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Synthesis and Properties of a Dithiirane *trans*-1,2-Dioxide, a Three-Membered *vic*-Disulfoxide

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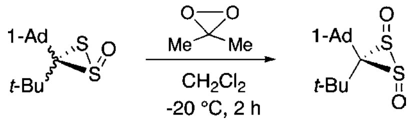
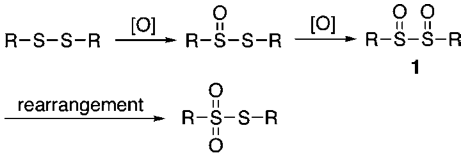
ABSTRACT



***cis*- and *trans*-3-(1-adamantyl)-3-*tert*-butyldithiirane 1-oxides were oxidized with dimethyldioxirane to give the *trans*-1,2-dioxide. Thermal decomposition of the 1,2-dioxide yielded the corresponding (*E*)- and (*Z*)-sulfines, thioketone, and *cis*- and *trans*-dithiirane 1-oxides. In the thermolysis, decomposition to the sulfines and SO was the main path and that to the thioketone and SO_2 was the minor one. The two decomposition processes and epimerization to the *cis*-1,2-dioxide were analyzed theoretically. SO generated in situ reacted with thioketones as additives to give the corresponding dithiirane 1-oxides.**

vic-Disulfoxide **1** has been recognized as an unstable intermediate in the oxidation of disulfide with electrophilic oxidants (Scheme 1),[1] and therefore has been drawing considerable attention experimentally[2−4] and theoretically.[1c,5] Freeman and Angeletakis reported that *vic*-disulfoxides derived from acyclic disulfides were stable in solution at low temperatures (−40 to −20 °C).[2] Folkins and Harpp observed a bicyclic *vic*-disulfoxide **2** by ^{1}H NMR spectroscopy.[3] We recently succeeded for the first time in the isolation of *vic*-disulfoxides **3**−**5**[6−8] under ambient conditions. All of the *vic*-disulfoxides have S(O)−S(O) moieties in five-membered-ring systems.

Scheme 1



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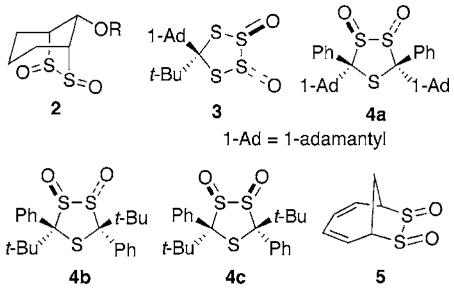
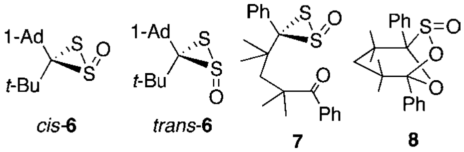
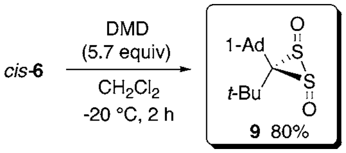
10.1021/ol052570f CCC: $33.50



We examined oxidation of dithiirane 1-oxides, *cis*-**6**, and *trans*-**6**,[6,9] with the expectation of obtaining the corresponding dithiirane 1,2-dioxide, a three-membered *vic*-disulfoxide. We previously reported the oxidation of 3-phenyl-3-(4-keto-*tert*-alkyl)dithiirane 1-oxide **7** with *m*-chloroperoxybenzoic acid to give bicyclic 1,4,2-dioxathiolane 2-oxide **8**.[10] Here we employed 3,3-di-*tert*-alkyldithiirane 1-oxides **6**, not possessing other functional groups, and dimethyldioxirane as an oxidant.



Dithiirane 1-oxide *cis*-**6** was treated with an acetone solution of dimethyldioxirane (DMD)[11] in dichloromethane at −20 °C. An excess amount of DMD (5.7 molar equiv) was necessary for complete consumption of *cis*-**6**. The ^{1}H NMR spectrum of the reaction mixture showed a singlet at δ 1.39, indicating formation of a new compound (**9**). The new compound was isolated in 80% yield by evaporation of the solvent, washing the residue with hexane, and then recrystallization from a mixed solvent of hexane and dichloromethane, where the manipulations were carried out at −20 °C (eq 1). Oxidation of *trans*-**6** with DMD provided the same compound **9**[12] in 42% isolated yield. In the oxidation of *cis*- and *trans*-**6**, trifluoroperoxyacetic acid was also available.



(1)

In the ^{1}H NMR of **9**, protons of *tert*-butyl (δ 1.39) and three methylenes (δ 2.19) (the 2-positions of 1-Ad) underwent low-field shifts owing to the respective sulfoxide groups orienting in the same direction. These values are very similar to those of *trans*-**6** (δ 1.44; cf. δ 1.09 for *cis*-**6**) and *cis*-**6** (δ 2.20; cf. δ 1.74 and 1.84 for *trans*-**6**),[6,9] respectively. The ^{13}C NMR spectrum of **9** showed a low-field shift of the dithiirane carbon by ca. 20 ppm (δ 106.9) compared with the corresponding carbons of *cis*-**6** (δ 86.2) and *trans*-**6** (δ 87.7). In the IR spectrum, strong absorptions were observed at 1064, 1084, and 1114 cm^{-1}, which were assignable to those due to S=O stretching vibrations.

The structure of **9** was finally determined by X-ray crystallography to be a dithiirane *trans*-1,2-dioxide (Figure 1).[12] There are two independent molecules in the unit cell. The averaged S−S bond length was 2.242(2) Å, which is longer than that [2.092(2) Å] of *trans*-**6** by 0.150 Å. In comparison with other *vic*-disulfoxides, the value is comparable to those of 1,2,4-trithiolane 1,2-dioxides **4a** [2.245(3) Å],[7a] **4b** [2.237(1) Å],[7b] and **4c** [2.241(1) Å][7b] and shorter than those of tetrathiolane 2,3-dioxide **3** [2.301(1) Å][6] and bicyclic *vic*-disulfoxide **5** [2.341(2) Å].[8] The averaged bond angle C2−C1−C12 widens up to 123.4(5)°, and the averaged dihedral angle O1−S1−S2−O2 is 149.6(3)°.

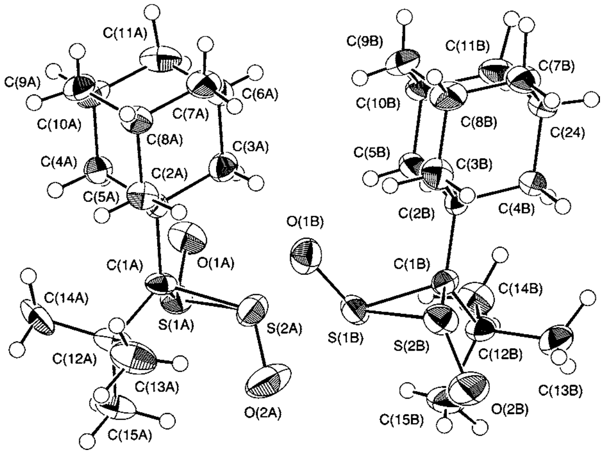


Figure 1. ORTEP drawing of 3-(1-adamantyl)-3-*tert*-butyldithiirane *trans*-1,2-dioxide (**9**) (50% ellipsoid).[12]

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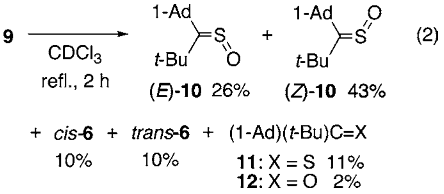
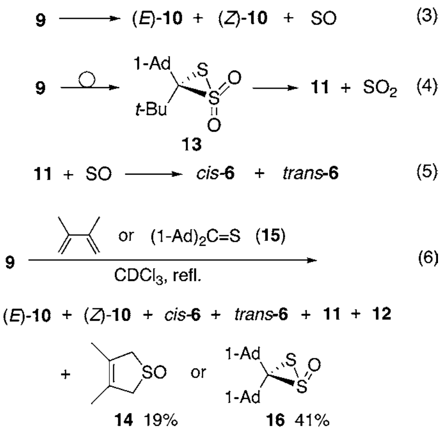
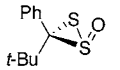
(12) Pale yellow crystals, mp 95 °C dec (hexane−dichloromethane). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (s, 9H), 1.71 (m, 6H), 2.04 (br s, 3H), 2.19 (br s, 6H); ^{13}C NMR ($CDCl_3$, 100.7 MHz) δ 29.02 (CH_3), 31.41 (br s, CH), 36.35 (CH_2), 41.10 (br s, CH_2), 42.17 (C), 46.08 (C), 106.92 (S−C−S); IR (KBr) 1064, 1084, 1114 cm^{-1} (S=O). Anal. Calcd for $C_{15}H_{24}O_2S_2$: C, 59.96; H, 8.05. Found: C, 60.18; H, 8.12. Crystallographic data for **9** (153 K): $C_{15}H_{24}O_2S_2$, $M = 300.48$, pale yellow plate, 0.30 × 0.16 × 0.02 mm^3, monoclinic, $P2_1/c$, $a = 11.504(1)$ Å, $b = 13.877(1)$ Å, $c = 19.440(2)$ Å, $\beta = 111.041(4)°$, $V = 2896.4(5)$ Å^3, $\rho_{calcd} = 1.378$ Mg m^{-3}, $Z = 8$, μ(Mo Kα) = 0.364 mm^{-1}, $R1 = 0.0968$, $wR2 = 0.2410$, GOF = 1.035. Relevant bond length (Å) and angle (deg) data: molecule A (left), S1A−O1A 1.476(5), S1A−C1A 1.855(6), S1A−S2A 2.241(2), S2A−O2A 1.469(5), S2A−C1A 1.860(6), C1A−C12A 1.578(8), C1A−C2A 1.580(7), O1A−S1A−C1A 115.6(3), O1A−S1A−S2A 113.6(2), C1A−S1A−S2A 52.99(19), O2A−S2A−C1A 116.6(3), O2A−S2A−S1A 115.0(2), C1A−S2A−S1A 52.79(18), C12A−C1A−C2A 123.3(5), C12A−C1A−S1A 110.2(4), C2A−C1A−S1A 114.8(4), C12A−C1A−S2A 113.8(4), C2A−C1A−S2A 110.2(4), S1A−C1A−S2A 74.2(2); molecule B (right), S1B−O1B 1.468(5), S1B−C1B 1.863(6), S1B−S2B 2.243(2), S2B−O2B 1.471(5), S2B−C1B 1.875(6), C1B−C12B 1.573(8), C1B−C2B 1.579(7), O1B−S1B−C1B 116.1(3), O1B−S1B−S2B 113.1(2), C1B−S1B−S2B 53.37(18), O2B−S2B−C1B 115.3(3), O2B−S2B−S1B 114.5(2), C1B−S2B−S1B 52.89(18), C12B−C1B−C2B 123.5(5), C12B−C1B−S1B 109.7(4), C2B−C1B−S1B 114.5(4), C12B−C1B−S2B 114.4(4), C2B−C1B−S2B 110.4(4), S1B−C1B−S2B 73.7(2).

Dithiirane 1,2-dioxide **9** was stable in the crystalline state but decomposed gradually in solution at room temperature; letting a solution of **9** in $CDCl_3$ stand at room temperature led to almost complete decomposition to (*E*)- and (*Z*)-sulfines **10**[6b] after 9 days. Heating **9** in refluxing $CDCl_3$ under argon produced (*E*)- and (*Z*)-sulfines **10** as the main products together with *cis*-**6**, *trans*-**6**, thioketone **11**, and ketone **12** in a ratio of 26/43/10/10/11/2 on the basis of the ^1H NMR integral ratio (eq 2).



The formation of sulfines **10** as the main products indicated straightforwardly that the decomposition of **9** into **10** and sulfur monoxide (SO) was the main path (eq 3). In the thermolysis, the formation of dithiirane 1-oxide **6** and thioketone **11** is significant. In our speculation, **9** isomerizes to dithiirane 1,1-dioxide **13** in a minor path, and **13** further decomposes to thioketone **11** and SO_2 (eq 4). Thioketone **11** thus formed reacts with SO, generated in eq 3, to give dithiirane 1-oxides **6** (eq 5).





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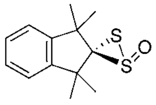

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To verify the above speculation, thermolysis of **9** was examined in the presence of a 1,3-butadiene[13] or thioketones[14] to trap SO (eq 6). In the case of 2,3-dimethyl-1,3-butadiene (7.2 equiv), the SO-trapping product, 2,5-dihydrothiophene 1-oxide **14**,[13] was formed in 19% yield, together with (*E*)-**10** (37%), (*Z*)-**10** (40%), *cis*-**6** (5%), *trans*-**6** (5%), **11** (10%), and **12** (3%).[15] In the presence of di-1-adamantyl thioketone **15** (4.6 equivs), SO was trapped more effectively to furnish dithiirane 1-oxide **16**[9] in 41% yield together with (*E*)-**10**, (*Z*)-**10**, *cis*-**6**, *trans*-**6**, and **11**.[16] The use of other thioketones, *tert*-butyl phenyl thioketone,[17] and 1,1,3,3-tetramethylindane-2-thione[18] gave the corresponding dithiirane 1-oxides (**17**[19] and **18**[20]), albeit in lower yields (24% and 21% yields, respectively) probably due to their instability under the conditions. The yields of these SO adducts were calculated on the assumption that 1 mol of **9** generates 1 mol of SO. The above results not only verify the generation of SO (eq 3) but also provide an alternative route for the synthesis of dithiirane 1-oxides (eq 5).[19,21] Decomposition pathways of dithiirane *trans*-1,2-dioxide **9** were analyzed theoretically with DFT calculations[22] on 3,3-di-*tert*-butyldithiirane *trans*-1,2-dioxide (**19**) as the model compound. Inverting one of the sulfoxide groups of **19** outside of the dithiirane ring leads to epimerization into *cis*-1,2-dioxide **20**, which is higher in energy than **19** by 4.6 kcal mol^{-1}. This epimerization proceeds through a large-barrier transition state (TS1) (54.3 kcal mol^{-1}) on the singlet potential energy surface. On the other hand, inverting the sulfoxide group inside of the ring leads to ring expansion to 2,1,3-oxadithietane **21** (6.7 kcal mol^{-1}), a three-membered *OS*-sulfenyl sulfinate, through TS2 (23.4 kcal mol^{-1}), followed by further isomerization to dithiirane 1,1-dioxide **22** (6.7 kcal mol^{-1}) through TS3 (47.9 kcal mol^{-1}). Isomerization of *vic*-disulfoxides to thiosulfonates through *OS*-sulfenyl sulfinates has been well studied theoretically and experimentally.[1−5] The 1,1-dioxide **22** decomposes to $t\text{-}Bu_2C{=}S$ and SO_2 (−26.5 kcal mol^{-1}) through TS4 (18.2 kcal mol^{-1}). When the S−S bond of **19** is elongated, an intersystem crossing (ISC) from the singlet potential energy surface to the triplet potential energy surface

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[14] It has been reported that thiirane oxide, which is a source of SO, and di-*p*-anisyl thioketone were heated in refluxing toluene to give 2,2-di-*p*-anisyl-1,3-dithiolane and its 1,1-dioxide: Aalbersberg, W. G. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 2792−2794.

[15] The yields were determined by measuring the ^1H NMR spectrum of the pyrolysate with 1,2-diphenylethane as the internal standard.

[16] Dithiirane 1-oxide **16** was isolated by means of silica gel column chromatography followed by HPLC as a mixture with *cis*-**6**, *trans*-**6**, **12**, and di-1-adamantyl ketone in the molar ratio of 86/1.3/1.3/1.3/10. The yield (41%) was calculated based on the weight of the mixture and the molar ratio detemined by ^1H NMR spectroscopy. The molar ratio of **16**/(*E*)-**10**/(*Z*)-**10**/*cis*-**6**/*trans*-**6**/**11** in the reaction mixture was 55/37/41/2/2/18.

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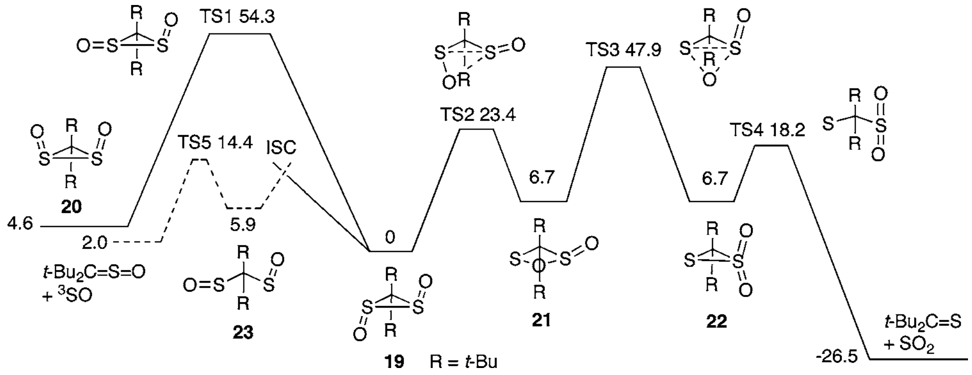

Figure 2. Relative energy (kcal mol^{-1}) of intermediates and transition states in decomposition of 3,3-di-*tert*-butyldithiirane *trans*-1,2-dioxide (**19**), calculated at the B3LYP/6-311++G** level including zero-point vibrational energy corrections: (—) singlet potential energy surface; (- - -) triplet potential energy surface.

takes place to give biradical **23** (5.9 kcal mol^{-1}). The intermediate **23** decomposes to *t*-$Bu_2C{=}S{=}O$ and ^3SO (2.0 kcal mol^{-1}) through TS5 (14.4 kcal mol^{-1}).

Thus, calculations show that decomposition to *t*-$Bu_2C{=}S$ and SO_2 was much more favorable energetically than decomposition to *t*-$Bu_2C{=}S{=}O$ and ^3SO and isomerization to *cis*-1,2-dioxide **20**. Simultaneously, however, the calculations exhibit that decomposition to *t*-$Bu_2C{=}S{=}O$ and ^3SO was much more favorable kinetically than the other two pathways (decomposition to *t*-$Bu_2C{=}S$ and SO_2 has a lower TS than epimerization to **20**). These theoretical results are in harmony with the experimental results that decomposition to *t*-$Bu_2C{=}S{=}O$ and ^3SO is the main path and that to *t*-$Bu_2C{=}S$ and SO_2 is the minor one. We did not observe compounds corresponding to **20**, **21**, or **22** experimentally. Incidentally, generation of triplet SO by thermal decomposition of thiirane oxide was proposed,[23] though an argument arose.[14]

In summary, we have succeeded in the synthesis of the first isolable dithiirane 1,2-dioxide, a three-membered *vic*-disulfoxide. The thermal decomposition of the 1,2-dioxide was investigated experimentally and theoretically. Work on synthesis of dithiirane 1,2-dioxides from other isolable dithiirane 1-oxides is in progress.

Supporting Information Available: Experimental details of oxidation of *cis*-**6** with DMD to give **9** and thermal decomposition of **9** in the presence of **15** to give **16**, and X-ray crystallographic analyses for *trans*-**6** and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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