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REARRANGEMENT MECHANISMS OF 1,3-DITHIOLANE SULFOXIDES.

Wha Suk Lee,* Koo Lee, Kee Dal Nam, and Yang Joon Kim
Organic Chemistry Research Laboratory
Korea Institute of Science and Technology
P.O.Box 131, Cheongryang, Seoul, Korea

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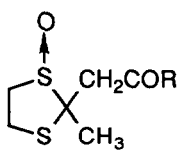
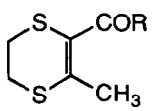
Abstract: *Oxidation of sulfide* **4** *gave a mixture of cis and trans monosulfoxides* **5** *and* **6** *as major and minor products, respectively, plus a small amount of disulfoxides* **7**. *The structural assignments of cis and trans sulfoxides* **5** *and* **6** *were based on* ^1H *NMR spectroscopy and the regiospecific deuterations of the two isomers . Under neutral conditions cis sulfoxides* **5** *underwent a sigmatropic rearrangement with 2-methylene hydrogens to give sulfenic acids* **18**, *followed by cyclization to dihydro-1,4-dithiins* **2** . *The trans sulfoxides* **6** *rearranged involving 2-methyl hydrogens to form isomeric dihydrodithiins* **3** *via sulfenic acids* **19**. *In the reactions of both the sulfoxides, sulfides* **4** *and disulfides* **11** *were also formed as minor side products. In the presence of acid catalyst cis sulfoxides* **5** *produced* **2** *in quantitative yields plus a small amount of* **3** , *while the trans sulfoxides* **6** *gave* **2** *as major product and* **3** *as minor. The mechanisms of formation of* **2**, **3**, **4** *and* **11** *are discussed.*

Introduction

The ring expansion reaction of appropriately substituted cyclic sulfoxides has been the subject of considerable interest from the synthetic as well as mechanistic viewpoints. Recently we have reported the rearrangement of 1,3-oxathiolane sulfoxides[1] and 1,3-thiazolidine sulfoxides[2]. We now report thermal and acid catalyzed rearrangements of 1,3-dithiolane sulfoxides **1**. Although the conversion of simple 1,3-dithiolane sulfoxides to the corresponding dihydro-1,4-dithiins has been reported[3,4], 1,3-dithiolane sulfoxides derived from acetoacetanilide or acetoacetic ester have not been reported.



1



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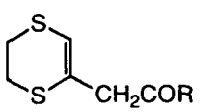


3

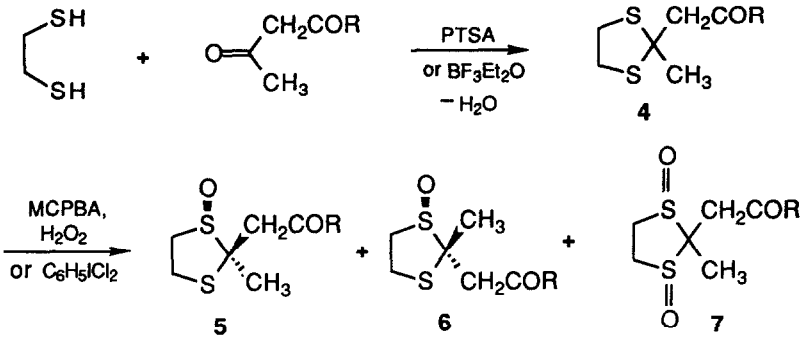
R = a NHC_6H_5 ; b OCH_3

An important feature of the new 1,3-dithiolane sulfoxide **1** is the presence of both carbonyl-activated methylene and unactivated methyl hydrogens β to the C-S bond being ruptured. Depending on the stereochemistry of sulfoxides **1** and reaction conditions under which the ring expansion takes place, either six-membered dihydrodithiins **2** or isomeric compounds **3** would result. Besides, the mode of ring opening of **1**, whether it is concerted or stepwise, will be mechanistically significant. Thus, it seemed of interest to investigate the rearrangements of these new sulfoxides and compare them with those of two previous series[1,2]

Results and Discussion

1,3-Dithiolane Sulfoxides. The parent 1,3-dithiolanes **4** were obtained by the usual methods for preparation of dithioketals [5]. Oxidation of the sulfides **4** with m-chloroperbenzoic acid (MCPBA) or hydrogen peroxide gave a mixture of cis and trans monosulfoxides **5** and **6** as major and minor products, respectively, in good yield in addition to a small amount of disulfoxide **7** (Scheme I). By contrast, oxidation of 1,3-dithiolane anilide **4a** by iodobenzene dichloride in aqueous pyridine afforded trans sulfoxide **6a** as the major product [6]. We have arbitrarily named the isomers as cis when the sulfoxide oxygen and the CH_2COR group are on the same face of the dithiolane ring and trans when they are on opposite faces.

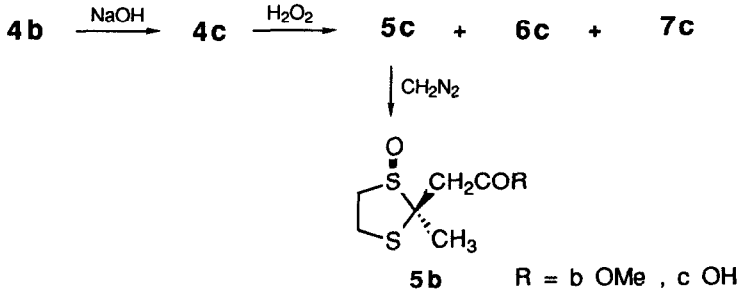
Scheme I



R = a NHC_6H_5 ; b OCH_3 ; c OH

The cis and trans sulfoxide amides **5a** and **6a** could be separated from each other by fractional crystallization or preparative TLC while attempts to separate cis and trans sulfoxide esters **5b** and **6b** were unsuccessful. However, the trans isomer **6b** could be isolated in pure form by refluxing a mixture of **5b** and **6b** in benzene with PTSA as catalyst until the cis isomer was completely transformed to dihydrodithiin **2b**. The unreacted trans isomer **6b** was then obtained by preparative TLC or column chromatography. Pure cis sulfoxide ester **5b** was obtained by the procedure shown in Scheme II.

Scheme II



Thus, when the sulfide acid **4c**, obtained by hydrolysis of **4b**, was oxidized, there was produced a mixture of cis and trans sulfoxide acids **5c** and **6c**, and a small amount of disulfoxide **7c**. From this mixture the cis sulfoxide acid was separated by fractional crystallization, and esterified to provide **5b**.

Structural assignments of the cis and trans isomers were made by ^{1}H NMR spectroscopy and deuterium incorporation in the 2-methylene and 2-methyl groups. In the ^{1}H NMR spectra the amide proton in the cis sulfoxides appeared at appreciably lower field than in the trans isomers possibly due to hydrogen bonding between NH protons and the sulfoxide oxygens (see Figure 1). Benzene-induced solvent shift[7] values provided further evidence in support of cis and trans configuration of S=O bond as in the case of 1,3-oxathiolane sulfoxides[1]. Confirmatory evidence for the stereochemistry of the cis and trans sulfoxides was found in the deuteration reactions of the two isomers as will be discussed later (see Scheme VI) .

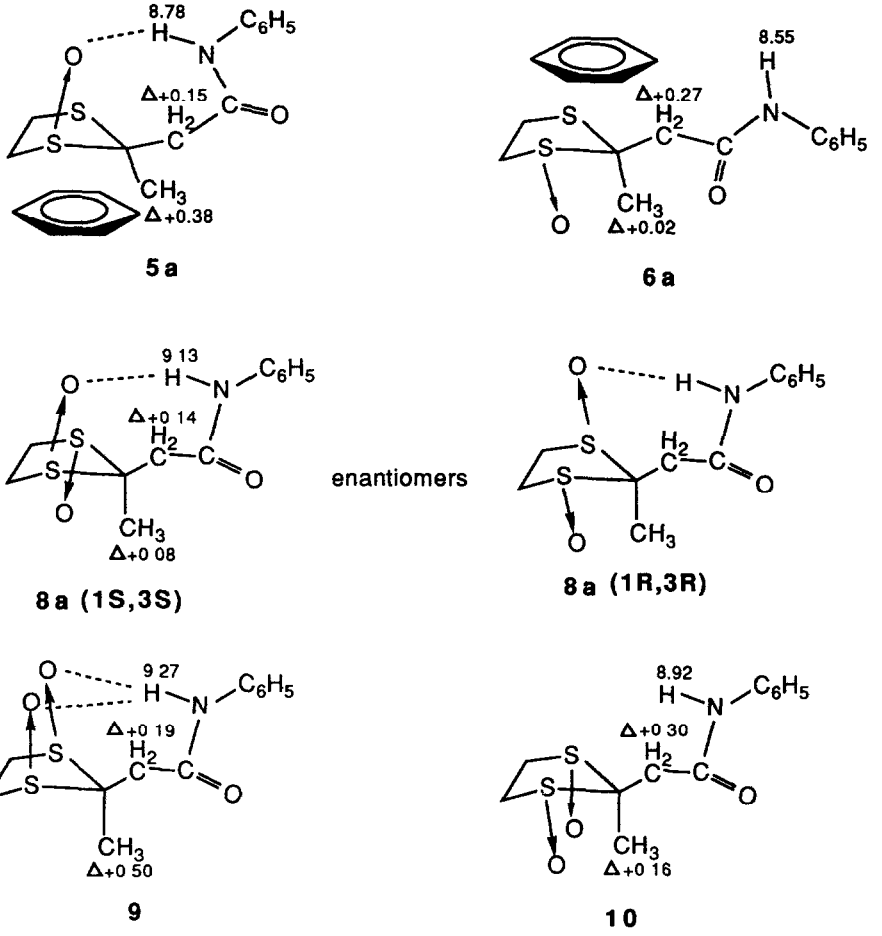


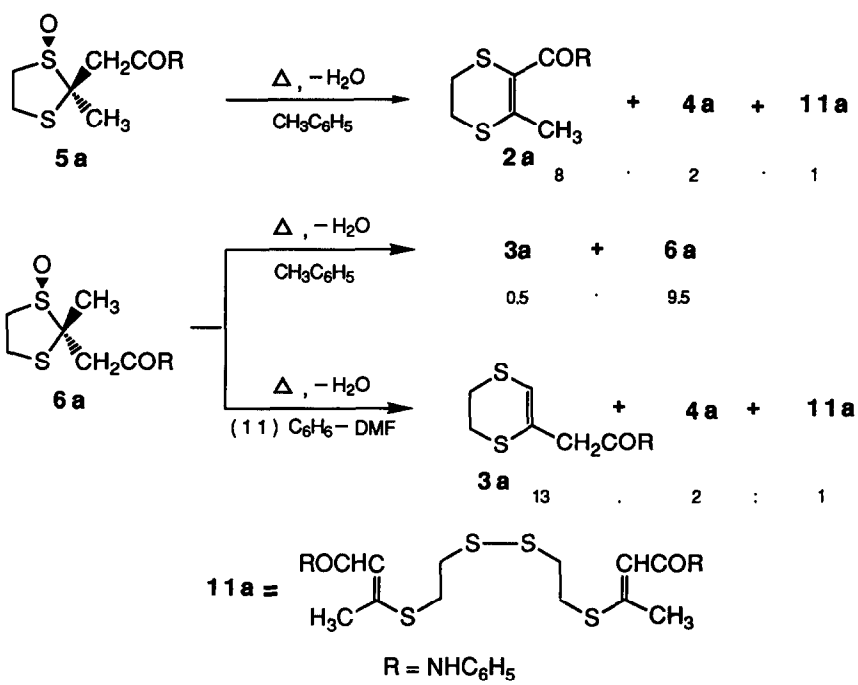
Figure 1. Perspective view of the cis and trans sulfoxides (**5a** and **6a**) and disulfoxides (**8a, 9** and **10**) and benzene - induced ^{1}H NMR shifts, $\Delta = \delta(CDCl_3) - \delta(C_6D_6)$

Disulfoxides. In the foregoing oxidation of the 1,3-dithiolanes **4**, the disulfoxide **7** was formed as a side product even when one equivalent of oxidizing agent was used for the starting sulfide **4**. It was found that the disulfoxide amide **7a** was a mixture of three different products **8a**, **9** and **10** as shown in Figure 1. There was also obtained a 3:1 mixture of **8a** and **9** plus a trace of **10** when the sulfide **4a** was treated with two equivalents of MCPBA. Isomer **10** was the major product when iodobenzene dichloride (two equivalents for **4a**) was used.

Assignments of the disulfoxide isomers were based on IR and ^{1}H NMR spectroscopy including aromatic solvent induced shift[7]. The amide proton of the disulfoxide **9** resonates at lower field than that of isomer **8a** owing to the double hydrogen bonding with two sulfoxide oxygens. On the other hand, the amide proton of **10**, in which hydrogen bonding between NH proton and sulfoxide oxygen is unfavored, appeared at higher field than that of **8a** or **9**. Benzene-d_6 induced solvent effects are best illustrated with the 2-methyl or 2-methylene protons. Thus the methyl proton resonance of the isomer **9** was shifted upfield as a result of anisotropy whereas those of **8a** and **10** were not appreciably affected in changing from $CDCl_3$ to C_6D_6. Interestingly, in the disulfoxide **8a** both the 2-methyl and 2-methylene protons are not affected since the benzene-d_6 molecule cannot approach from either side because of two S=O bonds sticking up in opposite directions (see Figure 1). Similarly, structures of disulfoxide ester **7b** and acid **7c** were identified by ^{1}H NMR spectroscopy, and these showed the same NMR pattern as did **8a**.

Sulfoxide to Dihydro-1,4-dithiin Conversion. Thermal reactions of cis and trans sulfoxides **5** and **6** under neutral conditions produced the expected dihydrodithiins **2** and **3**, respectively in good yields, plus sulfides **4** and disulfides **11** as side products[8]. The results are summarized in Scheme III.

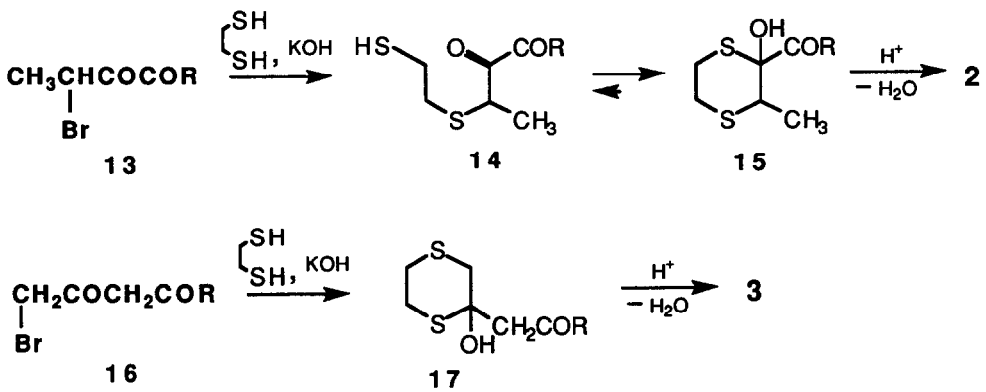
Scheme III



When the cis sulfoxide **5a** was heated in toluene solution at reflux with azeotropic removal of water for 45 h about 8:2:1 mixture of **2a**, **4a** and **11a**, respectively, was obtained as shown by TLC and ^{1}H NMR spectroscopy. Under the same conditions as above the trans sulfoxide **6a** afforded the isomeric dihydrodithiin **3a** in only 5 % yield with 95 % recovery. However, in refluxing 1:1 C_6H_6 - DMF (azeotropic removal of water) for 45 h **6a** gave approximately 13:2:1 mixture of **3a**, **4a** and **11a**, respectively. Similar results were obtained for the sulfoxide esters **5b** and **6b** from the reactions as described above.

The structures of the dihydro-1,4-dithiins **2** were identified by ^{1}H NMR spectroscopy as well as independent synthesis involving the reaction of 3-bromo-2-oxo-butanamide or ester **13** with ethanedithiol to form 1,4-dithian **15** via **14**, followed by acid-catalyzed dehydration[9]. The structures of isomeric dihydrodithiins **3** were confirmed also by independent synthesis by way of 4-bromoacetoacetanilide or ester **16** and dithian **17** (Scheme IV). The structures of disulfides **11** followed from elemental and spectral analysis.

Scheme IV



R = a NHC_6H_5 ; b OCH_3

In the presence of a catalytic amount of PTSA the cis sulfoxide **5a** in benzene solution at reflux (azeotropic removal of water) for 7 h gave the expected ring expansion product **2a** in quantitative yield plus a small amount of isomeric dihydrodithiin **3a**. Under the same conditions the trans isomer **6a** gave **2a** as major product and **3a** as minor. Each reaction of **5** or **6** also contained a mixture of the cis and trans sulfoxides **5a** and **6a** probably due to isomerization between them during the reaction. The results are summarized in Scheme V. The change in product ratios with time in the reactions of **5a** and **6a** are listed in Table 1.

Scheme V

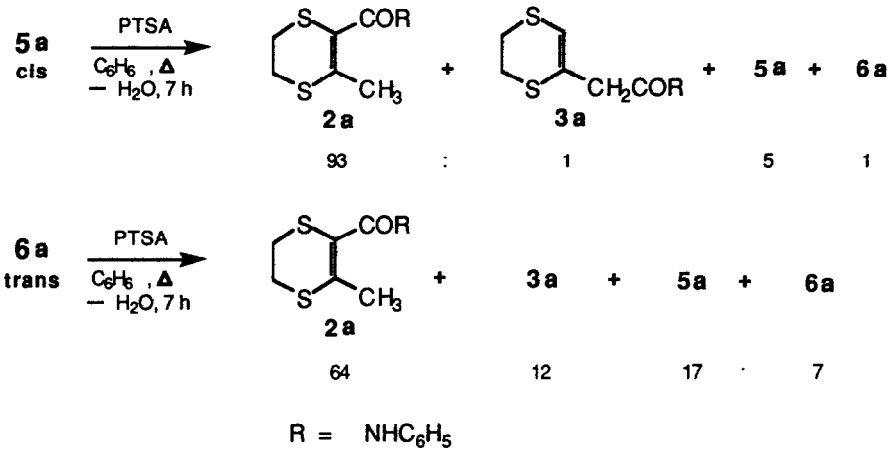


Table 1. Variation in product ratios in the reactions of cis sulfoxide **5a** and trans sulfoxide **6a** with PTSA[a].

Cis Sulfoxide **5a**

time (h)	**5a**	**6a**	**2a**	**3a** , %[b]
0	100.00	0.00	0.00	0.00
1	67.07	2.60	30.15	0.17
2	48.22	5.43	45.93	0.40
3	32.50	4.21	62.76	0.54
4	21.26	4.23	73.60	0.92
5	13 15	3.37	82.60	0.86
6	8.94	2.75	87.03	1.29
7	4.66	1.07	93.12	1.16

Trans Sulfoxide **6a**

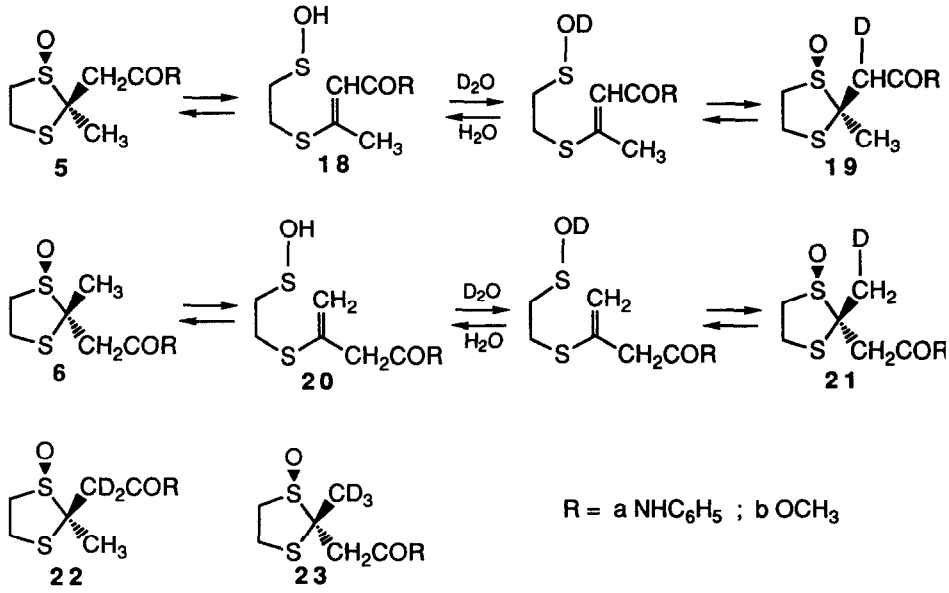
time (h)	**6a**	**5a**	**2a**	**3a** , %[b]
0	100.00	0.00	0.00	0.00
1	77.51	13.82	7.86	0.81
2	60.11	21.16	14.79	3.94
3	45.93	23.92	24.02	6.13
4	32 75	26.32	33.04	7.89
5	22.78	23.92	42.37	10.93
6	13.33	19.89	56.23	10.56
7	7.08	16.84	63.80	12.28
8	4.07	11.34	70.64	13.95
9	1.53	6.16	78.27	14.03

a In refluxing benzene solution of **5a** or **6a** with 0.05 molar equivalents of PTSA.

b Ratios were determined by NMR spectroscophy (300 MHz).

Deuteration Reactions of the Sulfoxides. In order to obtain mechanistic information for the foregoing reactions of the cis and trans sulfoxides **5** and **6** (Scheme III) deuteration reactions of the two isomers were carried out under various conditions, and the results are summarized in Table 2 while the deuterium exchange process is shown in Scheme VI.

Scherme VI



When the cis isomer **5** was heated in an appropriate solution containing a large excess of D_2O, only the 2-methylene group was deuterated to give **19** (as determined by ^1H NMR spectroscopy)[10]. The reaction very likely proceeds via sulfenic acid intermediate **18** formed by a reversible sigmatropic rearrangement[4,11] involving the carbonyl activated methylene hydrogens. In the presence of D_2O hydrogen-deuterium exchange in the sulfenic acid, followed by recyclization results in deuterium incorporation into the 2-methylene group. Under the same conditions the trans isomer **6** reacted much more slowly and incorporated deuterium only in the 2-methyl group to give **21** (shown by ^1H NMR)[10]. The reaction may proceed by way of sulfenic acid **20** formed by a reversible sigmatropic rearrangement with unactivated 2-methyl hydrogens. Based on these stereospecific deuterations and the relative ease of reactions of the two isomers the stereochemistry of cis and trans sulfoxides was assignable as mentioned previously.

Table 2. Deuterium incorporation in the cis and trans sulfoxides

sulfoxide	solvent [a]	temp. (°c)	time (h)	deuterium incorpo. (%) [b]		sulfoxide recovery (%)
				2−CH_2	2−CH_3	
5a	C_6H_6	80	24	95		100
6a	C_6H_6	80	72		60	100
5b	C_6H_6	80	12	95		100
6b	C_6H_6	80	72		75	100
5a	$CH_3C_6H_5$	111	12	100		100
6a	$CH_3C_6H_5$	111	48		95	?
6a	DMF-C_6H_6 (1 : 1)	98	48		45	
6b	DMF-C_6H_6 (1 : 1)	98	48		65	

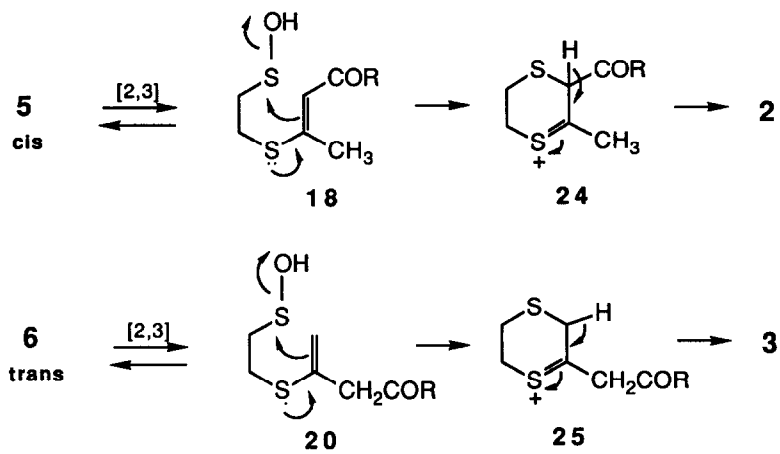
a D_2O − Solvent (0.3 : 3 v/v) ; b by ^1H NMR spectrum
c The sulfoxide was mostly recovered with a small amount of by-products as a mixture of probable 3 + 2 + 4 + 11

In all cases shown in Table 2 the recovered sulfoxide had the same stereochemistry as the starting sulfoxide indicating that no isomerization occurred to interconvert cis and trans sulfoxides **5** and **6** under these conditions. The stereospecific recyclization of the sulfenic acids **18** and **19** to their parent sulfoxides **5** and **6**, respectively, may arise from the geometrical requirements of the reacting bond and atom in the reverse sigmatropic rearrangement[12]. That the thermal reactions of the sulfoxides **5** and **6** are sigmatropic was substantiated by determining the kinetic deuterium isotope effect for **5a/22a** and **6a/23a** and the K_H/K_D was found to be 2.08 and 2.10[13], respectively, which are in the range of expected values for primary isotope effect in β-cis eliminations .

The data in Table 2 also shows something noteworthy. Unlike the D_2O free reactions of **5** and **6** in refluxing toluene which produced ring expansion products and by-products as shown in Scheme III the corresponding products were not formed in the deuteration reactions of **5** and **6**. It is possible that as the deuteration progresses the reaction is slowed down due to the deuterium isotope effect. More important reason, however, seems to be that a large excess of D_2O present in the reaction mixture may prevent ring expansion product from forming by dehydration. The D_2O may also interfere with the dimerization (producing water) of sulfenic acid to thiosulfinate (see Scheme VIII) which would be precursor of by-products. At the lower temperature of refluxing benzene with or without D_2O, no ring expansion products or by-products (Scheme III) were formed from the sulfoxides **5** or **6** (see the Mechanism below).

Mechanism of Sulfoxide Rearrangement The ring expansion reaction of the cis sulfoxides **5** under neutral conditions in refluxing toluene or C_6H_6-DMF proceeds via sulfenic acid **18** as generated by [2,3] sigmatropic rearrangement with the 2-methylene group, followed by cyclization to the sulfonium ions **24** which probably serve as precursors to **2** (see Scheme VII). Although the ring opening occurred in refluxing benzene (80°C) to give **18** as evidenced by the results of the deuteration reactions they did not produce dihydrodithiins **2**. Therefore, in harmony with the conclusion from the deuteration study, the cyclization of **18** is the slow step, requiring the higher temperature of refluxing toluene (111°C) to force the S_N2 displacement at the sulfur atom by the internal double bond to give **24**. Likewise, in the rearrangement of the trans sulfoxides **6** in C_6H_6-DMF at reflux, a sigmatropic ring opening occurs involving the 2-methyl group to form sulfenic acids **20** which cyclize to sulfonium ions **25** to give the expected isomeric dihydrodithiins **3** (Scheme VII).

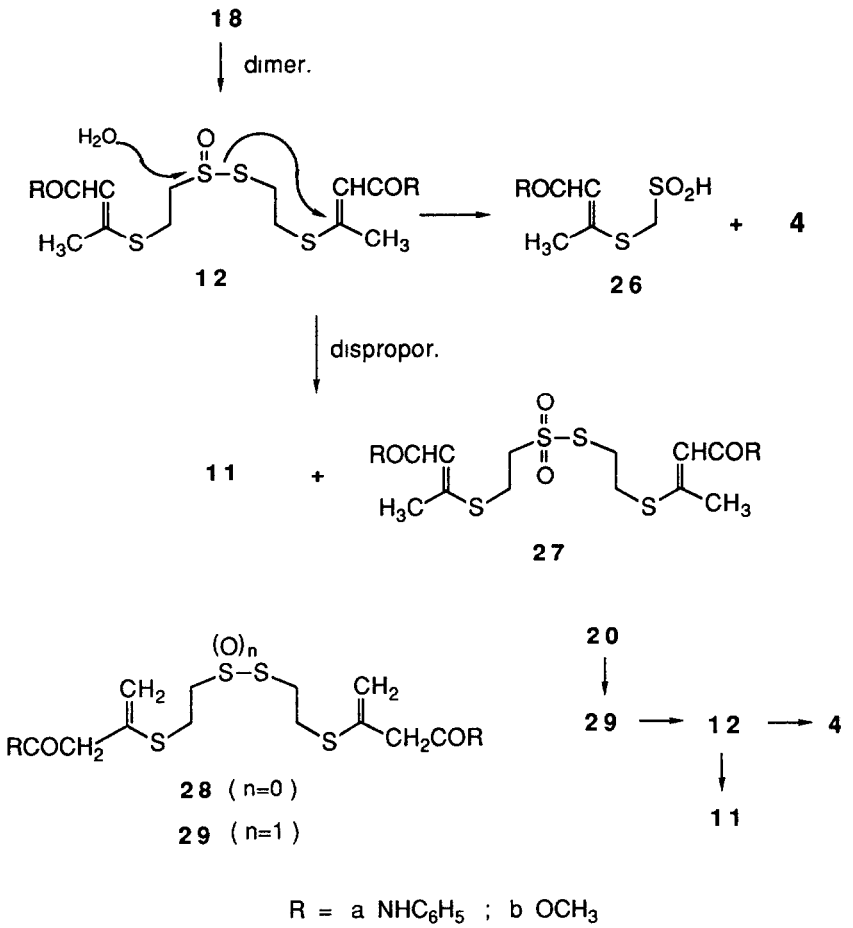
Scheme VII



R = a NHC_6H_5 ; b OCH_3

The probable origins of by-products **4a** and **11a** in the ring expansion reactions of **5a** and **6a** are shown in Scheme VIII according to the known transformations of sulfenic acids and thiosulfinates[15]. Thus, in the reaction of **5a** some of the initially formed sulfenic acid molecules **18** may have dimerized to thiosulfinate **12a** which is not isolable under the reaction conditions. Most likely, **11a** was formed along with thiosulfonate **27a** from disproportionation of **12a**. It is probable that the sulfide **4a** was formed from the thiosulfinate **12a** by water attack at the sulfinyl sulfur with liberation of sulfinic acid **26**. Although the thiosulfinate **29** or disulfide **28** was not found in the reaction mixture from **6a**, it is conceivable that some of the sulfenic acid **20** dimerized to the corresponding thiosulfinate **29**, followed by tautomerization to **12a**. Thus, **4a** and **11a** are formed from **12a** in the same way as in the reaction of **5a**.

Scheme VIII

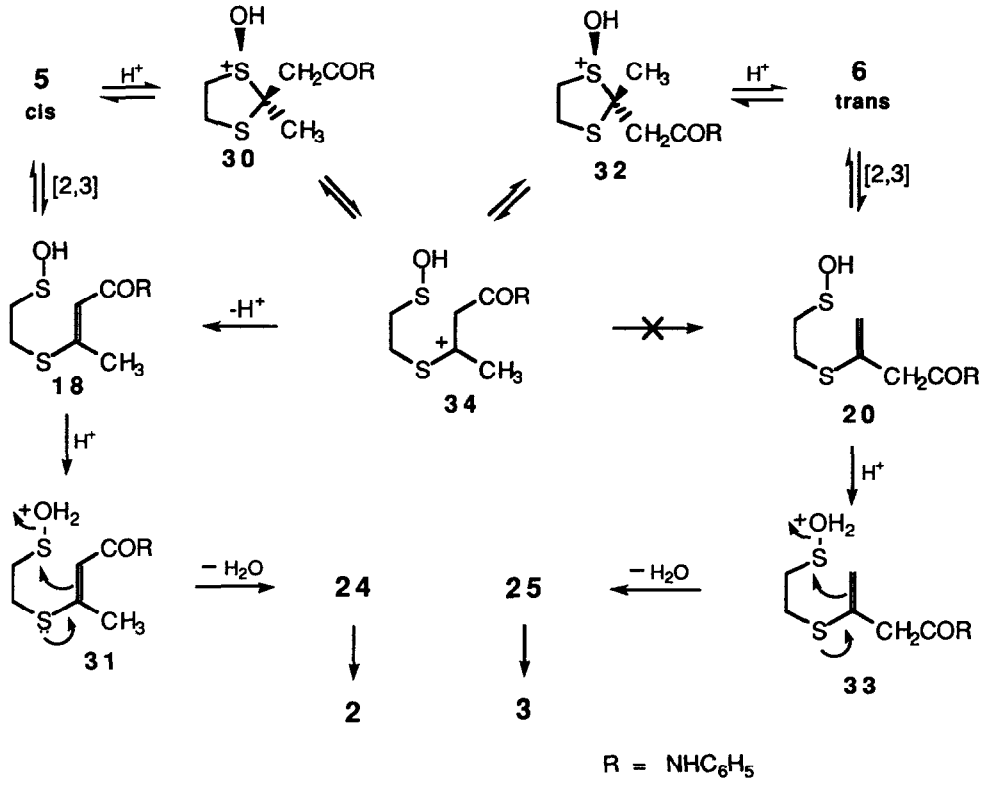


R = a NHC_6H_5 ; b OCH_3

In the presence of acid catalyst, it is likely that ring expansion reactions of both the cis and trans sulfoxides **5** and **6** proceed by two competitive mechanistic pathways. An overall mechanism is summarized in Scheme IX.

The ring opening of the cis sulfoxides **5** would take place via protonated sulfoxides **30** to form carbocation **34** from which sulfenic acid **18** is formed with loss of acidic β-hydrogen. The carbocation may also undergo nonstereospecific recyclization to give a mixture of the cis and trans isomers[2,16]. The sulfenic acid **18** could also be formed directly by sigmatropic ring opening of **5** involving 2-methylene hydrogens. The sulfenic acid undergoes acid catalyzed ring closure to sulfonium ion **24** to produce dihydrodithiin **2**. Likewise, from the trans sulfoxide **6** carbocation **34** is formed via protonated sulfoxides **32** to give sulfenic acid **18** which leads to **2**. The ring opening of **6** could also occur by sigmatropic rearrangement with 2-methyl group to give sulfenic acid **20** which, by acid catalyzed dehydration, produces isomeric dehydrodithiins **3** via **25**.

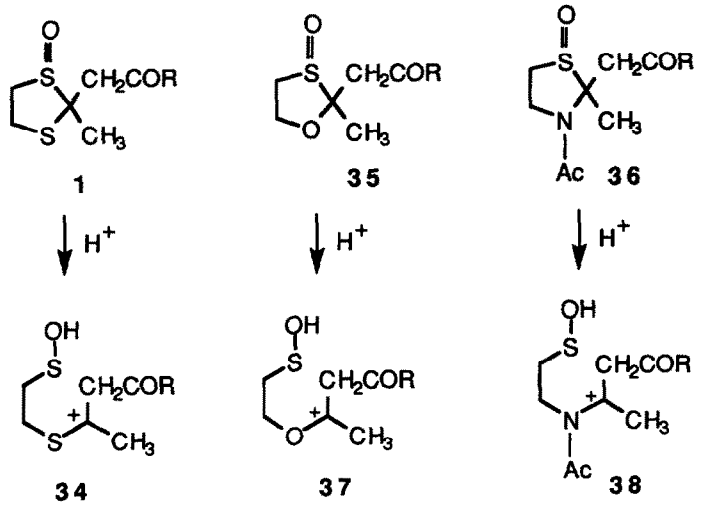
Scheme IX



Evidence for the carbocation **34** intermediacy was provided by the observed isomerization to interconvert **5** and **6** during the acid catalyzed reaction (see Table 1)[17]. The data in Table 1 show that the ring expansion product **2** forms much faster from the cis sulfoxide **5** than from the trans isomer **6**. This suggests that the sulfenic acid **18** is formed not exclusively via carbocation **34**. If **34** were only the reaction pathway the rate of formation of **2** from **5** and **6** should be equal. The fact that the cis sulfoxide **5** produces **2** much faster than the trans isomer **6** can be supporting evidence that sulfenic acid **18** is formed from **5** by a facile sigmatropic ring opening involving activated 2-methylene hydrogen as well as by stepwise mechanism involving carbocation **34**.

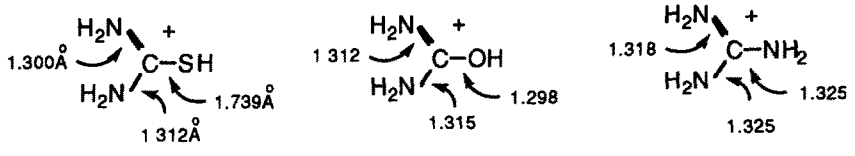
On the other hand, the trans sulfoxide **6** produces **18** only via carbocation **34**. and also reacts by a slow sigmatropic ring opening involving unactivated 2-methyl hydrogen to give sulfenic acid **20** leading to **3**. It is unlikely that carbocation **34** loses a 2-methyl proton to give sulfenic acid **20**. For if this were the case the product ratio **2/3** in the reactions of both **5** and **6** shuld be comparable with each other. Further support for these two reaction pathways in the ring expansion of **6** is the fact that product **2** increases with the amount of PTSA at the expense of **3** as we previously observed. Thus, at higher acid catalyst concentration the chance for **6** to react by sigmatropic ring opening with 2-methyl group to give **20** is decreased as compared to stepwise ring opening to give **18**.

Scheme X



R = NHC_6H_5

Relative stability : **34** ≪ **37** > **38**



Single bond values = C–SH 1.81 C–OH 1.43 $C–NH_2$ 1.48

ΔL = −0.07 −0.132 −0.155

∴ Delocalization order : S ≪ O < N

In the related series 1,3-oxathiolane sulfoxides **35**[18] and 1,3-thiazolidine sulfoxides **36**[2], isomerization also occurs to interconvert cis and trans sulfoxides in the presence of a acid catalyst, indicating involvement of carbocations **37** and **38** (Scheme X). Comparison of the reactivity of sulfoxides **1**, **35** and **36** for water in the presence of acid catalyst is interesting. When the sulfoxides **35** was heated in benzene at reflux with PTSA as a catalyst, a mixture of acetoacetanilide as major product and ring expansion product as minor resulted even though water was removed azeotropically during the reaction. This indicates that carbocation **37** was hydrolyzed fast. In contrast, under the same conditions sulfoxides **1** and **36** give ring expansion products in quantitative yield. These results can be related to the stability of carbocations **34**, **37** and **38**. Thus, more stable carbocation, forming faster,would undergo water attack more readily to give the parent ketone.

The relative stability of **34** , **37** and **38** can be verified indirectly from bond length data[19] on the salts of thiourea, urea and guanidine as illustrated in Scheme X. Consistent with resonance structures all three bond distances in each of the salts exhibit partial double bond character. Thus, substracting C-S, C-O and C-N single bond length values from the corresponding bond length in the resonance structures gives ΔL values, which indicate that the delocalization is in increasing order from sulfur to nitrogen and that the oxygen and nitrogen atoms have by far greater effect on stabilizing a cation compared with the sulfur atom. On the basis of these data the carbocation **34** is much less stable than **37** and **38**.

For comparing the carbocation **37** with **38** no data relative $R\text{-}CO\text{-}N\text{-}^{+}C$ are available to us at present, but considering the parent sulfoxide **35** was more reactive than **36** for water in the presence of a acid catalyst it seems probable that ether oxygen is more effective than amide nitrogen at stabilizing a cation. Thus, it can be concluded that the relative stability of the carbocations is **34 << 37 > 38**.

Experimental

General procedure. All melting points were obtained with an Electro thermal melting point apparatus and are uncorrected. Infrared spectra were recorded on a Analect Model FX-6160 FT-IR spectrophotometer. ^1H NMR spectra were recorded on a Varian Model EM 360 (60 MHz), a Brucker AM-system (200 MHz) or a Varian Gemini 300 (300 MHz) using Me_4Si as an internal standard and all are reported in δ. Elemental analyses of new compounds are within 0.4 % of the theoretical values unless otherwise noted. All chromatographic isolations were accomplished by preparative thin-layer or column chromatography, using Kieselgel GF 254 silica gel or Wakogel Q-23 silical gel, respectively.

Material. All solvents were freshly distilled and stored under a nitrogen atmosphere. Benzene and toluene were purified respectively by being shaken with concentrated H_2SO_4 until free of thiophene and predried over Na wire, heated at reflux over Na wire, and distilled at atmospheric pressure. Acetoacetanilide, methyl acetoacetate and 1,2-ethanedithiol were purchased from Aldrich Chemicals.

Synthesis of 2-Methyl-N-phenyl -1,3 -dithiolane -2-acetamide (4a).

To a refluxing solution of acetoacetanilide (10.63 g, 0.06 mol) and 1,2-ethanedithiol (7.35 g, 0.08 mol) in anhydrous ether (150 mL) was added borontrifluoride etherate (7.1 mL, 0.06 mol) dropwise over 20 min. The mixture was refluxed further for 1 h and cooled. The solid precipitate was filtered and the filtrate was evaporated under reduced pressure to give an oily residue, which was dissolved in methylene chloride. The solution was washed with sodium bicarbonate solution, followed by water, and dried (Na_2SO_4) The solvent was removed to give a white solid (1.3 g). The combined solid was crystallized from ethanol to obtain white needles **4a** (14.4g, 95 %): mp 156-158 °C; ^1H NMR (60 MHz) ($CDCl_3$) δ 1.90 (s, 3, 2-CH_3), 3.00 (s, 2, 2-CH_2), 3.37 (s, 4, 4-CH_2, 5-CH_2), 7.0-7.6 (m, 5, ArH), 8.10 (s, 1, NH) ; IR (KBr) 1650 (C=O) cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 56.88; H, 5.97; N, 5.70; S, 25.31. Found: C, 56.9; H, 6.02; N, 5.80; S, 25.46.

Synthesis of 2-Methyl-1,3-dithiolane-2-acetic acid Methyl Ester (4b).

A solution of methyl acetoacetate (10.45 g, 0.09 mol) and 1,2-ethanedithiol (8.48 mL, 0.09 mol) in benzene (50 mL) containing p-toluenesulfonic acid monohydrate (PTSA) (0.17 g) was refluxed with a Dean-Stark water trap for 3 h. The solution was washed with sodium bicarbonate solution and water, and dried (Na_2SO_4). The solvent was evaporated to give a pale yellow oil (17.15 g). Fractional distillation of this residue under reduced pressure gave a colorless oil **4b** (14.4 g, 83 %): bp 96 °C / 7 mmHg: ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.94 (s, 3, 3-CH_3), 3.05 (s, 2, 2-CH_2), 3.40 (s, 4, 4-CH_2, 5-CH_2), 3.74 (s, 3, OCH_3); IR (KBr) 1735 (C=O) cm^{-1}. Anal. Calcd for $C_7H_{12}O_2S_2$: C, 43.75: H, 6.25: S, 33.33. Found: C, 43.7; H, 6.28; S, 33.4.

Synthesis of 2-Methyl-N-phenyl-1,3-dithiolane-2-acetamide 1-Oxides (5a and 6a).

Method A. A solution of 1,3-dithiolane **4a** (5.07 g, 0.02 mol) in acetic acid (70 mL) was cooled to 15-20 °C in an ice bath. Hydrogen peroxide (35 %) (2.44 mL, 0.022 mol) in water was added dropwise over 15 min. Stirring was continued at the same temperature for 1 h. To the resulting mixture in the same bath was added dropwise 6 N NaOH solution until the mixture reached pH 7. The product was extracted with methylene chloride, and the extract was washed with water and dried (Na_2SO_4). The solvent was evaporated to give a white foamy solid (5.35 g, 90 % for **5a** and **6a**) as a mixture (ca. 7:3:1) of cis and trans monosulfoxides, **5a** and **6a**, respectively, and disulfoxides **7a** as determined by ^{1}H NMR spectrum. These isomeric monosulfoxides were separated by preparative TLC. Thus 1.0 g of the mixture was chromatographed on silica gel plates using 50:1 chloroform-methanol (v/v) as developing solvent to obtain 0.45 g of cis isomer **5a** and 0.1 g of trans isomer **6a** (crystallized from ethyl acetate and petroleum ether).

For **5a** : mp 141-143°C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.80 (s, 3, 2-CH_3), 3.16 (s, 2, 2-CH_2), 3.2-3.9 (m, 4, 4-CH_2, 5-CH_2), 7.0-7.7 (m, 5, ArH), 8,78 (s, 1, NH) ; IR (KBr) 1681 (C=O), 1041 (S=O) cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C; 53.50; H, 5.61; N, 5.20; S, 23.81. Found. C, 53.3; H, 5.61; N, 5.1; S, 23.91.

For **6a** : mp 142-144 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.76 (s, 3, 2-CH_3), 2.95 (d, 2, 2-CH_2), 3.1-3.8 m, 4, 4-CH_2, 5-CH_2), 7.0-7.7 (m, 5, ArH), 8.55 (S, 1, NH); IR (KBr) 1681 (C=O), 1039 (S=O) cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 53.50; H, 5.61; N, 5.20; S, 23.81. Found: C, 53.4; H, 5.62; N, 5.1; S, 23.69.

Method B. To a stirred suspension of **4a** (2.53 g, 0.01 mol) in chloroform (50 mL) cooled in an ice bath was added a cool solution of 80-90 % MCPBA (2.23 g, ca. 0.011 mol) in chloroform (80 mL) dropwise over 30 min. After stirring for 2 h the resulting reaction mixture was washed with sodium bicarbonate solution, water and dried (Na_2SO_4). The solvent was evaporated to give a white solid (2.71 g) as a mixture of **5a**, **6a** and **7a** (ca. 9:1:1 by NMR spectrum).

Method C. A solution of iodobenzene dichloride[20] (2.28 g, 0.01 mol) in pyridine (6 mL) was added to a stirred solution of **4a** (2.0 g, 7.89 mL) in 3:1 pyridine-water (20 mL) dropwise over 15 min at 15-25 °C. The mixture was stirred for an additional 30 min and diluted with methylene chloride (50 mL). The solution was washed with 1 N sulfuric acid (50 mL) once and with water three times, and dried (Na_2SO_4). The solvent was evaporated to give a pale yellow solid (2.13 g, 79 %) as a mixture of cis and trans (ca. 3:7) isomeric sulfoxides **5a** and **6a**.

Synthesis of 2-Methyl-1,3-dithiolane-2-acetic Acid Methyl Ester 1-Oxides (5b and 6b) and Isolation of 6b.

These compounds were prepared by the same procedure as described in method B for **5a** and **6a**. To a stirred solution of **4b** (9.62 g, 0.05 mol) in chloroform (200 mL) at 0-5°C was added dropwise a solution of 80-90 % MCPBA (12.18 g, ca. 0.06 mol) in chloroform (500 mL) over 1.5 h. Stirring was continued at the same temperature for 2 h. After workup there was obtained a 7:3:1 mixture of cis, trans sulfoxides **5b**, **6b** and disulfoxides **7b**, respectively (by NMR spectrum), which was dissolved in ethyl ether, and the precipitate was filtered to give **7b** as a white solid. The filtrate was removed to give a coloress oil (9.93 g, 95 %) as a mixture of **5b** and **6b**. A solution of this mixture and PTSA (0.29 mg) in dry benzene (100 mL) was refluxed with Dean-Stark water trap for 2.5 h. The resulting solution was washed with sodium bicarbonate solution and with water, and then dried (Na_2SO_4). Evaporation of the solvent yielded an oily residue (9.19 g) as a 3:1 mixture of dihydrodithiin **2b** and trans sulfoxide **6b**, followed by column chromatography on silica gel with 1:1 n-hexane-ethyl acetate (v/v) to obtain **6b** (1.88 g, overall 18 %) as a yellow oil. In the refrigerator this oil crystallized.

For **6b**: mp 23-25 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.80 (s, 3, 2-CH_3), 2.83 (d, 2, 2-CH_2), 3.1-3.6 (m, 4, 4-CH_2, 5-CH_2), 3.77 (s, 3, OCH_3); IR (NaCl) 1742 (C=O), 1049 (S=O) cm^{-1}. Anal. Calcd for $C_7H_{12}O_3S_2$: C, 40.36; H, 5.81; S, 30.78. Found: C, 40.3; H, 5.75: S, 30.90.

For **7b**: 153-154°C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.62 (s, 3, 2-CH_3), 3.07 (s, 2, 2-CH_2), 3.5-4.0 (m, 4, 4-CH_2, 5-CH_2), 3.74 (s, 3, OCH_3): IR (NaCl) 1733 (C=O), 1033 (S=O) cm^{-1}. Anal. Calcd for $C_7H_{12}O_4S_2$: C, 37.5; H, 5.36; S, 28.57. Found: C, 37.3; H, 5.37; S, 28.3.

Synthesis of 2-Methyl-1,3-dithiolane-2-acetic Acid Methyl Ester 1-Oxide (5b).

Step 1. Preparation of 2-Methyl-1,3-dithiolane-2-acetic Acid (4c).

A solution of 1,3-dithiolane **4b** (9.62 g, 0.05 mol) and 1 N aqueous sodium hydroxide (75 mL) was refluxed for 4 h. The resulting mixture was washed with methylene chloride and acidified to pH 2 with 1 N hydrochloric acid, then extracted with methylene chloride and dried (Na_2SO_4). The solvent was removed to obtain 1,3-dithiolane **4c** as a crystalline solid (8.63 g, 97 %): mp 68-69: ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.95 (s, 3, CH_3), 3.08 (s, 2, CH_2), 3.37 (s, 4, 4-CH_2, 5-CH_2), 11.64 (s, 1, OH); IR (KBr) 3300 (OH), 1655 (C=O) cm^{-1}. Anal. Calcd for $C_6H_{10}O_2S_2$: C, 40.45; H, 5.62; S, 35.96. Found: C, 40.45; H, 5.07; S, 35.8.

Step 2. Preparation of 2-Methyl-1,3-dithiolane-2-acetic Acid 1-Oxide (5c).

To a stirred solution of **4c** (1.78 g, 0.01 mol) in methylene chloride (30 mL) cooled in an ice bath at 0 °C was added 35 % H_2O_2 (1.17 mL, 0.01 mol) in water. The reaction mixture was stirred for 1 h at the same temperature and dried over Na_2SO_4. Evaporation of the solvent gave a gummy residue as a 13:56:8:23 mixture of cis, trans sulfoxides **5c**, **6c**, disulfoxide **7c** and starting **4c**, respectively as determined by ^{1}H NMR spectroscopy, which was crystallized from methylene chloride and petroleum ether to give cis sulfoxide acid **5c** (0.76 g, 39 %) as a white crystal: mp 120-121 °C, ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.71 (s, 3, CH_3), 3.15 (d, 2, 2 CH_2), 3.0-3.9 (m, 4, 4-CH_2, 5-CH_2), 9.83 (s, 1, OH); IR (KBr) 3300 (OH), 1662 (C=O), 1053 (S=O) cm^{-1}. Anal. Calcd for $C_6H_{10}O_3S_2$: C, 37.11; H, 5.15; S, 32.99. Found; C, 36.9; H, 5.18; S, 32.6.

Step 3. Preparation of Cis Sulfoxide Ester 5b.

A stirred solution of **5c** (0.50 g, 2.58 mmol) in methylene chloride was cooled in an ice bath. To this was added dropwise an ethereal solution of diazomethane until yellow color remained in the solution. After removing the solvent, **5b** (0.53 g, 99 %) was obtained as a pale yellow oil: ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.80 (s, 3, CH_3), 3.15 (d, 2, 2-CH_2), 3.2-3.7 (m, 4, 4-CH_2, 5-CH_2), 3.77 (s, 3, OCH_3); IR (NaCl) 1741 (C=O), 1048 (S=O) cm^{-1}. Anal. Calcd for $C_7H_{12}O_3S_2$: C, 40.36; H, 5.74. Found: C, 40.1: H, 5.74.

Synthesis of 2-Methyl-N-phenyl-1,3-dithiolane-2-acetamide 1,3-Dioxides (8a and 9).

To a stirred solution of **4a** (1.27 g, 0.005 mol) in chloroform (30 mL) was added dropwise a solution of 80-90 % MCPBA (2.03 g, ca. 0.01 mol) in chloroform (150 mL). After workup a white solid (1.30 g) was obtained as a 3:1 mixture of disulfoxides **8a, 9** and a trace of **10** (by NMR spectrum and TLC). These isomeric disulfoxides were separated by preparative TLC eluting with 50:2 chloroform - methanol (flowrate: **8a** > **10** > **9**) to obtain **8a** (0.75 g) and **9** (0.3 g).

For **8a**: mp 135-136 °C; ^{1}H NMR (200 MHz) ($CDCl_3$) δ 1.64 (s, 3, CH_3), 3.09 (d, 2, 2-CH_2), 3.66-3.89 (m, 4, 4-CH_2, 5-CH_2),7.03-7.58 (m, 5, ArH), 8.65 (s, 1, NH); ^{1}H NMR (200 MHz) (C_6D_6) δ 1.54 (s, 3, CH_3), 2.97 (d, 2, CH_2), 2.57-3.42 (m, 4, 4-CH_2, 5-CH_2), 6.87-8.09 (m, 5, ArH), 9.81 (s, 1, NH); IR (KBr) 1650 (C=O), 1036 (S=O) cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 50.5; H, 5.29; N,4.91; S, 22.47. Found: C, 50.5; H, 5.31; N, 4.9; S, 22.59.

For **9**: mp 150-151 °C; ^{1}H NMR (200 MHz) ($CDCl_3$) δ 1.53 (s, 3, CH_3), 3.23 (s, 2, 2-CH_2), 3.43-3.76 (m, 4, 4-CH_2, 5-CH_2), 7.03-7.58 (m, 5, ArH), 9.26 (s, 1, NH); ^{1}H NMR (200 MHz) (C_6D_6) δ 1.10 (s, 3, CH_3), 3.32 (s, 2, CH_2), 2.76-3.21 (m, 4, 4-CH_2, 5-CH_2), 6.87-8.09 (m, 5, ArH), 10.21 (s, 1, NH); IR (KBr) 1685 (C=O), 1036 (S=O) cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 50.5; H, 5.29; N, 4.91; S, 22.47. Found: C, 50.6; H, 5.32; N, 4.82; S, 22.70.

Synthesis of 2- Methyl-N-phenyl-1,3-dithiolane-2-acetamide 1,3-Dioxide (10).

To a stirred solution of **4a** (2.53 g, 0.01 mol) in 3:1 pyridine-water (40 mL) was added a solution of iodobenzene dichloride (6.50 g, 0.02 mol) in pyridine (6 mL). After the reaction mixture was stirred for 2 h, the solvent was removed *in vacuo* to give an oily residue, which was dissolved in ethyl acetate. The brown precipitates were filtered and crystallized from methanol to obtain **10** as white crystals (2.38 g, 80 %) : mp 191-192 °C.

For **10** : ^{1}H NMR (200 MHz) ($CDCl_3$) δ 1.52 (s, 3, CH_3), 3.31 (s, 2, 2-CH_2), 3.41-3.86 (m, 4, 4-CH_2, 5-CH_2), 7.09-7.52 (m, 5, ArH), 8.09 (s, 1, NH); ^{1}H NMR (200 MHz) (C_6D_6) δ 1.67 (s, 3, CH_3), 3.02 (s, 2, CH_2), 3.12-3.41 (m, 4, 4-CH_2, 5-CH_2), 7.07-8.02 (m, 5, ArH), 9.65 (s, 1, NH); IR (KBr) (S=O), 1043, 1680 (C=O) cm^{-1} Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 50.5; H, 5.29; N, 4.91; S, 22.47. Found: C, 50.5; H, 5.26; N, 5.1; S, 22.67.

Reaction of Trans Sulfoxide 6a in 1:1 C_6H_6-DMF.

A solution of trans sulfoxide **6a** (1.62 g, 6.0 mmol) in 1:1 C_6H_6-DMF (30 mL) was heated at reflux for 2 days. The solvent was removed *in vacuo* to give a brown oily residue as approximately a 13:2:1 mixture of isomeric dihydro-1,4-dithiin **3a**, 1,3-dithiolane **4a** and disulfide **11a** (by NMR spectrum and TLC), which was dissolved in methylene chloride to give a yellow suspension The solid precipitate was filtered to give a white solid, which

was crystallized from methylene chloride and petroleum ether to give white needles **3a** (1.06 g, 71 %). The filtrate was removed to give an oily residue (0.79 g). The residue was chromatographed on silica gel plates using 100:1 chloroform-methanol. The first band (Rf 0.7), the second band (Rf 0.5) and the third band (Rf 0.3) were respectively extracted with 1:1 mixture of methylene chloride and methanol to give **3a** (60 mg), **4a** (77 mg) and **11a** (50 mg).

For **3a**: mp 162-164 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 3.17 (s, 6, 5–CH_2, 6–CH_2, CH_2CO), 6.16 (s, 1, olefinic CH), 7.0-7.6 (m, 5, ArH), 7.65 (s, 1, NH); IR (KBr) 1656 (C=O), 1602 (C=C) cm^{-1}. Anal. Calcd for $C_{12}H_{13}NOS_2$: C, 57.34; H, 5.21; N, 5.57; S, 25.51. Found: C, 57.2; H, 5.16; N, 5.5; S, 25.48.

For **11a** : mp 178-180 °C; ^{1}H NMR (60 MHz) ($CDCl_3$-$DMSOd_6$) δ 2.45 (s, 6, CH_3), 2.9-3.3 (m, 8, CH_2), 5.93 (s, 1, olefinic CH), 6.9-7.7 (m, 10, ArH), 8.6 (s, 2, NH); IR (KBr) 1647 (C=O), 1598 (C=C) cm^{-1}. Anal. Calcd for $C_{24}H_{28}O_2N_2S_4$: C, 57.0; H, 5.54; N, 5.54; S, 25.41. Found: C, 56.8; H, 5.57; N, 5.51; S, 25.75.

Reaction of Trans Sulfoxide 6a under Neutral Conditions.

A solution of trans sulfoxide **6a** (0.1 g, 0.372 mmol) in dry toluene (10 mL) was refluxed with a Dean-Stark water trap for 48 h. The solvent was removed to give white solid residue (94 mg) as a 5:95 mixture of dihydro-1,4-dithiin **3a** and trans sulfoxide **6a** as determined by NMR spectroscopy and TLC.

Reaction of Cis Sulfoxide 5a under Neutral Conditions.

A solution of cis sulfoxide **5a** (0.27 g, 1.0 mmol) in dry toluene (15 mL) was refluxed with a Dean-Stark water trap for 45 h. The solvent was evaporated to give a pale brown oily residue (0.24 g) as a 8:2:1 mixture of dihydro-1,4-dithiin **2a**, 1,3-dithiolane **4a** and disulfide **11a** (by NMR spectrum and TLC). The mixture was crystallized from methylene chloride and petroleum ether to give white crystals **2a** (85 mg).

For **2a** : mp 100-102 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 2.34 (s, 3, 2-CH_3), 2.9-3.1 (m, 4, 5-CH_2, 7-CH_2), 7.0-7 7 (m, 5, ArH), 8.18 (s, 1, NH); IR (KBr) 1644 (C=O), 1595 (C=C) cm^{-1}. Anal. Calcd for $C_{12}H_{13}NOS_2$: C, 57.34; H, 5.21; N, 5.57; S, 25.51. Found: C, 57.3; H, 5.16; N, 5.5; S, 25.57.

Reaction of Trans Sulfoxide 6b in 1:1 C_6H_6-DMF.

A solution of trans sulfoxide **6b** (0.21 g, 1.0 mmol) in 1:1 C_6H_6-DMF (10 mL) was refluxed for 3 days. The solvent was removed to give an oily residue, which was dissolved in methylene chloride, washed with water, and dried (Na_2SO_4). The solvent was evaporated to give a dark oily residue (0.20 g), which was a 73:17:10 mixture of isomeric dihydro-1,4-dithiin **3b**, disulfide **11b** and 1,3-dithiolane **4b**, respectively (NMR spectrum). These were separated by preparative TLC (eluent, n-hexane and ethyl acetate, 2:1) from which **3b** (0.14 g, 68 %) and **11b** (85 mg) were obtained.

For **3b** : ^{1}H NMR (60 MHz) ($CDCl_3$) δ 3.19 (s, 6, 2-CH_2, 5-CH_2, 6-CH_2), 3.78 (s, 3, OCH_3), 6.12 (s, 1, olefinic CH); IR (NaCl) 1739 (C=O), 1614 (C=C) cm^{-1}. Anal. Calcd for $C_7H_{10}O_2S_2$: C, 44.21; H, 5.26; S, 33.68. Found: C, 43.9; H, 5.28; S, 33.5.

For **11b**: ^{1}H NMR (60 MHz) ($CDCl_3$) δ 2.40 (S, 6, CH_3), 2.8-3.2 (m, 8, CH_2), 3.70 (S, 6, OCH_3), 5.65 (S, 2, olefinic CH); IR (NaCl) 1712 (C=O), 1604 (C=C) cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_4S_4$: C, 43.98; H, 5.76; S, 33.51. Found : C, 43.8; H, 5.81; S, 33.5.

Reaction of Cis Sulfoxide 5a in the Presence of Acid Catalyst

A solution of cis sulfoxide **5a** (100 mg, 0.371 mmol) in anhydrous benzene (15 mL) containing PTSA (3.52 mg, 0.0185 mmol) was refluxed with a Dean-Stark water trap for 7 h. The resulting solution was evaporated to obtain a mixture of **2a** (93.85 %), **5a** (4.69), **6a** (1.08), and **3a** (0.39) as determined by TLC and ^{1}H NMR (300 MHz) spectroscopy. For the change in product ratios with time, see Table 1.

Reaction of Trans Sulfoxide 6a in the Presence of Acid Catalyst

A solution of trans sulfoxide **6a** (100 mg, 0.371 mmol) in anhydrous benzene (15 mL) containing PTSA (3.52 mg, 0.0185 mmol) was refluxed with a Dean-Stark water trap for 7 h. The resulting solution was evaporated to obtain a mixture of **2a** (69.5 %), **5a** (18.3), **6a** (7.71), and **3a** (4.46) as determined by TLC and ^{1}H NMR (300 MHz) spectroscopy. For the change in product ratios with time, see Table 1.

Independent Synthesis of Dihydro-1,4-dithiin 2a.

Step 1. Preparation of 3-Hydroxy-N-phenyl-1,4-dithian-3-carboxamide (15).

To a stirred solution of 3-bromo-2-oxo-N-phenylbutanamide (1.03 g, 4 mmol) in benzene (50 mL) was added a solution of potassium hydroxide (0.23 g), 1,2-ethanedithiol (0.33 mL, 4 mmol) in methanol (2 mL). The reaction mixture was stirred for 30 min and the solvent was evaporated. The residue was dissolved in benzene, washed with water, and dried (Na_2SO_4). On removing the solvent there was obtained **15** as a white solid (1.04 g, 96 %): mp 97-99°C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.08 (d, 3, J=7Hz, 2-CH_3), 2.6-3.4 (m, 4, 5-CH_2, 6-CH_2), 4.08 (q, 1, J=7Hz, 2-CH), 4.15 (s, 1, OH), 7.1-7.8 (m, 5, ArH), 8.83 (s, 1, NH); IR (KBr) 4300 (OH), 1735 (C=O) cm^{-1}.

Step 2. Preparation of 5,6-Dihydro-1,4-dithiin 2a.

A solution of 1,4-dithian **15** (1.0 g, 3.7 mmol) and PTSA (35 mg) in dry benzene (80 mL) was refluxed with a Dean-Stark water trap for 2 days. The solution was cooled, washed with water, dried (Na_2SO_4). The solvent was removed to give **2a** as a pale yellow solid (1.89 g, 94 %), identical in ^{1}H NMR and IR spectra with the compound obtained by the previous method.

The isomeric dihydro-1,4-dithiin **3b** was obtained by essentially the same procedure as described above involving the reaction of 4-bromoacetanilide **16** with 1,2-ethanedithiol to form dithian **17**, followed by acid catalyzed dehydration in refluxing benzene.

Deuteration Reactions. Typical Procedure:

To a solution of cis sulfoxide **5a** (200 mg, 0.742 mmol) in toluene (35 mL) was added deuterium oxide (0.67 mL, 37.1 mmol). The mixture was refluxed at 111°C for 19 h. After cooling the mixture was washed with water and dried (Na_2SO_4). The solvent was removed to give a colorless solid residue (190 mg, 95 %) of the cis sulfoxide in which the 2-methylene group was deuterated in 94.8 % as determined by ^{1}H NMR spectroscopy The oily residue was crystallized from ethyl acetate and petroleum ether to obtain pure cis sulfoxide **22a** (160 mg).

Hydrogen Exchange Reaction of Deuterated Sulfoxides.

Example: The preceding deuterium exchange reaction was carried out in the reverse manner[21]. Thus, a solution of deuterated cis sulfoxide **22a** (200 mg, 0.737 mmol) in toluene (35 mL) was added water (0.66 mL, 36.9 mmol). The mixture was refluxed at 111°C for 10 h. After cooling the mixture was washed with water and dried ($MgSO_4$). Solvent was removed to give colorless solid residue (192 mg, 96 %) of the cis sulfoxide **5a** in which 2-methylene group incorporated hydrogen in 63.2 % as determined by ^1H NMR spectroscopy.

Determination of k_H / k_D for 5a / 22a and 6a / 23a

From the deuteration and hydrogen exchange reaction as previously illustrated, the first order rate constants were obtained : k_H for **5a** = 5.36 x 10^{-5} sec^{-1}; k_D for **22a** = 2.58 x 10^{-5} sec^{-1}. Thus k_H / k_D for **5a / 22a** = 2.08. Likewise, k_H for 6a = 8.86 x 10^{-6} sec^{-1}; k_D for **23a** = 4.22 x 10^{-6} sec^{-1}. Thus k_H / k_D for **6a / 23a** = 2.10.

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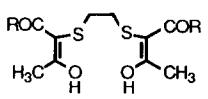
(8) Beside these side products a small amount of unidentified compounds were seen on TLC and NMR spectra, which could not be isolated. From mechanistic considerations these compounds are presumably sulfinic acid **26** and thiosulfonate **27** (see Scheme VIII).

(9) Prior to this, attempts were made to prepare **2** from the reaction of 2-chloroacetoacetanilide or ester analog with 1,2-ethanedithiol, but the bridged compound **i** was formed as the major product, and the yield of **2** was less then 5%



R = a NHC_6H_5 , b OCH_3

i

(10) Deuterium substituted structures **19** and **21** are symbolic. The actual product should be a mixture of d_0, d_1, d_2 and d_3 products unless completely deuterated.

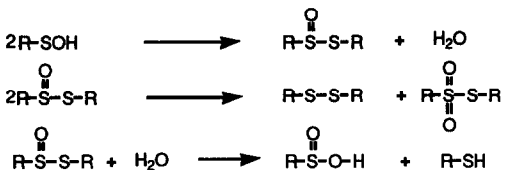
(11) Cooper, R. D. G. *J. Am. Chem. Soc.* **1970**, 92, 5010.

(12) So called microscopic reversibility principle can also explain these stereospecific process.

(13) Previously, we reported[14] that k_H/k_D values for **5a/22a** and **6a/22a** were 2.52 and 5.25, respectively. But after repeating the experiments under better conditions using 300 MHz NMR, the values 2.08 and 2.10 were found to be more reliable.

(14) Lee, W. S.; Lee, K.; Nam, K. D. Phosphorus, Sulfur, and Silicon **1991**, 59, 189.

(15) General equations for these transformations are:



For more details see Davis, F. A.; Jenkins, R. H., Jr.; Rizvi, S.Q.A.; Yocklovich, S. G. *J. Org. Chem.* **1981**, 46, 3467 and references there in.

(16) In other 1,3-dithiolane sulfoxides M. Hori's group has well demonstrated nonstereospecific ring opening and closure causing isomerization of the diastereomeric sulfoxides via carbocation: see Ueda, N.; Shimizu, H.; Kataoka, T.; Hori, M. *Tetrahedron Lett.* **1984**, 25, 757.

(17) In our preliminary report[14] on this subject we mistakenly proposed that the ring opening of protonated sulfoxides **30** and **32** occurred by a concerted mechanism to form sulfenic acid **18** without involvement isomerization of carbocation **34**. At that time we were unable to observe isomerization to interconvert cis and trans sulfoxides **5** and **6** mainly because the data in Table 1 could not be obtained by 60 MHz NMR spectroscopy. As we examined the reaction mixtures at a later stage of reaction small amounts of **5a** and **6a** could not be detected on 60 MHz NMR. Therefore, we had been misled to a wrong mechanism.

(18) Lee, W. S. et al., Unpublished results.

(19) (a) M. Sundaralingam and A. K. Chwang in Carbonium Ions, Ed. G. A. Olah and Paul von R. Shleyer, Wiely Interscience, New York, **1976**, Vol. 5, Chapt. 39, pp 2427 - 2476. (b) Weast, R. C., Ed. *Handbook of Chemistry and Physics*, 70th ed., CRC Press, Inc., Florida, **1989**, F-188-189.

(20) Horning, E. C., Ed. *Org. Synth.*; John Wiley and Sons, Inc.: New York, **1955**, Vol. 3, pp 482-484.

(21) For this type of reaction we propose use of new term "protation" derived from protium, as was deuteration from deuterium.