Formation of Kinetically Stabilized Dithiiranes by Treating Thione *S*-Oxides Bearing a Bulky Substituent with Lawesson's Reagent

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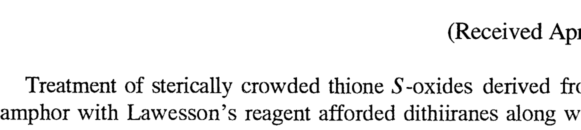
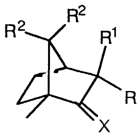
Treatment of sterically crowded thione *S*-oxides derived from *d*-camphor with Lawesson's reagent afforded dithiiranes along with deoxygenation of the starting materials, and the mixtures were subjected to mCPBA oxidation to give the corresponding dithiirane *S*-oxides and thione *S*-oxides.

Generation and synthesis of thione *S*-sulfides (thiosulfines) **B** and chemically-correlated dithiiranes **C** have gathered considerable interests in the light of their structural features and the potential use as novel intermediates for the synthesis of heterocycles.[1,2] However, there found only limited evidences on direct observation of such reactive species and the experimental observation on the thermodynamic preference of **C** to **B**. It was naturally expected that the generation of **B** would be achieved by the treatment of thione *S*-oxides **A** with a suitable sulfurating reagent possessing O-S exchanging ability. In this paper, we would like to describe a formation of kinetically stabilized dithiiranes **C** by treating thione *S*-oxides **A** bearing bulky substituents, R and R', with Lawesson's reagent.[3] Isolation and characterization of stable dithiirane *S*-oxides derived from **C** are also reported in this paper.



Sterically-crowded ketones (**1a**, **1b**) were at first prepared from *d*-camphor (**1c**).[4] A toluene or a xylene solution of **1a**, **1b**, **1c**, or **1d** was then treated with Lawesson's reagent (2 mol amt.) at refluxing temperature to give thiones **2a**-**d** in high yields. Subsequently, a CH_2Cl_2 solution of **2** was treated with mCPBA (1.1 mol amt.) to give thione *S*-oxides **3a**-**d** efficiently. Both **3a** and **3b** were obtained as the mixture of separable geometrical isomers (major-**3a**:minor-**3a**=3:2, *Z*-**3b**:*E*-**3b**=4:3),[5] and, especially, the orientation of the S-O bond of *E*-**3b** was determined by X-ray crystallographic analysis.[6] **3c** and **3d** were also given as sole geometrical isomers.[7] However, **3c** underwent gradual conversion into ketone **1c** along with extrusion of elemental sulfur during the standing even at room temperature for several hours.



1 (X=O)
2 (X=S)
3 (X=SO)

a: R^1-R^1=-$(CH_2)_4$-, R^2=CH_3
b: R^1-R^1=-CH_2(*o*-C_6H_4)CH_2-, R^2=CH_3
c: R^1=H, R^2=CH_3
d: R^1=CH_3, R^2=H

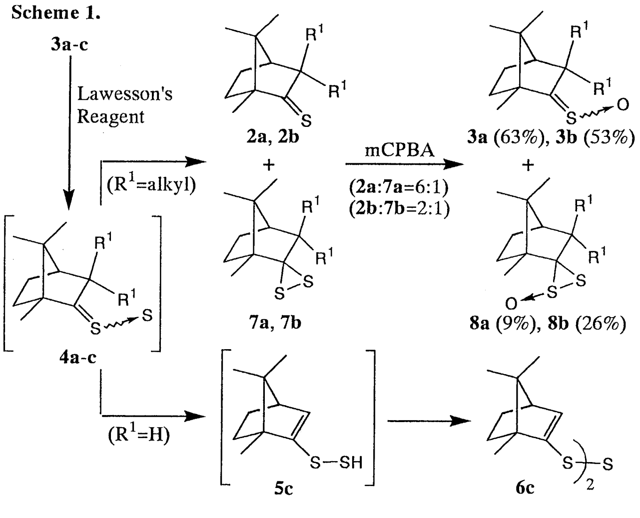
When a benzene solution of the mixture of *E*- and *Z*-isomers of thione *S*-oxide **3d** was treated with Lawesson's reagent (5 mol amt.) at room temperature for 3h, thione **2d** was given in quantitative yield.[1c] In contrast, a similar treatment of **3c** with the reagent gave unstable trisulfide **6c** in 30% yield besides **2c**(53%).[1e] It was suggested that **6c** was afforded through the mechanism involving the generation of thione *S*-sulfide **4c** by the reaction of **3c** with Lawesson's reagent, intramolecular abstraction of the α-methylene proton of **4c**, and condensation of the resulting disulfane **5c**. However, all attempts for detection or trapping of the plausible intermediates, such as **4c**, **4d**, or **5c**, were unsuccessful.

On the other hand, a similar treatment of a benzene solution of the mixture of *E*- and *Z*-isomers of **3a** or **3b** (about 1:1 in each case) with Lawesson's reagent at room temperature for a few days gave dithiiranes **7a**-**b** and thiones **2a**-**b** as mixtures (**2a**:**7a**=3:1, **2b**:**7b**=4:1). However, all attempts for the isolation of **7a**-**b** were unsuccessful due to the gradual decomposition of **7** into **2a**-**b** and elemental sulfur during the chromatographic separation. The mass spectra of the mixture of **2a**-**7a** or **2b**-**7b** revealed a significant parent ion peak at *m/z* 256 for **7a** or *m/z* 302 for **7b**, and the ^{13}C NMR spectra of these mixtures also revealed new singlet sp^3 carbon signals at δ=91.9 ppm (**7a**) or δ=90.6 ppm (**7b**), respectively.[2] The signals assignable to the thiocarbonyl carbons were not observed in the ^{13}C NMR spectra of the mixture of **2** and **7** at all except for those of the thiocarbonyl carbons of **2**. However, both **7a** and **7b** were unstable and caused gradual decomposition to give **2a**-**b** along with extrusion of elemental sulfur during the usual work-up, chromatographic purification on silica gel or alumina, or even by standing at room temperature. Thus, it was strongly suggested that the formation of **2** through the treatment of **3** with Lawesson's reagent was attributed mainly to thermal decomposition of **7** in the reaction mixture. A similar treatment of **3a** with the reagent in the presence of an excess amount of a trapping agent, such as phenylacetylene, cyclohexene, and 2,3-dimethyl-1,3-butadiene, only gave similar results to those of the reactions carried out in the absence of such trapping agents, and no products originated from **3a** or **4a**, or **7a** were obtained in all cases.[8]

When a mixture of a CH_2Cl_2 solution of **2** and **7** (**2a**:**7a**=6:1, **2b**:**7b**=2:1) was treated with mCPBA (1 mol amt.) at -78 °C, the corresponding stable dithiirane *S*-oxides **8a**-**b** were obtained as sole stereoisomers along with **3a**-**b** in almost same ratios of the starting mixture of **2** and **7** (Scheme 1).[2c,2g] These results indicated that **7** were efficiently converted into **8** by mCPBA oxidation. The MS, IR, ^1H NMR, and ^{13}C NMR spectra were fully consistent with the structures of **8**, and the structural confirmation of **8** was finally achieved by X-ray crystallographic analysis of **8b**,[9] and the ORTEP drawing of **8b** is shown in Figure 1. Thus, it was apparent that mCPBA oxidation of **7** was carried out in regio- and stereoselective manner at the less-hindered sulfur atom and from the less-hindered side of the dithiirane ring to afford **8**. The bond lengths of C(10)-S(1), C(10)-S(2), S(1)-S(2), and S(2)-O(1) of **8b** revealed within the normal ranges as shown in Figure 1, but it is noteworthy that the S(1)-C(10)-S(2) bond angle of **8b** was 70.4°, which was much smaller than those of the reported S-C-S bond angles of non-strained cyclic dithioacetals such as 1,2,4,5-tetrathianes.[10] Such a characteristic structural feature of dithiirane ring of **8b** is fully consistent with those of the theoretical predictions[11,1q] and the reported dithiiranes[2b] and their *S*-oxides.[2a,2f,2h]

All of these results suggest that thione *S*-sulfides **4a**-**d** were generated at the primary stage of the reactions and were assumed to undergo facile pericyclic isomerization into thermodynamically more

Scheme 1.



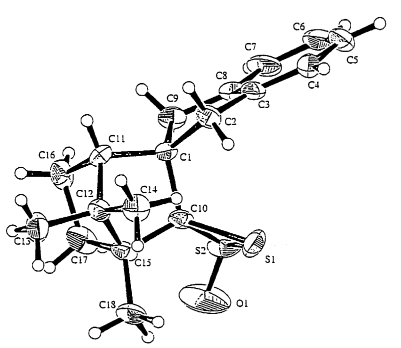


Figure 1. ORTEP Drawing of **8b**. Selected bond lengths (Å), bond angles (deg), and torsion angles (deg): S(1)-S(2), 2.093(4); S(1)-C(10), 1.829(9); S(2)-C(10), 1.80(1); S(2)-O(1), 1.42(1); S(2)-S(1)-C(10), 54.2(3); S(1)-S(2)-C(10), 55.4(3); S(1)-C(10)-S(2), 70.4(4); S(1)-S(2)-O(1), 117.2(6); O(1)-S(2)-C(10), 113.1(6); C(1)-C(10)-C(15), 105.6(7); S(1)-S(2)-C(10)-C(1), 111.0(7); S(1)-S(2)-C(10)-C(15), -115.3(7); S(2)-S(1)-C(10)-C(1), -113.7(7); S(2)-S(1)-C(10)-C(15), 114.6(8).

favored forms, i.e. **7a**-**b**^{12} or **5c**. The lack of plausible cycloaddition products of **4**, such as 1,2,4,5-tetrathianes or 1,2,4-trithiolanes, in the crude reaction mixtures can be explained by the steric bulkiness of **4a**-**d**. However, an alternative reaction pathway including the formation and thermal ring fission of oxadithiaphospholanes remains undeniable at this time.

In conclusion, we achieved a conversion of sterically-crowded thione *S*-oxides **3** into dithiiranes **7** by treating **3** with Lawesson's reagent. Further attempts to trap or detect the plausible precursors of **7** are under way in our laboratory.

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5 *E*-**3b** was partially isomerized into *Z*-**3b** by treating with BF$_3$•OEt$_2$ in CH$_2$Cl$_2$ at room temperature for several hours.

6 X-Ray crystallographic data for *E*-**3b**: Colorless plate, monoclinic, P2$_1$ (#4), a=8.705(3), b=7.93(1), c=22.477(4), β=93.67(2)°, V=1548(1) Å^3, Z=2, D$_{calc}$=1.160 g/cm^3, μ(MoKα)=1.34 cm^{-1}, R=0.033, R$_w$=0.031.

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8 Treating the mixture of **2a** and **7a** with various trapping agents also gave the recovery of the mixture.

9 X-Ray crystallographic data for **8b**: Colorless prism, monoclinic, P2$_1$(#4), a=8.724(1), b=15.820(4), c=12.235(3) Å, β=106.18(2)°, V=1621.7(6) Å^3, Z=4, D$_{calc}$=1.304 g/cm^3, μ(MoKα)=3.25 cm^{-1}, R=0.069, R$_w$=0.074.

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