Diastereoselective Episulfidation of Strained Cyclic Alkenes by a Thiophene Endoperoxide versus Epoxidation by Dimethyldioxirane

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Abstract: Thiophene endoperoxide **2**, which was prepared by photooxygenation of thiophene **1**, transfers a sulfur atom (up to 92%) to strained cycloalkenes to form thiiranes when thermolyzed in their presence. The diastereomeric pair *cis*/*trans*-cyclooctene (**5b**) reacted stereoselectively, which speaks for a concerted process rather than open dipolar and/or diradical intermediates. The set of chiral cyclooctenols **5c**−**e** was also investigated, and the relative configurations of the respective thiiranes were assigned by chemical correlation and NMR spectral and X-ray analysis. The first-order kinetics of the process clearly shows that the endoperoxide **2** itself is not the sulfur-transferring species, but it is thermally transformed to the intermediates **I** and **II**. Whereas intermediate **II** is responsible for the competitive formation of elemental sulfur, intermediate **I**, presumably an oxathiirane, is the active sulfur-transferring species. The episulfidation was compared with the epoxidation by the related dimethyldioxirane, and both show the same qualitative trends in the diastereoselectivity and the reactivity toward the alkenes **5a**−**e**.

Introduction

The epoxidation of alkenes is beyond doubt one of the most important and best investigated synthetic transformations. A variety of reagents are known, which may be used to transfer an oxygen atom directly to an alkene.[1−8] Several enantioselective epoxidations demonstrate the significance of this well-explored methodology in organic chemistry.[2−7] In contrast, the direct episulfidation of alkenes is reported only for a few special examples and has yet not been synthetically applied.[9,10] To transform alkenes to their episulfides, usually indirect methods are used, of which the preparatively more useful ones are the conversion of epoxides to their episulfides by thiocarbonyl-containing reagents (e.g., thiourea) or the addition of a sulfenyl chloride to an alkene and subsequent base-catalyzed ring closure.[10]

Recently, we have found that in the thermolysis of thiophene endoperoxide **2** a sulfur atom is transferred directly to strained cycloalkenes to form the corresponding thiiranes in moderate to good yields (Scheme 1).[11]

Presently we report the full experimental details on this novel sulfur transfer to a set of olefins for assessing the diastereoselectivity and to explore the mechanistic details of this potentially important reaction. Since oxathiiranes[12] have been postulated as intermediates in the thermolysis of endoperoxides[11,13] and since their sulfur-transfer potential has been already claimed,[14] these transients are postulated as the active sulfur-transferring agents in this episulfidation. Comparison with the related epoxidation by the analogous dimethyldioxirane (DMD) substantiates this claim.

Results

Episulfidations. Thiophene **1** reacted quantitatively with singlet oxygen at − 30 °C to form the endoperoxide **2**, which is persistent at − 20 °C in $CDCl_3$ solution for several days; it was characterized by its ^1H and ^{13}C NMR data.[11] The

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(1) Erden, I. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 1A, pp 97−171.
(2) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 193−246.
(3) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 247−308.
(4) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993, Chapter 4.2.
(5) Höft, E. *Top. Curr. Chem.* **1993**, *164*, 63−77.
(6) Pedragosa-Moreau, S.; Archelas A.; Furstoss R. *Bull. Soc. Chim. Fr.* **1995**, *132*, 769−800.
(7) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224−11235.
(8) Denmark, S. E.; Wu, Z. C.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem.* **1997**, *62*, 8288−8289.
(9) (a) Nakayama, J.; Ito, Y.; Mizumura, A. *Sulfur Lett.* **1992**, *14*, 247−250. (b) Abu-Yousef, I. A.; Harpp, D. N. *Tetrahedron Lett.* **1995**, *36*, 201−204. (c) Nau, W. M.; Bucher, G.; Scaiano, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 1961−1970.
(10) (a) Dittmer, D. C. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 7, pp 131−184. (b) Ando, W.; Choi, N. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 1A, pp 173−240. (c) Harring, S. R.; Livinghouse, T. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 1A, pp 241−258. (d) Capozzi, G.; Menichetti, S.; Nativi, C. In *Syntheses of Sulphones, Sulphoxides and Cyclic Sulphides*; Patai, S., Rappoport, Z., Eds.; Wiley & Sons: New York, 1994; pp 529−648.
(11) Adam, W.; Weinkötz, S. *J. Chem. Soc., Chem. Commun.* **1996**, 177−178.
(12) Murray, R. W.; Singh, M. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 1A, pp 429−456.
(13) (a) Gollnick, K.; Griesbeck, A. *Tetrahedron Lett.* **1984**, *25*, 4921−4924. (b) Matturro, M. G.; Reynolds, R. P.; Kastrup, R. V.; Pictroski, C. F. *J. Am. Chem. Soc.* **1986**, *108*, 2775−2776. (c) Matturro, M. G.; Reynolds, R. P. *Tetrahedron Lett.* **1987**, *28*, 4981−4984.
(14) Adam, W.; Weinkötz, S. *J. Org. Chem.* **1997**, *62*, 7084−7085.

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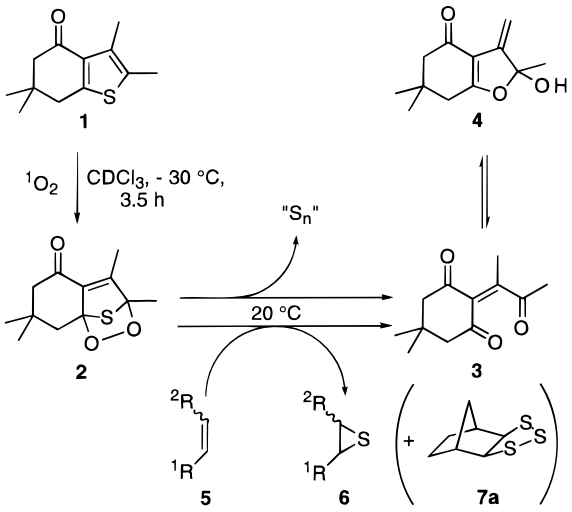
Scheme 1



endoperoxide **2** was isolated by silica gel chromatography at −30 °C as a yellow solid with a positive peroxide test (KI/HOAc).

The endoperoxide **2** decomposed readily already at 0 °C, both in isolated form and in solution. Its primary thermolysis products were elemental sulfur and the labile ene trione **3**; the latter rearranged to the hemiacetal **4** (Scheme 1) in a reversible reaction.[11] Although sulfines have been reported in the decomposition of a thiophene endoperoxide,[13] such products have not been found in the present work. The independently synthesized ene trione **3** (by oxidation of the corresponding furan with DMD at − 20 °C)[11,15] as well as the isolated **4** showed in $CDCl_3$ solution the presence of both species **3** and **4** after 2 h at room temperature (ca. 20 °C), together with small amounts of additional decomposition products. After one week at 20 °C, complete decomposition into a complex product mixture was observed, irrespective of whether one started from ene trione **3** or hemiacetal **4**.

For the sulfur-transfer experiments with the cycloalkenes **5a**−**e**, the endoperoxide **2** was generated at − 30 °C in $CDCl_3$ solution (0.10−0.15 M) and added to a mixture of the cycloalkene and dimethyl 1,3-benzenedicarboxylate (internal standard). After ^{1}H NMR analysis of the resulting solution at − 20 °C, it was kept at 25 °C for 2 h, and analyzed again by ^{1}H NMR spectroscopy (Table 1). The products **3**, **4**, **6**, and **7** were identified by comparison with authentic materials and quantified against the internal standard.[11,14] The pure new thiiranes **6c**−**e** were obtained by silica gel chromatography of the crude product mixture or by independent synthesis (see below, Table 2).

The thermolysis of endoperoxide **2** in the presence of norbornene (**5a**, Table 1, entries 1−3) and *cis*-cyclooctene (***cis*-5b**, entries 4−7) was run with different amounts of olefin to assess the efficacy of the sulfur transfer. The ratio of sulfur atom transfer to extrusion as elemental sulfur is reflected by the yield of thiirane **6**, which was independent of the olefin concentration within the analytical error (±5%). A constant yield of thiirane **6** (60 ± 5% referred to converted endoperoxide **2**) was also observed by monitoring the reaction progress versus time.

In the presence of *trans*-cyclooctene (***trans*-5b**), almost all of the available sulfur was trapped in the form of the thiirane ***trans*-6b** exclusively; not even traces of thiirane ***cis*-6b** were detected (Table 1, entry 8). Concomitantly, 6% of the starting olefin ***trans*-5b** isomerized to ***cis*-5b**. The *trans*/*cis* isomerization of the olefin was also observed when ***trans*-5b** was added to a completely thermolyzed (25 °C, 2.5 h) solution of endoperoxide **2** (contained **3** and **4**, their decomposition products, and elemental sulfur). Isomerization did not take place when the thermolysate was treated with Ph_3P to remove the elemental sulfur before the addition of ***trans*-5b**. Control experiments established that independently synthesized **3** and **4**[11] do not cause any isomerization of ***trans*-5b**, but elemental sulfur does. For this purpose, either the sulfur was activated before use by NH_3/DMF[16] or the solution of sulfur and ***trans*-5b** was heated to 60 °C.

To assess whether hydroxy-directing effects operate in the sulfur transfer, the chiral cyclooctenols **5c**−**e** were chosen as sulfur atom acceptors (Table 1, entries 9−11). 2-Cyclooctenol (**5c**) was transformed highly diastereoselectively into the thiirane ***trans*-6c**, whereas the regioisomers **5d**,**e** reacted unselectively to *cis*/*trans* mixtures of the corresponding thiiranes **6d**,**e**.

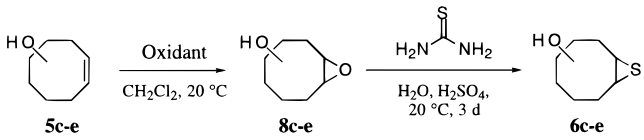
To assign the relative configurations of the thiiranes **6c**−**e**, they were prepared from the corresponding epoxides **8c**−**e** (Table 2). Thiourea was used as the sulfur source, which transforms the epoxide of 2-cyclohexenol to the corresponding thiirane in 35% yield.[17] It is known that cyclooctene epoxides

Table 1. Sulfur Transfer by Endoperoxide **2** to Cycloalkenes **5a**−**e**

entry	alkene	equiv	products (%)[a] 3	4	6[b]	dr of **6**[a] (*trans*:*cis*)
1	norbornene (**5a**)	1.3	26	38	57[c]	*d*
2		2.3	29	51	59[c]	*d*
3		3.6	24	53	63[c]	*d*
4	*cis*-cyclooctene (***cis*−5b**)	1.1	15	60	64	<5:95
5		2.3	19	61	64	<5:95
6		5.5	20	57	61	<5:95
7		10.3	14	55	61	<5:95
8	*trans*-cyclooctene (***trans*−5b**)	1.0	22	63	92[e]	>95:5
9	2-cyclooctenol (**5c**)	2.4	*f*	54	56	>95:5
10	3-cyclooctenol (**5d**)	2.4	*f*	50	57	42:58
11	4-cyclooctenol (**5e**)	2.6	*f*	53	53	47:53

[a] Determined from the ^{1}H NMR spectra of the crude products by comparison of characteristic signals with dimethyl 1,3-benzenedicarboxylate as internal standard; olefin mass balance >90%. [b] Based on endoperoxide **2**; sulfur mass balance >90%, determined by converting the extruded elemental sulfur with triphenylphosphine to the phosphine sulfide. [c] Traces of trithiolane **7a**. [d] Only the *exo* diastereomer was formed. [e] 6% of ***cis*-5b**. [f] Not determined because of overlapping NMR signals.

Table 2. Synthesis of Thiiranes **6c**−**e** from the Epoxides **8c**−**e**



olefin	oxidant	yield of **8** (%)	dr of **8**[a] (*cis*:*trans*)	yield of **6**[b] (%)	dr of **6**[a] (*cis*:*trans*)
5c	*m*CPBA	100 (100[c])	<5:95	10	>95:5
5c	*t*BuOOH, $VO(acac)_2$	82 (83[d])	>95:5	13	<5:95
5d	*m*CPBA	60[e] (58[c])	50:50	25	47:53
5e	*m*CPBA	43[e] (46[d])	>95:5[f]	9	<5:95

[a] Determined by ^{1}H NMR spectroscopy. [b] After silica gel chromatography and Kugelrohr distillation. [c] Reference 19. [d] Reference 21. [e] The crude epoxide **8** (yield determined by ^{1}H NMR spectroscopy) was treated with thiourea. [f] The cyclic ethers ***trans*-10e,e′** (ref 21) were observed as rearrangement products of the epoxide ***trans*-8e**.

(15) Sauter, M.; Adam, W. *Acc. Chem. Res.* **1995**, *28*, 289−298.

(16) Shields, T. C.; Kurtz, A. N. *J. Am. Chem. Soc.* **1969**, *91*, 5415−5416;.

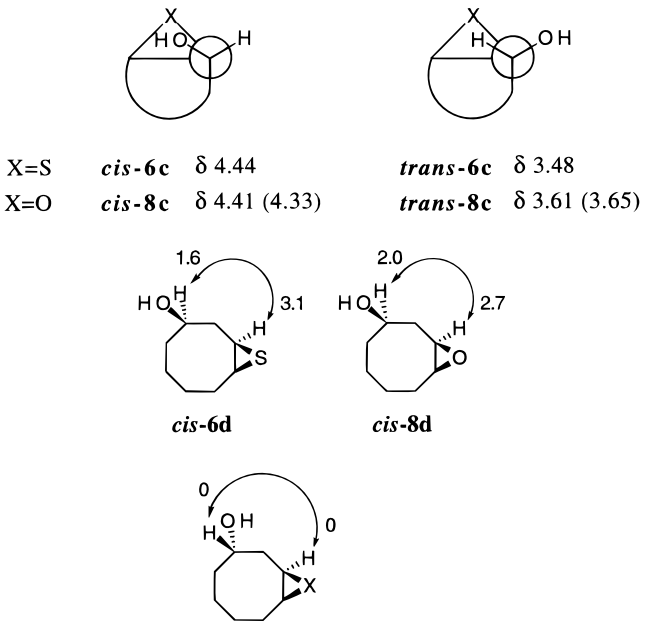


Figure 1. Characteristic δ_H(C*H*−OH) data and NOE effects (%) of selected thiiranes **6** and epoxides **8**, in parentheses data from ref 21.

are less reactive than cyclohexene epoxides in such reactions;[18] nevertheless, enough of the thiiranes **6c**−**e** were made available for their complete characterization and configurational assignment.

For this purpose, the 2-cyclooctenol (**5c**) was epoxidized by *m*CPBA to ***trans*-8c**,[19] which was treated with thiourea to form thiirane ***cis*-6c**. The transformation of an epoxide to a thiirane with thiourea is known to take place with inversion of the configuration.[20] Thiirane ***trans*-6c** was prepared by the same sequence, except *t*BuOOH/VO(acac)$_2$ instead of *m*CPBA was used as epoxidant, to afford the other diastereomer.[21] The configurations of ***cis*-** and ***trans*-6c** were assessed by ^{1}H NMR analysis (Figure 1). The resonance of the proton in the α position to the hydroxy group is shifted to higher field in ***trans*-6c** because of the anisotropic effect of the heterocycle. This effect is known for the epoxides ***cis*-** and ***trans*-8c**.[21]

The epoxidation of 3-cyclooctenol (**5d**) with *m*CPBA led to a 1:1 mixture of both diastereomeric epoxides ***cis*,*trans*-8d**, which were treated with thiourea to form the thiiranes ***cis*-** and ***trans*-8d** (47:53). The diastereomers were separated by silica gel chromatography, and their configurations were assigned by an NOE effect between the H-1 and H-3 protons in the thiirane ***cis*-6d**, which is absent in the *trans* diastereomer (Figure 1). The same effects were observed for the diastereomeric pair of the known ***cis*,*trans*-8d** epoxides, but their structures have not been rigorously determined.[19] This configurational assignment was confirmed by an X-ray analysis of the ***trans*-6d** thiirane (cf. Supporting Information).

When the 4-cyclooctenol (**5e**) was transformed to the thiirane by this route, only the diasteromer ***trans*-6e** was observed. The diasteromeric ***trans*-8e** epoxide rearranged in situ to the cyclic ethers ***trans*-10e**,**e′** under the reaction conditions of the *m*CPBA epoxidation.[21] Only epoxide ***cis*-8e** remained, which was transformed into the thiirane ***trans*-6e** by thiourea under inversion of the relative configuration.[20]

Epoxidations. For the epoxidations of the cycloalkenes **5a**−**e**, a solution of DMD in acetone (ca. 0.08 M) was used, which was added at room temperature to a stirred CH_2Cl_2 solution of the olefin. The crude reaction mixture was analyzed by gas chromatography to identify the products by comparison of the retention times with authentic material.

The cycloalkenes **5a**,**b** reacted rapidly with DMD to form the corresponding epoxides **8a**,**b** in very clean reactions (Table 3) and with retention of the original double-bond configuration of the olefins ***cis*-** and ***trans*-5b**.[22] 2-Cyclooctenol (**5c**) was diastereoselectively epoxidized to ***trans*-8c**,[19,23] but an excess of DMD overoxidized it to the epoxy ketone **9c**.[24] The other regioisomers **5d**,**e** did not react stereoselectively and formed 1:1 mixtures of the *cis*- and *trans*-epoxides. Excess DMD again caused overoxidation to the epoxy ketones **9d**,**e**.[25,26]

The epoxides **8a**−**e** are known, except ***trans*-8e**.[19,21−23] As mentioned above, ***trans*-8e** does not persist during the epoxidation of **5e** with *m*CPBA and rearranges to the cyclic ethers ***trans*-10e**,**e′**.[21,27] Due to the labile nature of ***trans*-8e** under acidic conditions, it was not possible to separate it from its ***trans*-8e** diastereomer by silica gel chromatography.

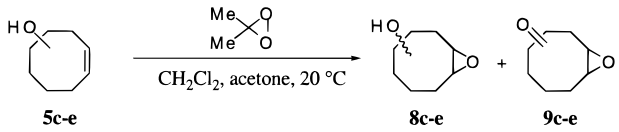
To establish the structure and the configuration of the ***trans*-8e**, an aliquot of the crude epoxide mixture, obtained in the epoxidation of **5e** with 1 equiv of DMD, was oxidized to the epoxy ketone **9e** by excess DMD and another one was treated with acid (Scheme 2). The latter caused quantitative rearrangement of ***trans*-8e** to ***trans*-10e**,**e′**, whereas ***cis*-8e** remained unchanged.

Kinetics. The episulfidation of norbornene by endoperoxide **2** was ^{1}H NMR-monitored by the disappearance of the signal at δ 2.00 relative to the signals of dimethyl 1,3-benzenedicarboxylate as internal standard. The rate of the disappearance of **2** follows a first-order rate law and was independent of the olefin concentration.

Competition experiments were performed to determine the relative rates of the olefins **5** in the episulfidation by endoperoxide **2** and in the epoxidation by DMD. A mixture of each olefin and *cis*-cyclooctene (***cis*-5b**), as reference olefin, was treated with less than 0.1 equiv of endoperoxide **2**, and after complete consumption of the endoperoxide **2**, the final **6**:***cis*-6b** thiirane ratio was determined by ^{1}H NMR spectroscopy directly on the crude reaction mixture. The relative rate constants (k_{rel}) were calculated by division of the **6**:***cis*-6b** final thiirane ratio by the initial **5**:***cis*-5b** olefin ratio (Table 4). The relative epoxidation rates for DMD were determined by the same

(17) Jankowski, K.; Harvey, R. *Can. J. Chem.* **1972**, *50*, 3930−3932.
(18) (a) Brimeyer, M. O.; Mehrota, A.; Quici, S.; Nigam, A.; Regen, S. L. *J. Org. Chem.* **1980**, *45*, 4254−4255. (b) Takido, T.; Kobayashi, Y.; Itabashi, K. *Synthesis* **1986**, 779−780. (c) Iranpoor, N.; Kazemi, F. *Synthesis* **1996**, 821−822.
(19) Whalen, D. L.; Cooper, J. D. *J. Org. Chem.* **1978**, *43*, 432−437.
(20) Claus, P. K.; Vierhapper, F. W. *J. Org. Chem.* **1977**, *42*, 4016−4023.
(21) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, *101*, 159−169.
(22) Shea, K. J.; Kim, J.-S. *J. Am. Chem. Soc.* **1992**, *114*, 3044−3051.
(23) (a) Adam, W.; Prechtl, F.; Richter, M. J.; Smerz, A. K. *Tetrahedron Lett.* **1993**, *34*, 8427−8430. (b) P. Chamberlain, M. L. Roberts, G. H. Whitham, *J. Chem. Soc. B* **1970**, 1374−1381.
(24) Cope, A. C.; Keough, A. H.; Peterson, P. E.; Simmons, H. E., Jr.; Wood, G. W. *J. Am. Chem. Soc.* **1957**, *79*, 0−3905.
(25) Mayer, W.; Meier, H. *Chem. Ber.* **1989**, *122*, 509−517.
(26) Meier, H.; Mayer, W.; Kolshorn, H. *Chem. Ber.* **1987**, *120*, 685−689.
(27) (a) Barrelle, M.; Apparu, M. *Bull. Soc. Chim. Fr.* **1972**, 2016−2024. (b) Best, S. P.; Bloodworth, A. J.; Spencer, M. D. *J. Chem. Soc., Chem. Commun.* **1990**, 416−418. (c) Kim, H.-J.; Schlecht, M. F. *Tetrahedron Lett.* **1987**, *28*, 5229−5232.

Table 3. Oxidation of Cycloalkenes **5a**−**e** by Dimethyldioxirane (DMD)



5c-e **8c-e** **9c-e**

alkene	DMD equiv	time (h)	conv of **5** (%)[a]	products (%)[a,b] **8**	**9**	dr of **8**[a] (*trans*:*cis*)
norbornene (**5a**)	1.0	0.2	>98	>98		
cis-cyclooctene (*cis*-**5b**)	1.0	0.2	>98	>98		<2:98
trans-cyclooctene (*trans*-**5b**)	1.0	0.2	>98	>98		>98:2
2-cyclooctenol (**5c**)	0.9	0.2	90	>98	<2	>98:2
	2.2	168	>95[c]	61[c]	39[c]	>95:5[c]
3-cyclooctenol (**5d**)	0.9	0.2	87[c]	93[c]	7[c]	47:53[c]
	2.1	24	>95[c]	<5[c]	>95[c]	
4-cyclooctenol (**5e**)	0.9	0.2	89	97	3	56:44
	2.2	24	>98	<2	85[d]	

[a] Determined by GC analysis of the crude product mixture. [b] Based on 100% conversion. [c] Determined by ^{1}H NMR analysis of the crude product mixture. [d] Estimated from the relative peak areas; 80% yield of isolated **9e**.

Scheme 2

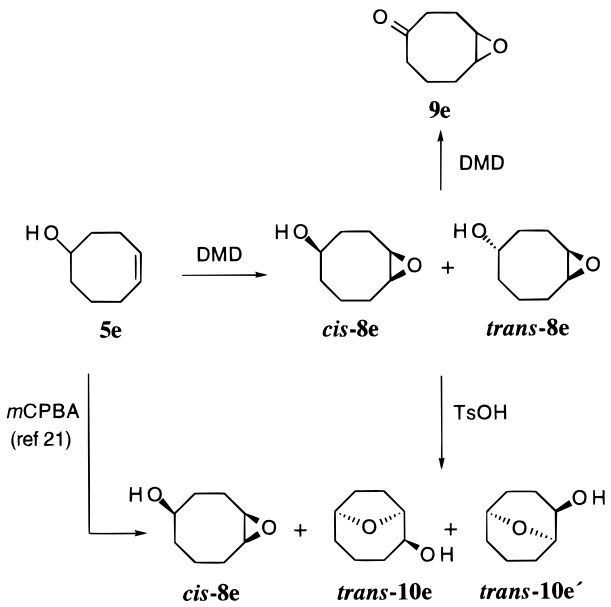


Table 4. Relative Rates of the Olefins **5** in the Episulfidation by Endoperoxide **2** and in the Epoxidations by DMD and *m*CPBA

olefin **5**	episulfidation[a] k_{rel}[b]	epoxidation k_{rel}(DMD)[c]	epoxidation k_{rel}(*m*CPBA)[d]
trans−**5b**	>50	100 ± 14[e]	112
cis−**5b**	1	1	1
5e	0.15 ± 0.05	0.60 ± 0.03	
5c	0.15 ± 0.04	0.56 ± 0.01	0.83[f]
5a	0.17 ± 0.03	0.51 ± 0.01	0.73
5d	0.13 ± 0.04	0.44 ± 0.04	

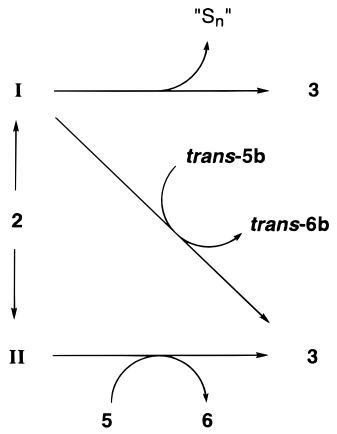
[a] By endoperoxide **2** in $CDCl_3$ at 25 °C relative to ***cis*-5b**. [b] Determined by ^{1}H NMR spectroscopy directly on the crude episulfide mixture relative to ***cis*-6b**. [c] Determined by gas chromatographic analysis on an SE-52 column, average of three independent competition experiments. [d] Calculated from the absolute rate constants of ref 22. [e] Reference 28. [f] Reference 23b.

procedure (Table 4). The final **8**:***cis*-8b** epoxide ratio was assessed by gas chromatography.

Discussion

Mechanism of the Episulfidation. The rate of endoperoxide **2** consumption, which follows first-order kinetics, is independent of olefin concentration. This indicates that the endoperoxide **2** itself is not attacked by the olefin and does not serve as the sulfur-transferring species. Instead, endoperoxide **2** decomposes in the rate-determining step to the two intermediates **I** and **II** (Scheme 3). Intermediate **I** is responsible for the formation of elemental sulfur, but the mechanism of such a sulfur extrusion is still obscure. Presumably, bimolecular processes are involved, since the expulsion of atomic sulfur is energetically an unlikely process.[13] The other intermediate **II** transfers a sulfur atom to the olefins **5** to form the thiiranes **6**. If a common intermediate were to intervene for both reaction modes, namely, *sulfur transfer* and *formation of elemental sulfur*, their ratio (reflected by the yield of thiirane **6** per converted endoperoxide **2** in Table 1) should depend on the starting olefin concentration and should decrease with reaction time. Both effects were not observed, and therefore, one common intermediate does not suffice to rationalize our results. The intermediates **I** and **II** are formed in a ratio of ca. 40:60, since the product composition (Table 1) indicates that ca. 40% of the available sulfur is extruded as elemental sulfur and ca. 60% is transferred to the olefins to yield thiirane **6**, which is independent of olefin type and concentration. The only olefin reactive enough to abstract a sulfur atom even from intermediate **I** is *trans*-cyclooctene (***trans*-5b**). This enhanced reactivity of the highly strained ***trans*-5b** in the episulfidation was confirmed by competition experiments ($k_{trans-5b}$:k_{cis-5b} > 50, Table 4) and is known for *m*CPBA and

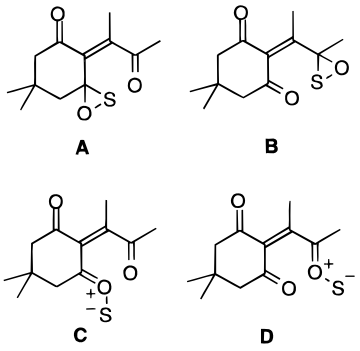
Scheme 3



DMD epoxidations.[22,28] Shea recently demonstrated by means of kinetics of the *m*CPBA epoxidation that the reactivity of strained olefins depends primarily on the strain-energy relief in the transition state, which correlates with the difference in the olefin and epoxide strain energies.[22]

The episulfidation of *trans*-cyclooctene (***trans*-5b**) led exclusively to the *trans*-thiirane **6b**. Unfortunately, no experimental and/or theoretical strain energies of fused-ring thiiranes are available;[10c] therefore, we assume that the isomer ***cis*-6b** is thermodynamically more stable than the ***trans*-6b** one. This assumption is based on the data reported for the corresponding olefins and epoxides (the difference in the strain energy for the cyclooctenes ***trans*/*cis*-5b** is 9.8 kcal/mol; for the corresponding epoxides ***trans*/*cis*-8b** it is 4.2 kcal/mol).[22] If a stepwise sulfur atom transfer were to take place through diradical or dipolar intermediates, bond rotation and, thus, *trans*/*cis* isomerization to the thermodynamically favored thiirane ***cis*-6b** would be expected.[28] This isomerization was not observed, and therefore, the sulfur atom transfer is presumed to be a concerted process.

Oxathiiranes and/or carbonyl *O*-sulfides have been postulated as transients in the thermolysis of 2,5-dimethylthiophene endoperoxide.[13] Both short-lived intermediates may serve as potential sulfur-transferring species.[13b] Consequently, in the thermolysis of the unsymmetric endoperoxide **2**, the two oxathiiranes **A** and **B** and the two carbonyl *O*-sulfides **C** and **D** would result.



From the experimental results it is not possible to decide unequivocally which of these species **A**−**D** serves as the sulfur-transferring and which as the sulfur-extruding agent, but as indicated above, it must be two distinct ones. However, from what is known about the analogous dioxiranes, which are highly efficient epoxidation reagents,[12,29] and carbonyl *O*-oxides, which tranfer oxygen only in some special cases,[30] a higher sulfur-transfer propensity should be ascribed to the oxathiiranes **A** and **B**. Indeed, recently we have demonstrated this efficacy of oxathiiranes, generated photochemically from thiocarbonyl *S*-oxides (sulfines).[14]

The diastereoselectivities of the episulfidations of the olefins **5a**−**e** (Table 1) follow qualitatively those for the epoxidations (Table 2). Furthermore, the reactivity of the olefins **5a**−**e**, which was confirmed by competition experiments (Table 4), follows the same trend in both reactions, i.e., ***trans*-5b** ≫ ***cis*-5b** > **5e** ≈ **5c** ≈ **5a** ≈ **5d**. These similarities in the episulfidation by endoperoxide **2** and the epoxidation by DMD suggest that the dioxirane-related oxathiiranes **A** and **B** function as active sulfur-transferring agents.

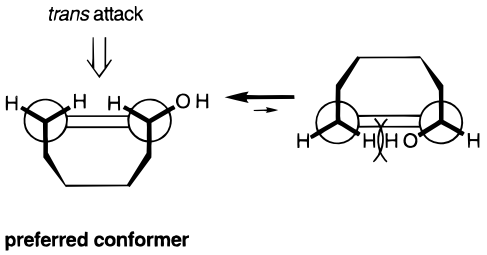


Figure 2. *Trans* selectivity for the episulfidation and epoxidation of cyclooctenol **5c**.

The carbonyl group of the endoperoxide **2** seems to play an essential role for the sulfur-transfer efficiency, since in the thermolysis of the 2,5-dimethylthiophene endoperoxide in the presence of a 10-fold excess of norbornene (**5a**) only 7% of thiirane **6a** was obtained,[13b] whereas endoperoxide **2** transferred ca. 60% of the available sulfur to norbornene (**5a**, Table 1). The additional carbonyl group enhances the electrophilicity of the sulfur-transferring intermediate and promotes the reaction with the nucleophilic olefin. A similar effect is observed in dioxirane chemistry: less reactive substrates are treated with methyl(trifluoromethyl)dioxirane instead of DMD.[31]

Diastereoselective Episulfidation and Epoxidation of Cyclooctenol 5c. Whereas 3- and 4-cyclooctenol (**5d**,**e**) reacted unselectively to give *cis/trans* mixtures of the corresponding episulfides **6** or epoxides **8**, both the episulfidation and epoxidation of 2-cyclooctenol (**5c**) occurred completely diastereoselectively (Tables 1 and 3). This *trans* selectivity is known for the *m*CPBA epoxidation of **5c**[21] and is dictated by the substrate.[32] In the preferred conformation of the cyclooctenol **5c**, the OH group avoids the repulsive transannular interaction and the sulfur or oxygen donor attacks from the *trans* side, which is not shielded by the methylene groups of the cyclooctene (Figure 2).

Epoxidation of Cyclooctenols 5c−e. In general, two reaction modes are known for the epoxidation of hydroxy-substituted alkenes by DMD, namely, epoxidation, which usually dominates, and C−H insertion to form alkenones.[23a] In the cyclooctenol series **5c**−**e**, epoxidation is favored due to the loss of strain energy,[22] and therefore, alkenone formation is not observed. Only when most of the cyclooctenols **5d**,**e** have already been converted to the hydroxy epoxides **8d**,**e** are the latter oxidized by C−H insertion to the keto epoxides **9d**,**e** (Table 3). For the epoxide **8c**, this C−H insertion is slower because of its deactivation by the inductive effect of the neighboring epoxy group.

Conclusions

Thiophene endoperoxide **2**, which can readily be prepared by photooxygenation of thiophene **1**, transfers a sulfur atom to norbornene (**5a**) and cyclooctenes (**5b**−**e**). The diastereomeric pair *cis/trans*-cyclooctene (**5b**) reacted stereoselectively, which indicates that the sulfur-transfer step is a concerted process and does not involve open dipolar and/or diradical intermediates. Kinetic investigations clearly showed that the endoperoxide **2** itself is not the sulfur-transferring species. Instead, it is thermally transformed to the intermediates **I** (formation of elemental sulfur) and **II** (sulfur transfer). An unequivocal structural assignment of these intermediates based on the present experimental facts is not possible, but the oxathiiranes **A** and

(28) Adam, W.; Curci, R.; D'Accolti, L.; Dinoi, A.; Fusco, C.; Gasparrini, F.; Kluge, R.; Paredes, R.; Schulz, M.; Smerz, A. K.; Veloza, L. A.; Weinkötz, S.; Winde, R. *Chem. Eur. J.* **1997**, *3*, 105−109.
(29) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg.* **1996**, *105*, 581−599.
(30) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335−362.
(31) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett.* **1995**, *36*, 5831−5834.
(32) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370.

B are the most likely species for intermediate **II**, since oxathiiranes are known to possess sulfur-transfer capacity. Credence for this mechanistic hypothesis provides a comparison of the episulfidation, presumably by oxathiiranes, with the epoxidation by the related dioxirane DMD, since both show the same qualitative trends in the diastereoselectivity and the reactivity toward the alkenes **5a**−**e**.

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Supporting Information Available: Experimental details (19 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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