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Oxidation of *cis*-3,5-di-*tert*-alkyl-3,5-diphenyl-1,2,4-trithiolanes: isolation and some properties of the 1-oxides and the 1,2-dioxides

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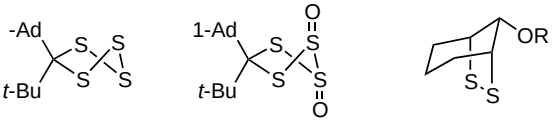
Abstract—Oxidation of *cis*-3,5-di-*tert*-alkyl-3,5-diphenyl-1,2,4-trithiolane with an excess amount of dimethyldioxirane gave the 1,2-dioxide, a *vic*-disulfoxide, and it was verified that the 1,2-dioxide was formed specifically from one of two stereoisomeric monoxides. The structures of the monoxides and the 1,2-dioxide were determined by X-ray crystallography.

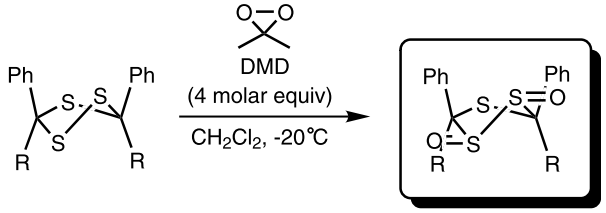
The chemistry of *vic*-disulfoxides [RS(O)S(O)R′] has been drawing much attention,[1–6] and recently we succeeded in the first isolation and structure determination of a compound bearing an S–S(O)–S(O)–S linkage by the oxidation of tetrathiolane **1** with dimethyldioxirane (DMD).[7] The two oxygen atoms of the tetrathiolane 2,3-dioxide **2** take the diaxial orientations characteristically, where the anomeric effect by adjacent sulfur atoms[7b,8,9] at the both ends seems to contribute to the stability of **2**. Naturally, our attention was turned to the synthesis of *vic*-disulfoxides not having such a special effect, that is, those which have a C–S(O)–S(O)–C linkage. The above-mentioned study, as well as the study by Folkins and Harpp on the oxidation of 4,5-dithiabicyclo[3.2.1]octanes **3**,[3] suggests that *vic*-disulfoxides derived from cyclic disulfides possess fair stability compared with those derived from acyclic disulfides,[4] thus leading us to investigate the oxidation of 1,2,4-trithiolanes.[10] Here we report the oxidation of tetrasubstituted 1,2,4-trithiolanes **4**,[11] which gives the desired *vic*-disulfoxides.



1 **2** **3**

Trithiolane **4a** was treated with an acetone solution of DMD[12] (4 molar equiv.) in CH_2Cl_2 at −20°C to give a dioxide (42%) which showed two strong absorptions due to the S=O stretching vibrations (1064 and 1104 cm^{-1}) in the infrared spectrum. Oxidation of **4b** with DMD proceeded similarly to give a dioxide in 60% yield. The structure of the dioxide of **4b** was finally determined by X-ray crystallography to be 1,2-dioxide **5b** (Scheme 1, Fig. 1). The structure of the dioxide of **4a** was thus elucidated to be **5a** based on the similarity of the ^{13}C NMR and IR data of **5a** with those of **5b**.[13]

In the crystalline state, the trithiolane ring of **5b** takes a near-envelope conformation [C(5)–S(4)–C(3)–S(2) 11.4(3)°]. In contrast to the structure of tetrathiolane 2,3-dioxide **2**, both the oxygen atoms of **5b** occupy the equatorial orientations, where the torsion angles of C(5)–S(1)–S(2)–C(3) and O(1)–S(1)–S(2)–O(2) were −57.3(2) and 73.6(3)°, respectively. The S(1)–S(2) bond



4a: R = *t*-Bu
4b: R = 1-Ad

5a: 42%
5b: 60%

Scheme 1.

Keywords: 1,2,4-trithiolane; oxidation; *vic*-disulfoxide; X-ray analysis; thermolysis.

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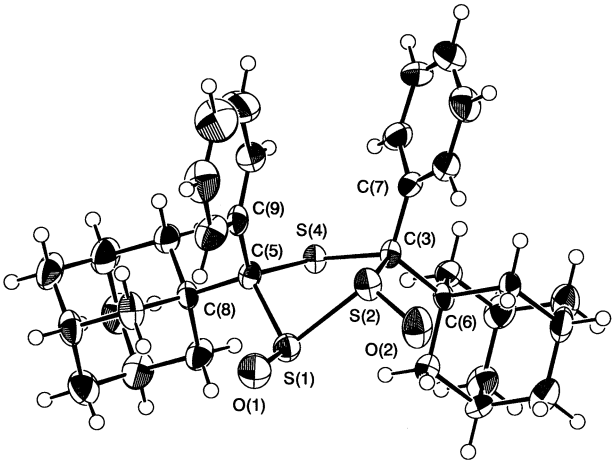
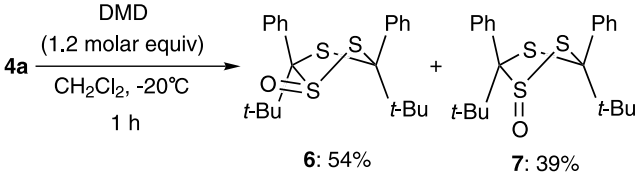


Figure 1. ORTEP drawing of **5b** (50% ellipsoids). Selected bond lengths (Å) and bond angles (°): S1–S2 2.249(2), S2–C3 1.860(6), C3–S4 1.862(6), S4–C5 1.829(5), C5–S1 1.838(5), C3–C6 1.603(7), C3–C7 1.503(9), C5–C8 1.567(7), C5–C9 1.520(7), S1–O1 1.468(5), S2–O2 1.455(5); S1–S2–C3 94.5(2), S2–C3–S4 105.4(3), C3–S4–C5 105.3(2), S4–C5–S1 96.5(2), C5–S1–S2 88.2(2), C6–C3–C7 113.9(4), C8–C5–C9 113.6(4).

length of 2.249(2) Å is elongated by approximately 10% compared with usual S–S bonds.[18] For reference, the S–S bond length of **4a** is 2.024(2) Å.[11a] The dioxides **5** was stable in the crystalline state for a long time in a refrigerator but decomposed gradually in solution at room temperature to give the corresponding thioketones.

In order to clarify the course of the formation of 1,2-dioxides **5**, we examined stepwise oxidation of trithiolane **4a**. Oxidation of **4a** with 1.2 molar amounts of DMD gave two stereoisomeric monoxides **6** and **7** in 54 and 39% yields, respectively (Scheme 2).[19] These two isomers were separated by silica-gel column chromatography, and their structures were determined definitely by X-ray crystallographic analyses (Figs. 2 and 3). A 1-oxide **6** takes a half-chair conformation with the oxygen atom being *cis* to the phenyl group and occupying the equatorial orientation. The S(1)–S(2) bond length was 2.1133(9) Å, and the C(5)–S(1)–S(2)–C(3) torsion angle was 45.82(9)°. The other 1-oxide **7** takes an envelope conformation [S(1)–S(2)–C(3)–S(4) 3.07(12)°], where the oxygen atom is *trans* to the phenyl group and occupies the axial orientation. The S(1)–S(2) bond length was 2.052(2) Å and the C(5)–S(1)–S(2)–C(3) torsion angle was −32.0(2)°. The S(1)–S(2) bond in **7** is meaningfully shorter than that in **6**, which would result in an anomeric effect in **7**.[7b,8,9] In the ^{13}C NMR spectra down to 203 K, signals due to 1,2,4-



Scheme 2.

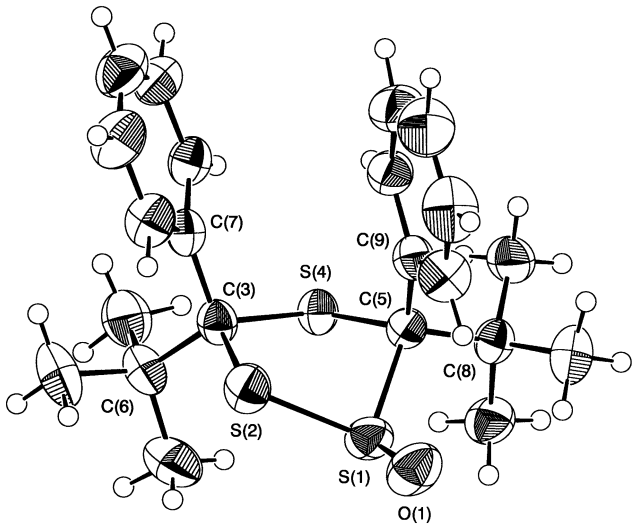


Figure 2. ORTEP drawing of **6** (50% ellipsoids). Selected bond lengths (Å) and bond angles (°): S1–S2 2.1133(9), S2–C3 1.838(2), C3–S4 1.855(2), S4–C5 1.814(2), C5–S1 1.880(2), C3–C6 1.586(3), C3–C7 1.522(3), C5–C8 1.584(3), C5–C9 1.514(3), S1–O1 1.457(2); S1–S2–C3 98.63(7), S2–C3–S4 107.13(11), C3–S4–C5 102.83(9), S4–C5–S1 96.72(10), C5–S1–S2 92.78(6), C6–C3–C7 111.7(2), C8–C5–C9 113.8(2).

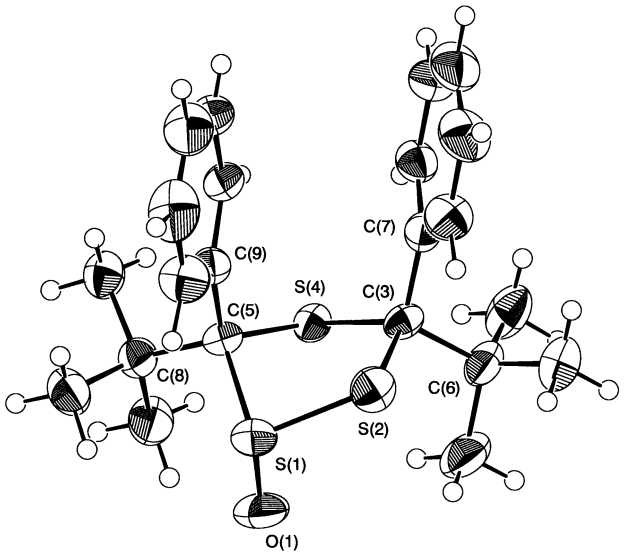
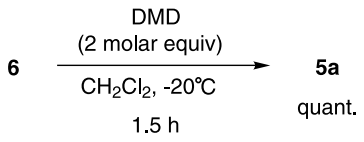


Figure 3. ORTEP drawing of **7** (50% ellipsoids). Selected bond lengths (Å) and bond angles (°): S1–S2 2.052(2), S2–C3 1.858(3), C3–S4 1.832(4), S4–C5 1.818(3), C5–S1 1.897(3), C3–C6 1.589(5), C3–C7 1.527(5), C5–C8 1.586(5), C5–C9 1.529(5), S1–O1 1.460(4); S1–S2–C3 104.94(12), S2–C3–S4 106.7(2), C3–S4–C5 101.4(2), S4–C5–S1 103.8(2), C5–S1–S2 93.10(12), C6–C3–C7 112.7(3), C8–C5–C9 112.9(3).

trithiolane carbons in **6** and **7** did not change on the chemical shifts and shape, indicating that they take respective single conformations in solution. We assume that the conformations are similar to those in the solid state. Recently, it was reported that the oxidation of 3,3,5,5-tetraphenyl-1,2,4-trithiolane with MCPBA yielded the 1-oxide with the oxygen atom possessing the axial orientation.[10b] Incidentally, there observed no for-



Scheme 3.

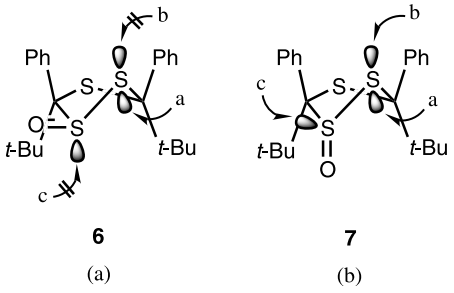
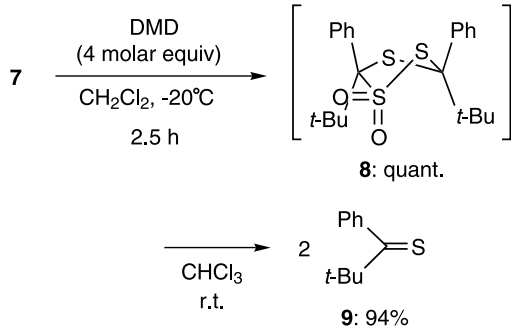


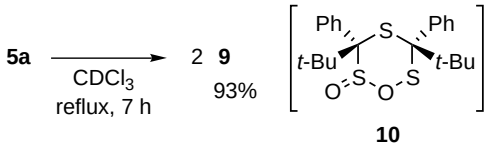
Figure 4.

mation of 4-oxides of **4a** in the present reactions in contrast to the oxidations of the parent[10a,d] and 3,3,5,5-tetramethyl-1,2,4-trithiolanes.[10c]

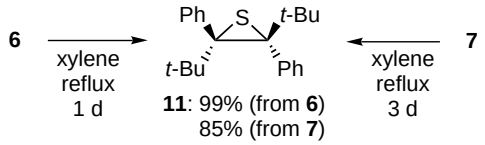
Trithiolane 1-oxides **6** and **7** thus obtained were allowed to react with DMD in CH_2Cl_2 at −20°C. We observed quite different results: oxidation of **6** with DMD (2 molar equiv.) yielded 1,2-dioxide **5a** quantitatively (Scheme 3), indicating that the oxidation occurred through path a (Fig. 4a) and not paths b or c. In contrast, the reaction of **7** with DMD was so slow that it required 4 molar amounts of DMD for the complete consumption of **7** to give thiosulfonate **8** (Scheme 4).[20] Although **8** was unstable in solution at room temperature to decompose quickly to thioketone **9** (94%), the yield of **8** was quantitative judging from the ^1H NMR spectrum of the reaction mixture measured at −20°C. The structure of **8** was also supported by the infrared spectrum indicating the presence of an $-S(O)_2-$ moiety (1312 and 1140 cm^{-1}). The lower reactivity of **7** compared with **6** might be attributed to a lowering of the energy level of the lone pair of electrons to be attacked owing to the anomeric effect described above. At present, there is no evidence whether **8** is formed by a rearrangement of 1,2-dioxides,[1] formed through paths a and/or b (Fig. 4b), or by the direct oxidation at the sulfinyl sulfur atom of **7** (path c).



Scheme 4.



Scheme 5.



Scheme 6.

In relation to the unexpected instability of 1,1-dioxide **8** compared with 1,2-dioxide **5**, the thermal reactions of **5a** and monoxides **6** and **7** were examined. Heating of **5a** in refluxing $CDCl_3$ yielded thioketone **9** in 93% yield (Scheme 5). The formation of 2 molar amounts of **9** is explained in terms of the extrusion of SO_2 from a rearrangement product, **8** or *OS*-sulfenyl sulfinate **10**.[1] Elemental sulfur was not detected by TLC in this thermolysis.

On the other hand, thermal reactions of **6** and **7** in refluxing xylene gave the identical *trans*-episulfide **11**[21] in high yields (Scheme 6). The *trans* stereochemistry of **11** was verified by the oxidation of **11** to give a single episulfoxide having nonequivalent *tert*-butyl groups. The stereospecific reactions of **6** and **7** would proceed through a common thiocarbonyl ylide intermediate in a manner similar to that in the N_2-extrusion reaction of 1,3,4-thiadiazolines reported by Kellogg and Wassenaar.[22]

In summary, we succeeded in the isolation and the structure determination of 1,2,4-trithiolane 1,2-dioxides **5** in addition to two stereoisomeric 1-oxides **6** and **7**. We also disclosed that the 1,2-dioxide **5a** is formed specifically from **6** and not from the epimer **7**. On this point, the present study provides not only a route to isolable *vic*-disulfoxides but also an important insight into the chemistry of multiple oxidations of cyclic polysulfides.

Acknowledgements

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13. Compound **5a**: Colorless crystals, mp >72°C (decomp.) (EtOH); ^{1}H NMR (400 MHz, $CDCl_3$, 253 K): δ 1.00 (br s, 9H), 1.29 (s, 9H), 6.55 (t, J=7.4 Hz, 1H), 7.01–7.23 (m, 5H), 7.26–7.34 (m, 1H), 7.46 (br s, 1H), 7.84 (br s, 1H), 8.28 (d, J=7.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 26.9 (CH_3), 27.5 (br s, CH_3), 41.1 (C), 42.5 (C), 73.7 (C), 78.3 (C), 126.9 (CH), 127.7 (CH), 128.4 (CH), 129.2 (CH), 136.1 (C), 139.1 (C) (two CH carbons appeared as very broad signals at 126.5 and 131.1); IR (KBr): 1064, 1104 cm^{-1} (S=O). Anal. calcd for $C_{22}H_{28}O_2S_3$: C, 62.82; H, 6.71. Found: C, 62.93; H, 6.70%. Compound **5b**: Colorless crystals, mp >80°C (decomp.) (CH_2Cl_2–hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53–1.73 (m, 15H), 1.80–2.25 (m, 15H), 6.43–6.60 (m, 1H), 6.93–7.85 (m, 8H), 8.13–8.33 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 28.6, 28.9, 36.3, 36.5, 37.6, 37.9, 43.2, 44.1, 73.3, 79.2, 125.3 (br s), 126.8, 127.2 (br s), 127.6, 128.3, 132.0 (br s), 135.5, 138.2; IR (KBr): 1066, 1102 cm^{-1} (S=O). Crystal data for **5b**:[14] $C_{34}H_{40}O_2S_3$, M_w 576.88, colorless plates, 0.26×0.20×0.06 mm, monoclinic, space group $P2_1/n$, a=7.2060(4), b=23.329(1), c=17.236(1) Å, β=99.657(3)°, V=2856.5(3) Å^3, Z=4, D_{calcd}=1.341 g cm^{-3}, μ(Mo Kα)=0.29 mm^{-1}. 5650 independent reflections, 352 parameters; R_1=0.0895 ($I>2\sigma(I)$, 2858 reflections), wR_2=0.2908 (for all), GOF=0.947; max./min. residual density=0.660/–0.609 e Å^{-3}.
14. General crystallographic information: Mac Science DIP3000 diffractometer with a graphite-monochromated Mo Kα radiation (λ=0.71073 Å), solved with direct methods (SIR-92[15]), and refined with full-matrix least-squares (SHELXL-97[16]) using all independent reflections. Absorption corrections were done by a multi-scan method (SORTAV[17]). Hydrogen atoms were placed at calculated positions. CCDC-176689 (**5b**), CCDC-176690 (**6**), and CCDC-176691 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223 336-033; e-mail: deposit@ccdc.cam.ac.uk].
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19. Compound **6**: Colorless crystals, mp 144–146°C (decomp.) ($CHCl_3$/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (br s, 9H), 1.29 (s, 9H), 6.84 (t, J=7.8 Hz, 2H), 6.97 (t, J=7.4 Hz, 1H), 7.03–7.15 (m, 3H), 7.26 (br s, 2H), 7.75 (d, J=7.6 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.3 (br s, CH_3), 28.4 (CH_3), 40.9 (C), 42.3 (C), 74.0 (C), 93.3 (C), 125.8 (CH), 126.0 (CH), 126.8 (CH), 127.3 (CH), 128.5 (CH), 130.8 (CH), 135.2 (C), 141.0 (C); IR (KBr): 1088 cm^{-1} (S=O). Anal. calcd for $C_{22}H_{28}OS_3$: C, 65.30; H, 6.97. Found: C, 65.32; H, 6.99%. Crystal data for **6**:[14] $C_{22}H_{28}OS_3$, M_w 404.66, colorless prisms, 0.34×0.20×0.16 mm, monoclinic, space group $C2/c$, a=22.2890(8), b=15.1610(7), c=12.6000(5) Å, β=97.738(2)°, V=4219.1(3) Å^3, Z=8, D_{calcd}=1.274 g cm^{-3}, μ(Mo Kα)=0.36 mm^{-1}. 4185 independent reflections, 235 parameters; R_1=0.0426 ($I>2\sigma(I)$, 3044 reflections), wR_2=0.1178 (for all), GOF=1.028; max./min. residual density=0.340/–0.223 e Å^{-3}. Compound **7**: Colorless crystals, mp 180–182°C (decomp.) ($CHCl_3$/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (br s, 9H), 1.28 (s, 9H), 6.43 (br s, 1H), 6.89 (t, J=7.3 Hz, 2H), 6.94–7.88 (m, 7H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 28.9 (CH_3), 29.4 (CH_3), 41.1 (C), 41.7 (C), 96.5 (C), 110.4 (C), 125.8 (br s, CH), 126.1 (CH), 126.9 (CH), 127.2 (CH), 129.8 (br s, CH), 131.5 (br s, CH), 134.6 (C), 141.1 (C); IR (KBr): 1108 cm^{-1} (S=O). Anal. calcd for $C_{22}H_{28}OS_3$: C, 65.30; H, 6.97. Found: C, 65.31; H, 7.03%. Crystal data for **7**:[14]

$C_{22}H_{28}OS_3$, M_w 404.66, colorless plates, 0.30×0.14×0.08 mm, triclinic, space group $P\bar{1}$, $a=6.5660(7)$, $b=9.3890(9)$, $c=18.138(3)$ Å, $\alpha=75.005(4)$, $\beta=85.167(4)$, $\gamma=72.838(4)°$, $V=1032.0(2)$ Å^3, $Z=2$, $D_{calcd}=1.302$ g cm^{-3}, μ(Mo Kα)= 0.37 mm^{-1}. 3750 independent reflections, 235 parameters; $R_1=0.0629$ ($I>2\sigma(I)$, 2311 reflections), $wR_2=0.1876$ (for all), GOF=0.974; max./min. residual density=0.329/–0.355 e Å^{-3}.

20. Compound **8**: Colorless crystals; ^{1}H NMR (400 MHz, $CDCl_3$, 253 K): δ 1.16 (br s, 9H), 1.28 (s, 9H), 6.56 (t, $J=7.6$ Hz, 1H), 6.78 (d, $J=7.9$ Hz, 1H), 6.97 (t, $J=7.7$ Hz, 1H), 7.04 (t, $J=7.3$ Hz, 1H), 7.16–7.24 (m, 2H), 7.31 (d, $J=8.3$ Hz, 1H), 7.39 (t, $J=7.6$ Hz, 1H), 8.00 (d, $J=7.8$ Hz, 1H), 8.22 (d, $J=8.1$ Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 253 K): δ 29.4, 31.3, 42.4, 42.8, 75.0, 103.1, 125.5, 126.0, 126.3, 126.5, 127.4, 127.8, 128.0, 128.5, 129.9, 131.5, 132.8, 139.0; IR (KBr, rt): 1312, 1140 cm^{-1} (SO_2).
21. Compound **11**: Colorless crystals, mp 149–151°C (hexane/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.62 (s, 18H), 7.25–7.30 (m, 6H), 7.49–7.53 (m, 2H), 7.62–7.66 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 29.7 (CH_3), 39.5 (C), 74.1 (C), 125.1 (CH), 126.8 (CH), 127.4 (CH), 131.6 (CH), 134.6 (CH), 139.9 (C). Anal. calcd for $C_{22}H_{28}S$: C, 81.42; H, 8.70. Found: C, 81.30; H, 8.75%.
22. Buter, J.; Wassenaar, S.; Kellogg, R. M. *J. Org. Chem.* **1972**, *37*, 4045–4060.