α-Disulfoxides and Other Intermediates in the Oxidation of Disulfides

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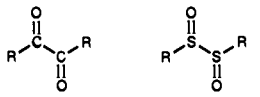
Abstract: The results of the electrophilic oxidation of eight bridged bicyclic thiosulfinates provide strong proof for the existence of α-disulfoxides as the initially formed intermediates. Bridged bicyclic α-disulfoxides from thiosulfinate **7b** are more stable than other α-disulfoxides reported, as they were shown to exist (ca. 10%) at temperatures up to 30 °C. Strong evidence for the formation of *O,S*-sulfenyl sulfinates as rearrangement products of α-disulfoxides was also demonstrated.

Introduction

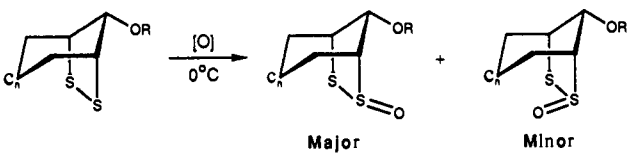
α-Dicarbonyl compounds (**1**) have been well-investigated since the early 1900s;[1] however the corresponding sulfur analogs, RS(O)S(O)R (**2**), have only been detected as reactive intermediates within the past 10 years.[2] The hunt for these elusive species has occupied the attention of several groups, and the topic has been extensively reviewed by Freeman.[2a,3] The major impediment to their investigation has been the low stability of the α-disulfoxide intermediate and its ease of transformation into more stable species through radical and ionic pathways.[2]



(1) (2)

We recently reported a general methodology for the synthesis of [2.2.1], [3.2.1], and [4.2.1] bridged bicyclic disulfides with the general structure **3**.[4] The compounds isolated as the first oxidation products of **3** were the bridged bicyclic thiosulfinate esters **4–10** (Scheme I). Their synthesis was achieved by the addition of 1 equiv. of *m*-CPBA, and they were shown to be unusually stable compounds.[4,5]

Scheme I



(3)

(4a) R=H, n=0 (10%) (4b) (2%)
(5) R=H, n=1 (88%)
(6) R=PNB, n=1 (90%)
(7a) R=Hex, n=1 (77%) (7b) (12%)
(8) R=H, n=2 (90%)
(9) R=PNB, n=2 (93%)
(10) R=Hex, n=2 (92%)

PNB = *p*-NO_2-C_6H_4-C(O)-; Hex = *n*-C_5H_{11}-C(O)-

While α-disulfoxides have not yet been isolated, their existence as reaction intermediates in the oxidation of thiosulfinates has been established.[2] Recently, we reported our initial observations concerning the formation of α-disulfoxides and other intermediates in the *m*-CPBA oxidation of bridged bicyclic thiosulfinates **7a** and **7b**.[2b] Here we present a detailed analysis of the oxidation of [2.2.1], [3.2.1], and [4.2.1] bridged bicyclic thiosulfinates.[6]

Results and Discussion

The general procedure used for the *m*-CPBA oxidation of bridged bicyclic thiosulfinates **4–10** is similar to that used by Freeman for the oxidation of dialkyl thiosulfinates.[7] Details are found in the Experimental Section. The initial reaction temperature ranged from −30 to −40 °C; the reaction mixture was slowly brought to room temperature by 10-deg increments in the NMR probe. Peak assignments were made by following the rate of appearance of the signals; those that showed a common abundance throughout the experiment and had the required number of peaks in the different regions of the spectrum were considered to be the same species. Each intermediate was labeled as symmetric or unsymmetric about the center plane of the molecule depending on the number of peaks in the ^{13}C spectrum for the ring carbons. This data is presented in Table I.

The oxidation of [3.2.1] thiosulfinates **5–7** provided the most information concerning the mechanism of this reaction; fewer intermediates were detected in the oxidation of the [2.2.1] and [4.2.1] analogs. In the latter examples we believe this is due to the rapid conversion of the intermediates to final products. In the [2.2.1] case, there were several reactive species formed; however, the concentration of each was too low to permit a

(1) (a) Schimmel & Co. *Chem. Zentralbl.* **1913**, 1972. (b) Suomalainen, H.; Jännes, L. *Nature* **1946**, *157*, 336. (c) *The Chemistry of Carbonyl Compounds*; Zabicky, J., Ed.; Interscience Publishers: New York, 1970; Vol. 2 and references cited therein.

(2) For a thorough historical review of this topic see: (a) Freeman, F. *Chem. Rev.* **1984**, *84*, 117. More recent papers on this topic include: (b) Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 8998. (c) Block, E.; Bayer, T. *J. Am. Chem. Soc.* **1990**, *112*, 4584. (d) Harpp, D. N.; Bodzay, S. J. *Sulfur Lett.* **1988**, *7*, 73. (e) Freeman, F.; Lee, C. *J. Org. Chem.* **1988**, *53*, 1263. (f) It should be pointed out that kinetic evidence was offered by Modena suggesting α-disulfoxides as intermediates in the oxidation of aromatic disulfides over 30 years ago: Marangelli, U.; Modena, G.; Todesco, P. E. *Gazz. Chim. Ital.* **1960**, *90*, 1.

(3) The first controversy over the α-disulfoxide structure occurred with the dioxide of cystine: (a) Toennies, G.; Lavine, T. F. *J. Biol. Chem.* **1936**, *113*, 571. (b) Lavine, T. F. *J. Biol. Chem.* **1936**, *113*, 583. (c) Emiliozzi, R.; Pichat, L. *Bull. Soc. Chim. Fr.* **1959**, 1887. (d) Utzinger, G. E. *Experientia* **1961**, *17*, 374. A reinvestigation of this problem has clearly shown the structure of the dioxide of cystine to be the thiosulfonate: Folkins, P. L.; Harpp, D. N. Unpublished results.

(4) Folkins, P. L.; Harpp, D. N. *J. Org. Chem.* **1992**, *57*, 2013. In all examples, the major product resulted from attack of the oxidizing agent on the exo face of these molecules (Scheme I). The endo face is blocked by the ring hydrogens; thus the endo diastereomers could only be accessed when there was a relatively large R group (e.g. **7b**, Scheme I) or if the ring was small (e.g. **4b**, Scheme I). Even in these examples, the endo isomer was only a minor product.

(5) Folkins, P. L.; Harpp, D. N.; Vincent, B. R. *J. Org. Chem.* **1991**, *56*, 904.

(6) The oxidation reactions were followed by low-temperature ^1H and ^{13}C NMR spectroscopy.

(7) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1983**, *105*, 4039.

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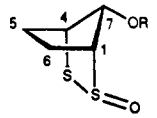
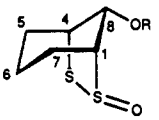
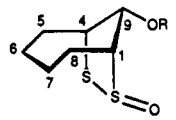
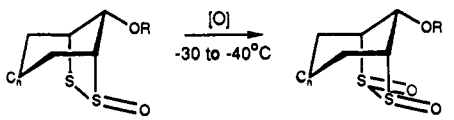
Table I. Number of Peaks in the ^{13}C NMR Spectrum of Bicyclic Species

		Symmetric	Unsymmetric
	[2.2.1]	3 C1 and C4 C5 and C6 equivalent	5
	(3.2.1]	4 C1 and C4 C5 and C7 equivalent	6
	[4.2.1]	4 C1 and C4 C5 and C8 C6 and C7 equivalent	7

Scheme II



(4a) R=H, n=0 (11)
(5) R= H, n=1 (12)
(6) R=PNB, n=1 (13)
(7a) R=Hex, n=1 (14)
(8) R=H, n=2 (15)
(9) R=PNB, n=2 (16)
(10) R=Hex, n=2 (17)

PNB = *p*-NO_2-C_6H_4-C(O)-
Hex = *n*-C_5H_{11}-C(O)-

Table II. ^{13}C NMR Chemical Shifts for α-Disulfoxides **11–17** (ppm)

		C1	C4	C5	C6	C7	C8	C9
[2.2.1]	**11**	59.7	59.7	16.7	16.7	95.8		
[3.2.1]	**12**	68.2	68.2	25.3	19.3	25.3	91.9	
	13	66.5	66.5	25.4	19.2	25.4	89.9	
	14	66.6	66.6	*a*	*a*	*a*	89.4	
[4.2.1]	**15**	76.0	76.0	25.6	24.9	24.9	25.6	91.1
	16	74.3	74.3	25.9	24.9	24.9	25.9	89.3
	17	74.2	74.2	*a*	*a*	*a*	*a*	88.2

[a] Region too complex to make appropriate assignments.

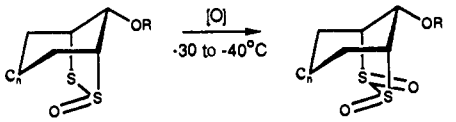
structural assignment. Figure 1 illustrates a representative example of the spectra from the oxidation of [3.2.1] thiosulfinate **5**. In all cases, ^{13}C and ^{1}H NMR results were internally consistent.[8] The data from the ^{1}H NMR experiments is conveniently summarized in composition profiles. These plots illustrate percent composition as a function of temperature on the basis of integration of the ^{1}H NMR spectra.

In all oxidations involving an exo isomer, the first species formed was a symmetric intermediate (not the thiosulfonate). This indicates that the oxidation of these molecules occurs on the exo face to give symmetric α-disulfoxide intermediates **11–17** (Scheme II). Preference for reactions to occur on this face has already been established;[4,5] thus this result was not unexpected. This suggests that the mutual dipolar repulsion of the adjacent sulfur–oxygen bonds must not be sufficiently strong to inhibit the attack of oxygen parallel to it and that the endo face must be relatively hindered. The ^{13}C chemical shifts of α-disulfoxides **11–17** are presented in Table II.

The oxidation of **7b**, the only endo thiosulfinate that could be separated from its corresponding exo isomer in pure form, provided several important clues for the elucidation of the pathway leading from α-disulfoxide to final product (thiosulfonate).[2b] The first

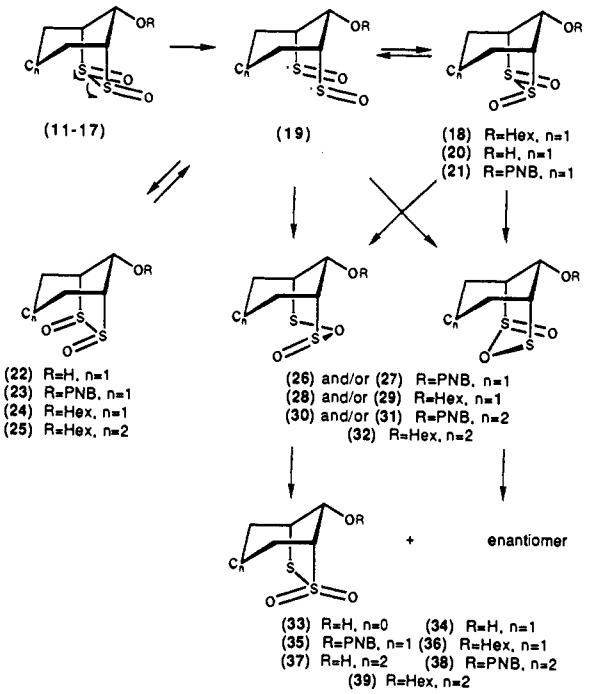
(8) Due to the shorter experimental acquisition time for the ^{1}H NMR spectra, the intermediates occasionally remained in the mixture at temperatures higher than those observed in the ^{13}C experiment. Over time, the equilibrium mixture from each experiment became identical in composition.

Scheme III



(7b) R=Hex, n=1 (18)
Hex = *n*-C_5H_{11}-C(O)-

Scheme IV



(11-17) (19) (18) R=Hex, n=1
(20) R=H, n=1
(21) R=PNB, n=1
(22) R=H, n=1
(23) R=PNB, n=1
(24) R=Hex, n=1
(25) R=Hex, n=2
(26) and/or (27) R=PNB, n=1
(28) and/or (29) R=Hex, n=1
(30) and/or (31) R=PNB, n=2
(32) R=Hex, n=2
+ enantiomer
(33) R=H, n=0 (34) R=H, n=1
(35) R=PNB, n=1 (36) R=Hex, n=1
(37) R=H, n=2 (38) R=PNB, n=2
(39) R=Hex, n=2

species formed in the oxidation of **7b** was unsymmetric intermediate **18**, which would be expected from attack of the second oxygen atom on the exo face of this molecule (Scheme III). The fascinating α-disulfoxide **18** is expected to be more stable than symmetric α-disulfoxides **11–17** because the repulsion between the adjacent sulfur oxygen bonds is no longer present. This is supported by the higher concentration (*as great as 69% of the reaction mixture*) of unsymmetric α-disulfoxide **18** in the oxidation of **7b**. This is depicted in the composition profile in Figure 2 and can be compared with the concentration of **14** (never greater than 47%, Figure 3) in the oxidation of **7a**. The temperature at which **18** remains in the reaction mixture (30 °C) is also higher than that of **14** (10 °C).[9]

Unsymmetric α-disulfoxide **18** was also seen in the oxidation of **7a** as the second species, formed after symmetric α-disulfoxide **14** (Figure 3).[2b] A reasonable way to envisage the formation of **18** from **14** is via biradical **19**.[10,11] The S–S bond in bridged bicyclic α-disulfoxides is expected to be relatively weak; thus homolysis can readily occur to give two sulfinyl radicals that can recombine to give several possible species (Scheme IV).[12] Rotation

(9) In time (ca. 1 h), rearrangement of **18** to other intermediates occurred so that all attempts to isolate it were unsuccessful.

(10) α-Disulfoxide **18** could also be formed by a direct attack of the oxidizing agent on the endo side of the sulfur–sulfur bond of **7a**; however, reactions from this side of these molecules have been shown to be unfavorable (refs 1 and 2). Thus, this mechanism should not account for the formation of a significant amount of **18** from **7a**.

(11) A concerted rearrangement of α-disulfoxide **14** is not likely, as the sulfinyl oxygen is not able to reach an empty orbital on the adjacent sulfur atom due to the rigidity of the system.

(12) Sulfinyl radicals have been proposed as intermediates in the disproportionation of aryl arenethiosulfinates (Koch, P.; Ciuffarin, E.; Fava, A. *J. Am. Chem. Soc.* **1970**, *92*, 5971) and in the rearrangement of α-disulfoxides to thiosulfonates in the oxidation of diaryl thiosulfinates (ref 3d). Chau, M. M.; Kice, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 7711. Gill, B.; Ramsden, M. *J. Chem. Ind.* **1979**, *21*, 283. Oae, S.; Toshikazu, T.; Kim, Y. H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2484.

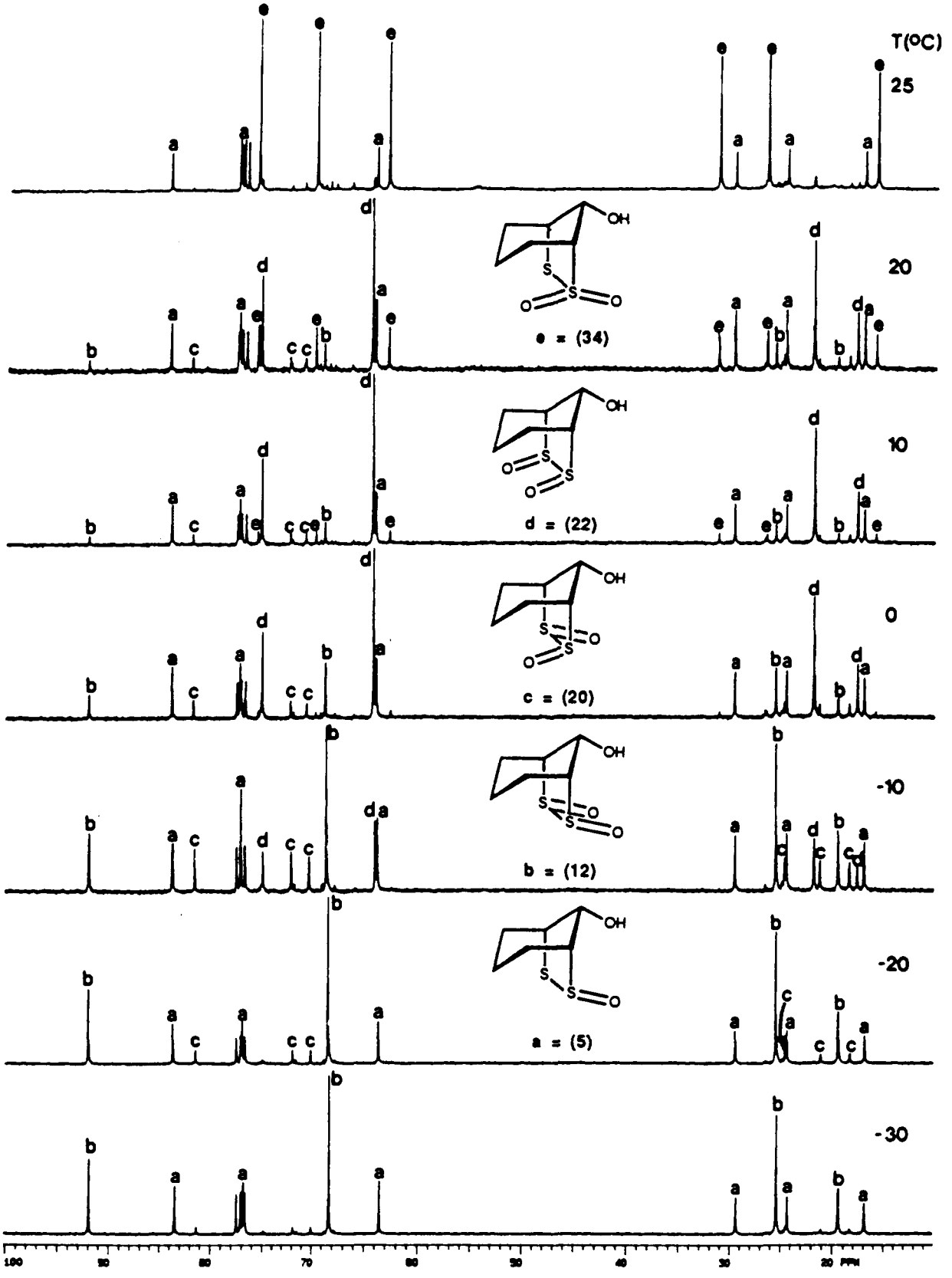


Figure 1. Low-temperature, *m*-CPBA oxidation of **5**; ^{13}C spectra.

about one C–S bond, followed by head-to-head radical recombination, would provide an unsymmetric α-disulfoxide **18**.

This process was detected in all of the oxidations performed on the [3.2.1] bicyclic thiosulfinates **5–7** in this study but not in the oxidation of [4.2.1] thiosulfinates **8–10**. The ^{13}C NMR chemical shifts for these intermediates are shown in Table III, illustrating the consistency in these values and therefore adding support to the structural assignments.

If rotation about both C–S bonds occurred, followed by head-to-head radical recombination, then a symmetric endo α-disulfoxide would be formed (Scheme IV). Symmetric species were detected in the oxidations of [3.2.1] thiosulfinates **5–7a** and **7b** and [4.2.1] thiosulfinate **10** at temperatures ranging from −10 to 25 °C. Intermediates **22–25** have been assigned this structure, and their ^{13}C chemical shifts are also presented in Table III.

The two sulfinyl radicals may also recombine in a head-to-tail

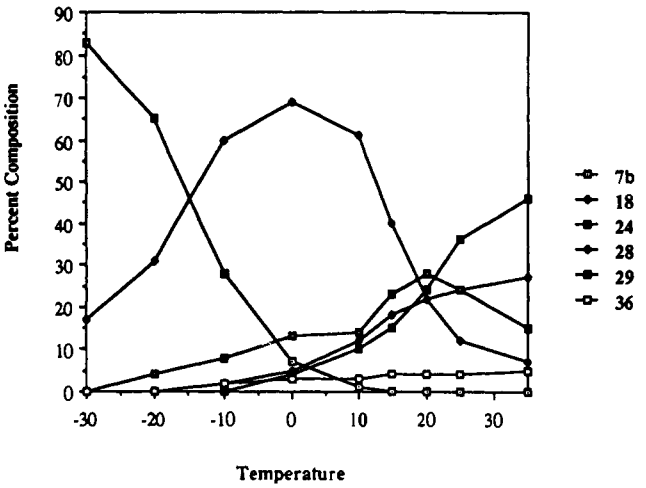


Figure 2. Percent composition vs temperature for the *m*-CPBA oxidation of **7b**.

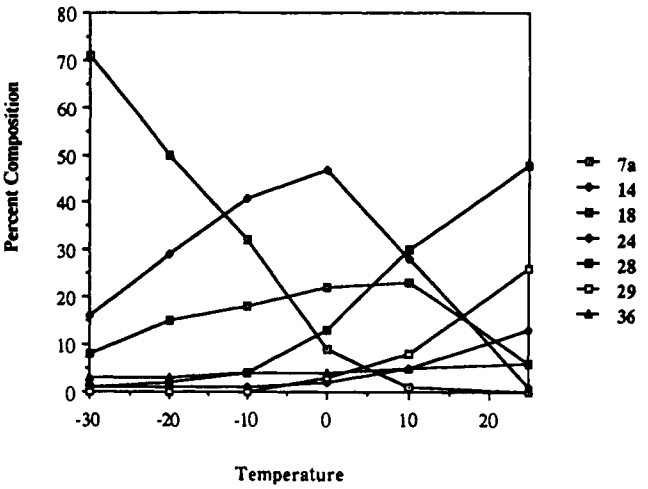


Figure 3. Percent composition vs temperature for the *m*-CPBA oxidation of **7a**.

fashion. This would provide compounds known as *O,S*-sulfenyl sulfinates.[13] There are two possible diastereomeric *O,S*-sulfenyl sulfinates (along with their corresponding enantiomers) that can be formed from biradical **19** (Scheme IV). These species can also be formed directly from unsymmetric α-disulfoxides **18–22** in a concerted-type fashion and are expected to be unsymmetric. Such an intermediate was detected in the oxidations of [3.2.1] thiosulfinates **6**, **7a**, and **7b** and [4.2.1] thiosulfinates **9** and **10**.

The ^{13}C NMR chemical shifts of *O,S*-sulfenyl sulfinates **26–28** and **32** are presented in Table IV.[14] It is important to note that the amount of these species remaining at the end of the experiment was greater in the oxidation of the hydroxy-substituted thiosulfinates. In fact, for the [3.2.1] thiosulfinates **6**, **7a**, and **7b**, *O,S*-sulfenyl sulfinates dominated at the end of the experiment. Over a period of 2–3 h after the experiment, the thiosulfonate became the major product, and all attempts to isolate the *O,S*-sulfenyl sulfinates were unsuccessful.[15]

The final product isolated from all oxidations of bridged bicyclic thiosulfinates was the corresponding thiosulfonate (**33–39**, Scheme IV). The formation of thiosulfonates most likely occurs via a concerted rearrangement of *O,S*-sulfenyl sulfinates **26–32** (Scheme IV). The product was purified by chromatographic workup on silica gel, and the yields were inversely proportional to the concentration of intermediates at the end of the experiment.

Oxidation of bridged bicyclic thiosulfinates using *m*-CPBA at low temperatures (−30 to −40 °C) produced a species that was not the corresponding thiosulfonate but was converted, through a series of intermediates, to this expected product. There is no doubt that oxidation occurred on the "softer" sulfenyl sulfur atom to give an α-disulfoxide intermediate. The quantity of α-disulfoxide formed and the temperatures at which signals were observed for its presence (30 °C in some examples) were higher than in any previous work.[2]

Some of the important details about the oxidation of the different bicyclic species are of special interest. First, there were fewer intermediates detected in the oxidation of [4.2.1] thiosulfinates than in the other two cases. For example, in the oxidation of **8**, the mechanism appears to involve clean formation of α-disulfoxide **15** (it is the only bicyclic species present at 10 °C) followed by complete conversion to thiosulfonate **37**. This does not rule out the possibility of the formation of other intermediates; however, their rearrangement into thiosulfonate (which is obviously more stable) occurs rapidly. This may be due to the greater conformational mobility of the [4.2.1] species.

Second, substitution at the hydroxy functionality appears to add stability to the intermediates in all cases. For example, in the oxidation of [3.2.1] thiosulfinates, complete conversion to the final product had occurred by the end of the experiment when R = H (**5**). When R was a *p*-nitrobenzoyl (**6**) or *n*-hexanoyl group (**7a** and **7b**), slower rearrangement to final product was observed. In fact, it was the *O,S*-sulfenyl sulfinates that were dominant at room temperature in the oxidation of **6**, **7a**, and **7b**. These compounds could not be isolated by column chromatography on silica or alumina gel, and their presence caused a lowering of the yield of thiosulfonate.[15] In the [4.2.1] examples, other intermediates besides α-disulfoxides were detected only when the OH group was protected (**9**, **10**). Their concentration was certainly far less than in the [3.2.1] examples, as they never reached a composition of greater than 20%.

Table III. ^{13}C NMR Chemical Shifts for Unsymmetrical α-Disulfoxides **18–21** and Symmetrical endo α-Disulfoxides **22–25** (ppm)

	C1	C4	C5	C6	C7	C8	C9
			Unsymmetrical α-Disulfoxides				
18	69.0	67.0	*a*	*a*	*a*	82.0	
20	71.9	70.1	21.0	18.2	24.4	81.4	
21	69.2	67.4	21.9	17.7	25.3	83.2	
			Symmetrical endo α-Disulfoxides				
22	64.2	64.2	21.7	17.6	21.7	75.0	
23	62.0	62.0	22.7	18.4	22.7	78.5	
24	62.0	62.0	*a*	*a*	*a*	77.0	
25	66.8	66.8	*a*	*a*	*a*	*a*	80.0

[a] Region too complex to make appropriate assignments.

Table IV. ^{13}C NMR Chemical Shifts for *O,S*-Sulfenyl Sulfinates **26–29** and **32** (ppm)

	C1	C4	C5	C6	C7	C8	C9
26	69.7	66.5	25.3	18.6	27.1	75.7	
27	69.5	66.7	*a*	*a*	*a*	74.9	
28	65.4	64.0	22.6	17.4	24.8	72.8	
29	65.3	63.7	*a*	*a*	*a*	71.7	
32	72.8	71.9	*a*	*a*	*a*	*a*	74.6

[a] Region too complex to make appropriate assignments.

Conclusion

The results reported here for the electrophilic oxidation of bridged bicyclic thiosulfinates represents the clearest evidence to date for the complete story of this important oxidation process. Strong proof is provided to support the existence of α-disulfoxides as the initial intermediate formed in this oxidation. Bridged

(13) These were also detected in the *m*-CPBA oxidation of dialkyl thiosulfinates (ref 2d) as well as in a tin-mediated coupling process (ref 2c). In addition, they have been suggested as reactive intermediates in onion extract: Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135.

(14) Due to the lower sensitivity of the ^{13}C experiment, the *O,S*-sulfenyl sulfinates (**30**, **31**) formed during the oxidation of **9** were detected only in small amounts in the ^{1}H NMR experiment.

(15) *O,S*-Sulfenyl sulfinates remaining at the end of the experiment may react with the solid support during chromatography possibly through an esterification reaction.

bicyclic α-disulfoxides (from thiosulfinate **7b**) are more stable than other α-disulfoxides previously reported;[2a] they were detected (ca. 10%) at temperatures up to 30 °C. This may provide a means to probe the reactivity of these hitherto elusive species via other low-temperature experiments. Strong evidence for the formation of *O,S*-sulfenyl sulfinates as rearrangement products of α-disulfoxides was also demonstrated.

Experimental Section[16]

The preparation of bridged bicyclic thiosulfinates **4a**, **4b**, **5**, **6**, **7a**, **7b**, and **8** along with analytical data for bridged bicyclic thiosulfonates **33**, **34**, and **37** was previously published.[4,5] Confirmation of structures **9**, **10**, **35**, **36**, **38**, and **39** was obtained by appropriate derivatization of the corresponding alcohol (HRMS confirmed) and a comparison with appropriate spectral data.

Oxidation of Bridged Bicyclic Thiosulfinates Using *m*-CPBA. The bicyclic thiosulfinate was dissolved in 2 mL of $CDCl_3$ and cooled to –40 °C in a dry ice/isopropanol bath under an atmosphere of nitrogen. *m*-CPBA (1 equiv) was then added as a solid to the cooled solution, and this mixture was stirred for a further 15 min at this temperature. The solution was then filtered as quickly as possible into an NMR tube previously cooled to –40 °C. The sample was then placed into the spectrometer probe that had been precooled to –40 °C, and acquisition was initiated. At least 15 min was allowed prior to spectral acquisition at each temperature in order for the sample to equilibrate at the desired temperature. An increment of 10 °C was used until the sample was brought to room temperature. Occasionally the sample was heated slightly above room temperature.

Preparation of *syn*-2,3-Dithia-9-[(*p*-nitrobenzoyl)oxy]bicyclo[4.2.1]nonane *S*-Oxide (9). *syn*-2,3-Dithia-9-[(*p*-nitrobenzoyl)oxy]bicyclo[4.2.1]nonane (70.0 mg, 0.215 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C under an atmosphere of nitrogen, and a solution of *m*-CPBA (37.1 mg, 0.215 mmol) in CH_2Cl_2 was added (dropwise). The solution was allowed to warm to room temperature, and stirring was continued for 1 h, after which the solution was absorbed onto silica and the product purified by column chromatography using 7:3 hexanes/EtOAc as the eluent. Compound **9** was obtained as a white solid (68.3 mg, 93%): mp 138–139 °C; R_f ($CHCl_3$) 0.13; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.46–2.29 (m, 2 × H5, H6, H7, and H8, 8 H), 4.30 (dt, J_1 = 10.4 Hz, J_2 = 1.23 Hz, H4, 1 H), 4.91 (t, J = 3.17 Hz, H1, 1 H), 6.19 (s, H9, 1 H), and 8.25 (q, aromatic protons, 4 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ 22.2 (C6), 24.3 (C7), 24.8 (C5), 34.5 (C8), 59.6 (C4), 73.6 (C1), 75.0 (C9), 123.6 (C3′ and C7′), 131.5 (C4′ and C6′), 134.7 (C2′), 150.8 (C5′), and 164.0 (C1′, C=O) ppm; IR (KBr) 722 (NO_2), 1076 (S=O), 1105 (NO_2), 1271 (NO_2), 1524 (NO_2), and 1721 (C=O) cm^{-1}; MS [EI, direct inlet, 200 °C] *m/z* (% relative intensity, assignment) 341 (1.3, $M^{\cdot+}$), 150 (100, $M^{\cdot+}$ – $^{\cdot}C(O)$-C_6H_4-NO_2).

Preparation of *syn*-2,3-Dithia-9-[(*n*-hexanoyl)oxy]bicyclo[4.2.1]nonane *S*-Oxide (10). Compound **10** was prepared following the same procedure as for **9** using *syn*-2,3-dithia-9-[(*n*-hexanoyl)oxy]bicyclo[4.2.1]nonane as the starting material. The product was purified by column chromatography using 3:1 hexanes/EtOAc as the eluent and was isolated as a clear oil in 92% yield: R_f (3:1 hexanes/EtOAc) 0.16; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, $J_{H6'-H5'}$ = 6.5 Hz, 3 × H6′, 3 H), 1.15–2.00 (m, 2 × H3′, H4′, and H5′ and 2 × H5, H6, H7, and H8, 14 H), 2.33 (t, $J_{H2'-H3'}$ = 7.5 Hz, 2 × H2′, 2 H), 4.17 (d, J = 11.2 Hz, H4, 1 H), 4.77 (t, J = 3 Hz, H1, 1 H), and 5.88 (s, H9, 1 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.8 (C6′), 22.2 (C5′), 23.7 (C6), 24.2 (C4′), 24.2 (C7), 24.3 (C3′), 31.1 (C2′), 32.0 (C5), 34.1 (C8), 64.3 (C4), 79.9 (C1), 84.5 (C9), and 173.4 (C1′, C=O) ppm; IR ($CDCl_3$) 1098 (S=O), 1164, 1380, 1470, and 1733 (C=O) cm^{-1}; MS [EI, direct inlet, 100 °C] *m/z* (% relative intensity, assignment) 290 (13.8, $M^{\cdot+}$), 99 (100, $^+C(O)(CH_2)_4CH_3$).

(16) For general experimental procedures, see ref 4.

Isolation of *syn*-2,3-Dithia-8-[(*p*-nitrobenzoyl)oxy]bicyclo[3.2.1]octane *S,S*-Dioxide (35). Compound **35** was isolated from the product mixture of the low-temperature NMR *m*-CPBA oxidation experiments on **6**. Purification was performed by column chromatography using 3:2 hexanes/EtOAc as the eluent. Compound **35** was isolated as a white solid 18% yield: mp 157–159 °C; R_f (3:2 hexanes/EtOAc) 0.20; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.6–2.6 (m, 2 × H5, H6, and H7, 6 H), 3.78 (br s, H4, 1 H), 4.67 (br s, H1, 1 H), 5.54 (m, H8, 1 H), and 8.3 (q, aromatics, 4 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ 16.0 (C6), 26.9 (C5), 31.5 (C7), 58.1 (C4), 67.1 (C1), 76.9 (C8), 123.7 (C3′ and C7′), 131.7 (C4′ and C6′), 134.2 (C2′), 151.0 (C5′), and 163.6 (C1′, C=O) ppm; IR ($CDCl_3$) 1105 (NO_2), 1118 (SO_2), 1268 (NO_2), 1530 (NO_2), and 1730 (C=O) cm^{-1}; MS [EI, direct inlet, 180 °C] *m/z* (% relative intensity, assignment) 150 (100, $M^{\cdot+}$ – $C(O)C_6H_4NO_2$).

Isolation of *syn*-2,3-Dithia-8-[(*n*-hexanoyl)oxy]bicyclo[3.2.1]octane *S,S*-Dioxide (36). The product mixture from the low-temperature oxidation of **7a** was absorbed on silica gel and flash column chromatography performed using $CHCl_3$ as the eluent. The product, a clear oil (15 mg, 61%), was found in fractions 3–11: R_f (3:1 hexanes/EtOAc) 0.14; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, $J_{H6'-H5'}$ = 6.5 Hz, 3 × H6′, 3 H), 1.2–2.2 (m, 2 × H3′, H4′, and H5′ and 2 × H5, H6, and H7, 12 H), 2.41 (t, $J_{H2'-H3'}$ = 7.5 Hz, 2 × H2′, 2 H), 3.65 (br s, H4, 1 H), 4.5 (br s, H1, 1 H), and 5.2 (dd, J_1 = 2.6 Hz, J_2 = 1.6 Hz, H8, 1 H) ppm; ^{13}C NMR (200 MHz, $CDCl_3$) δ 13.8 (C6′), 16.5 (C6), 22.2 (C5′), 24.2 (C4′), 26.9 (C5), 31.1 (C3′), 31.7 (C7), 34.1 (C2′), 58.1 (C4), 67.2 (C1), 76.1 (C8), and 173.1 (C=O) ppm; IR (neat) 1137 (SO_2), 1308 (SO_2), and 1735 (C=O) cm^{-1}; MS [EI, direct inlet, 100 °C] *m/z* (% relative intensity, assignment) 99 (100, $^+C(O)(CH_2)_4CH_3$).

Isolation of *syn*-2,3-Dithia-9-[(*p*-nitrobenzoyl)oxy]bicyclo[4.2.1]nonane *S,S*-Dioxide (38). Compound **38** was isolated from the product mixture of the low-temperature NMR *m*-CPBA oxidation experiments on **9**. Purification of **38** was performed using column chromatography with 4:1 $CHCl_3$/EtOAc as the eluent. The product was a white solid (60% yield): R_f($CHCl_3$) 0.17; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5–2.6 (m, 2 × H5, H6, H7, and H8, 8 H), 3.91 (d, J = 8.42 Hz, H4, 1 H), 4.68 (s, H1, 1 H), 5.80 (t, H9, 1 H), and 8.25 (q, aromatic protons, 4 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ 22.2 (C6), 24.3 (C7), 24.8 (C5), 34.5 (C8), 59.6 (C4), 73.6 (C1), 75.0 (C9), 123.8 (C3′ and C7′), 130.9 (C4′ and C6′), 134.1 (C2′), 151.0 (C5′), and 164.0 (C1′, C=O) ppm; MS [EI, direct inlet, 180 °C] *m/z* (% relative intensity, assignment) 150 (100, $M^{\cdot+}$ – $C(O)C_6H_4NO_2$).

Isolation of *syn*-2,3-Dithia-9-[(*n*-hexanoyl)oxy]bicyclo[4.2.1]nonane *S,S*-Dioxide (39). Compound **39** was isolated from the product mixture of the low-temperature NMR *m*-CPBA oxidation experiments on **10**. Purification of **39** was performed using column chromatography with 3:1 hexanes/EtOAc as the eluent. Compound **39** was a clear oil (55% yield): R_f (3:1 hexanes/EtOAc) 0.30; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, $J_{H6'-H5'}$ = 6.5 Hz, 3 × H6′, 3 H), 1.23–2.17 (m, 2 × H3′, H4′, and H5′ and 2 × H5, H6, H7, and H8, 14 H), 2.39 (t, $J_{H2'-H3'}$ = 7.5 Hz, 2 × H2′, 2 H), 3.76 (d, J = 8.2 Hz, H4, 1 H), 4.51 (br s, H1, 1 H), and 5.48 (s, H9, 1 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.9 (C6′), 22.0 (C6), 22.2 (C5′), 24.27 (C4′), 24.32 (C7), 24.6 (C3′), 31.1 (C2′), 34.1 (C5), 34.7 (C8), 59.5 (C4), 73.5 (C1), 74.9 (C9), and 173.1 (C1′, C=O) ppm; IR ($CDCl_3$) 902, 1109, 1131 (SO_2), 1158, 1169, 1310 (SO_2), and 1737 (C=O) cm^{-1}; MS [EI, direct inlet, 60 °C] *m/z* (% relative intensity, assignment) 99 (27, $^+C(O)(CH_2)_4CH_3$).

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Supplementary Material Available: NMR spectra from the oxidations of **5–10** (12 pages). Ordering information is given on any current masthead page.