First Isolable Dithiiranes: 3-(1,1,3,3-Tetramethyl-4-oxo-4-phenylbutyl)-3-phenyldithiirane 1-Oxides

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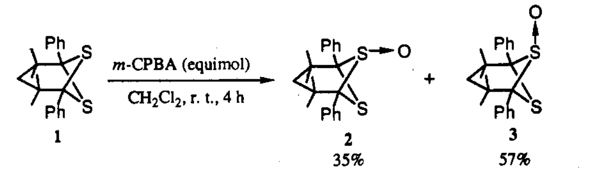
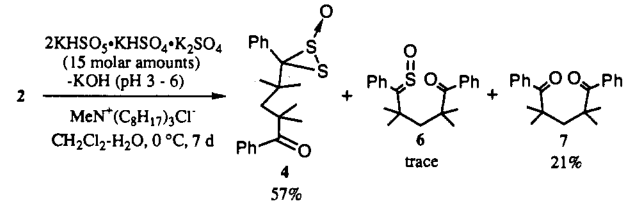
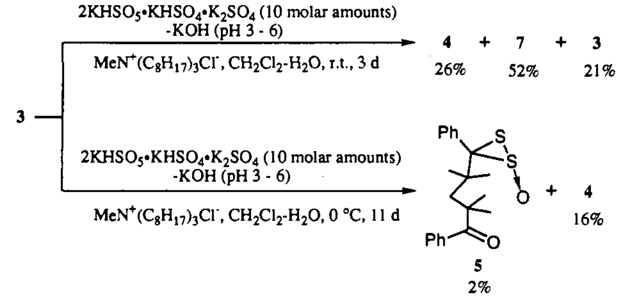
We report here the synthesis and characterization of the first isolable dithiirane derivative. Dithiiranes are the smallest cyclic disulfides, where the dihedral angle between two carbon–sulfur bonds is constrained to 0°, and therefore the large repulsive interaction between lone-pair electrons of the adjacent sulfur atoms is inevitable in addition to large angle strain.[1] The chemistry of dithiiranes, which are also of interest as isomers of thiosulfines and dithioesters, has been attracting considerable attention. Although some dithiiranes have been recognized as elusive intermediates, in spite of much effort, no isolable dithiiranes including their oxidized derivatives have been reported so far.[2,3] In our continuing study on bicyclic 1,3-dithietanes,[4] we have found that the oxidation of a 1,3-dithietane *S*-oxide with OXONE (Aldrich) ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$)[5,6] produces the first isolable dithiirane 1-oxide derivative.

Oxidation of the bicyclic 1,3-dithietane **1**[7] with *m*-chloroperbenzoic acid (*m*-CPBA) afforded *endo*- and *exo*-sulfoxides **3** and **2** in 35% and 57% yields, respectively. Further oxidation of the exo compound **2** with excess OXONE (15 equiv) in the presence of $MeN^+(C_8H_{17})_3Cl^-$ in CH_2Cl_2/H_2O at 0 °C, which was carried out by adjusting the pH of the mixture to 3–6 by addition of 1 M KOH, afforded the *cis*-dithiirane 1-oxide **4** in 57% yield along with a trace amount of the sulfine **6** and a 21% yield of the dicarbonyl compound **7**. When the oxidation was carried out without pH control, the yield of **4** decreased to 11% and compounds **6** and **7**, which result from the acid-catalyzed decomposition of **4**, became the major products. Oxidation of the endo compound **3** at room temperature also gave the dithiirane oxide **4** in 26% yield together with **7** (52%) under the pH-controlled conditions. Interestingly, the oxidation of **3** conducted at lower temperature (0 °C) gave the *trans*-dithiirane 1-oxide **5** though in 2% yield in addition to **4** (16%).







The dithiirane oxide **4** is a rather thermally stable, crystalline compound, mp 124–125 °C dec, while **5**, which is susceptible to isomerization to **4**, could not be obtained in pure form. The structure of **4** was unambiguously determined by spectroscopic means, chemical transformations, and X-ray single crystal structure analysis.[8] The structure of **5** was determined by comparison of its spectroscopic properties with those of **4**. An ORTEP drawing of **4** is given in Figure 1 along with the relevant bond distances and angles. In the X-ray structure analysis of **4**, disorder of the position of the sulfoxide oxygen is observed, that is, probabilities of observing the oxygen on S(1) and S(2) are 80% and 20%, respectively. In these circumstances, the observed bond distances of two C–S bonds of **4** are virtually equal and very similar, including the C–C bond distance, to the calculated bond distances of the parent dithiirane.[1]

The formation of dithiirane oxides can be formulated tentatively as shown below. The present oxidation did not proceed under neutral or alkaline conditions. Thus, protonation on the sulfoxide oxygen of **2** should take place first to assist nucleophilic attack of potassium hydrogen peroxomonosulfate on the bridgehead carbon,[6b,c,9] which is accompanied by ring-opening of the strained four-membered ring to give a sulfenic acid (**8**). Very fast intramolecular cyclization of **8** would give rise to **4** exclusively

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[1] (a) Snyder, J. P.; Carlsen, L. *J. Am. Chem. Soc.* **1977**, *99*, 2931. (b) So, S. P. *J. Mol. Struct. (THEOCHEM)* **1986**, *148*, 153. (c) Wilson, R. M.; Buchanan, D. N.; Davis, J. E. *Tetrahedron Lett.* **1971**, 3919 and references cited therein.

[2] (a) Senning, A.; Hansen, H. C.; Abdel-Megeed, M. F.; Mazurkiewicz, W.; Jensen, B. *Tetrahedron* **1986**, *42*, 739. (b) Senning, A. *Sulfur Lett.* **1986**, *4*, 213. (c) Senning, A. *Ibid.* **1990**, *11*, 83. (d) Kutney, G. W.; Turnbull, K. *Chem. Rev.* **1982**, *82*, 333.

[3] As to the next smallest cyclic disulfide, 1,2-dithietanes, only two isolable derivatives have been reported. (a) Block, E.; Bazzi, A. A.; Revelle, L. K. *J. Am. Chem. Soc.* **1980**, *102*, 2490. (b) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E.; Carroll, P. J. *Ibid.* **1987**, *109*, 3801.

[4] (a) Ishii, A.; Nakayama, J.; Ding, M.-X.; Kotaka, N.; Hoshino, M. *J. Org. Chem.* **1990**, *55*, 2421. (b) Ishii, A.; Ding, M.-X.; Maeda, K.; Nakayama, J.; Hoshino, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3343.

[5] For oxidation of sulfides with OXONE, see: (a) Kennedy, R. J.; Stock, A. *J. Org. Chem.* **1960**, *25*, 1901. (b) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287.

[6] For preparation of dioxiranes with oxidation of ketones with OXONE, see: (a) Edwards, J. O.; Pater, R. H.; Curci, R.; Di Furia, F. *Photochem. Photobiol.* **1979**, *30*, 63. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205. (c) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187.

[7] The dithietane **1** was prepared by treatment of 2,2,4,4-tetramethyl-1,5-diphenylpentane-1,5-dione with Lawesson's reagent.[4a]

[8] Selected spectral data are as follows. **4**: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.85 (s, 3H), 1.11 (s, 3H), 1.321 (s, 3H), 1.326 (s, 3H), 2.09 (d, $J = 14.5$ Hz, 1H), 2.26 (d, $J = 14.5$ Hz, 1H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.36–7.46 (m, 6H), 7.55 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.4 (CH_3), 27.2 (CH_3), 29.1 (CH_3), 29.2 (CH_3), 42.2 (C), 48.0 (C), 49.9 (CH_2), 87.8 (S-C-S), 127.8 (CH), 128.1 (CH × 2), 128.8 (CH), 131.1 (CH), 133.0 (C), 133.6 (CH), 138.4 (C), 209.1 (C=O); IR (KBr) 1673, 1142, 1125 cm^{-1}. Crystal data for **4**: triclinic, $P\bar{1}$; $a = 10.289(6)$ Å, $b = 10.455(4)$ Å, $c = 9.964(6)$ Å, $\alpha = 108.28(4)°$, $\beta = 109.89(4)°$, $\gamma = 88.00(4)°$, $V = 953.9(9)$ Å^3, $Z = 2$, $d_{calcd} = 1.297$ g cm^{-3}, μ(Cu Kα) = 26.10 cm^{-1}. The structure was solved using direct methods (SAPI 91) and refined by a full-matrix least-squares procedure, using 2165 data, to a conventional R value of 0.56 ($R_w = 0.090$). **5**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.27 (s, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.40 (s, 3H), 2.42 (d, $J = 14.4$ Hz, 1H), 2.64 (d, $J = 14.4$ Hz, 1H), 7.28 (s, 5H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.43 (t, $J = 7.4$ Hz, 1H), 7.62 (d, $J = 7.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.4 (CH_3), 28.0 (CH_3), 29.0 (CH_3), 29.6 (CH_3), 44.0 (C), 48.4 (C), 50.0 (CH_2), 84.3 (S-C-S), 128.0 (CH), 128.1 (CH), 128.3 (CH), 128.5 (CH), 131.0 (CH), 131.3 (CH), 136.9 (C), 138.7 (C), 208.5 (C=O); IR (KBr) 1669, 1118, 1099 cm^{-1}.

[9] For this ring-opening, a referee suggested a mechanism involving a stabilized carbocation intermediate followed by attack of the persulfate ion. We are grateful for this suggestion.

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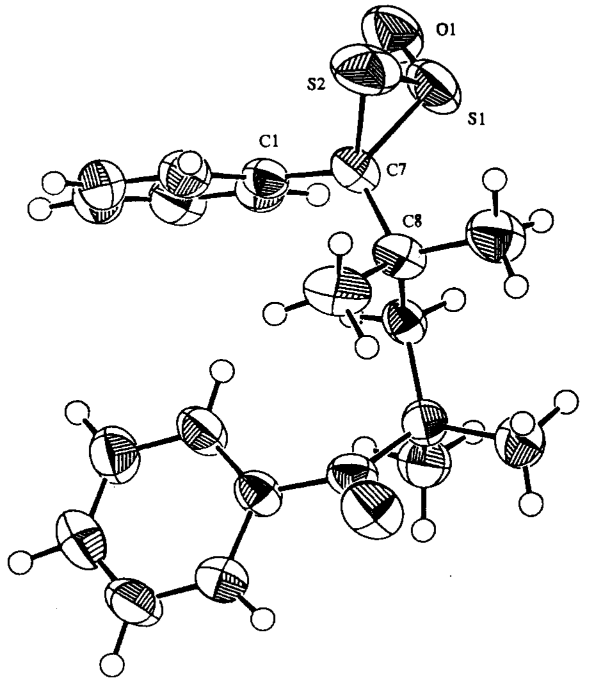
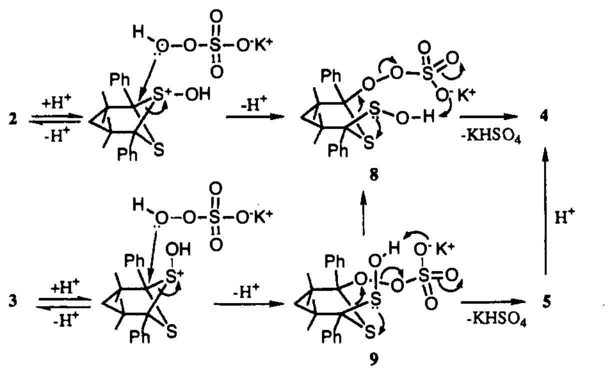


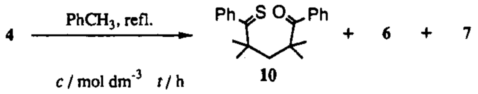
Figure 1. ORTEP view of *cis*-dithiirane *S*-oxide **4**. Selected bond distances (Å) and angles (deg): S(1)–S(2), 2.074(2); S(1)–O(1), 1.442(4); S(1)–C(7), 1.833(4); S(2)–C(7), 1.830(4); C(1)–C(7), 1.499(5); C(7)–C(8), 1.568(5); S(2)–S(1)–O(1), 111.2(0); S(2)–S(1)–C(7), 55.5(1); O(1)–S(1)–C(7), 113.9(2); S(1)–S(2)–C(7), 55.6(1); S(1)–C(7)–S(2), 69.0(1); S(1)–C(7)–C(1), 113.8(3), S(1)–C(7)–C(8), 116.2(3); S(2)–C(7)–C(1), 113.7(3); S(2)–C(7)–C(8), 116.4(3); C(1)–C(7)–C(8), 118.3(3).



in a stereospecific manner. In the case of **3**, the cyclization to a sulfenic acid (**9**) is slow, and conformation change to the rotamer **8** results in the formation of **4** exclusively or the formation of a mixture of **4** and **5**, depending on the reaction temperature. Another possibility may involve the stereospecific formation of **5** from **9**, followed by isomerization of **5** to the thermodynamically more stable **4**.

The divalent sulfur of **4** was readily eliminated by treatment with triphenylphosphine (1.3 equiv) in CH_2Cl_2 at room temperature, giving the sulfine **6** in 79% yield along with triphenylphosphine sulfide (δ_P 44). On the other hand, the dithiirane oxide **4** decomposes on heating to give the thioketone **10** and **6** with loss of sulfur monooxide and sulfur, respectively, in addition to the dicarbonyl compound **7** that is formed by further decomposition of **6** and **10** under the applied conditions.

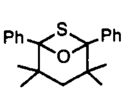
$$4 \xrightarrow[CH_2Cl_2,\ r.\ t.]{Ph_3P\ (1.3\ equiv)} \underset{79\%}{6} + \underset{(\delta_P\ 44)}{Ph_3P{=}S}$$



c / mol dm^{-3}	t / h	10	6	7
0.02	19	44%	9%	26%[a]
0.005	25	48%	14%	38%[b]

a : isolated yields; b : determined by ^{1}H NMR.

Thioketone **10** exists as an equilibrium mixture with the 1,3-oxathietane **11**.[10] Thermal stability of **4** in solution depends on concentration. Thus, although 100% decomposition of **4** in a 0.005 M toluene solution required refluxing for 25 h to give **10** (48%), **6** (14%), and **7** (38%), the decomposition of **4** in a more concentrated solution (0.02 M) was complete within 15 h to give the same compounds in a similar ratio. These observations are indicative of the presence of the decomposition pathway induced by the sulfur and/or sulfur monooxide formed. In fact, addition of sulfur (4 equiv) accelerated the decomposition of **4** in a dilute solution to give sulfine **6**, dicarbonyl compound **7**, and a trace amount of thioketone **10**.



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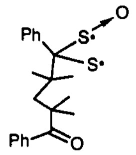

12

Thermal isomerization of **4** to **5** was also observed; heating a solution of **4** in toluene-d_8 at 110 °C for 0.5 h gave a mixture of **4**, **5**, **10**, **6**, and **7** in the ratio of 62:9:7:17:6. Biradical **12** must be involved as the common intermediate[11] leading to the isomerization and decomposition of **4**.

Serendipitous isolation of **4** and **5** should be largely attributed to steric protection by the bulky substituents[12] that prevents the highly reactive three-membered ring from being approached by reactant molecules.[13] We are currently investigating the preparation of a dithiirane derivative carrying no oxygen on the sulfur, where much greater repulsive interaction between lone-pair electrons of adjacent sulfur atoms would be expected.

Supplementary Material Available: Characterization data (IR, ^{1}H and ^{13}C NMR, and MS) for **2–6** and experimental procedures for the preparation of **3** and **4**; description of data collection, data reduction, structure solution, and refinement; tables of atomic coordinates, anisotropic displacement parameters, bond lengths, bond angles, and torsion angles for crystal structure determination of **3**; structural diagrams (26 pages). Ordering information is given on any current masthead page.

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(11) Hoffmann, R. W.; Barth, W. *J. Chem. Soc., Perkin Trans. II* **1983**, 1687.

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(13) Chew, W.; Harpp, D. N. *Tetrahedron Lett.* **1992**, *33*, 45.