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First Isolation of Eclipsed *vic*-Disulfoxide: 7,8-Dithiabicyclo[4.2.1]nona-2,4-diene 7-*exo*,8-*exo*-Dioxide

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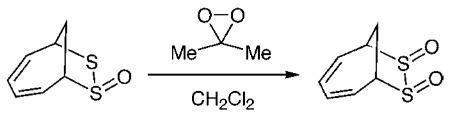
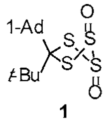
ABSTRACT

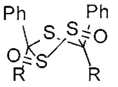


The oxidation of 7,8-dithiabicyclo[4.2.1]nona-2,4-diene 7-*exo*-oxide with dimethyldioxirane (DMD) provided the 7-*exo*-8-*exo*-dioxide, the structure of which was determined by X-ray crystallography [S–S 2.341(2) Å and ∠O–S–S–O 4.1(3)°]. The *exo* attack of DMD to give the *exo*,*exo*-dioxide was kinetically more favorable than the *endo* attack to give the *endo*,*exo*-dioxide. DFT calculations showed that the *exo*,*exo*-dioxide is thermodynamically more stable than the other stereoisomers.

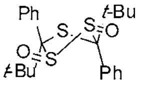
In the oxidation of disulfides ($RSSR'$) with an electrophilic agent, it has been proposed that initially formed thiosulfinates [RS(O)SR′] undergo a second oxidation at the sulfenyl sulfur atom to give unstable *vic*-disulfoxide intermediates [RS(O)S(O)R′] that rearrange to yield thiosulfonates $[RS(O)_2SR']$ as the final products. Thus, the chemistry of *vic*-disulfoxides has been drawing considerable attention in the viewpoints of their physical properties and the mechanism of the rearrangement to thiosulfonates.[1] Since 1999, we have succeeded in the isolation and the structure elucidation of tetrathiolane 2,3-dioxide **1**,[2] which was isolated for the first time as a compound having an −S(O)S(O)− linkage, and 1,2,4-trithiolane 1,2-dioxides **2**−**4**.[3] The recent theoretical study by Gregory and Jenks on *dl*- and *meso*-MeS(O)S(O)Me (**5**) showed that *dl*-**5** and *meso*-**5** with the most stable conformations were those with ∠O−S−S−O of 285 and 180°, respectively.[4] Incidentally, the stereochemistry of the *vic*-disulfoxide moiety in **1** corresponds to the conformation of *dl*-**5** with a ∠O−S−S−O of 165.5°. Similarly, those of **2b** and **3** correspond to the conformation of *dl*-**5** with ∠O−S−S−O of 73.6 and 59.8°, respectively, and that of **4** to the conformation of *meso*-**5** with a ∠O−S−S−O of 62.2°. The conformations with ∠O−S−S−O of 0° for *dl*-**5** and *meso*-**5** exist at high-energy, unstable states.[4] In that case, both the



1



2a: R = *t*-Bu
2b: R = 1-Ad



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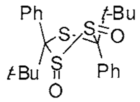

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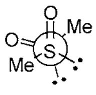
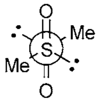
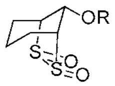


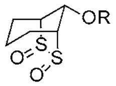
dl-**5**
∠O-S-S-O
= 285°



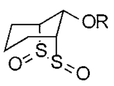
meso-**5**
∠O-S-S-O
= 180°



6a



6b



6c

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[1] For reviews, see: (a) Freeman, F. *Chem. Rev.* **1984**, *84*, 117−135. (b) Lacombe, S. In *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; Myu: Tokyo, 1999; Vol. 21, pp 1−41.

[2] (a) Ishii, A.; Nakabayashi, M.; Nakayama, J. *J. Am. Chem. Soc.* **1999**, *121*, 7959−7960. (b) Ishii, A.; Nakabayashi, M.; Jin, Y.-I.; Nakayama, J. *J. Orgamomet. Chem.* **2000**, *611*, 127−135.

[3] (a) Oshida, H.; Ishii, A.; Nakayama, J. *Tetrahedron Lett.* **2002**, *43*, 5033−5037. (b) Oshida, H.; Ishii, A.; Nakayama, J. *J. Org. Chem.* **2004**, *69*, 1695−1703.

10.1021/ol049031f CCC: $27.50

methyl groups and the oxygen atoms of *meso*-**5** are eclipsed to each other with respect to the S−S bond, to make it the most unstable conformation. This unfavorable situation of *meso*-**5** is improved by tying back the methyl groups to make a bicyclic system, where the rotation of the S−S bond is highly restricted. In fact, *cis*-*vic*-disulfoxides **6a** and **6b** were stable in solution up to 25 °C and were observed spectroscopically together with **6c**.[5] However, the disulfoxides **6** have not been isolated. Here we report the first isolation and structure determination of a *vic*-disulfoxide with eclipsed S═O groups.

Cycloheptatriene (**7**) was heated with S_8O[6,7] (0.33 molar equiv) in refluxing dichloromethane under argon for 1 h to give 7,8-dithiabicyclo[4.2.1]nona-2,4-diene 7-*exo*-oxide (**8**) in 20% isolated yield together with trisulfide **9** (5%) (eq 1). The reaction of **7** with elemental sulfur in pyridine at 70 °C has been reported to give **9**.[8] The structure of **8** was determined by X-ray crystallography (Figure 1).[9] Oxidation of 7-*exo*-oxide **8** was examined in expectation of obtaining the corresponding 7,8-dioxide(s). The oxidation with 1.5 molar equiv of an acetone solution of dimethyldioxirane (DMD)[10] in dichloromethane at −50 to −30 °C for 5 h furnished the desired 7,8-dioxide **10**[11] (48%) and a small amount of a mixture of 7,7-dioxide **11** and rearrangement products **12** and **13**, with recovery of **8** (31%) (eq 2). These byproducts **11**−**13** are derived from **10** as supported by following observations. First, an ^{1}H NMR spectrum, immediately measured after evaporation of the solvent, did not show signals due to **11**, and standing a solution of **10** in $CDCl_3$ at room temperature led to gradual appearance of the signals due to **11**, indicating that **11** is an isomerization product of **10**.[1]

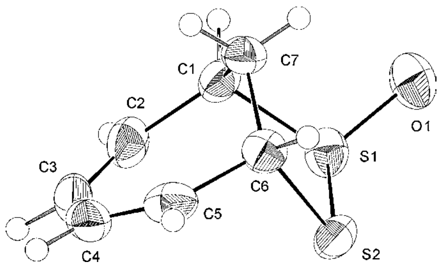
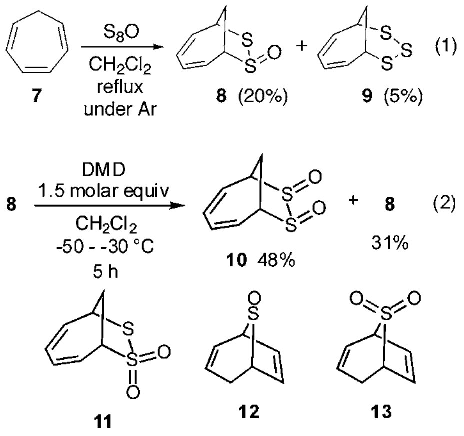
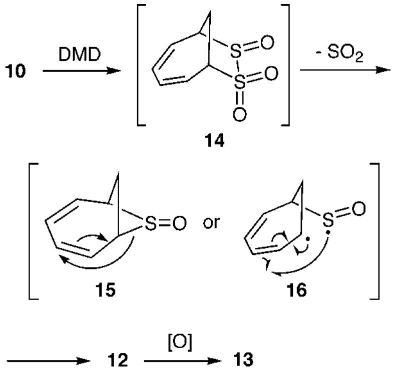


Figure 1. ORTEP drawing of 7,8-dithiabicyclo[4.2.1]nona-2,4-diene 7-*exo*-oxide (**8**) (50% ellipsoidal probability). Relevant bond length (Å) and bond angle (deg) data: S2−C6 1.8485(19); S2−S1 2.1038(9); S1−O1 1.4879(18); S1−C1 1.834(2); C6−S2−S1 98.94(7); O1−S1−C1 106.74(11); O1−S1−S2 110.92(9); C1−S1−S2 90.79(7); C5−C6−C7 113.64(19); C5−C6−S2 109.23(14); C7−C6−S2 106.96(14); C2−C1−C7 118.3(2); C2−C1−S1 106.19(16); C7−C1−S1 107.05(14); C1−C7−C6 110.07(18); C6−S1−S2−C1 −19.25(9).



Second, oxidation of **10** with 2.2 molar equiv of DMD at 0 °C for 3 h provided **13** in 88% yield. Thus, the formation mechanism for **12** and **13** is speculated as shown in Scheme 1: Oxidation of **10** yields **14**, which loses SO_2 to give 7-thiabicyclo[4.1.1]octa-2,4-diene 7-oxide (**15**) or biradical **16**, which undergoes a rearrangement or a recombination, respectively, to give **12**. Further oxidation of **12** gives **13**.

Scheme 1



The structures of **10**, **11**, and **13** were confirmed unambiguously by X-ray crystallography.[12] The structure of **12** was elucidated on the basis of its spectroscopic data and an experimental result that oxidation of **12** gave **13**. The

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(4) Gregory, D. D.; Jenks, W. S. *J. Phys. Chem.* **2003**, *107*, 3414−3423. For theoretical studies on *vic*-dislufoxides, see also papers cited therein.

(5) Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 8998−9000.

(6) Steudel, R.; Latte, J. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 603−604.

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(8) Fritz, H.; Weis, C. D. *Tetrahedron Lett.* **1974**, *18*, 1659−1660.

(9) Crystal data for **8**: orthorhombic, space group $Pca2_1$, $a = 11.1340(5)$, $b = 6.4980(2)$, $c = 10.4290(5)$ Å, $V = 745.52(6)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.517$ g cm^{-3}, μ(Mo Kα) = 0.627 mm^{-1}; 1487 independent reflections ($-12 \le h \le 10$, $-8 \le k \le 8$, $-13 \le l \le 12$) were collected with a Mac Science DIP3000 diffractometer using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) at 298 K; 124 parameters; $R1 = 0.0279$ ($I > 2\sigma(I)$, 1473 reflections), $wR2 = 0.0796$ (for all), GOF = 1.193; max/min residual density = 0.323/−0.289 e Å^{-3}.

(10) (a) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377. (b) Adam, W.; Hadjiarapoglou, L.; Smerz, A. *Chem. Ber.* **1991**, *124*, 227−232.

(11) Physical and spectral data of **10**: pale yellow needles; mp 98−101 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (d, $J = 14.5$ Hz, 1H), 3.72 (dt, $J = 14.4$, 5.4 Hz, 1H), 3.94 (t, $J = 6.3$ Hz, 2H), 6.06−6.13 (m, 2H), 6.23−6.29 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 33.9, 70.1, 121.4, 131.3.

stereochemistry of the S=O group in **12** was not determined. Figure 2 shows an ORTEP drawing of **10**, presenting the *exo*,*exo*-dioxide structure. The two independent molecules in the unit cell of **10** have almost the same geometries. The averaged S−S bond length was 2.341(2) Å, which is longer than that in **1** [2.302(2) Å], and the averaged O−S−S−O and C−S−S−C dihedral angles were 4.1(3) and 5.0(3)°, respectively. In the IR spectrum of **10**, two strong absorptions due to S=O stretching vibrations appeared at 1095 and 1039 cm^{-1}. DFT calculations on **10** at the B3LYP/6-311+G(3df) level[13] provided the symmetric and antisymmetric S=O stretching vibrations at 1146 and 1103 cm^{-1}, respectively (without scaling).

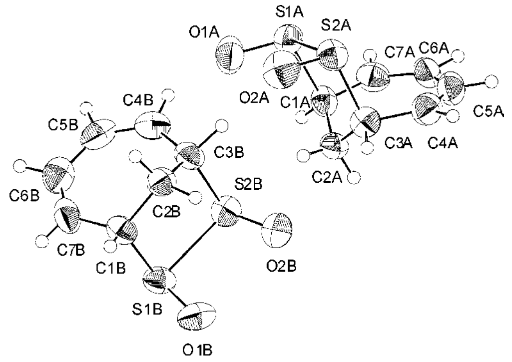
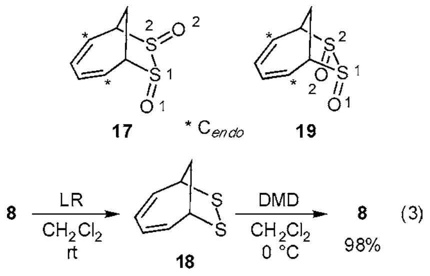


Figure 2. ORTEP drawing of 7,8-dithiabicyclo[4.2.1]nona-2,4-diene 7-*exo*, 8-*exo*-dioxide (**10**) (50% ellipsoidal probability). Relevant bond length (Å) and bond angle (deg) data: Molecule A: S1A−S2A 2.334(2); S1A−O1A 1.468(5); S2A−O2A 1.482(5); S1A−C1A 1.834(6); S2A−C3A 1.844(7); O1A−S1A−C1A 108.5(3); O1A−S1A−S2A 100.1(2); C1A−S1A−S2A 91.1(2); O2A−S2A−C3A 108.1(3); O2A−S2A−S1A 99.2(2); C3A−S2A−S1A 93.0(2); O1A−S1A−S2A−O2A −4.6(3); C1A−S1A−S2A−C3A −4.7(3); O1A−S1A−S2A−C3A 104.3(3); O2A−S2A−S1A−C1A −113.6(3); O1A−S1A−C1A−C2A −69.9(5); O1A−S1A−C1A−C7A 159.6(5); O2A−S2A−C3A−C4A −152.6(5); O2A−S2A−C3A−C2A 79.4(5). Molecule B: S1B−S2B 2.347(2); S2B−O2B 1.483(5); S1B−O1B 1.481(5); S2B−C3B 1.821(7); S1B−C1B 1.842(7); O2B−S2B−C3B 109.7(3); O2B−S2B−S1B 100.9(2); C3B−S2B−S1B 91.7(2); O1B−S1B−C1B 108.1(3); O1B−S1B−S2B 99.4(2); C1B−S1B−S2B 93.1(2); O1B−S1B−S2B−O2B −3.6(3); C1B−S1B−S2B−C3B −5.2(3); O2A−S2B−S1B−C1B 105.3(3); O1B−S1B−S2B−C3B −114.1(3); O2B−S2B−C3B−C2B −70.8(4); O2B−S2B−C3B−C4B 160.9(5); O1B−S1B−C1B−C7B −152.1(5); O1B−S1B−C1B−C2B 79.0(4).

In the oxidation of **8**, *endo*,*exo*-dioxide **17** was not obtained, indicating that the *exo* attack of DMD to give **10** took place exclusively. An exclusive *exo* attack of DMD was observed similarly in the oxidation of disulfide **18**, prepared by deoxygenation of **8** with Lawesson's reagent[14,15] in 75% yield, to give **8** stereoselectively and quantitatively (eq 3).



DFT calculations were carried out on **10**, **17**, and another stereoisomer **19** at the B3LYP/6-311+G(3df) level. Their energies and selected bond length and bond angle data are collected in Table 1. *exo*,*exo*-Dioxide **10**, which has a mirror plane going through the center of the S−S bond, is more stable than **17** and **19** by 2.68 and 6.41 kcal mol^{-1}, respectively. The calculated S−S bond length of 2.425 Å for **10** is longer by 3.6% than that obtained by X-ray

Table 1. Relative Energies (E_{rel}) and Selected Bond Length (Å) and Bond Angle (deg) Data of **10**, **17**, and **19** Calculated at the B3LYP/6-311+G(3df) Level

	10	**17**	**19**
E_{rel} (kcal mol^{-1})	0.0	2.68	6.41
S1−S2	2.425	2.364	2.402
S1−O1	1.480	1.478	1.477
S2−O2	1.480	1.486	1.477
S1−C	1.875	1.918	1.882
S2−C	1.875	1.864	1.913
C−S1−S2	91.7	93.0	90.5
C−S2−S1	91.7	91.2	92.2
S1−S2−O2	99.9	103.0	103.8
S2−S1−O1	99.9	111.7	104.1
C−S1−O1	107.8	109.2	110.2
C−S2−O2	107.8	106.7	110.1
C_{endo}−C−S1	107.4	110.5	111.7
C_{endo}−C−S2	107.4	108.6	110.5
O1−S1−S2−O2	0.0	−151.7	15.0
C−S1−S2−C	0.0	−11.2	15.2

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(12) Crystal data for **10**: orthorhombic, space group $Pca2_1$, $a = 19.794(2)$, $b = 6.2160(7)$, $c = 12.8890(13)$ Å, $V = 1585.9(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.577$ g cm^{-3}, μ(Mo Kα) = 0.613 mm^{-1}; 3002 independent reflections ($-25 \leq h \leq 25$, $-7 \leq k \leq 7$, $-16 \leq l \leq 16$) were collected with a Mac Science DIP3000 diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) at 298 K; 199 parameters, $R1 = 0.0690$ ($I > 2\sigma(I)$, 2606 reflections), $wR2 = 0.1868$ (for all), GOF = 1.024; max/min residual density = 1.003/−0.524 e Å^{-3}. Hydrogen atoms were placed at the calculated positions.

(13) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision B.04; Gaussian, Inc.: Pittsburgh, PA, 2003.

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crystallography. Isomers **17** and **19** have distorted C−S−S−C dihedral angles of 11.1 and 15.2°, respectively, and their calculated S−S bond lengths are 2.364 and 2.402 Å, respectively. Widening of the C−S−O and C_{endo}−C−S angles is shown for the *endo*-S═O moiety by 2−4° compared with the *exo*-S═O moiety, suggesting that the instability of **17** and **19** is ascribed to the 1,4-repulsion between the *endo*-O and the C_{endo}. The dipole−dipole repulsion between the cis-aligned S═O groups may be relieved to some extent by elongation of the S−S bonds in **10** and **19**.

In summary, bicyclic, eclipsed *vic*-disulfoxide **10** was prepared by oxidation of the corresponding thiosulfinate **8** with DMD. The formation of **10** from **8** by the *exo* attack of DMD was kinetically more favorable than the *endo* attack. DFT calculations showed that **10** is thermodynamically more stable than the other stereoisomers. The stabilization of the eclipsed *vic*-disulfoxide structure in **10** might be brought about by the structure tied with a 1,3-butadiene bridge, which opposes the bond stretching leading to spontaneous rupture of the S−S bond in **10**. The present results provide new insight into the study of the relationship between the structure and the stability of *vic*-disulfoxides.

Supporting Information Available: Physical and spectral data for **8**, **10**−**13**, and **18**, details of X-ray crystallographic analyses for **8**, **10**, **11**, and **13**, and optimized coordinates and structures of **10**, **17**, and **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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