of approximately 150 mL and extracted with 200 mL of 10% NaOH. Acidification of the basic extracts gave a 22.5% recovery of **25**. The $CHCl_3$ layer was washed with water, dried over $MgSO_4$ and evaporated in vacuo to give 27.03 g (68.4%) of white solid. Crystallization from hexane–EtOH with charcoal treatment afforded **26** as white, shiny leaflets, mp 125–126 °C; IR 1715 (ketone), 1330, 1172, 1140 cm^{-1} (sulfone); NMR δ 7.64–7.32 (m, 10, phenyls), 5.50 (d, 2, J = 10 Hz, H-2 and H-4), 3.90 (t, 1, J = 10 Hz, H-3), and 2.03 (s, 3, CH_3).

Anal. Calcd for $C_{17}H_{16}O_3S$ (300.37): C, 67.98; H, 5.37; S, 10.67.

Found: C, 68.15; H, 5.33; S, 10.64.

The oxime derivative **23** of **26** was prepared using a method from the literature.[31] Crystallization from water–EtOH gave **23** as small, white needles, mp 181–186 °C dec; IR 3440 (hydroxyl), 1315, 1170, 1135 cm^{-1} (sulfone); NMR (Me_2SO-d_6) δ 7.80–7.36 (m, 10, phenyl), 5.81 (d, 2, J = 10 Hz, H-2 and H-4), 4.08 (t, 1, J = 10 Hz, H-3), and 1.68 (s, 3, CH_3).

2,4-Diphenyl-3-(1-nitroethyl)thietane 1,1-Dioxide (21). A solution of 4.50 g (0.0176 mol) of **4** in 90 mL of nitroethane was diluted with 90 mL of ethanol and then 9.0 mL of a solution prepared by dissolving 1.0 g of KOH in a mixture of 10 mL of ethanol and 5 mL of nitroethane was added. The bright yellow solution was stirred for 7 h and acidified with 9.0 mL of glacial acetic acid. Evaporation in vacuo gave a white solid which was triturated with water, collected, and dried. Crystallization from hexane–benzene afforded 4.79 g (73.5%) of **21** as fine, white needles, mp 181–182 °C; IR 1554 (nitro group), 1324 (nitro group and sulfone), 1147 cm^{-1} (sulfone). The NMR spectrum showed a doublet at δ 7.48 (10, phenyl), two overlapping doublets, one at δ 5.33 (1, H_e, J_{eb} = 10 Hz) and the other at δ 5.14 (1, H_d, J_{db} = 11 Hz), a multiplet centered at δ 4.83 (1, H_c, J_{cb} = 8 Hz, J_{ca} = 7 Hz), a multiplet centered at δ 3.50 (1, H_b, J_{be} = 10 Hz, J_{bd} = 11 Hz, J_{bc} = 8 Hz), and a doublet at δ 1.33 (3, $C(H_a)_3$, J_{ac} = 7 Hz). The high-field signal of the doublet at δ 5.14 overlapped the low-field signal of the multiplet at δ 4.83. A singlet at δ 7.38 (3 H) was assigned to benzene. A solution prepared by dissolving 20.0 mg of crystalline **21** in 1.20 mL of anhydrous DMSO was calculated to contain 1.76 mg/mL of benzene. The solution was analyzed for benzene by GC using the 3% OV-225 column with the injection port, oven and detector at 250, 35, and 272 °C, respectively, and the nitrogen flow at 32 mL/min. One peak was observed which possessed a retention time and area identical with that recorded by injecting an equal volume of a reference solution containing 1.75 mg/mL of benzene in anhydrous DMSO. As insufficient **21** was on hand to crystallize from a solvent other than benzene, it was submitted for analysis as the benzene-containing crystals.

Anal. Calcd for $(C_{17}H_{17}NO_4S)_2$·C_6H_6 (740.89): C, 64.85; H, 5.44; N, 3.78; O, 17.28; S, 8.65. Found: C, 65.04; H, 5.31; N, 3.96; O, 17.33; S, 8.62.

2,4-Diphenyl-3-(1-dimethylaminoethyl)thietane 1,1-Dioxide (24). A solution of 4.00 g (0.0121 mol) of **21** in 30 mL of THF was diluted with 50 mL of EtOH and hydrogenated over 8 g of sponge nickel catalyst (W. R. Grace & Co., No. 986) at an initial hydrogen pressure of 52 psi using a Parr hydrogenator. After 7 h the catalyst was removed by filtration and the filtrate was evaporated under reduced pressure to give a viscous, pale yellow syrup. The syrup was dissolved in 20 mL of $CHCl_3$ and extracted with 40 mL of 4 N HCl followed by 20 mL of water. The pooled aqueous extracts were basified with 18 N NaOH and extracted with 50 mL of $CHCl_3$. The $CHCl_3$ extract was washed with 10% NaCl, dried over Na_2SO_4 and evaporated in vacuo to give 2.19 g (60%) of **22** as a pale yellow solid, mp 145–147 °C; IR 3440–3360 (NH_2), 1310, 1145 cm^{-1} (sulfone); NMR δ 7.67–7.30 (m, 10, phenyls), 5.26 (d, 1, J = 10 Hz, benzylic), 5.16 (d, 1, J = 10 Hz, remaining benzylic), 3.50–2.65 (m, 2, H-3 and CH_3CHNH_2), 1.22 (s, 2, NH_2), and 0.87 (d, 3, J = 6.5 Hz, CH_3). The $CHCl_3$ layer from the acid extraction was washed with water, dried over Na_2SO_4, and then evaporated under reduced pressure to give 1.36 g (36%) of beige solid. The IR and NMR spectra of the crystallized material (water–ethanol) was superimposable with those of *cis*-2,4-diphenyl-3-acetylthietane 1,1-dioxide oxime (**23**).

The amine **22** was dimethylated without further purification using a procedure similar to that described for the preparation of **9a**. After heating 2.2 g (0.007 mole) of **22** in 6.6 mL of 90.7% formic acid and 6.0 mL of 37% formaldehyde solution for 3 h, the reaction was worked up to give 1.9 g (79%) of pale beige solid. Crystallization from hexane–EtOH with charcoal treatment gave **24** as white needles, mp 145–146 °C; IR 1310, 1150 cm^{-1} (sulfone); NMR δ 7.60–7.31 (m, 10, phenyls), 5.26 (d, 1, J = 9 Hz, benzylic), 5.07 (d, 1, J = 9 Hz, remaining benzylic) 3.25–2.67 (m, 2, H-3 and $CH_3CHN(CH_3)_2$), 1.97 (s, 6, *N*-methyls), and 0.75 (d, 3, J = 6 Hz, CH_3).

Anal. Calcd for $C_{19}H_{23}NO_2S$ (329.46): C, 69.27; H, 7.04; N, 4.25. Found: C, 69.17; H, 7.03; N, 4.43.

Preparation of 24 Using 23. The procedure was investigated in a preliminary fashion. A stirred solution of 2.24 g (0.0071 mol) of **23** in 25 mL of dry THF was cooled in an ice–water bath and reacted with 2.0 mL of acetyl chloride[32] for 1.5 h. Evaporation of the solvent under reduced pressure gave an oil which was dissolved in 100 mL of Et_2O, washed with 200 mL of 3% $NaHCO_3$ solution, and dried over Na_2SO_4. Evaporation of the solvent gave an oil, the IR spectrum (neat) of which showed the absence of the oxime hydroxyl band and the presence of an ester functionality. A solution of 1.2 g (0.003 mol) of the crude ester in 20 mL of dry THF was reacted with 25 mL of 0.3 M diborane in THF for 16 h.[20] A dry nitrogen atmosphere was provided throughout the reaction period and the system was protected from moisture. The excess diborane was decomposed by drop-wise addition of water and then the colorless solution was gently refluxed for 1 h. Removal of the solvent in vacuo gave a white solid which was treated directly with 5 mL of 90.7% formic acid and 4.5 mL of 37% formaldehyde solution in a manner similar to that described for the preparation of **9a**. Work-up gave 0.16 g (14%) of pale yellow solid. Crystallization from hexane–EtOH afforded white needles, mp 144–145 °C. The IR spectrum of this material was superimposable with that of **24**.

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Registry No.—**1a**, 63268-45-1; **1b**, 63268-46-2; **2a**, 63231-37-8; **2b**, 63268-47-3; **3**, 63231-38-9; **4**, 18744-26-8; **5a**, 63250-64-6; **5b**, 63250-65-7; **6**, 63250-66-8; **7a**, 63284-66-2; **7b**, 63250-67-9; **7c**, 63250-68-0; **8a**, 63250-69-1; **8b**, 63250-62-4; **8b**, picrate, 63250-63-5; **8c**, 63284-69-5; **9a**, 63250-70-4; **9b**, 63250-71-5; **9c**, 63250-72-6; *cis*-**11a**, 614-46-0; *trans*-**11a**, 614-47-1; **13**, 63284-67-3; **13** dimethylamine salt, 63284-68-4; **14** isomer 1, 63250-73-7; **14** isomer 2, 63250-74-8; **15**, 5076-35-7; **16**, 63250-75-9; **18**, 63284-70-8; **19**, 63250-76-0; **20**, 52958-88-0; **21**, 63250-77-1; **22**, 63250-78-2; **23**, 63250-79-3; **24**, 63250-80-6; **25**, 63250-81-7; **25** acid chloride, 63250-82-8; **26**, 63250-83-9.

References and Notes

(1) (a) Taken in part from the Ph.D. thesis of J. E. Coates, University of British Columbia, 1972; (b) For previous paper, see: F. S. Abbott, J. E. Coates, and K. Haya, *J. Org. Chem.*, **42**, 3502 (1977); (c) L. Paquette and M. Rosen, *J. Org. Chem.*, **33**, 3027 (1968); (d) D. Dittmer and M. Christy, *J. Am. Chem. Soc.*, **84**, 399 (1962).

(2) When used in this paper with respect to thietane 1,1-dioxide derivatives, the terms cis and trans refer to the relationship of the aryl groups on the heterocyclic ring.

(3) Compound **4** has previously been prepared from 2,4-diphenyl-3-diethylaminothietane 1,1-dioxide: D. R. Eckroth and G. M. Love, *J. Org. Chem.*, **34**, 1136 (1969). Using 2-phenylthiete 1,1-dioxide[4] as a reference compound, it is apparent that their assignment of the heterocyclic protons in the NMR spectrum of **4** is reversed.

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(8) The mechanistic significance of the presence of some *cis*-chalcone in the thermolysates of **4**, **5a**, and **5b** is not clear at the present time because of the ease with which calcones undergo thermal and photochemical isomerization.[21]

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(15) Attack of thiol radicals is known to occur at the β-carbon atom of α,β-unsaturated carbonyl compounds; cf. R. Brown, W. E. Jones, and A. R. Pinder, *J. Chem. Soc.*, 2123 (1951).

(16) Thiols are known to react with carbonyl compounds to give α-hydroxy sulfides; cf. E. Campaigne in "Organic Sulfur Compounds", N. Kharasch, Ed., Vol. 1, Pergamon Press, London, 1961, p 134.

(17) J. L. Kice, in "The Chemistry of Organic Sulfur Compounds", N. Kharasch and C. Y. Meyers, Ed., Vol. 2, Pergamon Press, London, 1966, p 115.

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Photochemical Synthesis of Benzo[*f*]quinolines[1]

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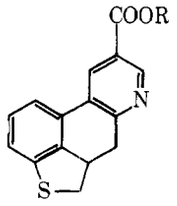
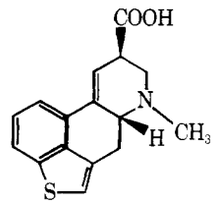
Benzo[*f*]quinolines with a sulfur-containing substituent at position 7 have been synthesized photochemically from the corresponding 2-stilbazoles. An improved synthesis of *o*-(methylthio)benzaldehyde is described.

In the course of a general study of the photochemistry of benzo[*b*]thiophene,[5] we became interested in the possibility of photochemical synthesis of a heterocyclic ring system, 1, capable of subsequent elaboration to 1-deaza-1-thialysergic acid (**2**).



1



2

Since benzo[*b*]thiophene is an isostere of indole, sulfur analogs of biologically active indole derivatives are obvious targets of research and their synthesis as well as pharmacology have been investigated extensively.[6] Among other derivatives, sulfur isosteres of various tryptamines, including serotonin, have been synthesized and found to have pharmacological properties similar to those of the nitrogen compounds.[7] In view of the extraordinary pharmacological activity of lysergic acid and many of its derivatives, it is not surprising that an attempt has been made to synthesize its sulfur isostere, 1-deaza-1-thialysergic acid (**2**). Campaigne and Knapp modeled their approach to **2**[8] after Kornfeld and Woodward's synthesis of lysergic acid,[9] but their effort could not be carried through to the desired compound.

In attacking the problem of the synthesis of a ring skeleton of **2**, we chose to construct first the benzo[*f*]quinoline system **8**, functionalized appropriately with a sulfur containing group at position 7, intending to close the sulfur ring after the simpler heterocycle was intact.

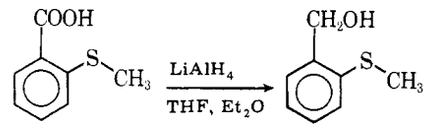
We present herein photochemical preparations of some benzo[*f*]quinolines as possible intermediates in the synthesis of a parent ring system of thiolysergic acid.

Results and Discussion

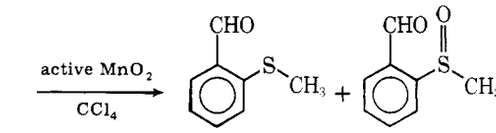
Our choice as a method of preparation of the three-ring system of **8** was the photocyclization of appropriate 2-stilbazoles. Because of its simplicity, this oxidative ring closure has been used on numerous occasions as a direct route to azaphenanthrenes,[10] in spite of generally modest yields. Thus, Kumler and Dybas prepared a variety of benzo[*f*]quinolines by photochemical ring closure of corresponding 2-stilbazoles.[11]

A suitable synthesis had to be developed for *o*-(methylthio)benzaldehyde (**5a**), the starting material for most of the stilbazoles we needed. The reported synthesis of **5a** by $LiAlH_4$ reduction of *N*-methyl-*o*-(methylthio)benzanilide in THF[12] failed in our hands, giving only trace quantities of the desired product. Lithium tri-*tert*-butoxyaluminohydride reduction of *o*-(methylthio)benzoyl chloride using Brown and Subba Rao's procedure[13] gave aldehyde **5a** in 37% yield, still not a particularly satisfactory yield for further synthetic use. An attempt to carry out a Reimer–Tiemann formylation of thiophenol combined with methylation of the mercapto group also was unsuccessful.

Good yields of the desired aldehyde were obtained, however, from a 2-step synthesis in which *o*-(methylthio)benzoic acid (**3**) was reduced to *o*-(methylthio)benzyl alcohol (**4**) which was



3 4



5a 5b

then oxidized to aldehyde **5a** using active manganese dioxide. The oxidation procedure[14] was adapted from Papadopoulos, Jarrar, and Issidorides[15] using the Morton[16] method to prepare active manganese dioxide.

Although certain sulfides are oxidized with active manganese dioxide,[17] we were able to arrive at conditions of solvent and temperature (Table I) in which very little oxidation to the corresponding sulfoxide **5b** occurred. Thus, treatment of 0.1 mol of **4** with a 5-fold (w/w) amount of active MnO_2 in CCl_4, at room temperature, led to reproducible, excellent yields of **5a** containing virtually no alcohol **4** and only traces of sulfoxide **5b**.

Because use of this procedure routinely resulted in overall conversion of about 80% starting from *o*-(methylthio)benzoic acid, we feel that it deserves consideration as a method of preparation of *o*-(methylthio)benzaldehyde. For purposes of identification, but also for use as starting material for the synthesis of appropriate benzo[*f*]quinolines, *o*-(methylsulfinyl)benzaldehyde (**5b**) was prepared in essentially quantitative yield by sodium metaperiodate oxidation of **5a**.[18]

The precursor 2-stilbazoles needed in our work were pre-