

Synthesis of 2,5-Disubstituted Thienosultines and Their Thermal Reactions with Dienophiles and Nucleophiles

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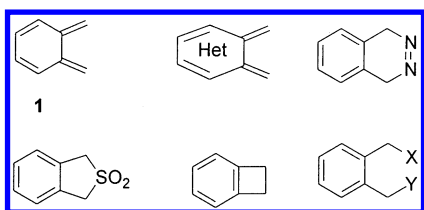
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The 2,5-disubstituted thienosultines (5,7-disubstituted 1,4-dihydro-1*H*-3 λ^4 -thieno[3,4-*c*][2,3]oxathiin-3-oxides) **5a–d** were prepared from the corresponding dichlorides **4a–d** with the commercially available Rongalite (sodium formaldehyde sulfoxylate) in 17–60% yields. When heated in the presence of electron-poor dienophiles, sultines **5a–d** underwent elimination of SO₂, and the resulting non-Kekulé biradicals **7a–d** were intercepted as the 1:1 adducts **8–12** in good to excellent yields. The pyrolysis of sultines and sulfolenes with different concentrations of dienophiles revealed that either a preequilibrium between starting reagents and biradical species or Diels–Alder and retro-Diels–Alder reaction mechanisms may be involved; however, more work is necessary to establish the proposed mechanisms. Reaction of sultine **5b** with *n*BuLi was found to undergo a nucleophilic ring-opening reaction to give sulfinyl alcohol **17** after H₂O workup. When sultine **5a** was heated in benzene in a sealed tube in the presence of methanol, methanol-*d*₄, or 2-mercaptoethanol, the respective 1:1 trapping adducts **19–21** as well as the rearranged sulfolene **6a** were isolated in similar amounts. The isolation of adducts **19–21** may be explained by the involvement of either biradical or ionic intermediates during the pyrolysis.

Introduction

The study of heterocyclic fused *o*-quinodimethane (*o*-QDM, **1**) has received considerable current interest,¹ and many methods have been developed for the generation of *o*-QDM; for example, azo compounds, sulfolenes, ben-



zocyclobutenes, and dihalides are popular precursors. Although azo compounds are popular for the generation of *o*-QDMs because of their clean thermal and photochemical reactions, they are notorious for their thermal instability in thieno- and pyrrolo-fused diazenes.^{2b,c} On the contrary, sulfolenes are so stable that harsh reaction conditions, such as flash vacuum pyrolysis or high-temperature pyrolysis, are usually required.^{1c,d,g} Benzo-

cyclobutenes are also useful precursors, but they often come from other precursors;^{1h,i} therefore, an extra step in synthesis is usually required. Dihalides are useful in thermal reactions; however, they usually require the addition of other catalysts^{1a,e,i} to enhance the reactivity. We choose sultines^{3–5} as precursors for *o*-QDM because they are usually stable above room temperature and yet react thermally at milder conditions than sulfolenes.

Pioneering studies on benzosultine and derivatives as *o*-QDM precursors had been explored by Durst et al. in the last two decades,⁴ but further development of other sultines was hampered by their tedious synthesis. The successful application of Rongalite in the conversion of

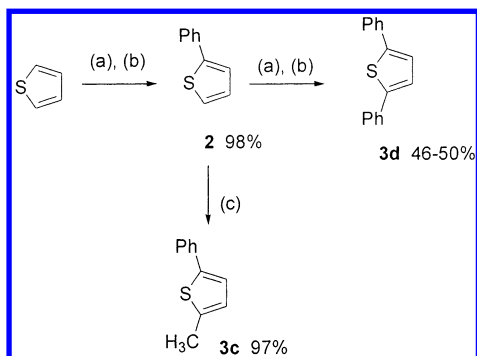
(1) For reviews of *o*-quinodimethanes, benzocyclobutenes, and related chemistry, see: (a) Segura, J. L.; Martín, N. *Chem. Rev.* **1999**, *99*, 3199. (b) Collier, S. J.; Storr, R. C. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Pergamon: New York, 1998; Vol. 10, pp 25–48. (c) Ando, K.; Kankake, M.; Suzuki, T.; Takayama, H. *Tetrahedron* **1995**, *51*, 129. (d) Chou, T.-S. *Rev. Heteroatom Chem.* **1993**, *8*, 65. (e) Martin, N.; Seoane, C.; Hanack, M. *Org. Prep. Proced. Int.* **1991**, *23*, 237. (f) Charlton, J. L.; Alauddin, M. M. *Tetrahedron* **1987**, *43*, 2873. (g) Funk, R. L.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, *9*, 41. (h) Kametani, T. *Pure Appl. Chem.* **1979**, *51*, 747. (i) Oppolzer, W. *Synthesis* **1978**, 793; *Heterocycles* **1980**, *14*, 1615.

(2) (a) Berson, J. A. *Acc. Chem. Res.* **1997**, *30*, 238. (b) In a study by Lu et al. the thiophene diazene was unstable below -10 °C: Lu, H. S. M.; Berson, J. A. *J. Am. Chem. Soc.* **1996**, *118*, 265. (c) The azo precursor was reported to be stable only below -20 °C by Bush et al.: Bush, L. C.; Heath, R. B.; Berson, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 9830.

(3) (a) Wu, A.-T.; Liu, W.-D.; Chung, W.-S. *J. Chin. Chem. Soc.* **2002**, *49*, 77. (b) Liu, J.-H.; Wu, A.-T.; Huang, M.-H.; Wu, C.-W.; Chung, W.-S. *J. Org. Chem.* **2000**, *65*, 3395. (c) Chung, W.-S.; Liu, J.-H. *Chem. Commun.* **1997**, 205. (d) Chung, W.-S.; Lin, W.-J.; Liu, W.-D.; Chen, L.-G. *J. Chem. Soc., Chem. Commun.* **1995**, 2537.

(4) For some earlier works on sultines, see: (a) King, J. F.; Rathore, R. *Tetrahedron Lett.* **1989**, *30*, 2763. (b) Durst, T.; Charlton, J. L.; Mount, D. B. *Can. J. Chem.* **1986**, *64*, 246. (c) Charlton, J. L.; Durst, T. *Tetrahedron Lett.* **1984**, *25*, 5287. (d) Jung, F.; Molin, M.; Van Den Elzen, R.; Durst, T. *J. Am. Chem. Soc.* **1974**, *96*, 935. (e) Connolly, T. J.; Durst, T. *Tetrahedron Lett.* **1997**, *38*, 1337. (f) Sharma, N. K.; De Reinach-Hirtzbach, F.; Durst, T. *Can. J. Chem.* **1976**, *54*, 3012. (g) Roversi, E.; Monnat, F.; Schenk, K.; Vogel, P.; Braña, P.; Sordo, J. A. *Chem.-Eur. J.* **2000**, *6*, 1858 and earlier references therein. (h) Megevand, S.; Moore, J.; Schenk, K.; Vogel, P. *Tetrahedron Lett.* **2001**, *42*, 673.

(5) For a review of sultines, see: Dittmer, D. C.; Hoey, M. D. *The Chemistry of Sulphinic Acids, Esters, and Their Derivatives*; Wiley: Chichester, U.K., 1990; pp 239–273.

SCHEME 1^a

^a Reagents and conditions: (a) *n*BuLi, THF, 0 °C, 3 h; ZnCl₂, rt, 2 h; (b) PhBr, Pd(PPh₃)₄, THF, 55 °C, 24 h; (c) *n*BuLi, THF, 0 °C, 3 h; CH₃I, 0 °C → rt, 24 h.

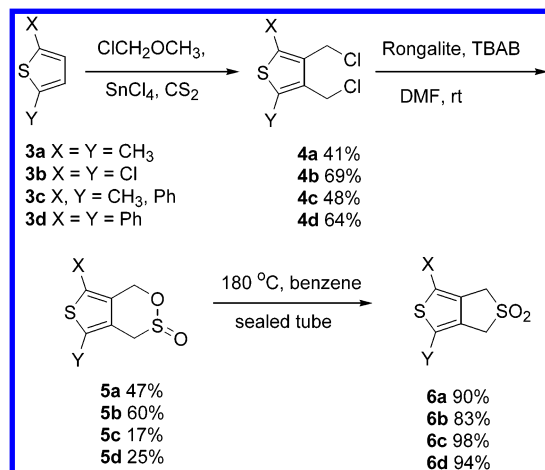
dihalides to sultines by Hoey and Dittmer^{5,6} makes it a convenient precursor for *o*-QDM. Although the application of sulfolenes and sultines as *o*-QDM precursors has been popular, important questions remain to be answered concerning their differences in reactivity and reaction mechanisms. In their pyrolysis studies of sulfolenes with alkenes, Takayama et al. reported^{1c,7} that Diels–Alder reaction occurred first on the aromatic moiety, followed by SO₂ extrusion, then a second Diels–Alder reaction to give 1:2 cycloadducts, and finally a retro-Diels–Alder reaction to give the 1:1 fused adducts (*vide infra*).

We have been interested in the application of heterocyclic fused *o*-QDM in Diels–Alder reactions,³ and in this work α,α' -disubstituted thienosultines are synthesized to find out whether sultines react through the mechanism proposed by Takayama for sulfolenes or through a biradical mechanism similar to those of diazenes.² On one hand, the bulky α,α' -disubstituents on thienosultines may have two functions: (1) they hinder the direct addition of dienophiles to α -positions of thiophene, and (2) the phenyl group(s) may stabilize the thus formed non-Kekulé biradicals. Therefore, if the 1:1 fused adducts are still formed with the bulky substituents, the biradical mechanism may be involved. Furthermore, concentration-dependent trapping studies on the pyrolysis of sulfolenes and sultines are carried out in the hope to differentiate their reaction mechanisms on the basis of whether their rate-determining steps are unimolecular or bimolecular reactions. We herein report our exploration of the scope of thienosultine derivatives and their thermal reaction with various dienophiles and nucleophiles.

Results and Discussion

The syntheses of 2,5-disubstituted thienosultines **5a–d** are shown in Schemes 1 and 2. 2,5-Dimethylthiophene (**3a**) and 2,5-dichlorothiophene (**3b**) are commercially

SCHEME 2



available. Butyllithium treatment of 2-phenylthiophene (**2**)^{8a} followed by methylation led to 2-methyl-5-phenylthiophene (**3c**) in 97% yield. 2,5-Diphenylthiophene (**3d**) was prepared by a known method using a palladium catalyst.^{8b} 2,5-Disubstituted 3,4-bis(chloromethyl)thiophenes **4a–d** were prepared by chloromethylation of the corresponding 2,5-disubstituted thiophenes **3a–d** adapted according to the procedures developed by Wynberg et al. in the synthesis of the corresponding sulfones **6**.^{9a,b} The key step in the synthesis of sultines **5a–d** is the use of Rongalite (sodium formaldehyde sulfoxylate) with the corresponding dichlorides **4a–d**. Unfortunately, the yields for the preparation of these sultines are relatively poor compared to that of ca. 70% for the preparation of benzosultine,^{5,6} and there is room for further improvement of the thienosultine synthesis.

The ¹H NMR spectra of sultines **5a–d** deserve some comments because they show two characteristic AB quartets of the 1,4-hydrogens near oxathiin-3-oxide functional groups. It has been reported that hydrogens on the carbon α to the oxygen of an oxathiin-3-oxide (sultine) have chemical shifts of 4.9–5.6 ppm, whereas hydrogens on the carbon α to the sulfinyl of an oxathiin-3-oxide have chemical shifts of 3.5–4.7 ppm.^{3–4,11b} The four α -hydrogens of sulfolenes **6a–d** have chemical shifts in the range of 4.1–4.4 ppm and appear as singlets (except those for **6c**, for which two singlets were observed) due to symmetry and lack of a nearby chiral center. In the five thienosultines we have studied, the chemical shifts of hydrogens in sultines **5a–d** fell into two regions, 3.6–4.4 and 4.9–5.5 ppm (see the Experimental Section), which are in good agreement with the above description. The magnitude of the geminal coupling constant of the hydrogens α to the oxygen, J_{ca} , is usually smaller than that of hydrogens α to the sulfinyl group of a sultine (i.e., J_{ab}). The former are in the range of 13.6–14.9 Hz, whereas the latter are in the range of 15.3–16.0 Hz (see Table 1). The assignments of thienosultine ¹H NMR chemical shifts are based on previous assignments by Pirkle on benzosultines^{11b} and the known propensity of

(6) (a) Hoey, M. D.; Dittmer, D. C. *J. Org. Chem.* **1991**, *56*, 1947. (b) Jarvis, W. F.; Hoey, M. D.; Finocchio, A. L.; Dittmer, D. C. *J. Org. Chem.* **1988**, *53*, 5750.

(7) (a) Ando, K.; Aakadegawa, N.; Takayama, H. *J. Chem. Soc., Chem. Commun.* **1991**, 1765. (b) Ando, K.; Kankake, M.; Suzuki, T.; Takayama, H. *Synlett* **1994**, 741. (c) Konno, K.; Kawakami, Y.; Hayashi, T.; Takayama, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1371. (d) Chou, T.-S.; Tseng, H.-J. *Tetrahedron Lett.* **1995**, *36*, 7105. (e) Chou, S.-S. P.; Lee, C.-S.; Cheng, M.-C.; Tai, H.-P. *J. Org. Chem.* **1994**, *59*, 2010.

(8) (a) Rossi, R.; Carpita, A.; Ciafalo, M.; Lippolis, V. *Tetrahedron* **1991**, *47*, 8443. (b) Campaigne, E.; Foye, W. *J. Org. Chem.* **1952**, *17*, 1405.

(9) (a) Wynberg, H.; Zwanenburg, D. J. *J. Org. Chem.* **1964**, *29*, 1919. (b) Zwanenburg, D. J.; Wynberg, H. *J. Org. Chem.* **1969**, *34*, 333. (c) Winn, M.; Bordwell, F. G. *J. Org. Chem.* **1967**, *32*, 1610.

TABLE 1. Characteristic Hydrogen Chemical Shifts and Geminal Coupling Constants of Thienosultines 5a-d and Other Heterocyclic Sultines

Sultine	H _a	H _b	J _{ab} ^a	H _c	H _d	J _{cd} ^a	Ref
	3.50	4.31	15.3	4.88	5.23	-	11b
	3.80–3.85	4.63–4.71	15.4–15.6	5.19–5.21	5.50–5.55	13.7–14.1	3b
R = H, Cl, Ph							
	3.58	3.88	15.3	4.93	5.16	14.1	this work
5a							
	3.66	3.73	16.0	4.94	5.08	14.9	this work
5b							
	3.79	4.15	15.5	5.05	5.26	14.0	this work
5c							
	3.60	4.05	15.6	5.03	5.44	14.1	this work
5c'							
	3.80	4.36	15.6	5.16	5.49	14.0	this work
5d							

^a Estimated accuracy for coupling constants is ca. ± 0.2 Hz. All measurements were done in CDCl₃ in a 300 MHz NMR spectrometer.

protons cis to a sulfinyl oxygen to be deshielded; therefore, H_b is downfield shifted from H_a and H_d is downfield shifted from H_c.^{11d}

Sealed tube reaction of sultines **5a–d** in benzene alone gave the corresponding sulfolenes **6a–d** in excellent yields (83–94%). The Diels–Alder reactions of sultines **5a–d** and sulfolenes **6a–d** with typical electron-poor dienophiles are presented in Scheme 3 and Table 2. For example, when heated in benzene (sealed tube, 180 °C, 24 h) in the presence of 3 equiv of *N*-phenylmaleimide, dimethyl fumarate, fumaronitrile, dimethyl acetylenedicarboxylate, or diethyl fumarate, the sultines **5a–d** all underwent extrusion of SO₂, and the resulting non-Kekulé biradicals **7a–d** were intercepted as the 1:1 fused adducts **8–12** in 37–91% yields (entries 1–3, 5–7, 9–12, and 14–17 of Table 2). In each case, small to substantial amounts of sulfolenes **6a–d** were also formed depending on the power of the dienophiles; that is, stronger dienophiles led to higher yields of fused adducts and less sulfolenes. It is important to note that sulfolenes **6a–d** did not react with any of these dienophiles under the same reaction conditions (entries 4, 8, 13, and 18 of Table 2). The low reactivity of sulfolenes **6a–d** is in sharp contrast with the high reactivity of sultines **5a–d** but is

consistent with those reported by Takayama,^{1c,7a–c} Chou,^{7d,e} and Wynberg⁹ in their early attempts. Furthermore, it is interesting to observe the great similarity of our results with sultines and those with diazenes reported by Berson et al.^{2,10} For example, in the trapping experiments of thiophene biradical **7e** (X = Y = H) derived from a diazene precursor,¹⁰ the sole adducts formed (85–100%) had the fused structure (such as **8**) but not the bridged structure **13** (see Scheme 4).

The pyrolysis results of these sultines may be explained by at least three possible reaction mechanisms. The most likely pathway is the formation of non-Kekulé biradicals **7a–d**, followed by the Diels–Alder reaction with a dienophile to form either bridged adducts **13** or fused adducts **8–12** (pathway A, Scheme 3). This mechanism resembles those proposed for thieno- or furano-

(10) (a) Haider, K. W.; Clites, J. A.; Berson, J. A. *Tetrahedron Lett.* **1991**, *32*, 5305. (b) Stone, K. J.; Greenberg, M. M.; Blackstock, S. C.; Berson, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 3659. (c) Greenberg, M. M.; Blackstock, S. C.; Berson, J. A. *Tetrahedron Lett.* **1987**, *28*, 4263. (d) Reynolds, J. H.; Berson, J. A.; Kumashiro, K. K.; Duchamp, J. C.; Zilm, K. W.; Scaiano, J. C.; Berinstain, A. B.; Rubello, A.; Vogel, P. *J. Am. Chem. Soc.* **1993**, *115*, 8073. (e) Greenberg, M. M.; Blackstock, S. C.; Berson, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 3671. (f) Cichra, D.; Platz, M. S.; Berson, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 8507.

SCHEME 3

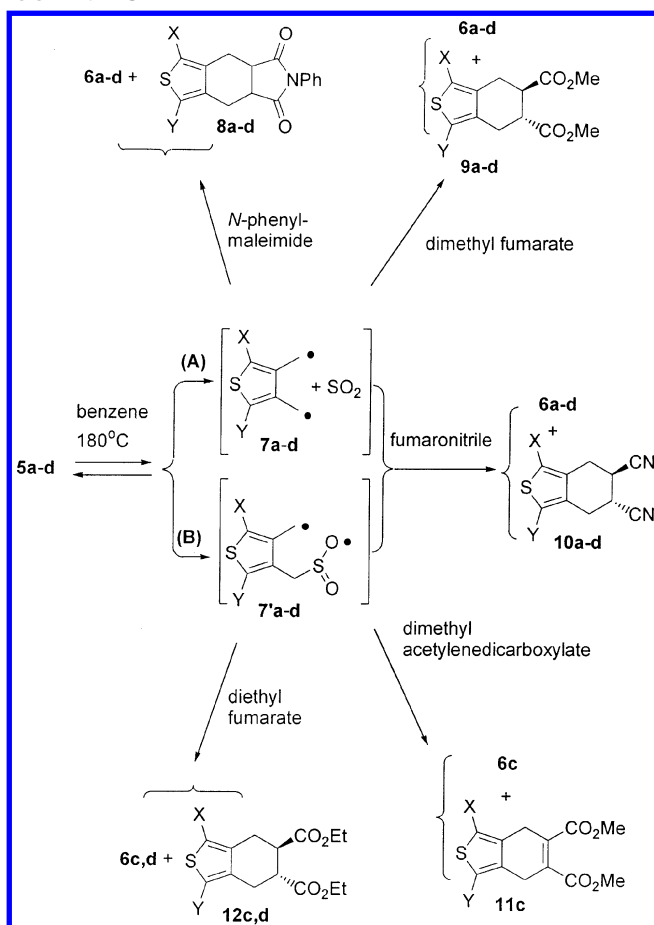


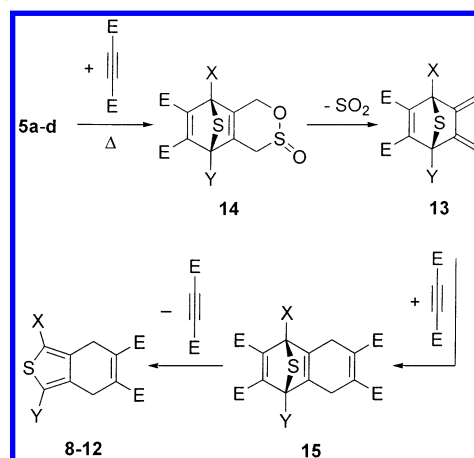
TABLE 2. Sealed Tube Reactions of 2,5-Disubstituted Thienosultines 5a–d and Sulfolenes 6a–d with Various Dienophiles (3 equiv) in Benzene^a

entry	diene	dienophile	products (yield, %)	total yield, %
1	5a	<i>N</i> -phenylmaleimide	6a (6) + 8a (91)	97
2	5a	dimethyl fumarate	6a (49) + 9a (40)	89
3	5a	fumaronitrile	6a (46) + 10a (43)	89
4	6a	various dienophiles ^b	no reaction	0
5	5b	<i>N</i> -phenylmaleimide	6b (7) + 8b (65)	72
6	5b	dimethyl fumarate	6b (4) + 9b (64)	68
7	5b	fumaronitrile	6b (16) + 10b (77)	93
8	6b	various dienophiles ^b	no reaction	0
9	5c	<i>N</i> -phenylmaleimide	6c (16) + 8c (76)	92
10	5c	fumaronitrile	6c (13) + 10c (75)	88
11	5c	dimethyl acetylenedicarboxylate	6c (47) + 11c (37)	84
12	5c	diethyl fumarate	6c (23) + 12c (69)	92
13	6c	various dienophiles ^b	no reaction	0
14	5d	<i>N</i> -phenylmaleimide	6d (6) + 8d (82)	88
15	5d	dimethyl fumarate	6d (12) + 9d (79)	91
16	5d	fumaronitrile	6d (21) + 10d (75)	96
17	5d	diethyl fumarate	6d (30) + 12d (67)	97
18	6d	various dienophiles ^b	no reaction	0

^a All reactions were carried out in benzene solution in a sealed tube at 180 °C for 24 h. ^b All the dienophiles used in the table were tested for sulfolenes 6a–d.

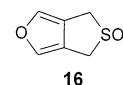
diazenes.^{2,10} Alternatively, sultines may undergo a one-bond (carbon–oxygen bond) cleavage to form alkyl sulfinyl biradicals of the type 7'a–d. The biradicals 7'a–d may then undergo either an intramolecular rearrangement to form sulfolenes 6a–d or an intermolecular trapping by olefins to form after losing SO₂ the 1:1 fused adducts

SCHEME 4



(pathway B, Scheme 3). The third possible reaction mechanism of thienosultines 5a–d is to undergo a Diels–Alder reaction on the aromatic moieties first followed by instantaneous SO₂ elimination to give bridged adducts 13. Compounds 13 further react with another dienophile to give the 1:2 adducts 15, and finally a retro-Diels–Alder reaction of 15 would occur to form fused adducts 8–12 (Scheme 4). The latter mechanism was proposed by Takayama to explain results with furano- and pyrrolisulfolenes.^{1c,7}

In the mechanisms involving biradical intermediates (pathways A and B in Scheme 3), the rate will be dependent only on the sultine concentration if the dienophile concentration is kept high and a steady-state approximation of the biradical concentration is satisfied. However, if the dienophile concentration is low, the rate of reaction will be dependent not only on the concentration of sultines but also on the concentration of dienophiles.^{11e} Alternatively, if a Diels–Alder reaction occurs first on the aromatic part of sultine and it happens to be the rate-determining step, the reaction would be second order and first order with respect to both the sultine and the dienophile. In the latter mechanism, the higher the dienophile concentration the faster products are formed and the faster starting sultines (or sulfolenes) are consumed. Because thienosulfolenes 6a–d required a much higher temperature to react with dienophiles, we used furanosulfolene 16^{3d} instead and thienosultine 5a for concentration-dependent kinetic studies.



Concentration-dependent studies on the thermolysis of thienosultine 5a (150 °C, 5 h) and furanosulfolene 16 (120 °C, 2 h) are shown in Figure 1. In the thermolysis of 5a, the yield of sulfolene 6a gradually decreased from 23% to ca. 2% when the concentration of fumaronitrile in-

(11) (a) Andersen, K. K.; Foley, J.; Perkins, R.; Gaffield, W.; Papanikalaou, N. *J. Am. Chem. Soc.* **1964**, *86*, 5637. (b) Pirkle, W. H.; Hoekstra, M. S. *J. Am. Chem. Soc.* **1976**, *98*, 1832. (c) Harpp, D. N.; Vines, S. M.; Montillier, J. P.; Chan, T. H. *J. Org. Chem.* **1976**, *41*, 3987. (d) Alternatively, one may envision that the lone pair electrons on sulfur of a sulfinyl group could act to shield a proton cis-vicinal to it. (e) For an excellent monograph on the kinetics of reactions involving intermediates, see: Wentrup, C. *Reactive Molecules*; Wiley: New York, 1984; Chapter 1.

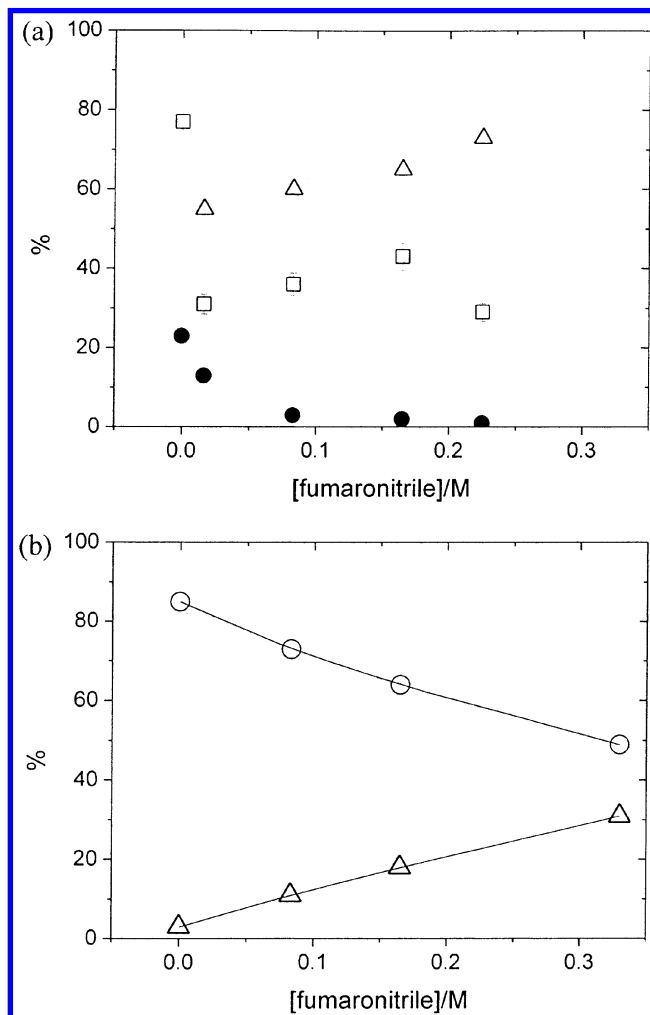
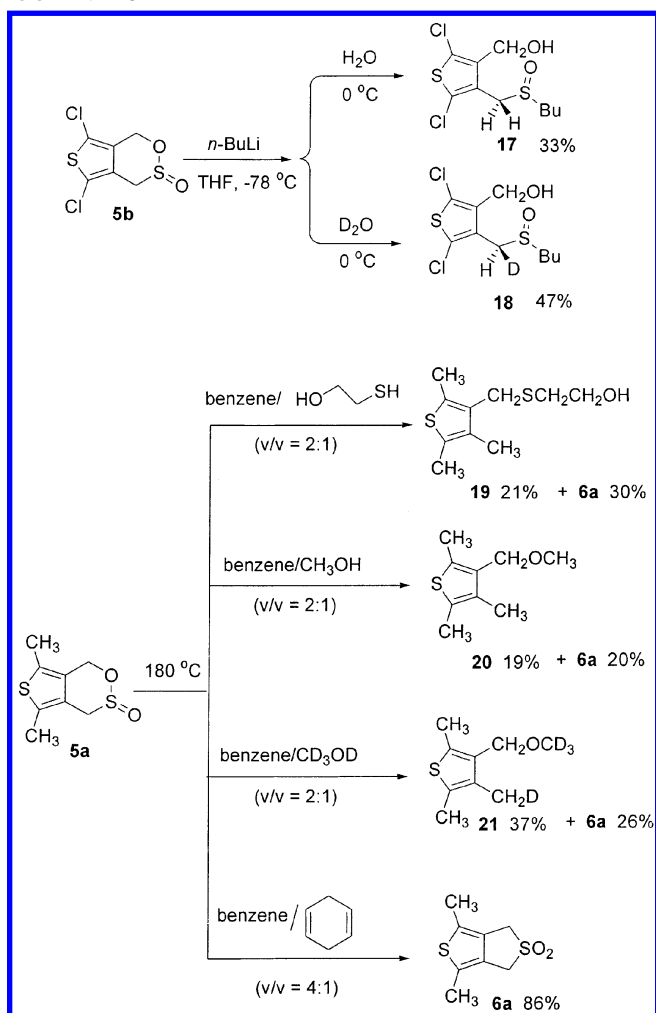


FIGURE 1. Product distributions of the sealed tube reactions of sultine **5a** and sulfolene **16** with various concentrations of fumaronitrile: (a) 2,5-dimethylthienosultine **5a** (16.5 mM in toluene), reacted at 150 °C for 5 h, where closed circles indicate the yield (%) of sulfolene **6a**, open triangles indicate the yield (%) of cycloadduct, and open squares indicate the yield (%) of the recovered sultine; (b) furanosulfolene **16** (15.8 mM in benzene), reacted at 120 °C for 2 h, where open circles indicate the yield (%) of recovered sulfolene and open triangles indicate the yield (%) of cycloadduct formed. All the reactions were stopped far before completion.

creased from 0 to 0.25 M (Figure 1a). Concurrently, the percentage yield of cycloadduct **10a** increased when the concentration of fumaronitrile increased. The results may be rationalized easily if diradical intermediates are invoked; that is, a competitive trapping of biradicals **7** by SO_2 or dienophile determines the relative amount of sulfolene **6a** and cycloadduct **10a**. A similar explanation may be applied in the Diels–Alder and retro-Diels–Alder reaction mechanism (Scheme 4), where a competitive trapping of reactive diene **13** by dienophile or SO_2 determines the relative product ratios. The consumption rate of furanosulfolene **16** is shown to be concentration dependent on both the sulfolene and fumaronitrile (Figure 1b). That is, higher dienophile (or sulfolene) concentration led to faster consumption of sulfolene and faster formation of cycloadducts. It would certainly be desirable to differentiate the above mechanisms; however, more accurate kinetic data are necessary for such an analysis.

SCHEME 5



Such an analysis would require direct spectroscopic measurement as has been elegantly demonstrated in the pyrolysis of a diazene.^{10f} However, we lack a proper thermostated optical cell for the in situ monitoring of high-temperature kinetics. Although laser flash spectroscopy and matrix isolation would also provide valuable information about the transient species, they are related to photochemical and photophysical properties of these sultines and may not be related to the thermolysis results discussed here. Clearly more work is necessary to establish these proposed mechanisms.

It has long been known that the reaction of an optically active reagent on sulfinates (sultines) will lead to sulfoxides of high optical purity, the so-called Andersen synthesis.^{11a} These reactions are stereospecific and proceed with inversion at sulfur.^{11b} Nucleophilic ring opening of heterocyclic fused sultines, however, has rarely been reported. Some of the few reported reactions of sultines with Grignard reagents as well as organocopper–lithium reagents^{11c} were mainly with aliphatic sultines. Reaction of sultine **5b** with $n\text{BuLi}$ gave the sulfinyl alcohol **17** after workup by H_2O ; however, it gave a deuterated sulfinyl alcohol, **18**, as the main product if worked up by D_2O (Scheme 5). Careful inspection of the ^1H NMR spectrum of **18** revealed that deuterium appeared only on the α -sulfinyl carbon, and no sign of deuterium scrambling in other carbons was found. The isolation of **18** as the

major product indicated that neighboring alkoxide might have undergone a H abstraction from the α -carbon of the sulfinyl group, giving hydroxyl and sulfinyl anion groups. The sulfinyl anion group eventually abstracts either a H from H₂O or a deuterium from D₂O to form **18** as the finally observed product. Although yields for the nucleophilic attack of cyclic sulfinate esters (sultines) by *n*BuLi are low (33–47%), they are comparable to the yields reported (40–70%) for aliphatic sultines.^{11a–c}

Sulfolenes are well-known to undergo alkylation readily at their α -sulfonyl position upon deprotonation with *n*BuLi followed by methyl iodide and ethyl, butyl, and benzyl bromides, respectively.⁷ By contrast, sultines undergo a nucleophilic attack if treated with a strong base such as a Grignard reagent or *n*BuLi; therefore, the synthesis of α -derivatives of sultines will not be straightforward. Reminiscences of the work done by Durst indicated that sulfinyl alcohols **17** and **18** (so-called δ -hydroxy sulfoxides)^{4d,f} may be useful intermediates in the synthesis of sultines.

To learn more about sultine chemistry and to determine the nature of the reactive intermediates, we further explored the reaction of sultine **5a** with radical trapping reagents such as methanol, 1,4-cyclohexadiene, and 2-mercaptoethanol.^{12–14} In the presence of 2-mercaptoethanol in a sealed tube reaction in benzene, sultine **5a** underwent SO₂ extrusion and gave a radical (or ionic) trapping product, **19**, as well as the rearranged sulfolene **6a** in a ca. 2:3 ratio, with a total yield of 50%. Similar trapping of the reactive intermediates by methanol gave **20** and sulfolene **6a** in a ca. 1:1 ratio. The abstractions of a hydrogen and a methoxy group in product **20** were confirmed by a methanol-*d*₄ trapping experiment, where the disappearance of a methyl ether signal and a decrease of the 3-methyl signal from an integration of three to two protons were observed in ¹H NMR spectra of adduct **21**. Although the formation of adducts **19–21** may be explained by a biradical trapping mechanism, alternatively, it may also be explained by ionic intermediates similar to those used by Myers in their trapping of α ,3-dehydrotoluene.^{13,14} The trapping of the reactive intermediate, resulting from the pyrolysis of sultine **5a**, by 1,4-cyclohexadiene was found to be inefficient even though it has been frequently used in the trapping of biradicals. The results implied that the biradicals might have been formed; however, they were either retrapped by SO₂ (**7a–d**) or underwent intramolecular rearrangement (through **7a–d**) to give only sulfolene **6a** in 86% yield. Alternatively, the latter results may favor the nucleophilic displacement by methanol or mercaptoethanol on the *O*-carbon atom to yield a sulfinic acid, which after losing SO₂ gives the observed products.¹⁵

In conclusion, we have synthesized 2,5-disubstituted thienosultines **5a–d** and studied their thermal reactions

(12) For examples of radical trapping by thiols, see: (a) Ottenheijm, H. C. J. *J. Org. Chem.* **1981**, *46*, 5408. (b) Tome, A. C.; Cavaleiro, J. A. S.; Storr, R. C. *Tetrahedron* **1996**, *52*, 1723.

(13) For efficient trapping of biradical intermediates using 1,4-cyclohexadiene, see: (a) Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057. (b) Myers, A. G.; Dragovich, P. S.; Kuo, E. Y. *J. Am. Chem. Soc.* **1992**, *114*, 9369.

(14) Storr et al. reported^{12b} a similar observation of conjugate addition of thiol nucleophiles on the pyrimidin-4-ones generated from the corresponding sulfolene with SO₂ extrusion.

(15) We thank one of the reviewers for the suggestion of this mechanism.

with electron-poor alkenes, alkynes, radical trapping agents, and nucleophiles. When heated in the presence of electron-poor dienophiles, sultines **5a–d** underwent elimination of SO₂, and the resulting biradicals (**7a–d** or **7'a–d**, Scheme 3) were intercepted as the 1:1 adducts **8–12** in good to excellent yields. In each case, small to substantial amounts of sulfolenes **6a–d** were also formed. When sultine **5a** was heated in benzene in a sealed tube in the presence of methanol or 2-mercaptoethanol, the respective trapping adducts **19–21** as well as the rearranged sulfolene **6a** were isolated. Reaction of sultine **5b** with *n*BuLi was found to undergo a nucleophilic ring-opening reaction to give sulfoxide alcohol **17** after H₂O workup. Sulfoxide alcohols can be further transformed into other sultine derivatives.^{4d,f} Concentration-dependent trapping of sultines and sulfolenes through thermolysis revealed that different reaction mechanisms may be involved. We are in the process of studying the photochemistry and transient absorption spectroscopy of these and other heterocyclic fused sultines,³ and the results will be reported in due course.

Experimental Section

General Procedures. Melting points were determined on a melting point apparatus and are uncorrected. ¹H NMR spectra were recorded at 300 MHz, ¹³C and DEPT NMR spectra were recorded at 75.4 MHz, and the chemical shifts are reported in parts per million (δ) relative to that of CDCl₃ (δ = 7.25 ppm for proton, and δ = 77.00 ppm for carbon) or tetramethylsilane as internal standard. Coupling constants are reported in hertz (Hz). High-resolution mass spectra were recorded on a spectrometer of the instrument center of either National Tsing-Hua University or National Chung-Hsin University. C, H, and N combustion analyses were determined, and all analyzed compounds are within $\pm 0.4\%$ of the theoretical value unless otherwise indicated. Column chromatography was performed on silica gel of 70–230 or 230–400 mesh. The preparation of **2** followed a literature^{8a} procedure. The synthesis of dihalides **4a** and **4b** followed a literature procedure.^{9b,c}

Data for 2-Phenylthiophene (2): 98% yield; white solid; mp 31–32 °C (lit.^{8a} mp 36 °C); ¹H NMR (300 MHz, CDCl₃) δ 7.03–7.05 (1H, m), 7.23–7.37 (5H, m), 7.58–7.61 (2H, m); ¹³C NMR (75.4 MHz, CDCl₃) δ 123.03 (CH), 124.75 (CH), 125.90 (CH), 127.41 (CH), 127.96 (CH), 128.84 (CH), 134.35 (C_q), 144.38 (C_q).

Synthesis of 2-Methyl-5-phenylthiophene (3c). To a solution of **2** (4.36 g, 27.26 mmol) in THF (60 mL) at 0 °C was slowly added *n*-butyllithium (2.5 M in hexane, 30 mmol) via syringe under nitrogen. After the solution was stirred for 3 h, methyl iodide (8.1 g, 54 mmol) in THF (4 mL) was added dropwise with vigorous stirring. The reaction mixture was gradually warmed to ambient temperature and stirred overnight. The solution was poured into 50 mL of ice–water, the two layers were separated, and the aqueous layer was extracted with ether (3 \times 50 mL). The organic layers were combined, dried over MgSO₄, filtered, and concentrated. Flash column chromatography on silica gel (hexane) gave 4.6 g (26 mmol, 97%) of **3c** as a white solid: mp 39–41 °C; ¹H NMR δ 2.47 (3H, s), 6.70–6.69 (1H, m), 7.07–7.08 (1H, m), 7.21–7.55 (5H, m); ¹³C NMR δ 15.45 (CH₃), 122.85 (CH), 125.47 (CH), 126.16 (CH), 126.96 (CH), 128.78 (CH), 134.68 (C_q), 139.48 (C_q), 141.96 (C_q).

Synthesis of 2,5-Diphenylthiophene (3d). A hexane solution of *n*-butyllithium (34.3 mmol) was added via syringe to a stirred solution of 2-phenylthiophene (5.0 g, 31.2 mmol) in anhydride THF (50 mL) at 0 °C under nitrogen. The mixture was stirred at this temperature for 3 h, and then transferred via syringe to a stirred solution of zinc chloride (4.68 g, 34.3 mmol) in 20 mL of anhydride THF at room temperature. The

solution was stirred at ambient temperature for another 2 h and then added via syringe to an oven-dried 250 mL round-bottom flask containing tetrakis(triphenylphosphine) palladium (108 mg, 0.0936 mmol) and bromobenzene (5.0 g, 31.2 mmol) in 20 mL of dry THF. The reaction mixture was then slowly heated to 55 °C and kept at this temperature for 24 h. Dilute hydrochloric acid (0.1 N, 30 mL) was added to the cooled reaction mixture. The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 30 mL). The organic layers were combined, washed with saturated sodium bicarbonate solution (30 mL) and water (3 × 30 mL), dried over MgSO₄, filtered, and concentrated. Recrystallization in hot 2-propanol gave 3.4 g (14.4 mmol, 46%) of **3d** as a pale yellow powder: mp 149–150 °C (lit.^{8b} mp 149–150 °C); ¹H NMR δ 7.26–7.66 (12H, m); ¹³C NMR δ 123.97 (CH), 125.60 (CH), 127.50 (CH), 128.90 (CH), 134.27 (C_q), 143.58 (C_q); MS (EI) *m/z* 237 (M⁺ + 1, 58), 236 (M⁺, 100), 202 (8).

General Procedure for the Synthesis of 2,5-Disubstituted 3,4-Bis(chloromethyl)thiophenes 4a–d.^{9c} The procedure for **4c** is given as an example. Compound **3c** (5.0 g, 28.7 mmol) was dissolved in carbon disulfide (10 mL), and chloromethyl methyl ether (7.3 g, 86 mmol) was added. The solution was cooled to 0 °C. A solution of tin tetrachloride (11.3 g, 43.05 mmol) in 10 mL of carbon disulfide was added dropwise via an additional funnel under nitrogen. The mixture turned dark green upon addition. The reaction mixture was stirred at 0 °C for 1 h and then warmed to room temperature for 2 h. The heterogeneous dark green mixture was poured into ice–water (20 mL), and CH₂Cl₂ (40 mL) was added. After the mixture was stirred for 10 min, the layers were separated and the organic layer was washed with water (20 mL) and dried over MgSO₄. The solvent was distilled off in vacuo to yield 3.7 g (1.37 mmol, 48%) of **4c** as a viscous green oil. Product **4c** decomposed after chromatography on silica gel; therefore, crude product was used without further purification. The isolated yields based on starting materials **3a–c** are as follows: **4a**, 41%; **4b**, 69%; **4c**, 48%; **4d**, 64%.

Data for 3,4-Bis(chloromethyl)-2,5-dimethylthiophene (4a): white solid; mp 59–61 °C; ¹H NMR δ 2.40 (6H, s), 4.60 (4H, s); ¹³C NMR δ 12.75 (CH₃), 37.23 (CH₂), 131.95 (C_q), 135.91 (C_q). Anal. Calcd for C₈H₁₀Cl₂S: C, 45.95; H, 4.82. Found: C, 46.00; H, 4.85.

Data for 2,5-Dichloro-3,4-bis(chloromethyl)thiophene (4b): white solid; mp 38–39 °C (lit.^{9b} mp 41–42 °C); ¹H NMR δ 4.63 (4H, s); ¹³C NMR δ 35.66 (CH₂), 126.94 (C_q), 132.88 (C_q). Anal. Calcd for C₆H₄Cl₄S: C, 28.83; H, 1.61. Found: C, 29.05; H, 1.62.

Data for 3,4-Bis(chloromethyl)-2-methyl-5-phenylthiophene (4c):^{2b} viscous green oil; ¹H NMR δ 2.48 (3H, s), 4.63 (2H, s), 4.69 (2H, s), 7.36–7.52 (5H, m); ¹³C NMR δ 12.96 (CH₃), 37.12 (CH₂), 38.55 (CH₂), 128.21 (CH), 128.83 (CH), 129.02 (CH), 131.63 (C_q), 132.89 (C_q), 133.07 (C_q), 138.92 (C_q), 140.49 (C_q); MS (EI) *m/z* 272 (M⁺ + 2, 17), 271 (M⁺ + 1, 30), 270 (M⁺, 25), 269 (36), 234 (64), 185 (100).

Data for 3,4-Bis(chloromethyl)-2,5-diphenylthiophene (4d): white solid; 64% yield; mp 108.1–108.7 °C; ¹H NMR δ 4.76 (4H, s), 7.42–7.61 (10H, m); ¹³C NMR δ 38.45 (CH₂), 128.55 (CH), 128.94 (CH), 129.08 (CH), 132.50 (C_q), 132.58 (C_q), 143.22 (C_q); MS (EI) *m/z* 336 (M⁺ + 3, 4), 335 (M⁺ + 2, 7), 334 (M⁺ + 1, 27), 333 (M⁺, 17), 332 (42), 298 (20), 297 (47), 248 (100), 247 (62), 129 (69). Anal. Calcd for C₁₈H₁₄Cl₂S: C, 64.87; H, 4.23. Found: C, 64.70; H, 4.62.

General Procedure for the Synthesis of 5,7-Disubstituted 1,4-Dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxides (Sultines) 5a–d. A solution of **4a–d** (0.30 g for **4a**, 1.43 mmol), Rongalite (0.44 g, 2.86 mmol), and TBAB (0.69 g, 2.15 mmol) in DMF (50 mL) was stirred at room temperature for 2 h. The mixture was diluted with H₂O (40 mL) and extracted three times (3 × 20 mL) with ether. The organic layer was dried over MgSO₄, concentrated, and purified by column chromatography (25–5:1 hexane/ethyl acetate) to give 0.14 g (0.67 mmol, 47%) of **5a**. Corresponding yields for other

substituents are as follows: 60% for **5b**, 17% for **5c** and **5c'** (as a 1:1 mixture), and 25% for **5d**.

Data for 5,7-Dimethyl-1,4-dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxide (Sultine 5a): white solid; mp 70–71 °C; ¹H NMR δ 2.27 (6H, s), 3.58 (1H, A'B', *J* = 15.3 Hz), 3.88 (1H, A'B', *J* = 15.6 Hz), 4.93 (1H, AB, *J* = 14.1 Hz), 5.16 (1H, AB, *J* = 14.1 Hz); ¹³C NMR δ 12.11 (2 CH₃), 50.92 (CH₂), 58.73 (CH₂), 119.13 (C_q), 125.40 (C_q), 128.72 (C_q), 133.15 (C_q); MS (EI) *m/z* 202 (M⁺, 6.0), 138 (M⁺ – SO₂, 100); HRMS *m/z* calcd for C₈H₁₀O₂S₂ 202.0122, found 202.0116. Anal. Calcd for C₈H₁₀O₂S₂: C, 47.50; H, 4.98. Found: C, 47.29; H, 5.06.

Data for 5,7-Dichloro-1,4-dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxide (Sultine 5b): white solid; mp 86–87 °C; ¹H NMR δ 3.66 (1H, A'B', *J* = 16.0 Hz), 3.73 (1H, A'B', *J* = 16.1 Hz), 4.94 (1H, AB, *J* = 14.9 Hz), 5.08 (1H, AB, *J* = 14.9 Hz); ¹³C NMR δ 49.50 (CH₂), 57.04 (CH₂), 120.44 (C_q), 121.23 (C_q), 125.51 (C_q), 126.36 (C_q); MS (EI) *m/z* 242 (M⁺, 11.4), 178 (M⁺ – SO₂, 100); HRMS *m/z* calcd for C₆H₄Cl₂O₂S₂ 241.9030, found 241.9024. Anal. Calcd for C₆H₄Cl₂O₂S₂: C, 29.64; H, 1.66. Found: C, 29.66; H, 1.94.

Data for 7-Methyl-5-phenyl-1,4-dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxide (Sultine 5c): pale yellow solid; mp 91–92 °C; ¹H NMR δ 2.41 (3H, s), 3.79 (1H, A'B', *J* = 15.5 Hz), 4.15 (1H, A'B', *J* = 15.5 Hz), 5.05 (1H, AB, *J* = 14.0 Hz), 5.26 (1H, AB, *J* = 14.0 Hz), 7.35–7.45 (5H, m); ¹³C NMR δ 12.71 (CH₃), 51.59 (CH₂), 58.81 (CH₂), 121.02 (C_q), 126.42 (C_q), 127.79 (CH), 128.40 (CH), 128.94 (CH), 133.00 (C_q), 135.01 (C_q), 136.02 (C_q); MS (EI) *m/z* 264 (M⁺, 5), 200 (M⁺ – SO₂, 96), 119 (96), 185 (M⁺ – SO₂ – CH₃, 100); HRMS *m/z* calcd for C₁₃H₁₂O₂S₂ 264.0279, found 264.0280. Anal. Calcd for C₁₃H₁₂O₂S₂: C, 59.07; H, 4.58. Found: C, 59.32; H, 4.71.

Data for 5-Methyl-7-phenyl-1,4-dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxide (Sultine 5c'): pale yellow solid; mp 95–97 °C; ¹H NMR δ 2.37 (3H, s), 3.60 (1H, A'B', *J* = 15.6 Hz), 4.05 (1H, A'B', *J* = 15.6 Hz), 5.03 (1H, AB, *J* = 14.1 Hz), 5.44 (1H, AB, *J* = 14.1 Hz), 7.29–7.46 (5H, m); ¹³C NMR δ 12.59 (CH₃), 51.54 (CH₂), 58.75 (CH₂), 121.04 (C_q), 126.42 (C_q), 127.71 (CH), 128.33 (CH), 128.86 (CH), 132.96 (C_q), 134.93 (C_q), 135.91 (C_q); MS (EI) *m/z* 264 (M⁺, 6), 200 (M⁺ – SO₂, 78), 199 (100), 185 (75).

Data for 5,7-Diphenyl-1,4-dihydro-1H-3λ⁴-thieno[3,4-d][2,3]oxathiin-3-oxide (Sultine 5d): clear crystal after recrystallization from a solvent of CH₂Cl₂ and hexane; mp 176–177 °C; ¹H NMR δ 3.80 (1H, A'B', *J* = 15.6 Hz), 4.36 (1H, A'B', *J* = 15.6 Hz), 5.16 (1H, AB, *J* = 14.0 Hz), 5.49 (1H, AB, *J* = 14.0 Hz), 7.37–7.49 (10H, m); ¹³C NMR δ 53.22 (CH₂), 59.43 (CH₂), 121.22 (C_q), 127.78 (C_q), 128.24 (CH), 128.31 (CH), 128.66 (CH), 128.95 (CH), 129.00 (CH), 129.05 (CH), 132.59 (C_q), 132.67 (C_q), 137.87 (C_q), 140.95 (C_q); MS (EI) *m/z* 326 (M⁺, 1.5), 262 (34), 261 (100), 228 (28); HRMS *m/z* calcd for C₁₈H₁₄O₂S₂ 326.0436, found 326.0433. Anal. Calcd for C₁₈H₁₄O₂S₂: C, 66.23; H, 4.32. Found: C, 66.18; H, 4.39.

General Procedure for the Trapping Experiments of 2,5-Dimethylthienosultine 5a with Dienophiles Such as *N*-Phenylmaleimide, Dimethyl Fumarate, and Fumaronitrile. A solution of 2,5-dimethylthienosultine **5a** (50 mg, 0.25 mmol), with or without the respective dienophiles (0.74 mmol), in benzene (3 mL) was kept in a sealed tube at 180 °C for 24 h. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using hexane/ethyl acetate (from 16:1 to 4:1) as the eluent. Sulfolene **6a** was obtained in 90% yield (no quencher). For the trapping by dienophiles, the respective yields are as follows: *N*-phenylmaleimide, 6% **6a** and 91% **8a**; dimethyl fumarate, 49% **6a** and 40% **9a**; fumaronitrile, 46% **6a** and 43% **10a**.

Data for 4,6-Dimethyl-1,3-dihydro-1H-2λ⁶-thieno[3,4-c]thiophene-2,2-dione (6a): white solid; mp 187–188 °C; ¹H NMR δ 2.34 (6H, s), 4.11 (4H, s); ¹³C NMR δ 13.54 (CH₃), 54.71 (CH₂), 126.59 (C_q), 133.57 (C_q); MS (EI) *m/z* 202 (M⁺, 21.7), 138 (M⁺ – SO₂, 100); HRMS *m/z* calcd for C₈H₁₀O₂S₂ 202.0122, found 202.0119. Anal. Calcd for C₈H₁₀O₂S₂: C, 47.50; H, 4.98. Found: C, 47.29; H, 5.06.

Data for 1,3-Dimethyl-6-phenyl-4a,5,6,7,7a,8-hexahydro-4H-thieno[3,4-f]isoindole-5,7-dione (8a): white solid; mp 149–151 °C; $^1\text{H NMR}$ δ 2.20 (6H, s), 2.57–2.63 (2H, m), 3.12–3.18 (2H, m), 3.20–3.30 (2H, m), 6.82–6.86 (2H, m), 7.24–7.33 (3H, m); $^{13}\text{C NMR}$ δ 12.14 (CH₃), 24.47 (CH₂), 40.23 (CH), 126.38 (CH), 128.51 (CH), 129.01 (CH), 129.24 (C_q), 130.64 (C_q), 131.78 (C_q), 178.77 (C_q); MS (EI) m/z 311 (M⁺, 100), 163 (60); HRMS m/z calcd for C₁₈H₁₇NO₂S 311.0980, found 311.0984.

Data for Dimethyl (5*R,6*R**)-1,3-Dimethyl-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate (9a):** white solid; mp 106–108 °C; $^1\text{H NMR}$ δ 2.17 (6H, s), 2.21–2.48 (2H, m), 2.84–2.97 (4H, m), 3.66 (6H, s); $^{13}\text{C NMR}$ δ 12.46 (CH₃), 27.70 (CH₂), 42.68 (CH), 50.00 (CH₃), 128.37 (C_q), 130.58 (C_q), 175.13 (C_q); MS (EI) m/z 282 (M⁺, 71.0), 222 (67), 163 (100); HRMS m/z calcd for C₁₄H₁₈O₄S 282.0926, found 282.0921. Anal. Calcd for C₁₄H₁₈O₄S: C, 59.55; H, 6.43. Found: C, 59.19; H, 6.38.

Data for (5*R,6*R**)-1,3-Dimethyl-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarbonitrile (10a):** white solid; mp 214–215 °C; $^1\text{H NMR}$ δ 2.92 (6H, s), 2.87–2.95 (2H, m), 3.11–3.27 (4H, m); $^{13}\text{C NMR}$ δ 12.58 (CH₃), 26.74 (CH₂), 28.87 (CH₃), 118.55 (C_q), 126.30 (C_q), 130.58 (C_q); MS (EI) m/z 216 (M⁺, 21.7), 138 (100); HRMS m/z calcd for C₁₂H₁₂N₂S 216.0727, found 216.0722.

General Procedure for the Trapping Experiments of 2,5-Dichlorothienosultine 5b with Dienophiles Such as *N*-Phenylmaleimide, Dimethyl Fumarate, and Fumaronitrile. A solution of 2,5-dichlorothienosultine **5b** (50 mg, 0.21 mmol), with or without the respective dienophiles (0.62 mmol), in benzene (3 mL) was kept in a sealed tube at 180 °C for 24 h. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using 25:1 hexane/ethyl acetate as the eluent. Sulfolene **6b** was obtained in 95% yield (no quencher). For the trapping by dienophiles, the respective yields are as follows: *N*-phenylmaleimide, 7% **6b** and 65% **8b**; dimethyl fumarate, 4% **6b** and 64% **9b**; fumaronitrile, 16% **6b** and 77% **10b**.

Data for 1,6-Dichloro-1,3-dihydro-1*H*-2*l*⁶-thieno[3,4-*c*]thiophene-2,2-dione (6b): white solid; mp 157–160 °C; $^1\text{H NMR}$ δ 4.22 (4H, s); $^{13}\text{C NMR}$ δ 55.09 (CH₂), 123.07 (C_q), 128.05 (C_q); MS (EI) m/z 242 (M⁺, 18.5), 178 (M⁺ – SO₂, 100); HRMS m/z calcd for C₆H₄Cl₂O₂S₂ 241.9030, found 241.9039. Anal. Calcd for C₆H₄Cl₂O₂S₂: C, 29.64; H, 1.66. Found: C, 29.66; H, 1.94.

Data for 1,3-Dichloro-6-phenyl-4a,5,6,7,7a,8-hexahydro-4H-thieno[3,4-f]isoindole-5,7-dione (8b): white solid; mp 195–196 °C; $^1\text{H NMR}$ δ 2.77–2.85 (2H, m), 3.31–3.46 (4H, m), 7.06–7.09 (2H, m), 7.36–7.45 (3H, m); $^{13}\text{C NMR}$ δ 24.06 (CH₂), 39.24 (CH), 121.26 (C_q), 126.18 (CH), 128.69 (CH), 129.10 (CH), 131.49 (C_q), 131.84 (C_q), 177.52 (C_q); MS (EI) m/z 351 (M⁺, 100), 169 (52), 134 (47); HRMS m/z calcd for C₁₆H₁₁SO₂Cl₂N 350.9987, found 350.9887. Anal. Calcd for C₁₆H₁₁SO₂Cl₂N: C, 54.56; H, 3.15; N, 3.98. Found: C, 54.57; H, 3.54; N, 4.09.

Data for Dimethyl (5*R,6*R**)-1,3-Dichloro-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate (9b):** white solid; mp 88–89 °C; $^1\text{H NMR}$ δ 2.52–2.71 (2H, m), 2.93–3.15 (4H, m), 3.75 (6H, s); $^{13}\text{C NMR}$ δ 26.77 (CH₂), 41.57 (CH), 52.23 (CH₃), 120.56 (C_q), 131.81 (C_q), 174.03 (C_q); MS (EI) m/z 322 (M⁺, 55.1), 262 (100), 203 (99), 168 (74); HRMS m/z calcd for C₁₂H₁₂SO₄Cl₂ 321.9833, found 321.9828. Anal. Calcd for C₁₂H₁₂SO₄Cl₂: C, 44.60; H, 3.74. Found: C, 44.65; H, 3.89.

Data for (5*R,6*R**)-1,3-Dichloro-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarbonitrile (10b):** white solid; mp 192–194 °C; $^1\text{H NMR}$ δ 3.00–3.21 (4H, m), 3.35–3.39 (2H, m); $^{13}\text{C NMR}$ δ 25.84 (CH₂), 27.86 (CH), 117.53 (C_q), 123.02 (C_q), 127.72 (C_q); MS (EI) m/z 256 (M⁺, 85.4), 178 (100); HRMS m/z calcd for C₁₀H₆Cl₂N₂S 255.9629, found 255.9633.

General Procedure for the Trapping Experiments of 2-Methyl-5-phenylthienosultine 5c with Dienophiles Such as *N*-Phenylmaleimide, Fumaronitrile, Dimethyl Acet-

ylenedicarboxylate, and Diethyl Fumarate. A solution of 2-methyl-5-phenylthienosultine **5c** (50 mg, 0.189 mmol), with or without the respective dienophiles (0.567 mmol), in toluene (3 mL) was kept in a sealed tube at 180 °C for 24 h. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using hexane/ethyl acetate (from 6:1 to 4:1) as the eluent. Sulfolene **6c** was obtained in 98% yield (no quencher). For the trapping by dienophiles, the respective yields are as follows: *N*-phenylmaleimide, 16% **6c** and 76% **8c**; fumaronitrile, 13% **6c** and 75% **10c**; dimethyl acetylenedicarboxylate, 47% **6c** and 37% **11c**; diethyl fumarate, 23% **6c** and 69% **12c**.

Data for 4-Methyl-6-phenyl-1,3-dihydro-1*H*-2*l*⁶-thieno[3,4-*c*]thiophene-2,2-dione (6c): clear crystal; mp 197–198 °C (CH₂Cl₂/hexane); $^1\text{H NMR}$ δ 2.44 (3H, s), 4.17 (2H, s), 4.38 (2H, s), 7.44–7.32 (5H, m); $^{13}\text{C NMR}$ δ 13.89 (CH₃), 53.89 (CH₂), 56.21 (CH₂), 125.69 (C_q), 126.88 (CH), 127.98 (CH), 128.37 (C_q), 129.13 (CH), 132.94 (C_q), 133.78 (C_q), 136.67 (C_q); MS (EI) m/z 265 (M⁺ + 1, 3), 264 (M⁺, 25), 200 (M⁺ – SO₂, 100), 199 (80), 185 (M⁺ – SO₂ – CH₃, 64), 184 (53); HRMS m/z calcd for C₁₃H₁₂O₂S₂ 264.0279, found 264.0278. Anal. Calcd for C₁₃H₁₂O₂S₂: C, 59.07; H, 4.58. Found: C, 59.13; H, 4.67.

Data for 1-Methyl-3,6-diphenyl-4a,5,6,7,7a,8-hexahydro-4H-thieno[3,4-f]isoindole-5,7-dione (8c): yellow oil; $^1\text{H NMR}$ δ 2.38 (3H, s), 2.76–2.88 (2H, m), 3.29–3.58 (4H, m), 6.95–6.98 (2H, m), 7.29–7.42 (8H, m); $^{13}\text{C NMR}$ δ 12.37 (CH₃), 24.32 (CH₂), 24.94 (CH₂), 40.11 (CH), 126.33 (CH), 127.26 (CH), 128.60 (CH), 128.68 (CH), 129.04 (CH), 130.46 (C_q), 131.77 (C_q), 131.95 (C_q), 132.30 (C_q), 133.60 (C_q), 134.89 (C_q), 178.54 (C_q), 178.63 (C_q); MS (EI) m/z 374 (M⁺ + 1, 18), 373 (M⁺, 100), 225 (40), 187 (14); HRMS m/z calcd for C₂₃H₁₉NO₂S 373.1137, found 373.1136.

Data for (5*R,6*R**)-1-Methyl-3-phenyl-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarbonitrile (10c):** pale yellow solid; mp 158.2–160.0 °C; $^1\text{H NMR}$ δ 2.37 (3H, s), 2.97–3.40 (6H, m), 7.26–7.45 (5H, m); $^{13}\text{C NMR}$ δ 12.87 (CH₃), 26.81 (CH₂), 28.10 (CH₂), 28.76 (CH), 29.03 (CH), 118.32 (C_q), 118.55 (C_q), 126.40 (C_q), 127.39 (C_q), 127.63 (CH), 128.44 (CH), 128.82 (CH), 133.38 (C_q), 133.68 (C_q), 135.75 (C_q); MS (EI) m/z 278 (M⁺, 100), 199 (57), 185 (45), 165 (26); HRMS m/z calcd for C₁₇H₁₄N₂S 278.0879, found 278.0871.

Data for Dimethyl 1-Methyl-3-phenyl-4,7-dihydrobenzo[*c*]thiophene-5,6-dicarboxylate (11c): yellow solid; mp 101–102 °C; $^1\text{H NMR}$ δ 2.40 (3H, s), 3.54–3.75 (4H, m), 3.79 (3H, s), 3.83 (3H, s), 7.28–7.45 (5H, m); $^{13}\text{C NMR}$ δ 12.95 (CH₃), 27.25 (CH₂), 29.00 (CH₂), 52.42 (CH₃), 127.12 (CH), 128.41 (CH), 128.71 (CH), 129.80 (C_q), 131.78 (C_q), 131.93 (C_q), 133.84 (C_q), 134.23 (C_q), 168.19 (C_q), 168.71 (C_q); MS (EI) m/z 342 (M⁺, 77), 310 (100), 309 (65), 282 (34), 251 (44), 224 (87); HRMS m/z calcd for C₁₉H₁₈O₄S 342.0926, found 342.0929.

Data for Diethyl (5*R,6*R**)-1-Methyl-3-phenyl-4,5,6,7-tetrahydrobenzo[*c*]thiophene-5,6-dicarboxylate (12c):** pale yellow solid; mp 72–73 °C; $^1\text{H NMR}$ δ 1.19–1.32 (6H, m), 2.34 (3H, s), 2.83–3.18 (6H, m), 4.10–4.23 (4H, m), 7.27–7.40 (5H, m); $^{13}\text{C NMR}$ δ 12.82 (CH₃), 14.09 (CH₃), 14.15 (CH₃), 27.70 (CH₂), 29.41 (CH₂), 42.70 (CH), 43.08 (CH), 60.82 (CH₂), 126.93 (CH), 128.37 (CH), 128.57 (CH), 130.93 (C_q), 131.65 (C_q), 131.87 (C_q), 133.48 (C_q), 134.29 (C_q), 174.56 (C_q), 174.63 (C_q); MS (EI) m/z 372 (M⁺, 46), 327 (11), 298 (20), 225 (100); HRMS m/z calcd for C₂₁H₂₄O₄S 372.1395, found 372.1395.

General Procedure for the Trapping Experiments of 2,5-Diphenylthienosultine 5d with Dienophiles Such as *N*-Phenylmaleimide, Dimethyl Fumarate, Fumaronitrile, and Diethyl Fumarate. A solution of 2,5-diphenylthienosultine **5d** (50 mg, 0.153 mmol), with or without the respective dienophiles (0.459 mmol), in toluene (3 mL) was kept in a sealed tube at 180 °C for 24 h. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using hexane/ethyl acetate (from 10:1 to 6:1) as the eluent. Sulfolene **6d** was obtained in 94% yield (no quencher). For the trapping by dienophiles, the respective yields are as follows: *N*-phenylmaleimide, 6% **6d**

and 82% **8d**; dimethyl fumarate, 21% **6d** and 75% **9d**; fumaronitrile, 12% **6d** and 79% **10d**; diethyl fumarate, 30% **6d** and 67% **12d**.

Data for 4,6-Diphenyl-1,3-dihydro-1H-2λ⁶-thieno[3,4-c]thiophene-2,2-dione (6d): white solid; mp 214–215 °C; ¹H NMR δ 4.41 (4H, s), 7.35–7.46 (10H, m); ¹³C NMR δ 55.29 (CH₂), 127.10 (CH), 127.23 (C_q), 128.40 (CH), 129.22 (CH), 132.58 (C_q), 138.44 (C_q); MS (EI) *m/z* 326 (M⁺, 9), 262 (M⁺ – SO₂, 16), 261 (100), 228 (20); HRMS *m/z* calcd for C₁₈H₁₄O₂S₂ 326.0436, found 326.0434. Anal. Calcd for C₁₈H₁₄O₂S₂: C, 66.23; H, 4.32. Found: C, 66.01; H, 4.44.

Data for 1,3,6-Triphenyl-4a,5,6,7,7a,8-hexahydro-4H-thieno[3,4-f]isoindole-5,7-dione (8d): white solid; mp 214–217 °C; ¹H NMR δ 2.87–2.96 (2H, m), 3.47–3.49 (2H, m), 3.59–3.64 (2H, dd, *J* = 14.7, 6 Hz), 6.99–7.02 (2H, m), 7.34–7.52 (13H, m); ¹³C NMR δ 24.91 (CH₂), 40.16 (CH), 126.42 (CH), 127.75 (CH), 128.74 (CH), 128.88 (CH), 129.24 (CH), 131.55 (C_q), 131.77 (C_q), 133.32 (C_q), 137.85 (C_q), 178.58 (C_q); MS (EI) *m/z* 436 (M⁺ + 1, 11), 435 (M⁺, 100), 287 (16), 286 (20), 261 (13); HRMS *m/z* calcd for C₂₈H₂₁NO₂S 435.1294, found 435.1285. Anal. Calcd for C₂₈H₂₁NO₂S: C, 77.22; H, 4.86; N, 3.22. Found: C, 77.20; H, 5.04; N, 3.41.

Data for Dimethyl (5R*,6R*)-1,3-Diphenyl-4,5,6,7-tetrahydrobenzo[c]thiophene-5,6-dicarboxylate (9d): white solid; mp 184–185 °C; ¹H NMR δ 2.90–3.05 (4H, m), 3.24–3.30 (2H, m), 3.71 (6H, s), 7.29–7.49 (10H, m); ¹³C NMR δ 29.14 (CH₂), 42.79 (CH), 52.08 (CH₃), 127.42 (CH), 128.52 (CH), 128.66 (CH), 131.57 (C_q), 133.88 (C_q), 136.52 (C_q), 174.89 (C_q); MS (EI) *m/z* 406 (M⁺, 34), 346 (10), 287 (100), 252 (34); HRMS *m/z* calcd for C₂₄H₂₂O₄S 406.1240, found 406.1243. Anal. Calcd for C₂₄H₂₂O₄S: C, 70.91; H, 5.45. Found: C, 71.10; H, 5.49.

Data for (5R*,6R*)-1,3-Diphenyl-4,5,6,7-tetrahydrobenzo[c]thiophene-5,6-dicarbonitrile (10d): due to the severe overlap of **10d** with **6d** in column chromatography, we obtained only proton NMR data, δ 3.19–3.48 (6H, m), 7.36–7.49 (10H, m).

Data for Diethyl (5R,6R)-1,3-Diphenyl-4,5,6,7-tetrahydrobenzo[c]thiophene-5,6-dicarboxylate (12d): white solid; mp 145–146 °C; ¹H NMR δ 1.25 (6H, t, *J* = 7.1 Hz), 2.90–3.04 (4H, m), 3.24–3.29 (2H, dd, *J* = 15, 2.7 Hz), 4.17 (4H, q, *J* = 7.1 Hz), 7.32–7.49 (10H, m); ¹³C NMR δ 14.07 (CH₃), 29.16 (CH₂), 42.95 (CH), 60.85 (CH₂), 127.38 (CH), 128.52 (CH), 128.65 (CH), 131.74 (C_q), 133.95 (C_q), 136.45 (C_q), 174.43 (C_q); MS (EI) *m/z* 435 (M⁺ + 1, 9), 434 (M⁺, 59), 287 (100), 286 (79), 253 (46); HRMS *m/z* calcd for C₂₆H₂₆O₄S 434.1553, found 434.1553. Anal. Calcd for C₂₆H₂₆O₄S: C, 71.86; H, 6.03. Found: C, 72.07; H, 6.14.

Reaction of 5b with *n*-BuLi Followed by Quenching with H₂O or D₂O To Give Products 17 and 18. To a 25 mL two-necked bottle were added 100 mg (0.42 mmol) of **5b** and 5 mL of dry THF. The solution was cooled to –78 °C, 248 μL (0.62 mmol) of *n*BuLi was added via syringe, and the resulting solution was stirred at this temperature for 1 h. It was then stirred at 0 °C for 1 h and at rt for another 1 h. The solution was quenched with either brine (1 mL) or D₂O (1 mL) in an ice bath, and the product was extracted with ethyl ether (3 × 5 mL). The combined organic extracts were washed with water (2 × 5 mL) and brine (5 mL) and then dried with MgSO₄. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using hexane/ethyl acetate (4:1) as the eluent to yield 42 mg (0.14 mmol) of **17** or 60 mg (0.20 mmol) of **18**.

Data for 4-[(Butylsulfinyl)methyl]-2,5-dichloro-3-thienylmethanol (17): 33% yield; white solid; mp 85–86 °C; ¹H NMR δ 0.98 (3H, t, *J* = 7.5 Hz), 1.46–1.60 (2H, m), 1.73–1.84 (2H, m); 2.47 (2H, t, *J* = 7.2 Hz), 3.94, 4.10 (2H, AB, *J* = 14.0 Hz), 4.49 (2H, d, *J* = 6.9 Hz), 4.70 (1H, t, *J* = 6.6 Hz); ¹³C NMR δ 13.63 (CH₃), 21.99 (CH₂), 24.55 (CH₂), 48.59 (CH₂), 51.07 (CH₂), 55.50 (CH₂), 125.80 (C_q), 126.18 (C_q), 127.06 (C_q), 138.68 (C_q); MS (EI) *m/z* 301 (M⁺ + 1, 7), 117 (100); HRMS *m/z* calcd for C₁₀H₁₄S₂O₂Cl₂ 299.9812, found 299.9804; *R*_f = 0.1 (hexane:ethyl acetate = 4:1).

Data for 4-[(Butylsulfinyl)methyl-*d*₁]-2,5-dichloro-3-thienylmethanol (18): 47% yield; white solid; mp 88–90 °C; ¹H NMR δ 0.95 (3H, t, *J* = 7.2 Hz), 1.54–1.55 (2H, m); 1.73–1.83 (2H, m); 2.74 (2H, t, *J* = 7.8 Hz), 3.96, 4.08 (1H, AB, *J* = 13.8 Hz), 4.47 (2H, d, *J* = 6.6 Hz), 4.70 (1H, t, *J* = 6.6 Hz); ¹³C NMR δ 13.63 (CH₃), 21.99 (CH₂), 24.55 (CH₂), 48.39 (t, C–D), 51.13 (CH₂), 55.56 (CH₂), 125.83 (C_q), 126.15 (C_q), 127.09 (C_q), 138.71 (C_q); MS (EI) *m/z* 302 (M⁺ + 1, 4), 117 (100); *R*_f = 0.1 (hexane:ethyl acetate = 4:1).

General Procedure for the Trapping Experiments of 2,5-Dimethylthienosultine 5a by Radical Trapping Agents Such as 2-Mercaptoethanol, Methanol, Methanol-*d*₄, and 1,4-Cyclohexadiene. A solution of **5a** (50 mg, 0.25 mmol) with the respective radical trapping agents (each 1 mL except 0.5 mL for 1,4-cyclohexadiene) in benzene (2 mL) was kept in a sealed tube at 180 °C for 24 h. The solvent was evaporated under vacuum, and the residue was subjected to silica gel chromatography using hexane/ethyl acetate (from 16:1 to 1:1) as the eluent. The trapping yields are as follows: 21% **19** and 30% **6a** by 2-mercaptoethanol, 19% **20** and 20% **6a** by methanol, 37% **21** and 26% **6a** by methanol-*d*₄, and 86% sulfolene **6a** by 1,4-cyclohexadiene.

Data for 2-[(2,4,5-Trimethyl-3-thienyl)methyl]sulfanyl-1-ethanol (19): colorless liquid; ¹H NMR δ 2.14 (3H, s), 2.28 (3H, s), 2.35 (3H, s), 2.69 (2H, t, *J* = 5.7 Hz); 3.60 (2H, s), 3.68–3.88 (2H, br s); ¹³C NMR δ 12.43 (CH₃), 13.05 (CH₃), 13.16 (CH₃), 27.79 (CH₂), 34.93 (CH₂), 60.45 (CH₂), 129.21 (C_q), 131.28 (C_q), 132.27 (C_q); MS (EI) *m/z* 216 (M⁺, 10), 139 (100); HRMS *m/z* calcd for C₁₀H₁₆OS₂ 216.0643, found 216.0639.

Data for 3-(Methoxymethyl)-2,4,5-trimethylthiophene (20): colorless liquid; ¹H NMR δ 2.07 (3H, s), 2.27 (3H, s), 2.38 (3H, s), 3.33 (3H, s), 4.27 (2H, s); ¹³C NMR δ 12.10 (CH₃), 12.80 (CH₃), 12.89 (CH₃), 57.56 (CH₃), 66.27 (CH₂), 128.74 (C_q), 132.93 (C_q), 133.49 (C_q), 133.58 (C_q); MS (EI) *m/z* 170 (M⁺, 1), 138 (100); HRMS *m/z* calcd for C₉H₁₄OS 170.0765, found 170.0763.

Data for 3-(Methoxy-*d*₃-methyl)-2,5-dimethyl-4-methyl-*d*₁-thiophene (21): colorless liquid; ¹H NMR δ 2.05 (2 H, t, *J* = 2.1 Hz), 2.27 (3H, s), 2.38 (3H, s), 4.26 (2H, s); ¹³C NMR δ 11.88 (t, *J*_{CD} = 20 Hz, CH₂D), 12.84 (CH₃), 12.93 (CH₃), 66.19 (CH₂) 128.78 (C_q), 132.91 (C_q), 133.53 (C_q); MS (EI) *m/z* 174 (M⁺, 23), 139 (60), 84 (100); HRMS *m/z* calcd for C₉H₁₀D₄OS 174.1017, found 170.1017.

Procedure for the Concentration-Dependent Trapping of Thienosultine 5a and Furanosulfolene 16 by Fumaronitrile. Stock solutions of **5a** and **16** were first prepared by adding 60 mg (0.30 mmol) of **5a** to 18 mL of toluene or 45 mg (0.28 mmol) of **16** to 18 mL of benzene. The stock solution was then equally divided into six thick-walled tubes, and each contained a 3 mL solution of **5a** (16.5 mM) in toluene or **16** (15.8 mM) in benzene. Tubes a and b were without fumaronitrile, and tubes c–f were with different amounts of fumaronitrile: (c) 4 mg (0.05 mmol, 16.7 mM), (d) 20 mg (0.26 mmol), (e) 40 mg (0.51 mmol), (f) 60 mg (0.77 mmol). After three cycles of freeze–pump–thaw, these tubes were sealed under vacuum, all reacted at the same time in an oil bath thermostated at (1) 150 ± 2 °C, 5 h for **5a**, and (2) 120 ± 2 °C, 2 h for **16**, and then cooled to room temperature. The solvent of these tubes was removed by rotary evaporation, and to each of them was added 1 mL of CDCl₃ with 50 mM *N*-phenylmaleimide as internal standard for ¹H NMR analysis. The data shown in Figure 1 are the average of at least two runs.

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Supporting Information Available: ¹H and ¹³C (or DEPT) NMR spectra for compounds **8a**, **8c**, **10a–d**, **11c**, **12c**, and **17–21**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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