0.1 mol), 50 g of KOH, and 300 ml of EtOH was heated under reflux for 2 hr and poured into water. The clear solution was acidified (HOAc), cooled, and filtered, and the precipitate was washed with water and recrystallized from EtOH, mp 236–238°, yield 16.3 g (76%).

Anal. Calcd for $C_{12}H_9NO_3$: C, 66.97; H, 4.22; N, 6.51. Found:, 67.27; H, 4.26; N, 6.72.

3-*o*-Hydroxyphenyl(2-1*H*-pyridinon-3-yl) Ketoxime (3). A solution of 21.5 g (0.1 mol) of ketone **10**, 10.4 g (0.15 mol) of $HONH_2{\cdot}HCl$, and 36 g of KOH in 200 ml of EtOH was refluxed for 2 hr, poured into 250 ml of H_2O, and acidified (HOAc). The precipitated product was recrystallized from EtOH, mp 257–258°.

This same product was obtained from **10** (0.1 mol) by refluxing with 0.15 mol of $HONH_2{\cdot}HCl$ in 200 ml of pyridine and 100 ml of EtOH.

4-Azaxanthone 5-Oxime. One gram of 4-azaxanthone, 0.5 g of $HONH_2{\cdot}HCl$, 20 ml of pyridine, and 40 ml of EtOH were refluxed on the steam bath for 6 hr. The excess solvents were removed in vacuo and ice water was added. The product was filtered, washed with H_2O, and recrystallized from dilute EtOH, yield 0.8 g, mp 152–154°.

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 68.30; H, 3.78; N, 13.47.

2-Azaxanthone 5-Oxime. This compound was prepared by same method as above, yield 0.6 g, mp 259–260°.

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: 67.88; H, 3.66; N, 13.21.

Acknowledgment. The authors are grateful to Professor Sir Derek Barton, Imperial College, London, and to Professor Leon Mandell, Emory University, Atlanta, Ga., for their helpful discussions and suggestions during the course of this work.

Registry No.—**1**, 6537-46-8; **2**, 54999-68-7; **3**, 54999-69-8; **4**, 42374-49-2; **5**, 54999-70-1; **6**, 54999-71-2; **7**, 54999-72-3; **8**, 54999-73-4; **9**, 54999-74-5; **10**, 54999-75-6; **13**, 5698-68-0; **14**, 54999-76-7; **15**, 54629-30-0; **16**, 54999-77-8; 2-bromochlorobenzene, 694-80-4; 3-pyridinealdehyde, 500-22-1; α-(3-pyridyl)-2-chlorobenzyl alcohol, 54999-78-9; 4-azaxanthone 5-oxime, 54999-79-0; 4-azaxanthone, 54629-31-1; 2-azaxanthone 5-oxime, 54999-80-3; 2-azaxanthone, 54629-29-7.

References and Notes

(1) For part 1 in this series see F. J. Villani et al., *J. Med. Chem.*, **18**, 1 (1975).

(2) For convenience and consistent with the numbering system adopted in this and related series of compounds (see ref 1 and references cited therein), we prefer to use the numbering system shown in **1**.

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(6) G. A. Archer, A. Stempel, S. S. Ho, and L. H. Sternbach, *J. Chem. Soc. C*, 1031 (1966).

The Behavior of Thioxanthenol Sulfoxides and Related Compounds in 96% Sulfuric Acid[1]

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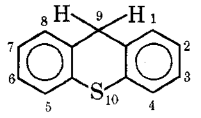
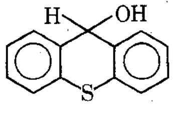
Thioxanthen-9-ol 10-oxides react with 96% sulfuric acid to produce, after quenching, thioxanthone (85%) as the major product. The mechanism, studied by NMR, absorption, and fluorescence spectroscopy, involves the loss of H_3O^+ from sulfinyl-O-protonated thioxanthen-9-ol 10-oxide. Minor components arise via a hydride transfer from starting material to O-protonated thioxanthone. Based upon isotope exchange studies, a thiaanthracene analog of thioxanthenol sulfoxide is considered an unlikely intermediate in this dehydration.

The course of the reaction of derivatives of thioxanthene (**1**) with acids depends upon the nature of both the derivative and the acid. For example, **1** and its 9-alkyl and 9,9-dialkyl derivatives react with "magic acid" to produce the corresponding S-protonated thioxanthene derivatives (and *not* thiaanthracenes).[2] Sulfuric acid converts 9,9-dialkylthioxanthenes into the corresponding radical cations.[3] On the other hand, **1**, thioxanthenol (**2**), and thioxanthene sulfoxide (**3**) react with concentrated sulfuric acid to produce the thioxanthylium cation (**4**).[4] In contradistinction, trifluoroacetic acid converts **2**, but not **3**, into **4**.[5]

As part of our continuing study of the chemistry of the thioxanthene ring system and of the reactions of organosulfur compounds in acidic media,[6] we now present an account of the behavior of the isomeric thioxanthenol sulfoxides (**5**)[7] and related compounds in concentrated (96%) sulfuric acid.[8]



1



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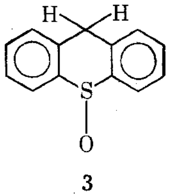
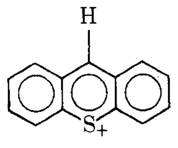


3

Results

cis- or *trans*-thioxanthenol sulfoxide (**5**) reacts with concentrated sulfuric acid (or its deuterated analog) to produce, after 1 hr, a solution whose NMR spectrum is similar to, but not identical with, that of thioxanthone (**6**) in the same medium.[9] A salient difference is the presence, in solutions of **5**, of a highly structured group of absorptions in the aryl region and a sharp singlet at δ 9.98. Both of these features are characteristic of solutions of the thioxanthylium



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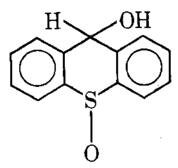
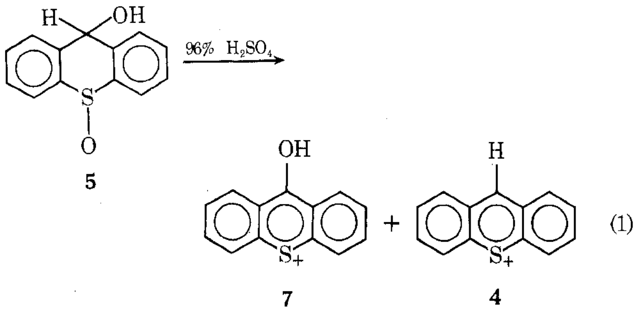


5

cation, **4**, in concentrated sulfuric acid.[10] These NMR results suggest, therefore, that the major species present in a solution of *cis*- or *trans*-**5** in 96% sulfuric acid are **4** and O-protonated thioxanthone, **7** (eq 1). The relative integrated intensity of the singlet at δ 9.98 compared to the integrated intensity of the aryl protons (1:18) implies that the concentration of **4** is slightly less than the concentration of **7** in these solutions.



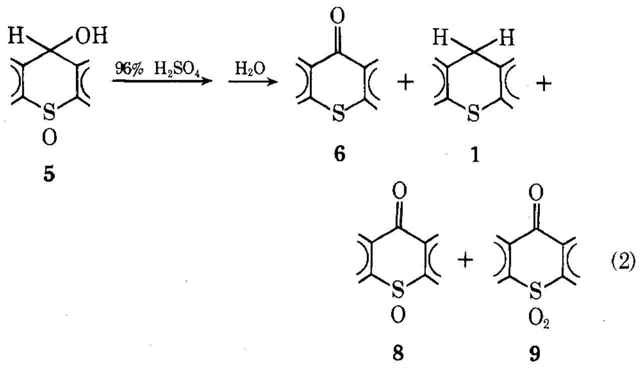
5 **7** **4**

To test this view, a solution of a mixture of **1** and **6** in 96% sulfuric acid also was examined. (Such a solution is expected to produce a mixture of **4** and **7**.) The NMR spectrum of an approximately equimolar mixture of **1** and **6** in 96% sulfuric acid is different from that of either pure **1** or pure **6** in 96% sulfuric acid but is very similar to that of *cis*- or *trans*-**5** in this medium. This, therefore, supports our contention.

The presence of **4** and **7** in solutions of **5** in 96% sulfuric acid is further supported by ultraviolet spectral data. A solution of both **1** and **6** in 96% sulfuric acid (0.25×10^{-5} and 0.5×10^{-5} *M*, respectively) exhibits an ultraviolet spectrum which, after 24 hr, is almost indistinguishable from that of a solution of **6** in 96% sulfuric acid and also is very similar to a 24 hr old solution of **5** in sulfuric acid. At concentrations of 0.75×10^{-5} *M, cis*- and *trans*-**5** react with 96% sulfuric acid to produce solutions with a weak, broad absorption band (219–223 nm) which disappears with time.[11] In addition to this change, weak bands at 242 and 349 nm, and a strong band at 275 nm, appear with time. (The electronic absorption spectrum appears to be nearly constant after 3 hr.) Using a 5×10^{-5} *M* solution, three bands appear in the visible region with time (381, 448, and 469 nm). All of these are ascribable to either **4** or **7**. The changes in the ultraviolet spectrum of **5** pass through an isosbestic point at 236 nm.

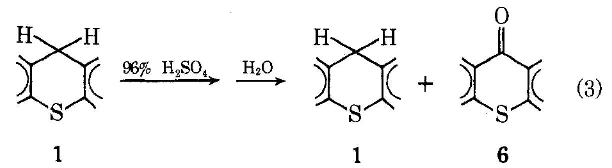
The fluorescence excitation spectrum of either *cis*- or *trans*-**5** (0.75×10^{-5} *M*) in 96% sulfuric acid initially has peaks corresponding to the absorption spectrum (275, 350, 380, 450, and 470 nm). The peaks grow with time but eventually reach maximum intensities. The fluorescence emission spectrum also changed with time and appeared eventually to correspond closely to that of **7** obtained from solutions of **6** in 96% sulfuric acid.

Quenching a solution of either *cis*- or *trans*-**5** in 96% sulfuric acid with water produces about 85% **6** and lesser amounts of **1** and thioxanthone sulfoxide (**8**) (eq 2). In addition, *trace* amounts of what appeared to be thioxanthone sulfone (**9**) also were detected (TLC).



5 **6** **1** **8** **9**

Dilution, with water, of a 10% solution of **1** in 96% sulfuric acid, which was 24 hr old, produces a mixture of **1**, **6**, and three *trace* components (eq 3). One of these was identified (TLC) as **8**. As already noted,[9] **6** is recovered quantitatively from solutions of **6** in 96% sulfuric acid.



1 **1** **6**

Because they were detected as minor products of the reaction of water with solutions of **5** in 96% sulfuric acid, the behavior of **8** and **9** in 96% sulfuric acid also was examined. Dilution, with water, of a 10% (w/v) solution of **8** in 96% sulfuric acid which had been stored for 15 min at 25° produces a very large quantity of starting material along with a small amount of **6**. A third, trace component was identified (TLC) as **9**. The NMR spectrum of **8** in 96% sulfuric acid, taken immediately after preparation of the solution, is not unlike that of **8** in deuteriochloroform or in deuteriochloroform containing 10% of 96% sulfuric acid. Thus, a 10% (w/v) solution of **8** in 96% sulfuric acid exhibits two structured multiplets at δ 7.9–8.4 and 8.4–8.8 (external Me_4Si). In deuteriochloroform **8** exhibits the corresponding multiplets at δ 7.6–8.1 and 8.1–8.5 (internal Me_4Si).

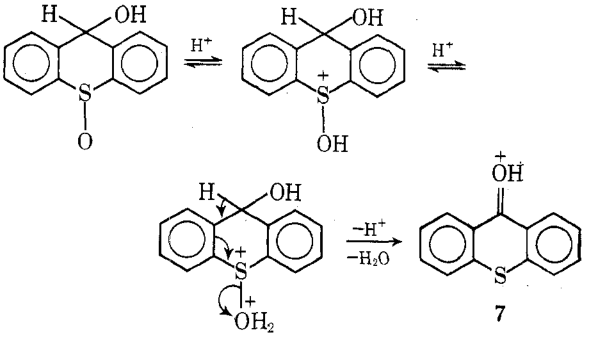
A solution of **8** (2.5×10^{-5} *M*) in 96% sulfuric acid exhibits an initially strong absorption at 246 nm, a weak absorption at 274 nm, and a very broad band at 320 nm. The spectrum changes slowly with time—the peak at 246 nm diminishes slightly, the absorption at 320 nm increases slightly, and the maximum at 274 nm increases greatly. Absorptions at 445 and 469 nm appear in the visible region with the passage of time, using solutions of 5×10^{-5} *M*.

Dilution, with water, of a 5% (w/v) solution of **9** in 96% sulfuric acid which was 24 hr old produces essentially pure (TLC) starting material. A solution of **9** (0.5×10^{-5} *M*) in 96% sulfuric acid possesses an absorption spectrum with broad bands at 268 and 305 nm. Electronic absorption spectra of such solutions are time-invariant.

Discussion

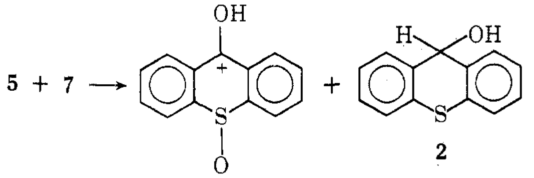
The data presented above indicate that either *cis*- or *trans*-thioxanthenol sulfoxide (**5**) is dehydrated by 96% sulfuric acid to produce, after dilution with water, thioxanthone (**6**) along with lesser amount of thioxanthene (**1**), thioxanthone sulfoxide (**8**), and *traces* of thioxanthone sulfone (**9**).[12] Both absorption and fluorescence spectra and the NMR data indicate that the major species present in solutions of **5** in 96% sulfuric acid are O-protonated thioxanthone (**7**) and the thioxanthylium ion (**4**). The isomers of **5** may be viewed as hydrates of **6** and their dehydration in sulfuric acid is not, therefore, unexpected.[13] However, the formation of 1 and 8 is somewhat surprising and suggests a process which has a competing redox component.

The sequence presented below (eq 4–6) accounts for the formation of the major species (i.e., 4 and 7) observed in solutions of 5 in sulfuric acid and, when considered in light of eq 7, accounts for the major product isolated when these solutions are quenched with water. While this scheme requires the presence of O-protonated thioxanthone sulfoxide (10) in solutions of 5 in 96% sulfuric acid, the spectral properties of 4 and 7, when coupled with the large quantity of these present, make it difficult to establish unequivocally that a small quantity of 10 is present in these solutions.



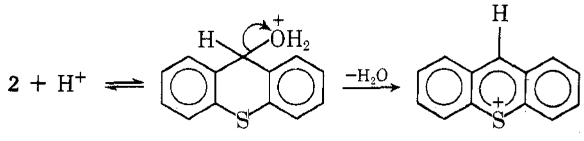
7

(4)



10 2

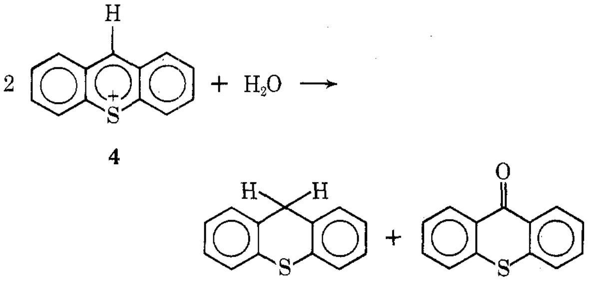
(5)



4

(6)

The 6 which is formed upon addition of water to these solutions has at least two origins. First, there is the deprotonation of 7 (eq 4) with water. Second, 4 reacts with water to produce 2, which is known to disproportionate under a variety of conditions,[14] including the presence of acid,[4] to yield 1 and 6. The disproportionation of 4 (eq 7) also accounts for the formation of 1 upon addition of water to solutions of 5 in sulfuric acid.

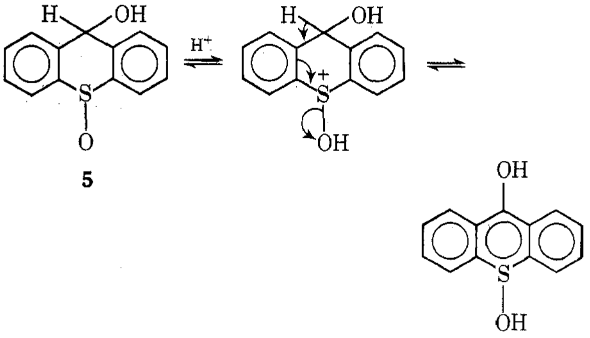


4 1 6

(7)

A hydride transfer between 5 and 7, similar to that between 4 and 2,[4] leads to 10 (eq 5) and deprotonation of 10 by water affords 8. The production of traces (<1%) of 9 is more difficult to explain and we are not yet able to set out reliably the way in which it was formed in these systems.

One may view thioxanthone sulfoxide as a thiaquinone, i.e., as a sulfur analog of anthraquinone.[15] This idea is supported by the formation[16] of the radical anion of 8. This same species also is presumed to be formed during the base-catalyzed dehydration of 5.[13] One might, as an extension of this idea, suggest that thioxanthenol sulfoxides are isomeric tautomers of the corresponding hydroquinone, 11. Thus far we have not been able to detect 11 in solutions of either isomer of 5 in a variety of organic solvents or in the solid state.[5,7] The NMR spectra of solutions of 5 in solvents such as CCl_4, CS_2, $CDCl_3$, and C_6D_6 display characteristics of a secondary diarylcarbinol (a methine proton and, where detectable, an O–H resonance). One might, however, suggest that in a strongly acidic medium 5 could be protonated at the sulfinyl oxygen[6] and, by deprotonation at C-9, convert to 11 (eq 8).

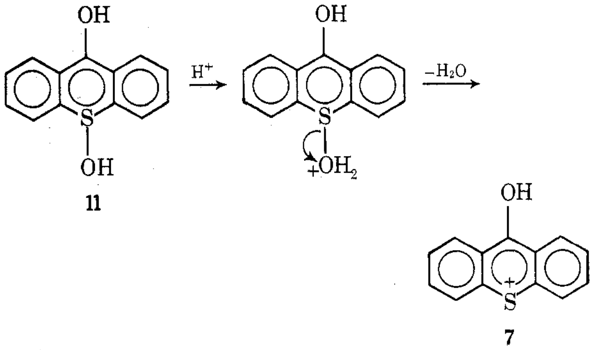


5 11

(8)

Our observation that the NMR spectrum of 5 in D_2SO_4 exhibits the C-9 H resonance characteristic of the thioxanthylium ion (4) suggests that 11 is *not* in rapid equilibrium with 5 in this medium. Had the equilibrium depicted in eq 8 been established rapidly, the 4 produced in the reaction of 5 with deuterated sulfuric acid should have lacked a proton at C-9.

To the extent that 11 can be precluded in this equilibrium, it seems reasonable that 11 does not serve as a significant precursor to 7 in sulfuric acid even though one can construct a pathway for converting 11 to 7 (eq 9). This is consistent with the view that compounds such as 11 should not be viewed as aromatic (i.e., highly stabilized) sulfur analogs of anthracene.[17]



11 7

(9)

Experimental Section

Syntheses. All of the compounds employed in this study have already been described.[4,5,7]

Electronic Spectra.[19] The various compounds were dissolved in 95% ethanol and diluted to an appropriate concentration. An aliquot was pipetted into a volumetric flask and evaporated to dryness to leave a film of substance on the surface of the flask. Sulfuric acid was added to the mark and the solutions were transferred to 1-cm, ground-glass stoppered cells. Absorption spectra were recorded on a Beckman Model DK-2A or a Cary Model 15; fluorescence spectra were recorded on an Aminco-Bowman spectrofluorometer.

Nuclear Magnetic Resonance Spectra. Solutions were prepared by dissolving the sample directly in the solvent in the NMR tube. Spectra were recorded (Varian Models A-60, T-60, and Ha-100) within 5 min of the preparation of the solution unless otherwise indicated.

Thin Layer Chromatography. Thin layer chromatographies were performed employing glass plates coated with 0.25 mm of Kieselgel (A. H. Thomas Co.). Elution was accomplished with benzene, chloroform, ethyl acetate, and chloroform–ethyl acetate (5:1) mixtures. Substances were identified by comparing their R_f values with those of authentic compounds on the same chromatogram. Visualization was achieved using both ultraviolet light and iodine vapor.

In a typical experiment, 80–100 mg of a substance was dissolved in 0.3 ml of sulfuric acid and, after 5 min, the resulting solution was diluted with water. The resultant solid was removed by filtration and dissolved in chloroform, and the solution was analyzed by TLC as described above. An alternate work-up procedure, involving extraction of the aqueous phase with methylene chloride, produced identical results.

Reaction of Thioxanthenol Sulfoxide (5) with 96% Sulfuric Acid. Product Study. A 10% solution of **5** in 96% sulfuric acid was maintained at 26° for 7 days. The solution was diluted with water and the resulting solid was removed by filtration. A solution of this solid in methylene chloride was analyzed by TLC as described above, using several eluents including ethyl acetate. The major component was found to be thioxanthone (**6**), with other spots being ascribed to **1**, **5**, and **8**. A *very* weak spot had an R_f value similar to that of **9** and is assigned to **9**. Several different reactions afforded 80–85% **6** after recrystallization from ethanol.

Reaction of *cis*-5 with 96% Sulfuric Acid. NMR Analysis. A small amount of *cis*-**5** was added to frozen sulfuric acid in an NMR tube. The sample was placed in the probe and spectra were obtained periodically. Initially, the solution contained an aryl multiplet extending from δ 7.66 to 8.49 and a singlet at δ 6.88. After 1 hr, the structure of the multiplet had altered and its position "shifted" to δ 7.84–9.02. This was accompanied by the disappearance of the singlet at δ 6.88 and the appearance of a singlet at δ 9.98. The singlet at δ 6.88 is ascribed to C-9 H of the starting material while the singlet at δ 9.98 is ascribed to C-9 H of **4**.

Acknowledgments. The research at the University of Texas at Arlington was supported by Grant Y-484 from the Robert A. Welch Foundation; the NMR spectrometer was purchased by an award from the Research Corporation. This support is gratefully acknowledged. Support at Texas Tech University by the Robert A. Welch Foundation (Grant D-028) is gratefully acknowledged. We thank Dr. W. Kurtin (now at Trinity University, San Antonio, Texas) for the fluorescence spectra.

Registry No.—*cis*-**5**, 13096-56-5; *trans*-**5**, 13096-57-6.

Supplementary Material Available. Full electronic spectral data will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-1737.

References and Notes

(1) A portion of this work was presented at the VI Symposium on Organic Sulphur Chemistry, Bangor, Wales, July 1974.

(2) D. Deavenport, S. A. Evans, and A. L. Ternay, Jr., manuscript in preparation.

(3) D. Deavenport, J. T. Edwards, A. L. Ternay, Jr., E. T. Strom, and S. A. Evans, *J. Org. Chem.*, **40**, 103 (1975).

(4) H. J. Shine and L. Hughes, *J. Org. Chem.*, **31**, 3142 (1966).

(5) A. L. Ternay, Jr., and D. W. Chasar, *J. Org. Chem.*, **33**, 3641 (1968).

(6) For reviews of this area see, for example, (a) H. J. Shine, *Organosulfur Chem.*, 93 (1967); (b) G. Modena, *Int. J. Sulfur Chem., Part C*, **7**, 95 (1972).

(7) A. L. Ternay, Jr., D. W. Chasar, and M. Sax, *J. Org. Chem.*, **32**, 2465 (1967).

(8) In an earlier report[5] we noted that *cis*- and *trans*-**5** are converted to a mixture (1:4) of the corresponding *cis*- and *trans*-**9**-trifluoroacetoxythioxanthene sulfoxides in trifluoroacetic acid.

(9) Solutions of **6** in sulfuric acid are known[4] to produce only O-protonated thioxanthone (the 9-hydroxythioxanthylium ion, **7**). These solutions, which have absorption maxima at 218, 243, 274, 348, 448, and 469 nm, do not change their absorption spectra with time. Dilution with water of a 5% (w/v) solution of **6** in 96% sulfuric acid which was 24 hr old produces essentially pure (TLC) **6**.

(10) Solutions of **4** in 96% sulfuric acid may be produced by dissolving **1** in the acid.[4] These solutions exhibit a characteristic C-9 H methine resonance near δ 10. A solution of **1** in 96% sulfuric acid (0.75×10^{-5} *M*) has a fluorescence excitation spectrum with maxima at 260 and 380 nm and a broad band with maxima at 475 and 525 nm. The fluorescence emission spectrum of this solution exhibits a slender peak with a maximum at 545 nm.

(11) This corresponds to unreacted starting material.

(12) *cis*- and *trans*-**9**-trimethylsiloxythioxanthene sulfoxides react with sulfuric acid to produce, after dilution with water, **6**, **1**, and **8**. Another component, identified as **9** by TLC, was produced in *trace* quantities: A. L. Ternay, Jr., and D. W. Chasar, unpublished results.

(13) Thioxanthenol sulfoxide dehydrates in alkaline solution: A. L. Ternay, Jr., and D. W. Chasar, *J. Org. Chem.*, **32**, 3814 (1967).

(14) Thioxanthenol is converted to **1** and **6** during gas chromatography: A. L. Ternay, Jr., unpublished results.

(15) A. L. Ternay, Jr., and D. W. Chasar, Abstracts, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 9–14, 1967, No. 0-105.

(16) A. Trifunac and E. T. Kaiser, *J. Phys. Chem.*, **74**, 2236 (1970).

(17) A 1,4-sigmatropic shift of a hydroxy group from sulfur to C-9 could, in principle, convert **11** to **7** via the *gem*-diol of **6**. This would parallel the mechanism of the isomerization of *S*-alkyl "thiaanthracenes" to 9-alkylthioxanthenes.[18] However, our inability to detect **4** containing a deuteron at C-9 where dehydration is carried out in 96% D_2SO_4 (this manuscript) *and* our inability to detect even the transient formation of "thiaanthracene" from 9,9-dideuterothioxanthene and HSO_3F–SbF_5–SO_2 (−50°) suggest that this is unlikely.[2] We are grateful to Professor Mislow for discussions of his results with us.

(18) G. H. Senkler, Jr., J. Stackhouse, B. E. Maryanoff, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 5650 (1974), and subsequent papers in this series.

(19) See paragraph at end of paper regarding supplementary material.