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A New Route to Dithiirane 1-Oxides: Oxidation of Tetrathiolanes with Dimethyldioxirane

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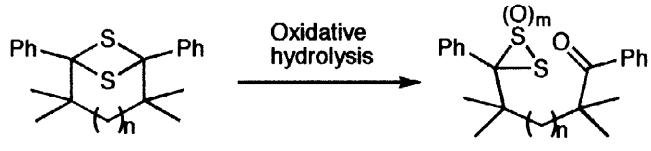
Abstract: Oxidation of di-1-adamantyltetrathiolane with dimethyldioxirane (DMD) in dichloromethane and acetone gave di-1-adamantyldithiirane 1-oxide. Similarly, reaction of 1-adamantyl-*t*-butyltetrathiolane with DMD gave (1*RS*,3*SR*)- and (1*RS*,3*RS*)-1-adamantyl-*t*-butyldithiirane 1-oxides. In the reactions, intermediary formation of tetrathiolane 1-oxides was suggested by low-temperature ^{13}C NMR.

We have reported the first synthesis of isolable, stable dithiiranes **2** by oxidative hydrolysis of bicyclic 1,3-dithietanes **1**.[1] Detailed examination of this synthesis has revealed it to be successfully applicable only to bicyclic 1,3-dithietanes, which inevitably yield carbonyl group-containing dithiiranes.[1] Although the carbonyl groups are considered to be independent of the stability of dithiirane rings from the crystal structures of **2** (n=1, m=0,1),[1a,b,c] they sometimes take part in some reactions of the dithiiranes. For example, thermolysis of the dithiirane **2** (n=1; m=0) in solution affords the corresponding bicyclic 1,3,4-oxadithiolane probably via the 1,3-dipolar cycloaddition of the intermediary thioketone *S*-sulfide ($R_2C{=}S^{+}\text{-}S^{-}$),[1b,2] the ring-opening isomer of **2**, with the intramolecular C=O group; the inevitable existence of a carbonyl group within **2** impedes investigation of the intermolecular reactivities of dithiiranes and their highly reactive, related species such as thioketone *S*-sulfides. Therefore, we are continuing study to develop new, more general methods for the preparation of dithiirane derivatives which do not possese other functional groups. Recently, we found that certain hydrazones, which carry bulky groups on the carbon atom, gave tetrathiolanes, albeit in moderate yields, by modified Okazaki's thioketone synthesis.[3,4] The chemistry of cyclic polysulfides has drawn much attention and oxidation of these compounds is a subject of current interest.[5] We have now found that oxidation of these tetrathiolanes with dimethyldioxirane (DMD) leads to a new synthesis of dithiirane 1-oxides.



1
n = 0,1,2

2
n = 0,1; m = 0
n = 2; m = 1

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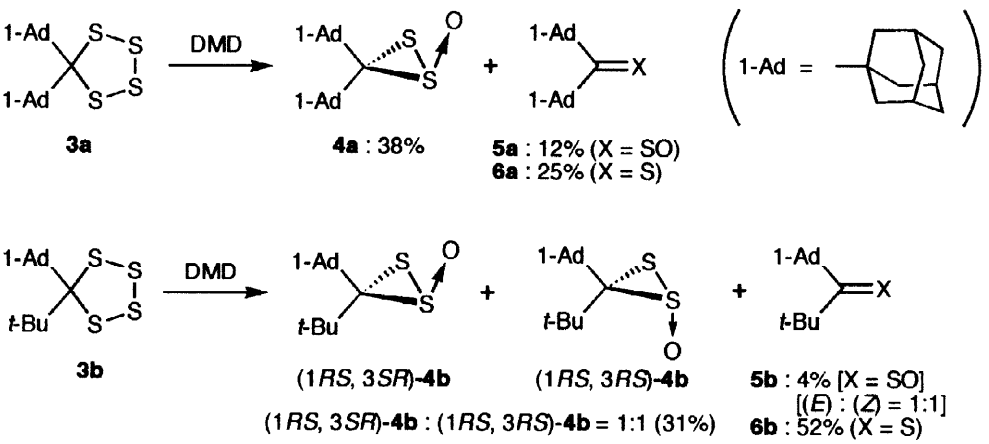
PII: S0040-4039(98)00522-X

5,5-Di-1-adamantyltetrathiolane (**3a**) was treated with 1.2 equiv of DMD[6] at –78 °C for 5 h in a mixture of CH_2Cl_2 and acetone. Removal of the solvent and careful purification of the residue with HPLC gave dithiirane 1-oxide **4a** in 38% yield along with thioketone *S*-oxide **5a** (12%) and thioketone **6a** (25%) with recovery of **3a** (14%). The dithiirane 1-oxide **4a** is rather thermally stable, colorless plates. This is the first example of dithiirane 1-oxides that carry no functional group such as a carbonyl. The structure of **4a** was determined by its spectroscopic data[7] and finally by an X-ray single-crystal structure analysis (Figure 1).[8] The bond lengths and bond angles of the dithiirane 1-oxide part are comparable with those found in other dithiirane 1-oxides.[1a,c] The C2-C1-C3 bond angle is expanded to as large as 123.6° because of repulsion between the bulky 1-adamantyl groups and of connection to the three-membered ring. On the other hand, the oxidation of tetrathiolane **3b** gave a 1:1 mixture of (1*RS*,3*SR*)- and (1*RS*,3*RS*)-dithiirane 1-oxides **4b** (31%), a 1:1 mixture of (*E*)- and (*Z*)-thioketone *S*-oxides **5b** (4%), and thioketone **6b** (52%). The isomers of **4b**[7] were separated by HPLC. The *tert*-butyl signal of (1*RS*,3*SR*)-**4b** appears at a 0.36 ppm higher field than that of (1*RS*,3*RS*)-**4b** because of anisotropy of the SO group,[9] whereas three broad singlets due to the adamantyl of (1*RS*,3*RS*)-**4b** appear at 0.10-0.23 ppm higher fields than those of (1*RS*,3*SR*)-**4b**. The above assignment was further supported by aromatic solvent[10a-c] and $Eu(fod)_3$[10a,b,d] induced shift studies. Assignment of (*E*)- and (*Z*)-thioketone *S*-oxides **5b** was done similarly by ^1H NMR analyses.



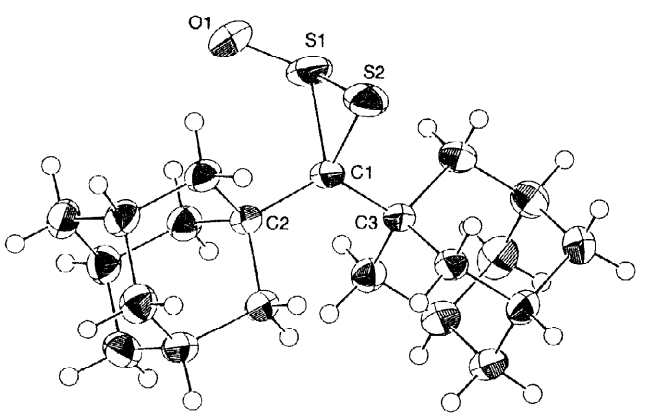
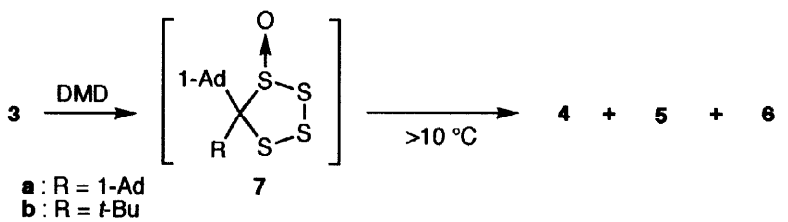


Figure 1. ORTEP view of **4a** (ellipsoids at 50% probability).

Selected bond lengths [Å] and angles [°]: S1-S2 2.098(1), S1-C1 1.860(1), S1-O1 1.407(2), S2-C1 1.863(1), C1-C2 1.606(2), C1-C3 1.592(2), S2-S1-C1 55.8(1), S2-S1-O1 117.5(1), C1-S1-O1 118.8(1), S1-S2-C1 55.6(1), S1-C1-S2 68.6(1), S1-C1-C3 112.7(1), S1-C1-C2 113.3(1), S2-C1-C3 111.6(1), S2-C1-C2 114.2(1), C2-C1-C3 123.6(1) (there is a disorder of the position of the oxygen atom: probabilities of observing the oxygen on S1 and S2 are 64 and 36%, respectively. The oxygen on S2, which appears *trans* to O1, is omitted in this figure to avoid confusion).

The dithiirane 1-oxides **4** decompose at their melting points to give thioketone *S*-oxides **5**, thioketones **6**, and the corresponding carbonyl compounds. In solution, thermal isomerization between (1*RS*,3*SR*)-**4b** and (1*RS*,3*RS*)-**4b** took place in addition to decomposition. Thus, heating pure (1*RS*,3*SR*)-**4b** in $CDCl_3$ at 60 °C for 20 h gave a mixture of (1*RS*,3*SR*)-**4b** (36%), (1*RS*,3*RS*)-**4b** (21%), (*E*)-**5b** (10%), (*Z*)-**5b** (11%), **6b** (2%), and 1-adamantyl *t*-butyl ketone (20%). A similar result was also obtained by heating (1*RS*,3*RS*)-**4b** in $CDCl_3$. Desulfurization of (1*RS*,3*SR*)-**4b** and (1*RS*,3*RS*)-**4b** by Ph_3P gave quantitatively the (*Z*)- and (*E*)-thioketone *S*-oxides **5b**, respectively, with complete retention of configuration.[11]

In the present oxidation reaction, tetrathiolane 1-oxides **7** would be the precursor for dithiirane oxides **4**. When an oxidation mixture of **3a** was carefully evaporated below –10 °C and the residue was analyzed by ^{13}C NMR at –10 °C, a signal assignable to the quaternary carbon (S-*C*-S) of **7a** was observed at δ 127.7. In the case of **3b**, two signals due to two epimers of **7b** were observed at δ 125.5 and 125.6. These signals appear at ca. 11 ppm lower fields than those due to the corresponding quaternary carbons of **3**.[3a,12] On raising the temperature (>10 °C), these signals turned weak, and new signals due to **4**, **5**, and **6** began to appear instead.[13]



We are now investigating removal of the oxygen atom within **4** and the pathway of the decomposition of the intermediates **7** to the products.

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7. All new compounds gave satisfactory analytical data. Selected physical data are as follows: **4a**: colorless plates; m.p. 143—144 °C dec (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50—1.85 (m, 18H), 1.90—2.10 (m, 6H), 2.10—2.40 (br s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.70 (CH), 29.73 (CH), 36.41 (CH_2), 36.61 (CH_2), 39.54 (CH_2), 42.0 (CH_2, br s), 44.14 (C), 44.68 (C), 87.43 (S-*C*-S). (1*RS*,3*SR*)-**4b**: colorless solid; m.p. 106—107 °C dec (EtOH); ^{1}H NMR δ 1.08 (s, 9H; *t*-Bu), 1.70 (br s, 6H), 2.05 (br s, 3H), 2.20 (br s, 6H); (C_6D_6) δ 0.75 (s, 9H; *t*-Bu), 1.61 (br s, 6H), 1.92 (br s, 3H), 2.16 (br s, 6H); ($CDCl_3$, Eu(fod)$_3$, 0.3 equiv) δ 1.58 (s, 9H; *t*-Bu), 2.15 (br s, 6H), 2.45 (br s, 3H), 3.80 (br s, 6H); ^{13}C NMR δ 29.42 (CH_3), 29.65 (CH), 36.57 (CH_2), 41.72 (CH_2, br s), 41.74 (C), 43.97 (C), 86.24 (S-*C*-S). (1*RS*,3*RS*)-**4b**: colorless solid; m.p. 99—100 °C dec (EtOH); ^{1}H NMR δ 1.44 (s, 9H; *t*-Bu), 1.61 (br s, 6H), 1.80 (br s, 6H), 1.97 (br s, 3H); (C_6D_6) δ 1.38 (s, 9H; *t*-Bu), 1.35 (br s, 6H), 1.52 (br s, 6H), 1.65 (br s, 3H); ($CDCl_3$, Eu(fod)$_3$, 0.3 equiv) δ 3.92 (s, 9H; *t*-Bu), 2.03 (br s, 6H), 2.42 (br s, 3H), 3.06 (br s, 6H); ^{13}C NMR δ 28.64 (CH), 32.2 (br s, CH_3), 36.37 (CH_2), 39.48 (CH_2), 41.92 (C), 43.46 (C), 87.73 (S-*C*-S).
8. Crystal data for **4a**: $C_{21}H_{30}OS_2$, monoclinic, $P2_1/c$, a = 6.4700(3), b = 13.549(1), c = 20.985(2) Å, β = 92.985(6)°, V = 1803.2(2) Å^3, Z = 4, ρ_{calcd} = 1.335 g cm^{-3}, μ(Mo$_{K\alpha}$) = 2.893 mm^{-1}. A colorless plate with dimensions 0.30×0.30×0.06 mm was mounted on a Mac Science DIP3000 diffractometer with a graphite-monochromater. Oscillation and nonscreen Weissenberg photographs were recorded on the imaging plates of the diffractometer by using Mo$_{K\alpha}$ radiation (λ = 0.71073 Å) at 25 °C and the data reduction was made by the MAC DENZO program system. Intensity data of 4344 unique reflections were collected in the range of $0 \le h \le 6$, $0 \le k \le 19$, $-29 \le l \le 29$. Cell parameters were determined and refined by using the MAC DENZO for all observed reflections. The structure was solved by direct methods using SIR in the CRYSTAN-GM program system. The atomic coordinates and anisotropic thermal parameters of the non-H atoms were refined by full-matrix least squares to minimize the functions, $\Sigma(|F_O|-|F_C|)^2$, for 3297 reflections [$I \ge 2\sigma(I)$] (346 parameters). The final R (R_w) = 0.047 (0.053) and GOF = 1.995; max/min residual electron density = 0.71/–0.48 e Å^{-3}.
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11. For retention of configuration in desulfurization of episulfides by Ph_3P, see (a) Neureiter, N. P.; Bordwell, F. G. *J. Am. Chem. Soc.* **1959**, *81*, 578; (b) Meyers, A. I.; Ford, M. E. *J. Org. Chem.* **1976**, *41*, 1735.
12. In the oxidation study of $Me_3CS(S)_nSCMe_3$ to $Me_3CS(O)(S)_nSCMe_3$ (n=1,2) were observed a similar regioselectivity of the oxidation and a comparable degree of down-field shift of carbon atoms α to the sulfur atoms oxidized. See: Derbesy, G.; Harpp, D. N. *Sulfur Lett.* **1995**, *19*, 1; *Sulfur Reports* **1995**, *16*, 363.
13. Although **7** is storable at about –20 °C for a few days, no single crystals of **7** suitable for X-ray diffraction analysis were obtained in spite of much effort.