Allium Chemistry: Structure, Synthesis, Natural Occurrence in Onion (*Allium cepa*), and Reactions of 2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane *S*-Oxides

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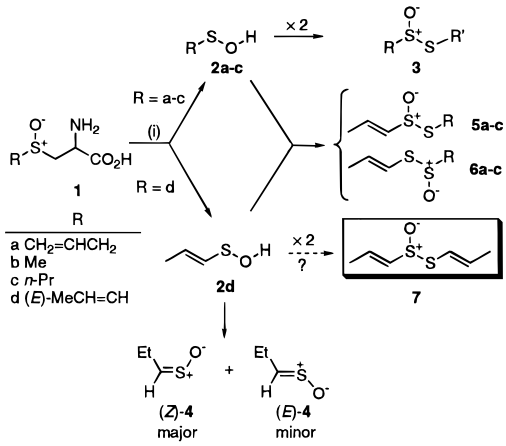
Abstract: Peracetic acid oxidation of di-1-propenyl disulfide (**8**) gives (±)-(1α,2α,3β,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide (**10a**; 10%) and (1α,2α,3α,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide (**11a**; 11%), both also isolated from extracts of homogenized onion. Compound **10a** could be converted into bissulfoxides (±)-(1α,2α,3β,4α,5α,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (**16**) and (±)-(1α,2α,3β,4α,5β,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (**17a**); these could be oxidized further to (±)-(1α,2α,3β,4α,5α,5β,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**18a**) and (±)-(1α,2α,3β,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**18b**) from **16** and **18a** from **17a**. Extended oxidation of **10a** gave (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide (**19**). Oxidation of **11a** gave (1α,2α,3α,4α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (**21a**) which was further oxidized to trioxides (1α,2α,3α,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**23a**) and (1α,2β,3β,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**23b**) and a bissulfone (*cis*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide (**24**)). The structures of **18a**, **19**, **21a,** and **23a** were determined by X-ray crystallography. With the proof of the structure of **18a**, structures for **17a** and **10a** are thereby unequivocally established.

Introduction

When garlic (*Allium sativum*) is crushed, the alliinase enzyme acts on precursor **1a** to generate the flavorant allicin (**3**, R = R′ = CH_2═$CHCH_2$; Scheme 1) via self-condensation of 2-propenesulfenic acid (**2a**).[1,2] Upon cutting an onion (*Allium cepa*), a similar reaction ensues, transforming precursor **1d** to onion lachrymatory factor propanethial *S*-oxide (**4**, LF)[1,3] via rearrangement of (*E*)-1-propenesulfenic acid (**2d**). At the same time, isomeric alk(en)yl 1-propenethiosulfinates CH_3CH═$CHS(O)$-SR and 1-propenyl alkane(ene)thiosulfinates CH_3CH═$CHSS$-(O)R (R = CH_2═$CHCH_2$, Me, or *n*-Pr; **5a**−**c** and **6a**−**c**, respectively) are formed by cocondensation of **2d** with 2-propene-, *n*-propane-, or methanesulfenic acid (**2a**−**c**, respectively). Compounds **5a**−**c** and **6a**−**c** are major flavorants of onion and related *Allium* species.[3c−e] Curiously, nothing is known concerning the possible role in *Allium* chemistry of 1-propenesulfinothioic acid *S*-1-propenyl ester (**7**, CH_3CH═$CHS(O)$-SCH═$CHCH_3$),[1] the self-condensation product of **2d**. The absence of **7** is all the more surprising in view of the significantly higher concentrations in onion extracts of the LF, and therefore precursor **2d**, relative to the concentrations of alkyl 1-propenethiosulfinates **5b**,**c** and 1-propenyl alkane(ene)thiosulfinates **6b**,**c**.[3c,d] This dilemma was resolved when it was recognized that a pair of compounds isolated by us during an attempt to prepare **7** by oxidation of di-1-propenyl disulfide (**8**) were spectroscopically identical to two unusual sulfur compounds isolated by Bayer and Wagner in Munich from extracts of chopped onion in the course of their characterization of the antiasthmatic agents from this plant.[4] With the Munich group,[5]

Scheme 1[a]



[a] (i) alliinase.

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[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1995.

(1) For background and leading references, see: (a) Block, E. *Sci. Am.* **1985**, *252*, 114. (b) Block, E. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *58*, 3. (c) Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135. (d) Block, E.; Naganathan, S.; Putman, D.; Zhao, S.-H. *Pure Appl. Chem.* **1993**, *65*, 625. (e) Block, E. In *Food Phytochemicals for Cancer Prevention*; Huang, M.-T.; Osawa, T.; Ho, C.-T.; Rosen, R. T., Eds.; ACS Symposium Series 546; American Chemical Society: Washington, DC, p 84, 1994. (f) Block, E.; Calvey, E. M. In *Sulfur Compounds in Food*; Mussinan, C. J.; Keelan, M. E., Eds.; ACS Symposium Series 564; American Chemical Society: Washington, DC, p 63, 1994.

(2) *Chemical Abstracts* names of compounds: **1a**, (+)-*S*-2-propenyl-L-cysteine *S*-oxide; **1d**, (+)-*S*-(*E*)-1-propenyl-L-cysteine *S*-oxide; **3**, 2-propene-1-sulfinothioic acid *S*-2-propenyl ester; **5a**, (*E*)-1-propenesulfinothioic acid *S*-2-propenyl ester; **5b**, (*E*)-1-propenesulfinothioic acid *S*-methyl ester; **5c**, (*E*)-1-propenesulfinothioic acid *S*-*n*-propyl ester; **6a**, 2-propene-1-sulfinothioic acid *S*-(*E*)-1-propenyl ester; **6b**, methanesulfinothioic acid *S*-(*E*)-1-propenyl ester; **6c**, 1-propanesulfinothioic acid *S*-(*E*)-1-propenyl ester.

(3) (a) Block, E.; Penn, R. E.; Revelle, L. K. *J. Am. Chem. Soc.* **1979**, *101*, 2200. (b) Block, E.; Revelle, L. K.; Bazzi, A. A. *Tetrahedron Lett.* **1980**, *21*, 1277. (c) Block, E.; Naganathan, S.; Putman, D.; Zhao, S.-H. *J. Agric. Food Chem.* **1992**, *40*, 2418. (d) Block, E.; Putman, D.; Zhao, S.-H. *J. Agric. Food Chem.* **1992**, *40*, 2431. (e) Precursor **1a** is found in onion only in trace amounts; the amounts of compounds **5a** and **6a** formed from **1a** are correspondingly small.[3f] (f) Calvey, E.; Block, E.; Matusik, J.; White, K. D.; DeOrazio, R.; Sha, D. Manuscript in preparation.

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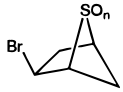
we dubbed these two compounds "zwiebelanes" ("zwiebel" is German for onion) and proposed that they are stereoisomers of 2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane *S*-oxide. These natural products are notable for the presence of a previously unknown type of strained sulfur heterobicyclic ring system. In this paper we examine the synthesis, structure, natural occurrence in freshly cut onion, properties, and reactions of zwiebelanes and other 2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane *S*-oxides. We consider elsewhere mechanistic details of the oxidation of disulfide **8** with the attendant formation of a number of curious compounds and intermediates relevant to the chemistry of onion and related *Allium* spp.[6]

Results and Discussion

Oxidation of Mixed Isomers of Di-1-propenyl Disulfide (8). Synthesis of Zwiebelanes, Flavorants in Fresh Onion. A 1:2:1 mixture of (*E*,*E*)-, (*E*,*Z*)-, and (*Z*,*Z*)-di-1-propenyl disulfide (**8**) was prepared in 41% yield from methyl (*E*,*Z*)-1-propenyl sulfide (**9**) by sequential treatment with lithium/ammonia followed by I_2/KI_3.[7] Oxidation of **8** with peracetic acid at −70 °C gave ca. 10% each of two compounds, **A** and **B**, both with fresh onion aromas and formula $C_6H_{10}OS_2$ by chemical ionization mass spectroscopy (CI-MS) and by GC−MS. Compound **A**, a low melting solid, showed IR bands at 1122 and 1080 cm^{-1} along with six ^{13}C NMR bands (δ 79.4, 77.7, 48.0, 39.4 (all CH) and 15.7, 14.2 (CH_3)) and a well-resolved ^1H NMR spectrum (see Table 1), all suggestive of an unsymmetrical saturated bicyclic sulfoxide. Compound **B**, a colorless oil, showed IR bands at 1090 and 1065 cm^{-1}, along with only three ^{13}C NMR bands (δ 79.5, 33.3 (CH) and 12.6 (CH_3)) and a ^1H NMR spectrum (see Table 1) consistent with the structure of a symmetrical saturated bicyclic sulfoxide. Through the use of a γ-cyclodextrin GC column, **A** was found to be chiral, giving two closely spaced peaks of identical mass by GC−MS.[1f] Compound **B** gave a single broadened peak under these same conditions, consistent with it being achiral.

We propose that compounds **A** and **B** are stereoisomers of 2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide (Scheme 2; **10a**,**b** and **11a**−**d**), on the basis of an analysis of the spectral data and comparison of long-range ^1H NMR coupling constants with those in the related compound *endo*-2-bromo-5-thiabicyclo-[2.1.1]hexane (**12a**) and its *S*-oxides **12b**,**c** (see Table 1).[8] On



12 a n = 0
b n = 1
c n = 2

the basis of $Eu(fod)_3$ shift reagent and aromatic solvent induced shift studies, as well as mechanistic considerations (see below), we propose that **A** is (±)-(1α,2α,3β,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide (**10a**) rather than (±)-(1α,2α,3β,4α,5α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5-oxide (**10b**). Similarly, we propose that **B** is (1α,2α,3α,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5-oxide (**11a**).[9a] Definitive proof of the stereochemical assignment of **A** as **10a** and **B** as **11a** is given below. The spectroscopic and chromatographic properties of compounds **10a** and **11a** are identical to those of the two isomeric zwiebelanes isolated from extracts of freshly chopped onions[9b] and easily detected in these extracts by GC−MS and LC−MS analysis.[3d]

Scheme 2 depicts a possible mechanism for the formation of **10a** and **11a** from **7** via a sulfoxide-accelerated [3,3]-sigmatropic (dithia-Claisen) rearrangement[9d−f] followed by an intramolecular [2+2] cycloaddition reaction, as in the formation of **13** shown in Scheme 3.[10a] These mechanisms are discussed in detail elsewhere.[6] With regard to the sulfoxide stereochemistry in **10a** and **11a**, it should be noted that, upon oxidation of **13**, *endo*-sulfoxide **14a** predominates over *exo*-isomer **14b** and is the thermodynamic product as well.[10b,c] Furthermore, we have previously found the preferred conformation of 1,3-dithietane 1-oxide (**15b**) to be puckered, with oxygen having an equatorial

15b

orientation.[11] Both of these observations may reflect intramolecular interactions between the sulfur atoms which are possible only when the sulfoxide oxygen is exo to the 1,3-dithietane ring. Such sulfur−sulfur interactions should also be optimum in structures **10a** and **11a**/**11c**. Additional information on the nature and extent of intramolecular sulfur−sulfur interactions in structures related to **10a** and **11a** is presented elsewhere.[12a]

Natural Product Chemistry of 10a and 11a. A typical cryogenic GC−MS analysis of ether extracts of the juice of a white onion, prepared as described elsewhere,[3c,d] showed the following (data given as nanomoles of the compound per gram of juice): **3** (R = R′ = Me), 4.3; **3** (R = R′ = *n*-Pr), 13.0; **3** (R = Me, R′ = *n*-Pr), 4.3; **3** (R = *n*-Pr, R′ = Me), 7.1; **4**, 332; **5b**, 44.5; **5c**, 10 (estimated); **6b**, 34.5; **6c**, 32.5; **10a**, 5.0; **11a**, 16.0. From these data it is seen that (1) the sum **10a** + **11a** represents 12% of the sum of **3** + **5b**,**c** + **6b**,**c** + **10a** + **11a**, (2) LF **4** is ca. twice as abundant as the sum of the thiosulfinates and zwiebelanes,[12b,c] and (3) **11a** is ca. 3 times as abundant as **10a**. Similar results were obtained for yellow and red onion and for shallots (*Allium ascalonicum* auct.); somewhat lower amounts of **10a** and **11a** were found in scallions (*Allium fistulosum* L.),

(4) Dorsch, W.; Wagner, H.; Bayer, T.; Fessler, B.; Hein, G.; Ring, J.; Scheftner, P.; Sieber, W.; Strasser, T.; Weiss, E. *Biochem. Pharmacol.* **1988**, *37*, 4479.

(5) (a) Preliminary communication: Bayer, T.; Wagner, H.; Block, E.; Grisoni, S.; Zhao, S. H.; Neszmelyi, A. *J. Am. Chem. Soc.* **1989**, *111*, 3085. (b) This work is extracted in part from the Ph.D. Thesis of Mohan Thiruvazhi (SUNY−Albany, 1993).

(6) Block, E.; Bayer, T.; Naganathan, S.; Zhao, S.-H. *J. Am. Chem. Soc.* **1996**, *118*, 0000 (accompanying paper in this issue).

(7) Brandsma, L.; Schuijl, P. J. W. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 513.

(8) Block, E.; Naganathan, S. *J. Heteroatom Chem.* **1993**, *4*, 33.

(9) (a) According to the Cahn−Ingold−Prelog convention, **11b**, **11c**, and **11d** are named (1α,2α,3α,4α,5α)-, (1α,2β,3β,4α,5α)-, and (1α,2β,3β,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide, respectively. (b) Structures **A** and **B** were originally assigned (following LAOCOON NMR simulation but in the absence of IR data!) as *trans*- and *cis*-3,4-dimethyl-7-oxa-2,5-dithiabicyclo[4.1.0]heptane.[9c] (c) Bayer, T. Ph.D. Dissertation, University of Munich, 1988. (d) Block, E.; Ahmad, S. *J. Am. Chem. Soc.* **1985**, *107*, 6731. (e) Garigipati, R. S.; Cordova, R.; Parvez, M.; Weinreb, S. M. *Tetrahedron* **1986**, *42*, 2979. (f) Hwu, R.; Anderson, D. A. *Tetrahedron Lett.* **1986**, *27*, 4965.

(10) (a) Ishii, A.; Nakayama, J.; Ding, M.; Kotaka, N.; Hoshino, M. *J. Org. Chem.* **1990**, *55*, 242. (b) Ishii, A.; Ding, M.; Maeda, K.; Nakayama, J.; Hoshino, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3343. (c) Calculations indicate that *endo*-6,7-dithiabicyclo[3.1.1]heptane 6-oxide is more stable than the corresponding *exo*-isomer by 5.2 kcal/mol.[10d] (d) Ishii, A.; Jin, Y.-N.; Hoshino, M.; Nakayama, J. *J. Heteroatom Chem.* **1995**, *6*, 161.

(11) Block, E.; Corey, E. R.; Penn, R. E.; Renken, T. L.; Sherwin, P. F.; Bock, H.; Hirabayshi, T.; Mohmand, S.; Solouki, B. *J. Am. Chem. Soc.* **1982**, *104*, 3119.

(12) (a) Block, E.; Glass, R. S.; Thiruvazhi, M.; Toscano, P. J.; DeOrazio, R.; Lichtenberger, D. L.; Pollard, J. R.; Russell, E. E.; Schroeder, T. B., Submitted for publication. (b) Randle, W. M.; Block, E.; Littlejohn, M. H.; Putman, D.; Bussard, M. *J. Agric. Food Chem.* **1994**, *42*, 2085. (c) It is likely that our procedure significantly underestimates the amount of LF in onion extracts, which may be as much as 20 times higher than what we find: N. E. Schmidt, personal communication.

Table 1. ^{1}H and ^{13}C NMR Spectral Data for 2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane Derivatives and Related Compounds

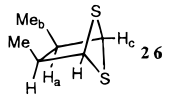
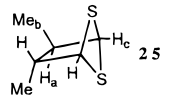
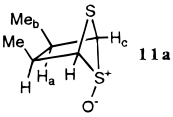
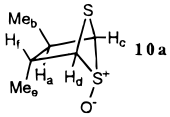
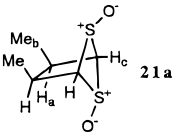
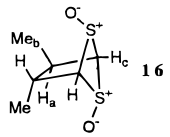
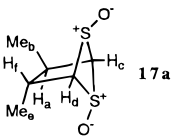
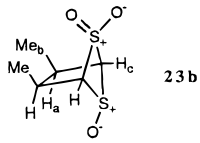
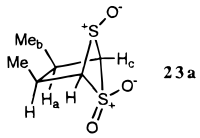
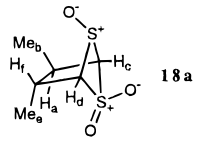
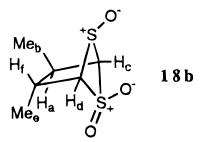
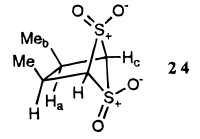
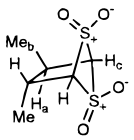
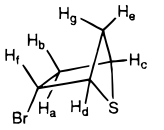
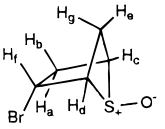
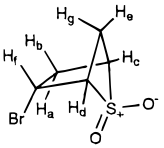
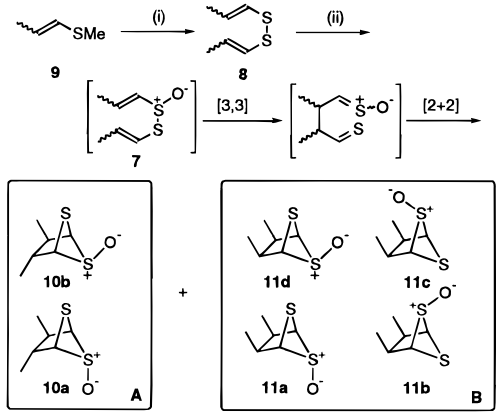
		^{1}H and ^{13}C chemical shifts					
compound	parameter[b]	a	b	c	d	e	f
 **26**	δ, ^{13}C	45.6	17.1	65.8			
	δ, ^{1}H ($CDCl_3$)	3.46	1.19	3.91			
 **25**	δ, ^{13}C	52.0	19.6	64.7			
	δ, ^{1}H ($CDCl_3$)	2.85	1.41	3.86			
	J_{HH}	ab 7					
	δ, ^{1}H (C_6D_6)	2.57	1.23	3.39			
	$\Delta\delta$	0.28	0.18	0.47			
 **11a**	δ, ^{13}C	33.3	12.6	79.5			
	δ, ^{1}H ($CDCl_3$)	2.95	1.15	4.12			
		ab 6.8					
		ac 0.3					
	δ, ^{1}H (C_6D_6)	2.60	0.65	3.15			
	$\Delta\delta$	0.35	0.5	0.97			
 **10a**	δ, ^{13}C	48.0	14.2	79.4	77.7	15.7	39.4
	δ, ^{1}H ($CDCl_3$)	2.85	1.37	4.25	4.21	1.45	2.33
	J_{HH}	ab 6.7		cd 6.7	df 1.1	ef 7.3	
		ac 0.9					
		af 4.0					
	δ, ^{1}H (C_6D_6)	2.55	0.94	3.42	3.34	1.26	1.74
	$\Delta\delta$	0.30	0.43	0.83	0.87	0.19	0.59
 **21a**	δ, ^{13}C	28.3	12.8	91.0			
	δ, ^{1}H ($CDCl_3$)	2.99	1.20	4.87			
	δ, ^{1}H (C_6D_6)	2.39	0.35	3.76			
	$\Delta\delta$	0.60	0.85	1.11			
 **16**	δ, ^{13}C	38.3	14.3	87.9			
	δ, ^{1}H ($CDCl_3$)	3.10	1.56	4.74			
	δ, ^{1}H (C_6D_6)	2.78	1.27	3.43			
	$\Delta\delta$	0.32	0.29	1.31			
 **17a**	δ, ^{13}C	35.8	15.2	91.7	88.8	16.9	37.1
	δ, ^{1}H ($CDCl_3$)	2.86	1.38	4.94	4.99	1.39	2.11
	J_{HH}	ab 6.1		cd 7.2	df 0.75	ef 6.1	
		ac 1.5					
		af 5.7					
	δ, ^{1}H (C_6D_6)	2.32	0.55	3.71	3.80	0.94	1.02
	$\Delta\delta$	0.54	0.83	1.23	1.19	0.45	1.09
 **23b**	δ, ^{13}C	28.7	11.0	95.8			
	δ, ^{1}H ($CDCl_3$)	3.11	1.47	4.66			
	δ, ^{1}H (C_6D_6)	2.43	0.88	3.20			
	$\Delta\delta$	0.68	0.59	1.46			
 **23a**	δ, ^{13}C	29.8	14.1	99.1			
	δ, ^{1}H ($CDCl_3$)	2.52	1.33	4.78			
	δ, ^{1}H (C_6D_6)	2.09	0.16	3.44			
	$\Delta\delta$	0.43	1.17	1.34			
 **18a**	δ, ^{13}C	39.3	14.4	94.5	96.1	14.0	36.3
	δ, ^{1}H ($CDCl_3$)	2.87	1.62	4.71	4.78	1.43	3.11
	J_{HH}	ab 5.6		cd 6.6		ef 5.6	
		ac 1.5					
		af 7.2					
	δ, ^{1}H (C_6D_6)	2.21	1.07	3.23	3.37	0.93	2.56
	$\Delta\delta$	0.66	0.55	1.48	1.41	0.50	0.55
 **18b**	δ, ^{13}C	35.3	17.8	98.4	98.4	16.5	33.2
	δ, ^{1}H ($CDCl_3$)	2.52	1.33	4.78	4.94	1.42	2.15
	J_{HH}	ab 7.2		cd 6.9	df 1.5	ef 7.2	
	δ, ^{1}H (C_6D_6)	1.69	0.32	3.54	3.64	0.75	0.84
	$\Delta\delta$	0.83	1.01	1.24	1.30	0.67	1.31
 **24**	δ, ^{13}C	32.5	11.1	93.0			
	δ, ^{1}H ($CDCl_3$)	3.54	1.46	4.35			
	δ, ^{1}H (C_6D_6)	2.55	0.71	2.59			
	$\Delta\delta$	0.99	0.75	1.76			

Table 1 (Continued)

compound	parameter[b]	^{1}H and ^{13}C chemical shifts a	b	c	d	e	f
 **19**	δ, ^{13}C	37.7	15.3	93.4			
	δ, ^{1}H ($CDCl_3$)	2.95	1.51	4.41			
	δ, ^{1}H (C_6D_6)	2.16	0.84	2.79			
	$\Delta\delta$	0.79	0.67	1.62			
 **12a**[a]	δ, ^{13}C	43.6[c]		54.6	62.4	49.0[c]	4.79
	δ, ^{1}H ($CDCl_3$)	2.53	2.87	3.80	3.89	3.09	4.79
	J_{HH}	ab 13	bc 1.7	cd 6.2	de 2.2	eg 7.5	
		ac 0.7	bf 7.3	ce 2.2	df 2.2		
		ae 2.2					
		af 2.2					
 **12b**[a]	δ, ^{13}C	22.8[c]		63.0	68.5	33.6[c]	41.3
	δ, ^{1}H ($CDCl_3$)	2.79	2.97	3.66	3.88	1.17	4.49
	J_{HH}	ab 13.4	bc 2.2	cd 6.1	dd 2.2	eg 12.3	
		ae 2.2	bf 7.8	cd 2.2	df 2.2		
		af 3.2					
 **12c**[a]	δ, ^{13}C	31.8[c]		72.0	78.5	33.6[c]	38.3
	δ, ^{1}H ($CDCl_3$)	2.65	2.76	3.98	4.14	2.76	4.49
	J_{HH}	ab 12.8	bf 10.7	cd 6.1	df 2.3	eg 12.8	
		ae 2.3		cd 2.3			
		af 4.6					

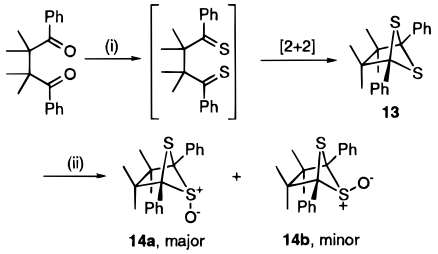
[a] Proton g in **12a**, **12b**, and **12c** appears at δ 1.88, 1.49, and 1.76 ppm, respectively. [b] $\Delta\delta$ refers to the difference in chemical shift in C_6D_6 and $CDCl_3$. [c] C_a refers to CH_aH_b; C_e refers to CH_eH_g; the other carbon atoms are identified by the unique letter of the attached hydrogen atom.

Scheme 2[a]



[a] (i) Li/NH_3; I_2/KI_3. (ii) CH_3CO_3H, 25 °C, 72 h.

Scheme 3[a]



[a] (i) Lawesson's reagent. (ii) *m*CPBA.

leeks (*Allium porrum* L.), and chives (*Allium schoenoprasum* L.).[3c] Zwiebelanes **10a** and **11a** are readily seen in supercritical carbon dioxide extracts of onion analyzed by both GC−MS and reversed-phase LC−MS using tandem MS (MS−MS) procedures.[13] Analysis of an onion extract by GC−MS using a γ-cyclodextrin GC column showed that natural zwiebelane **10a** occurs as a racemic mixture, as would be expected if **7** originates in cut onions from achiral **2d** (Scheme 1). While attempts to prepare an optically active sample of **10a** by asymmetric oxidation of *trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane (**26**)[12a] or di-1-propenyl disulfide (**8**) by the method of Kagan[14] were unsuccessful, an enantiomerically enriched sample of methanesulfinothioic acid *S*-methyl ester (MeS(O)SMe, **3**, R = R′ = Me),[14b] showed the same degree of enrichment on the chiral γ-cyclodextrin GC column as it did by NMR analysis. On this basis, we believe it likely that optically active **10a** would survive our GC analytical conditions.[14c]

To isolate **10a** and **11a**, onion bulbs were peeled, chopped, and, after ca. 30 min, squeezed to give onion juice, which was extracted with chloroform. The concentrated extract was then subjected (sequentially) to flash chromatography (C-18 silica gel, methanol; to remove triterpenes), chromatography on a Chromatotron (silica gel, chloroform), column chromatography (silica gel, 5:1 toluene/ethyl acetate), and finally HPLC (silica gel, 100:1 methylene chloride/acetone), affording **11a** together with lesser amounts of **10a**, and thiosulfinates **3**, **5b**,**c**, and **6b**,**c**, among other compounds.[4]

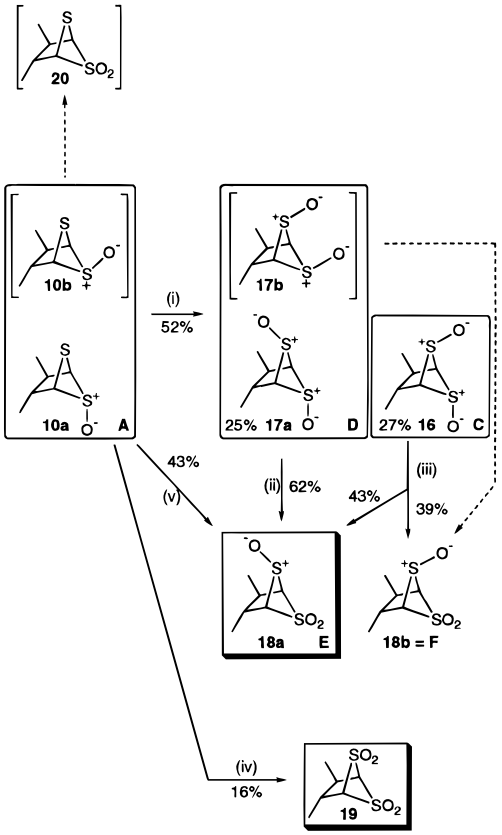
A mixture of **10a** and **11a** showed a 65−90% inhibition of thrombin-induced TXB_2 biosynthesis in human platelet rich plasma at a concentration of 0.1−1.0 mg/mL, similar to the level of inhibition by compounds **6b** and **6c**. However, in contrast to **6b** and **6c**, **11a** exerted no antiasthmatic activity (it altered neither PAF- nor ovalbumin-induced bronchial obstruction in animals at doses of 20 mg/kg).[4] Sensory testing indicates that **10a** has a green or raw onion and sweet sulfur taste with a 0.1 ppm threshold; **11a** imparts a sweet or brown sauté taste with liver and hydrogen sulfide notes with a 0.5 ppm threshold.[12b]

Further *S*-Oxidation of 2,3-Dimethyl-5,6-dithiabicyclo-[2.1.1]hexane *S*-Oxides A and B and Proof of Their Stereochemistry as 10a and 11a, Respectively. Because of the potential ambiguity associated with the assignment of the

(13) (a) Calvey, E. M.; Matusik, J. E.; Block, E.; Littlejohn, M. H. *Proceedings of the 41st Conference on Mass Spectrometry*, San Francisco, CA, May 1993; p 314. (b) Calvey, E. M.; Matusik, J. E.; Block, E.; Littlejohn, M. H. *Proceedings of the 1993 National Onion Research Conference*, Ithaca, NY, December 1993, p 103.

(14) (a) Pitchen, P.; Deshmukh, M.; Dunach, E.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188. (b) Nemecek, E.; Dunach, E.; Kagan, H. B. *New J. Chem.* **1986**, *10*, 761. (c) While **10a** and its reduction and oxidation products are all racemates, for convenience we have arbitrarily chosen to display these structures in one enantiomeric form.

Scheme 4[a]



[a] (i) *m*CPBA. (ii) excess CH_3CO_3H, 46 °C, 14 h. (iii) same but 45−50 °C, 24 h. (iv) same, but 55 °C, 3 days. (v) 3.4 equiv of CH_3CO_3H, 25 °C, 4 days.

stereochemistry of **A** and **B** by NMR methods, we sought an alternative approach based on X-ray crystallography.

A. *trans*-Series. Oxidation (CH_3CO_3H or *m*CPBA) of **A** affords two isomeric crystalline compounds, **C** and **D**, of formula $C_6H_{10}O_2S_2$. The former compound (mp 126 °C) has an IR band at 1067 cm^{-1} consistent with the presence of sulfoxide groups, six ^{13}C NMR bands (δ 91.7, 88.8, 37.1, 35.8 (all CH) and 16.9, 15.2 (CH_3), and a well-resolved ^1H NMR spectrum with six different resonances (see Table 1). The only unsymmetrical bissulfoxide possible from monooxidation of either **10a** or **10b** is (±)-(1α,2α,3β,4α,5α,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (**16**), the structure assigned to isomer **C** (Scheme 4).

Compound **D** (mp 162−163 °C) shows a strong IR band at 1046 cm^{-1} consistent with the presence of sulfoxide groups, three ^{13}C NMR bands (δ 87.9, 38.3 (CH) and 14.3 (CH_3)), and an ^1H NMR spectrum with three different resonances (see Table 1). Two symmetrical *trans*-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5,6-dioxides are possible, namely, the (±)-(1α,2α,3β,4α,5β,6α) and (±)-(1α,2α,3β,4α,5α,6β) isomers **17a** and **17b**, respectively. In **17a** the oxygens are both endo while in **17b** the oxygens are both exo. Compound **D** was found to be less polar than **C** (**16**), e.g., as shown by the respective TLC R_f values (in 16% EtOAc−CH_2Cl_2) of 0.31 and 0.56. Since the anticipated order of polarities should be **17b** > **16** > **17a**, we suspected that **D** had structure **17a**. Unfortunately, despite considerable effort, we were unable to prepare X-ray quality crystals of compound **D** to confirm this suspicion.

We therefore investigated the products from further oxidation of compound **D**. Treatment of **D** with peracetic acid at 46 °C for 14 h afforded a new compound, **E** (mp 152 °C), of formula $C_6H_{10}O_3S_2$, showing strong IR bands at 1317, 1149, and 1079 cm^{-1} consistent with the presence of both sulfoxide and sulfone groups, six ^{13}C NMR bands (δ 96.1, 94.5, 39.3, 36.3 (all CH) and 14.4, 14.0 (CH_3)), and a ^1H NMR spectrum with six different resonances (see Table 1). Single-crystal X-ray diffraction established the structure of **E** to be (±)-(1α,2α,3β,4α,5α,5β,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,5,6-trioxide (**18a**), with an *endo*-sulfinyl oxygen, rather than (±)-(1α,2α,3β,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5,5,6-trioxide (**18b**), with an *exo*-sulfinyl oxygen (Figure 1).[15a] *It therefore follows that compound **D** must have structure **17a**, with an endo sulfinyl oxygen [(±)-(1α,2α,3β,4α,5β,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,6-dioxide] and that compound **A** must have structure **10a** [(±)-(1α,2α,3β,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5-oxide], also with an endo-sulfinyl oxygen.*

To complete our characterization of the *S*-oxides of (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane, compound **16** was treated with peracetic acid at 45−50 °C for 24 h, giving a mixture of **18a** (43%) and a new compound, **F** (39%; mp 150−

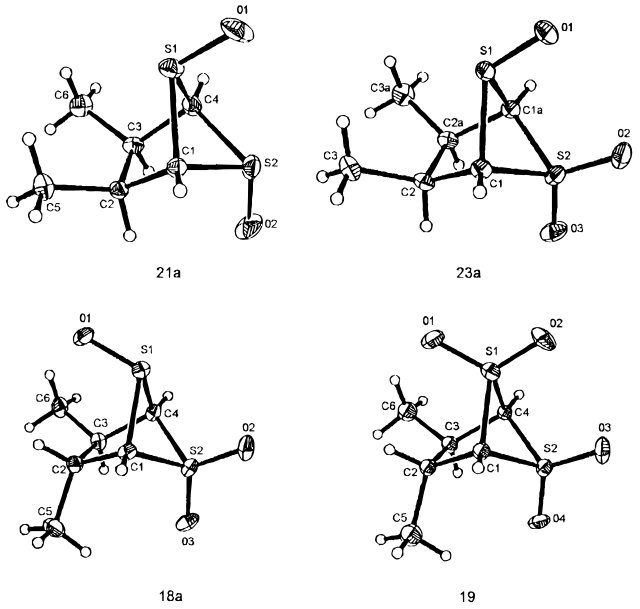


Figure 1. X-ray structures of (±)-(1α,2α,3β,4α,6α)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**18a**),[15a] (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide (**19**), (1α,2α,3α,4α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (**21a**), (1α,2α,3α,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5,5,6-trioxide (**23a**). Representative bond distances (Å) and angles (deg): (**18a**) C−S(O) (average), 1.870(3); C−SO_2 (average), 1.806(3); sulfoxide S−O, 1.456(2); sulfone average S−O, 1.431(3); sulfoxide C−S−C, 75.8(1); sulfone C−S−C, 79.0(1), O−S−O, 117.9-(2); (**19**) C−SO_2 (average), 1.82(1); S−O (average), 1.42(7); C−S−C (average), 78.1(4); O−S−O (av), 118.3(4); (**21a**) *endo*-C−S(O) (average), 1.836(4); *exo*-C−S(O) (average), 1.837(4); *endo*- and *exo*-S−O, 1.483(3); *endo*-sulfoxide C−S−C, 74.2(1); *exo*-sulfoxide C−S−C, 74.1(2); (**23a**) C−S(O), 1.868(2); C−SO_2, 1.792(2); sulfoxide S−O, 1.479(3); sulfone average S−O, 1.438(3); sulfoxide C−S−C, 74.4(1); sulfone C−S−C, 78.1(1), O−S−O, 118.0(1).

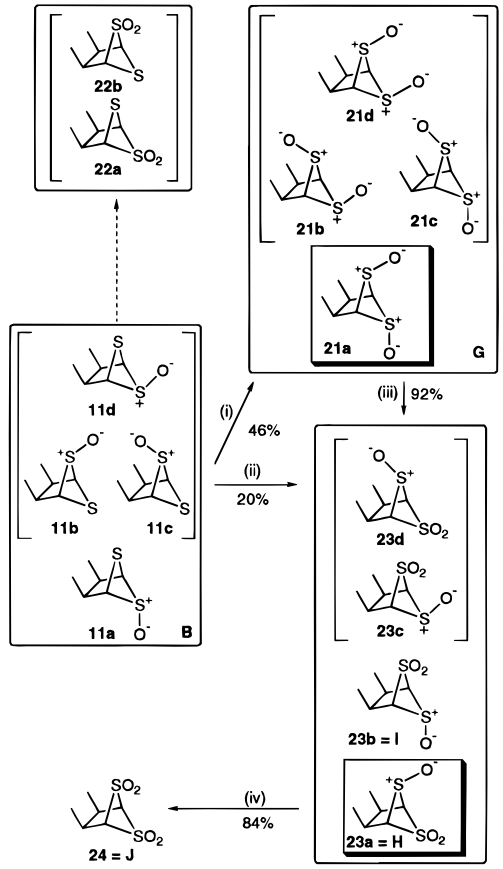
(15) (a) Bissulfone **19** (see below) cocrystallized at the same crystallographic sites as **18a**. The extra oxygen was modeled as having one-third the occupancy of the other atoms, which implies that the lattice sites had an occupancy ratio of two molecules of **18a** for every molecule of **19**, in agreement with the NMR spectroscopy for the crystals. As a consequence, the bond angles and bond lengths for **18a** may be less accurate than for the other structures in this paper. (b) For comparison, 2,2,5,5-tetramethyl-2,5-disila-7,8-dithiabicyclo[4.1.1]octane 7,7,8,8-tetraoxide shows very strong IR bands at 1328 and 1172 cm^{-1} and a ^{13}C NMR band (δ 96.6) for the bridgehead carbon atoms.[15c] (c) Frasch, M.; Sundermeyer, W. *Chem. Ber.* **1993**, *126*, 537. (d) Block, E.; DeOrazio, R.; Thiruvazhi, M. *J. Org. Chem.* **1994**, *59*, 2273.

153 °C dec), of formula $C_6H_{10}O_3S_2$, showing strong IR bands at 1310, 1195, 1120, and 1095 cm^{-1}, consistent with the presence of both sulfoxide and sulfone groups, six ^{13}C NMR bands (δ 98.4 (2CH), 35.2, 33.2 (all CH), and 17.8, 16.5 (CH_3)), and a ^1H NMR spectrum with six different resonances (see Table 1). Because of the degeneracy in the ^{13}C NMR spectrum, NMR assignments were clarified by HETCOR experiments. Compound **F** is assigned the structure **18b**. Finally, treatment of **10a** with excess peracetic acid in the presence of Na_2CO_3 (25 °C, 34 h; 55 °C, 3 days) gave a new compound, **19** (16%; mp 196 °C), of formula $C_6H_{10}O_4S_2$, showing strong IR bands at 1337 and 1170 cm^{-1}, consistent with the presence of sulfone groups, three ^{13}C NMR bands (δ 93.4, 37.7 (CH) and 15.3 (CH_3)), and a ^1H NMR spectrum with three different resonances (see Table 1). The identification of **19** as (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide was confirmed by single-crystal X-ray diffraction (Figure 1).[15b] Attempts were made to prepare one of the remaining unknown *S*-oxides of (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane, namely, (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,5-dioxide (**20**). However, neither treatment of **10a** with $KMnO_4$ itself, $KMnO_4/FeCl_3 \cdot 6H_2O$, or $KMnO_4/Zn(OAc)_2 \cdot 2H_2O$, (conditions previously shown by us to effect oxidation of sulfoxides to sulfones in the presence of sulfides)[11,15d] nor reduction of **14** with $LiAlH_4$ at −30 °C, $BH_3 \cdot THF$,[11] or Zn/(TMS)Cl[16] gave any indication of the formation of **20**.

B. *cis*-Series. In parallel with our study of the oxidation of **A**, now shown to have structure **10a**, we also sought by similar means to define the stereochemistry of *cis*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane *S*-oxide **(B)**. However, in contrast to the case of **10a** where the presence of a C_2 symmetry axis in bissulfoxide **17a** allowed the structure proof to rest on a single X-ray crystal structure (**18a**), the structure proof for **B** requires two X-ray structures, e.g., either of two of four possible bissulfoxides **21a**−**d**, or of one of these bissulfoxides along with a sulfone−sulfide (**22a** or **22b**; Scheme 5). Oxidation of **B** with 1 equivalent of *m*CPBA gave a single new compound, **G** (46%; mp 147−150 °C), of formula $C_6H_{10}O_2S_2$, showing strong IR bands at 1091 and 1072 cm^{-1} consistent with the presence of sulfoxide groups, three ^{13}C NMR bands (δ 91.0, 28.3 (CH) and 12.8 (CH_3)), and a ^1H NMR spectrum with three different resonances (see Table 1). No other new *S*-oxides were detected by ^1H NMR spectroscopic analysis of the crude product. Single-crystal X-ray diffraction established the structure of **G** to be (1α,2α,3α,4α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,6-dioxide (**21a**; Figure 1). The identification of the monooxidation product of **B** as **21a** limits the possible structure of **B** to **11a** or **11b**. For reasons addressed below, structure **11a** is favored.

In the absence of formation of a second bissulfoxide from **B** with either *m*CPBA or peracetic acid, we turned our attention toward synthesis of sulfone−sulfide **22a** or **22b**.[17,18] However, treatment of **B** with $KMnO_4$ itself, $KMnO_4/FeCl_3 \cdot 6H_2O$, $KMnO_4/Zn(OAc)_2 \cdot 2H_2O$,[11,15d] or potassium superoxide gave no indication of the formation of **22a**,**b**. Oxidation of **21a** with excess peracetic acid at 50 °C for 5 h gave three new compounds, **H**, **I**, and **J**, in a ratio of 24:12.5:1. Compound **H** (mp 182−186 °C), of formula $C_6H_{10}O_3S_2$, showed strong IR bands at 1317, 1149, and 1080 cm^{-1}, consistent with the presence of both sulfone and sulfoxide groups, three ^{13}C NMR bands (δ 99.1, 29.8 (CH) and 14.1 (CH_3)), and a ^1H NMR spectrum with three different resonances (see Table 1). X-ray diffraction showed the structure of **H** to be (1α,2α,3α,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**23a**; Figure 1). Compound **I** (mp 162−164 °C), also of formula $C_6H_{10}O_3S_2$, showed strong IR bands at 1308, 1143, and 1079 cm^{-1}, consistent with the presence of both sulfone and sulfoxide groups, three ^{13}C NMR bands (δ 95.8, 28.7 (CH) and 11.0 (CH_3)), and a ^1H NMR spectrum with three different resonances (see Table 1).

Scheme 5[a]



[a] (i) *m*CPBA. (ii) excess CH_3CO_3H, 25 °C, 72 h. (iii) same but 50 °C, 5 h. (iv) same but 65 °C, 36 h.

Since **I** and **H**, the latter now characterized as **23a**, are isomeric and are both derived from the same precursor, **21a**, compound **I** must have the structure (1α,2β,3β,4α,5α,5β,6β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-trioxide (**23b**). Compound **J**, identical with the compound formed by treatment of **21a** with excess peracetic acid at 50 °C for 5 h and at 65 °C for 36 h (84% yield; mp 192−194 °C), is a colorless solid of formula $C_6H_{10}O_4S_2$, showing strong IR bands at 1335, 1200, and 1170 cm^{-1}, consistent with the presence of sulfone groups, three ^{13}C NMR bands (δ 93.0, 32.5 (CH) and 11.1 (CH_3)), and a ^1H NMR spectrum with three different resonances (see Table 1), and was identified as *cis*-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5,5,6,6-tetraoxide (**24**). Attempts to obtain the other possible bissulfoxide and/or sulfone−sulfide from **B** failed, even under forcing conditions. For example, oxidation of **B** with peracetic acid (3.3 equiv) at room temperature for 3 days gave **21a**, **23a,** and **23b**, in 13%, 13%, and 7% yields, respectively, as the only isolable products. We further find that oxidation of **21a** first gives **23a** and then **23b**. On the basis of the structure of **23a**, it appears that oxidation of bissulfoxide

(16) Schmitt, A. H.; Russ, M. *Chem. Ber.* **1981**, *114*, 822.

(17) Named as (1α,2β,3β,4α,5α,5β)- and (1α,2α,3α,4α,5α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5-dioxide (**22a** and **22b**, respectively).

(18) (a) Nicolaou, K. C.; DeFrees, S. A.; Hwang, C.-K.; Stylianides, N.; Carroll, P. J.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 3029. (b) Ishii, A.; Akazawa, T.; Maruta, T.; Nakayama, J.; Hoshino, M.; Shiro, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 777. (c) Ishii, A.; Jin, Y.-N.; Nagaya, H.; Hoshino, M.; Nakayama, J. *Tetrahedron Lett.* **1995**, *36*, 1867.

21a occurs fastest with the oxidant approaching from the *exo*-direction on the sulfur furthest from the vicinal methyl groups; *endo*-oxidation of the sulfur atom closer to the methyl groups is slower due to steric hindrance posed by the methyl groups.

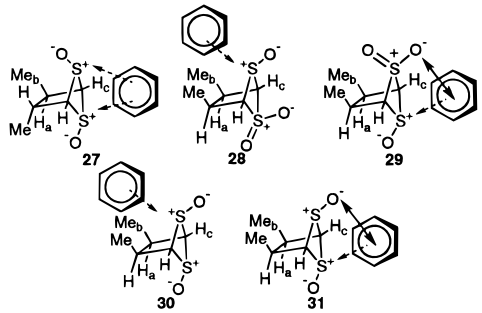
Comparative Structural and Spectroscopic Studies on 5,6-Dithiabicyclo[2.1.1]hexane Derivatives. Comparative X-ray Structural and NMR and IR Spectroscopic Data. The X-ray structures of **18a**, **19**, **21a**, and **23a** indicate the following: (1) The 1,3-dithietane rings possess angles between the two CSC planes of 51.2−56°. The highly puckered CSCS rings in these bicyclic 1,3-dithietanes contrast with the smaller puckering angle (39.3°) in 1,3-dithietane 1-oxide (**15b**) and with the near planar structure of 1,3-dithietane and its 1,1,3,3-tetraoxide (**15a** and **15c**). (2) While the S···S nonbonded distances (Å) in **21a**

15 a n = n' = 0
b n = 1, n' = 0
c n = n' = 2

(2.600(3)), **23a** (2.596), **15b** (2.600), and **15c** (2.590) are comparable, the analogous distances in **18a** (2.533(2)) and **19** (2.530(4)) are slightly shorter. An even shorter S···S nonbonded distance of 2.497 Å is found in 2,2,3,3-tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]hexane *endo*-*S*-oxide (**14a**).[10b] The bridgehead−bridgehead 2.214−2.296 Å C···C distances in the bicyclic 1,3-dithietanes are shorter than those in **15b** (2.37(2) Å) and **15c** (2.524(4) Å). (3) The C−S(O) distances in trioxides **18a** (average 1.837 Å/1.870 Å) and **23a** (1.868 Å) are longer than the C−SO_2 distances in **18a** (average 1.806 Å), **19** (1.82 Å), and **23a** (1.792 Å), while the C−S distance in **13** is intermediate in value (1.850 Å) (see Figure 1).

Table 1 gives NMR data for various 2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane derivatives. The ^{1}H NMR peak assignments for **10a** and **11a** were facilitated by LAOCOON III analyses of these 10 spin systems and by examination of the shifts induced by Eu(fod)$_3$ and benzene-d_6.[5] With added Eu(fod)$_3$ the 2.95 ppm peak of **11a** shows a much greater change than the 1.15 ppm CH_3 peak; similarly with **10a**, the 1.45 ppm CH_3 doublet and the 2.85 ppm multiplet show significantly larger changes than the 1.37 ppm CH_3 doublet and the 2.33 ppm multiplet.[19] The Eu(fod)$_3$ shifts are consistent with protons H_a in **11a** and H_a and Me_e in **10a** being close to the sulfoxide oxygen and H_f and Me_b in **10a** being more remote. Benzene-d_6 causes a reversal of the effect with **10a**: the shifts ($\Delta\delta$; Table 1) for Me_b and H_f, which are remote from the sulfoxide oxygen, are double the shifts experienced by the more proximate Me_e and H_a.[19b]

Proton chemical shifts for all of the compounds in Table 1 with the exception of *cis*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]-hexane (**26**)[20] were determined in C_6D_6 as well as in $CDCl_3$. As might be expected, effects ($\Delta\delta$) were small in bissulfide (±)-*trans*-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane (**25**)[20] and considerably larger in bissulfones **19** and **24**, with all protons experiencing a substantial upfield shift. Symmetrical bissulfoxide **16** showed a substantial upfield shift for the bridgehead protons but small effects for the other positions, consistent with interaction with benzene occurring remote from the two-carbon bridge with the orientation shown in **27** for the collision complex. Comparison of *cis*-dimethyl *endo*-sulfoxide−sulfone **23b** with *cis*-dimethyl *exo*-sulfoxide sulfone **23a** shows that, in **23a**, protons b are more strongly shifted than protons a. In the former compound, the overall extent of shielding is diminished and the order is reversed. This observation is consistent with the collision complexes shown in **28** and **29** in which the benzene ring is further from protons a and b in **29** compared to **28**. The reversal in the shielding effect of benzene on protons in **10a** and **23b** may be attributable to the presence of the sulfonyl group in the latter but not the former compound. The effect of benzene on the shifts in bissulfoxides **21a** and **17a** is clear: benzene is closer to protons b and, in **17a**, f, avoiding repulsive interactions on the opposite face of the ring with the sulfoxide oxygen (**30**, **31**). The above NMR data are also most consistent with compound **B**, Scheme 2, having structure **11a** rather than **11b** (e.g., compare benzene-d_6 data for **11a** with those for **17a**, **18a**, and **18b**).



The S═O IR bands (cm^{-1}) for compounds **10a** (1081), **11a** (1065, 1090), **16** (1046), **17a** (1067), **21a** (1072, 1091), **18a**,**b** (1079; 1095), and **23a**,**b** (1080; 1079), like the analogous values for 1,3-dithietane 1-oxide (**15b**; 1035, 1080), *cis*- and *trans*-1,3-dithietane 1,3-dioxides (1100, 1062; 1059), and 1,3-dithietane 1,1,3-trioxide (1085),[11] often lie outside the standard range of 1015−1061, presumably due to proximity effects. Similar effects were seen with **14a** (1077 cm^{-1}/1083 cm^{-1}) and **14b** (1096 cm^{-1}) (Scheme 3); stabilizing S···S interactions are invoked in **14a**.[10b] The lower frequency S−O band in *exo*-*endo* **16** (1046) compared to that in *endo*-*endo*-**17a** (1067) parallels results seen in bissulfoxides of **13** (bands at 1080 for the *exo*−*endo*- and 1100 cm^{-1} for the *exo*−*exo*-compounds).[10b] The sulfonyl bands for **18a**,**b**, **19**, **23a**,**b**, **24**, and related compounds[10b] lie within the normal ranges of 1110−1170 and 1290−1370 cm^{-1}.

Experimental Section

General Procedures. Reactions involving air-sensitive materials were carried out under dry nitrogen. NMR spectra were recorded in $CDCl_3$ on a Varian Gemini spectrometer operating at 300 MHz for proton and 75.1 MHz for carbon; chemical shifts (δ) are indicated in parts per million downfield from tetramethylsilane. Acetonitrile and dichloromethane were distilled from calcium hydride, diethyl ether and THF were distilled (under nitrogen) from sodium−benzophenone ketyl, hexanes were fractionally distilled (65−70 °C fraction used), and ethyl acetate was distilled before use. Anhydrous $MgSO_4$ was employed as the drying agent. Analytical TLC was performed on precoated silica gel plates (Art. No. 5715, Merck) with a 254 nm fluorescent indicator and was visualized with a *p*-anisaldehyde solution (18.5 mL of *p*-anisaldehyde, 25 mL of concentrated H_2SO_4, 7.5 mL of acetic acid, and 675 mL of ethanol). GC−MS data were collected using a Hewlett-Packard 5898 mass spectrometer ("MS Engine") interfaced to a dual-column Hewlett-Packard 5890 II GC with a programmable on-column injector and cryogenic cooling (CO_2) using a 30 m x 0.53 mm *i.d.* HP-1 (cross-linked methyl silicone gum) column with 99.995% helium as a carrier gas. The temperature profiles employed were as follows: 0−200 °C, 5 °C/min, injector under oven tracking control, transfer line at 100 °C, and a column head pressure of 5 psi. The MS source and

(19) For related work, see: (a) Juaristi, E.; Cruz-Sanchez, J. S.; Petsom, A.; Glass, R. S. *Tetrahedron* **1988**, *44*, 5653. (b) Block, E.; Wall, A. *J. Org. Chem.* **1987**, *52*, 809.

(20) (a) The preparation and unusual properties of **25** and **26** will be described elsewhere.[12a] The ^{1}H and ^{13}C NMR chemical shifts for **25** and **26** are included in Table 1 for completeness.

quadrupole magnet temperatures were maintained at 200 and 100 °C, respectively. Chiral separations were achieved using a γ-cyclodextrin capillary GC column (Advanced Separation Technologies Inc., "Chiraldex" G-PN 30 m × 0.32 mm) under the above GC−MS conditions.

Methyl (*E,Z*)-1-Propenyl Sulfide (9). Allyl methyl sulfide (66.0 g, 0.75 mol) in dimethyl sulfoxide (30.0 mL) was added dropwise to a mixture of potassium *tert*-butoxide (37.0 g, 0.3 mol) in dimethyl sulfoxide (120 mL), under argon. The dark brown mixture was stirred at 45 °C for 1 h and at room temperature for 24 h. The solution was poured into ice−water (300 mL), the aqueous portion was extracted with pentane (2 × 150 mL), and the pentane was removed by distillation. Further distillation gave the title compound **9** as a clear, foul-smelling liquid (48.6 g, 74%): bp 99−104 °C; ^{1}H NMR ($CDCl_3$) δ 6.1 (dq, 1 H), 5.7 (dq, 1 H), 5.5−6.2 (m, 2 H), 2.39 (s, 3 H), 2.33 (s, 3 H), 1.79 (m, 3 H), 1.76 (q, 3 H).

Di-1-propenyl Disulfide ((*E,E*)-, (*E,Z*)-, and (*Z,Z*)-8).[7] A solution of methyl (*E,Z*)-1-propenyl sulfide (**9** 11.4 g, 0.14 mol) in dry ether (100 mL) was added to a −80 °C blue solution prepared by reacting lithium (1.80 g, 0.26 mol) with liquid ammonia (200 mL). After 1.5 h, the mixture was warmed to room temperature stirred overnight to remove ammonia, and the residue was diluted with ether (100 mL) and water (100 mL), cooled to 0 °C, and treated with a solution of iodine (30 g) and catalytic KI in water. Excess iodine was added, if necessary, to maintain a brown-black color. After dilution with ether (100 mL) the aqueous layer was separated and extracted once with ether (100 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$ solution (3 × 50 mL) and water (50 mL). The organic layer was then separated, dried, filtered, and concentrated to yield a dark brown oil which was purified by flash column chromatography (silica gel, pentane; $R_f = 0.6$) to afford **8** (4.14 g, 41% yield) as a 1:2:1 mixture of isomers: ^{1}H NMR ($CDCl_3$) δ 6.29−5.53 (m, 4 H), 1.95−1.61 (m, 6 H); ^{13}C NMR δ 130.62, 128.72, 128.06, 124.79, 124.49, 18.11, 18.06, 14.37, 14.35; GC−MS (EI) *m/z* (rel intens) 146 (M^+).

(±)-(1α,2α,3*β*,4α,5*β*)- and (1α,2α,3α,4α,5*β*)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-Oxide (10a and 11a). A solution of peracetic acid in acetic acid[21] (35%; 2.6 g, 12.1 mmol) was added to a solution of mixed isomers of **8** (1:2:1; 3.2 g, 21.9 mmol) in CH_2Cl_2 (320 mL) and Na_2CO_3 (4.7 g, 43.8 mmol) at −70 °C. After 1 h at −70 °C the solution was warmed to −20 °C. Additional peracetic acid was added (2.6 g, 12.1 mmol), and the reaction mixture was kept at −20 °C for 1 h. The cooling bath was removed, and the reaction mixture was warmed to 0 °C during the course of 1 h. The mixture was then stirred at −78 °C for 18 h, warmed to room temperature, and washed successively with $NaHSO_3$ (2 × 60 mL) and $NaHCO_3$ (2 × 60 mL). The organic layer was dried, filtered, and concentrated to yield a residue which was *immediately* purified by flash column chromatography (30% EtOAc/hexanes) to give compounds **10a** (343 mg, 10%) and **11a** (375 mg, 11%).

Compound **10a** is a colorless, low melting solid with a fresh onion aroma: ^{1}H NMR ($CDCl_3$) δ 4.25 (dd, J = 6.7, 0.8,[22] 1 H, CHS_2), 4.21 (dd, J = 6.7, 1.0 Hz,[22] 1 H, CHS_2), 2.85 (qdd, J = 6.8, 4.0, 1.1 Hz,[22] 1 H, C*H*CH_3), 2.33 (qdd, J = 7.3, 4.0, 1.1 Hz,[22] 1 H, C*H*CH_3), 1.45 (d, J = 7.3 Hz,[22] 3 H, CH_3), 1.37 (d, J = 6.8 Hz,[22] 3 H, CH_3); ^{1}H NMR (C_6D_6) δ 3.42, 3.34 (AB, J_{AB} = 6.9 Hz, 2 H), 2.55 (qdd, J = 6.8, 3.8, 1.2 Hz, 1 H), 1.74 (m, 1 H), 1.26 (d, J = 7.3 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 79.4, 77.7, 48.0, 39.4 (CH) and 15.7, 14.2 (CH_3); MS (EI GC−MS) *m/z* (rel intens) 162 (M^+, 1), 130 (1), 116 (1), 115 (6), 114 (16), 113 (100), 99 (94), 97 (29), 85 (16), 79 (31), 77 (18), 74 (12), 73 (17), 72 (16), 71 (38), 69 (23), 67 (14), 65 (33), 64 (12), 59 (35), 58 (27), 57 (15), 55 (20), 53 (37); MS (NH_3, CI) *m/z* (rel intens) 180 (M + NH_4), 163 (M + H^+); IR 1122, 1082 cm^{-1} (vs, S═O); UV. GC−MS analysis on a β-cyclodextrin capillary column ("Chiraldex" G-PN, 30 m × 0.32 mm) showed a pair of peaks of equal area of retention times 28.36 and 29.19 min at a column temperature of 120 °C, each with a MS pattern characteristic of **10a**. From these retention times and the retained volume for the air peak under these conditions of 1.37 min, k_1 = 19.75, k_2 = 20.35, and α = 1.03.

Compound **11a** ((1α,2α,3α,4α,5*β*)-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5-oxide) is a colorless oil with a fresh onion aroma: IR 1065, 1085 cm^{-1} (S═O); UV λ_{max} 250 nm; ^{1}H NMR ($CDCl_3$) δ 4.12 (s 2 H, CHS_2), 2.95 (sextet, J = 6.8, 0.3 Hz,[22] 2 H, C*H*CH_3), 1.15 (dm, J = 6.8 Hz,[22] 6 H, CH_3); ^{1}H NMR (C_6D_6) δ 3.15 (s, 2 H), 2.60 (m, 2 H), 0.65 (dm, J = 6.9 Hz, 6 H); ^{13}C NMR δ 79.5 (CH), 33.3 (CH), 12.6 (CH_3); MS (EI GC−MS) *m/z* (rel intens) 162 (M^+, 1), 130 (1), 116 (1), 115 (4), 114 (19), 113 (65), 99 (100), 97 (21), 85 (12), 79 (18), 77 (10), 74 (10), 73 (17), 72 (13), 71 (32), 69 (16), 65 (27), 59 (26), 58 (23), 57 (11), 55 (12), 53 (29); MS (NH_3, CI) *m/e* 180 (M + NH_4), 163 (M + H^+). Anal. Calcd for $C_6H_{10}OS_2$: C, 44.4; H, 6.2; O, 9.9; S, 39.5. Found: C, 44.5; H, 6.1; O, 9.3; S, 38.2. GC−MS analysis on a β-cyclodextrin capillary column ("Chiraldex" G-PN 30 m × 0.32 mm) showed a single peak of retention time 45 min at a column temperature of 120 °C with a MS pattern characteristic of **11a**.

C. From Onion. Onion bulbs were peeled, chopped, and, after 30 min, squeezed to give onion juice, which was extracted with $CHCl_3$. The concentrated extract was then subjected sequentially to flash chromatography (C-18 silica gel, methanol to remove triterpenes), chromatography on a Chromatotron (silica gel, $CHCl_3$), column chromatography (silica gel, 5:1 toluene−ethyl acetate), and finally HPLC (silica gel, 100:1 CH_2Cl_2−acetone), affording **10a** and **11a**, among other compounds.

(±)-(1α,2α,3*β*,4α,5α,6α)- and (±)-(1α,2α,3*β*,4α,5*β*,6α)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,6-dioxide (16 and 17a). A solution of (±)-(1α,2α,3*β*,4α,5*β*,6*β*)-2,3-dimethyl-5,6-dithiabicyclo-[2.1.1]hexane 5-oxide (**10a**; 56 mg, 0.34 mmol) in CH_2Cl_2 (3 mL) was treated at −25 °C with *m*CPBA (100%, 63 mg, 0.37 mmol) in CH_2Cl_2 (5 mL), and the solution was warmed to 10 °C during 2 h. Additional CH_2Cl_2 (10 mL) was added, the mixture was washed successively with saturated $NaHSO_3$ (10 mL) and $NaHCO_3$ (15 mL), and the organic layer was separated, dried (Na_2SO_4), filtered, and concentrated, affording crude product (61 mg) which was chromatographed (silica gel, 16% EtOAc−CH_2Cl_2), giving **16** (R_f 0.56; 17 mg, 27%) and **17a** (R_f 0.31; 15 mg, 25%). Data for **16**: mp 162−163 °C dec, ^{1}H NMR ($CDCl_3$) δ 4.74 (s, 2 H), 3.10 (m, 2 H), 1.56 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 87.85, 38.27, 14.34; IR (KBr) 1046 (s) cm^{-1}. Anal. Calcd for $C_6H_{10}O_2S_2$: 40.42; H, 5.66. Found: C, 40.54; H, 5.73. Data for **17a**: mp 126 °C dec, ^{1}H NMR ($CDCl_3$) δ 4.99 (dd, J = 7.2, 0.75 Hz, 1 H), 4.94 (dd, J = 7.2, 1.5 Hz, 1 H), 2.86 (ddq, J = 6.1, 5.7, 1.5 Hz, 1 H), 2.11 (ddq, J = 6.1, 5.7, 0.75 Hz, 1 H), 1.39 (d, J = 6.1 Hz, 3 H), 1.38 (d, J = 6.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 91.72, 88.77, 37.10, 35.82, 16.89, 15.24; IR (KBr) 1067 (s) cm^{-1}. Anal. Calcd for $C_6H_{10}O_2S_2$: 40.42; H, 5.66. Found: C, 40.63; H, 5.53.

The ^{1}H NMR spectral assignments for **17a** were arrived at by comparison with data for **16**. The resonances at δ 2.86 and 2.11 ppm for **17a** were assigned to H_a and H_f, respectively, assuming that H_f experiences the greater chemical shift difference ($\Delta\delta_f = -0.99$ ppm) than H_a ($\Delta\delta_a = -0.24$ ppm) when compared to those of **16**. A decoupling experiment completed the ^{1}H NMR spectral assignment for **17a**. Irradiation at 2.86 ppm collapsed the peaks at 4.94 ppm (dd) and 1.38 ppm (d) to a doublet (J_{cd} = 7.2 Hz) and a singlet, respectively. Therefore, the resonances at 4.94 and 1.38 ppm (J_{ab} = 6.9 Hz) were assigned to H_c and Me_b, respectively. In a similar manner, the assignments for H_d, H_e, and Me_f were made. The ^{13}C NMR assignments for **17a** were deduced from HETCOR experiments.

(±)-(1α,2α,3*β*,4α,5α,5*β*,6α)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,5,6-Trioxide (18a). From **17a**. A solution of **17a** (25 mg, 0.14 mmol) in acetic acid (1 mL) was treated with 3 drops of peracetic acid (35%) and kept in an oven at 46 °C for 14 h. Dilution of the solution with EtOAc and washing with $NaHCO_3$ yielded the title compound (34 mg, 62%) after drying and concentration. An analytical sample, obtained by flash chromatography on silica gel, showed the following: mp 152 °C; ^{1}H NMR ($CDCl_3$) δ 4.78 (dd, J = 6.6, 1.5 Hz, 1 H), 4.71 (br d, 6.6 Hz, 1 H), 3.11 (ddq, J = 7.2, 5.6, 1.5 Hz, 1 H), 2.87 (br dq, J = 7.2, 5.6 Hz, 1 H), 1.62 (d, J = 5.6 Hz, 3 H), 1.43 (d, J = 5.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 96.08, 94.47, 39.30, 36.29, 14.38, 13.98; IR (KBr) 1149 (s), 1080 (s) cm^{-1}. Anal. Calcd for $C_6H_{10}O_3S_2$: C, 37.10; H, 5.19. Found: C, 37.20; H, 5.35.

From 10a. A solution of **10a** (92 mg, 0.57 mmol) in CH_2Cl_2 (5 mL) was treated with stirring at 0 °C with peracetic acid (35%, 423 mg, 2 mmol, 3.4 equiv) in CH_2Cl_2 (5 mL), and the solution was stirred

(21) Sodium metaperiodate could also be used as the oxidant for **8**, although somewhat less efficiently;[6] neither tetra-*n*-butylammonium (peroxymonosulfate) Oxone nor tetra-*n*-butylammonium periodate proved useful.

(22) Coupling constant from LAOCOON III analysis.[5a]

at room temperature for 3.75 days. The mixture was diluted with CH_2Cl_2 (10 mL) and stirred for 5 min with saturated $NaHSO_3$ (5 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 × 5 mL), and the organic layer was separated, dried, filtered, and concentrated to yield a solid residue which on purification by column chromatography gave the title compound **18a** as a colorless solid (48 mg; 43% yield).

(±)-(1α,2α,3β,4α,5α,5β,6β)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,5,6-Trioxide (18b). Peracetic acid (30.2 mg, 0.14 mmol; 35% solution in acetic acid) was added to a solution of **16** (15.0 mg, 0.084 mmol) in glacial acetic acid (0.5 mL), and the mixture was heated at 45−50 °C for 24 h. The reaction mixture was diluted with EtOAc (10 mL) and shaken with saturated $NaHCO_3$ (2 × 5 mL). The organic layer was then separated, dried, filtered, and concentrated to yield 19.4 mg of crude material which was purified by flash chromatography on silica gel. In addition to **18a** (7.0 mg, 43%), the title compound **18b** was isolated as a colorless solid (6.4 mg, 39%): mp 150−153 °C (dec), ^{1}H NMR ($CDCl_3$) δ 4.92 (dd, J = 6.9, 1.5 Hz, 1 H), 4.77 (dd, J = 6.9, 1.5 Hz, 1 H), 2.52 (m, 1 H), 2.15 (m, 1 H), 1.42 (d, J = 7.2 Hz, 3 H), 1.33 (d, J = 7.2 Hz, 3 H); ^{13}C ($CDCl_3$) δ 98.41 (2C), 35.22, 33.22, 17.84, 16.46; IR (KBr) 3026, 2975, 2934, 2875, 1453, (all m), 1310 (vs), 1195 (s), 1120 (vs), 1095 (s) cm^{-1}. Anal. Calcd for $C_6H_{10}O_3S_2$: C, 37.10; H, 5.19. Found: C, 37.11; H, 5.40.

The ^{1}H NMR chemical shifts for **18a** were assigned by comparison with those for **23b**. The proton H_a of **23b** resonating at δ 3.11 ppm is on the same side as the sulfoxide, but on the side opposite the sulfone. The resonance at δ 3.11 ppm for sulfone−sulfoxide **18a** is assigned to H_f because of its similarity to H_a of **23b**; e.g., H_f is on the same side as the sulfoxide and on the side opposite the sulfone. The other methine resonance of **18a** at δ 2.87 ppm is assigned to H_a. A decoupling experiment completed the ^{1}H NMR spectral assignments for **18a**. Irradiation at 2.87 ppm collapsed the peaks at 4.71 ppm (dd) and 1.43 ppm (d) to a doublet (J_{cd} = 6.6 Hz) and a singlet, respectively. Therefore, the resonances at δ 4.71 and 1.43 ppm (J_{ab} = 5.6 Hz) were assigned to H_c and Me_b, respectively. In a similar manner, the assignments for H_d, H_e, and Me_f were made. The ^{1}H shifts for **18b** were assigned by comparison with those of **24**, employing the same reasoning used for ^{1}H chemical shift assignments for **18a**. The ^{13}C NMR assignments for **18a** and **18b** were deduced from HETCOR experiments.

(±)-*trans*-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide (19). Peracetic acid (235 mg, 1.08 mmol; 35% solution in acetic acid) was added to an ice-cooled solution of **10a** (58.4 mg, 0.361 mmol) in CH_2Cl_2 (10 mL) containing Na_2CO_3. The mixture was stirred at room temperature for 20 h and then treated with additional peracetic acid (2 g) and Na_2CO_3 and stirred overnight. After standard workup, the residue was taken up in peracetic acid (35%, 5 mL), sealed, and placed in a 55 °C oven for 3 days. After dilution with EtOAc followed by $NaHCO_3$ wash, compound **19** was obtained as a colorless solid (12 mg, 16% yield): mp 196 °C; ^{1}H NMR ($CDCl_3$) δ 4.41 (s, 2 H), 2.95 (m, 2 H); 1.51 (m, 2 H); ^{13}C ($CDCl_3$) δ 93.4, 37.7, 15.3; IR (KBr) 3438 (w), 2982 (w), 2941 (w), 2882 (w), 1457 (w), 1337 (s), 1289 (w), 1170 (s), 1092 (m) cm^{-1}. Anal. Calcd for $C_6H_{10}O_4S_2$: C, 34.27; H, 4.79. Found: C, 34.18; H, 4.95.

(1α,2α,3α,4α,5β,6α)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]-hexane 5,6-Dioxide (21a). A solution of (1α,2α,3α,4α,5β)-2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxide (**11a**; 50 mg, 0.31 mmol) in CH_2Cl_2 (10 mL) was treated at −20 °C with solid *m*CPBA (92%, 60 mg, 0.33 mmol), and the solution was stirred at −20 °C for 30 min. The mixture was then slowly warmed to room temperature and stirred overnight. Additional CH_2Cl_2 (10 mL) was added, the mixture was washed with saturated $NaHCO_3$ (2 × 10 mL), and the organic layer was separated, dried, filtered, and concentrated, affording crude product which was purified by flash chromatography on silica gel (70% EtOAc−hexanes), giving the title compound **21a** (R_f 0.25; 25 mg, 46%): mp 147−150 °C; ^{1}H NMR ($CDCl_3$) δ 4.87 (s, 2 H), 2.99 (m, 2 H), 1.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 91.03, 28.26, 12.83; MS (NH_3, CI) *m/z* (rel intens) 374 (2M + NH_4^+, 3.98), 179 (M + H^+, 2.02); IR (KBr) 1263 (m), 1122 (m), 1091 (s), 1072 (s), 1054 (s) cm^{-1}.

Oxidation of a solution of **11a** (80 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) with peracetic acid (237 mg, 1.09 mmol; 35% solution in acetic acid) at room temperature for 2 days and workup as above also afforded **21a** (23 mg, 26%).

Oxidation of 11a with Excess Peracetic Acid: 21a, and (1α,2α,3α,4α,5α,5β,6α)- and (1α,2α,3α,4α,5β,6α,6β)-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6-Trioxide (23a and 23b, Respectively). Peracetic acid (0.6 g, 2.8 mmol; 35% solution in acetic acid) was added to a solution of **11a** (138 mg, 0.84 mmol) in CH_2Cl_2 (5 mL) at room temperature, and the solution was stirred at this temperature for 72 h. At this point analysis by TLC indicated complete absence of **11a**. The mixture was treated with K_2CO_3 (0.7 g) and a few crystals of $NaHSO_3$, stirred for 15 min, filtered, and washed with CH_2Cl_2. Concentration of the combined filtrate afforded 90 mg of residue which upon flash chromatography (silica gel, 90% EtOAc−10% hexanes) gave **21a** (19.3 mg, 13%), **23a** (21.2 mg, 13%), and **23b** (10.3 mg, 7%), all colorless, crystalline solids. Data for **23a**: mp 182−186 °C; ^{1}H NMR ($CDCl_3$) δ 4.82 (s, 2 H), 3.09 (br s, 2 H), 1.26 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 99.08, 29.83, 14.09; MS (NH_3, CI) *m/z* (rel intens) 406 (2M + NH_4^+, 26), 212 (M + NH_4^+, 100), 195 (M + H^+, 4.4); IR (KBr) 1330 (m), 1308 (s), 1211 (m), 1146 (m), 1123 (s) cm^{-1}. Anal. Calcd for $C_6H_{10}O_3S_2$: C, 37.10; H, 5.19. Found: C, 36.90; H, 5.19. Data for **23b**: mp 162−164 °C; ^{1}H NMR ($CDCl_3$) δ 4.66 (s, 2 H), 3.11 (m, 2 H), 1.47 (dd, J = 4.9, 2.4 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 95.82, 28.69, 11.03; MS (NH_3, CI) *m/z* (rel intens) 406 (2M + NH_4^+, 16), 212 (M + NH_4^+, 100%); IR (KBr) 1308 (m), 1143 (s), 1079 (s), 1026 (m) cm^{-1}. Anal. Calcd for $C_6H_{10}O_3S_2$: C, 37.10; H, 5.19. Found: C, 37.23; H, 5.40.

Oxidation of 22a with Excess Peracetic Acid: 23a and 23b. Peracetic acid (1.0 g, 4.6 mmol, 35 equiv 35% solution in acetic acid) was added to **21a** (23 mg, 0.13 mmol). The solution was kept at 50 °C for 5 h and then cooled to room temperature, diluted with ethyl acetate (20 mL), and washed successively with $NaHSO_3$ (2 × 10 mL) and $NaHCO_3$ (2 × 10 mL), dried, filtered, and concentrated. Analysis by ^{1}H NMR spectroscopy indicated that the product consisted of a 1:12.5:24 **21a**/**23b**/**23a** mixture. Flash silica gel chromatography afforded **23a** (15.2 mg, 60%) and **23b** (8.1 mg, 32%).

Oxidation of 21a with Excess Peracetic Acid: *cis*-2,3-Dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5,5,6,6-tetraoxide (24). Peracetic acid (1.0 g, 4.6 mmol; 35% solution in acetic acid) was added to **21a** (15.2 mg, 0.085 mmol), and the mixture was kept at 45−50 °C for 5 h. Since NMR analysis indicated the presence of **23a** and **23b** in addition to the title compound, additional peracetic acid (4.5 g added in 1.5 g batches every 12 h, 20.7 mmol total; 35% solution in acetic acid) was added, and the mixture was maintained at 65 °C for 36 h with periodic monitoring to gauge the reaction progress. The cooled reaction mixture was then diluted with ethyl acetate (20 mL) and washed successively with $NaHSO_3$ (2 × 10 mL) and $NaHCO_3$ (2 × 10 mL), dried, filtered, and concentrated to give the title compound as a colorless solid (15.2 mg, 84% yield): mp 192−194 °C; ^{1}H NMR ($CDCl_3$) δ 4.35 (s, 2 H), 3.54 (m, 2 H), 1.46 (m, 6 H); ^{13}C ($CDCl_3$) δ 93.00, 32.51, 11.09; IR (KBr) 3037 (m), 1335 (s), 1271 (m), 1200 (s), 1170 (s), 1144 (m) cm^{-1}. Anal. Calcd for $C_6H_{10}O_4S_2$: C, 34.27; H, 4.79. Found: C, 34.36; H, 4.91.

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Supporting Information Available: Text describing experimental procedures and tables of crystallographic parameters for the X-ray study of **18a**, **19**, **21a**, and **23a** and atomic positional parameters, bond angles, bond lengths, anisotropic temperature factors, and hydrogen atom coordinates for **18a**, **19**, **21a**, and **23a** (32 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering instructions and Internet access instructions.

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