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Preparation of some new bicyclic compounds of sulfur

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Reductive cleavage of the disulfide bond of 2,3-di-*tert*-butyl-5,6,7-trithiabicyclo[2.2.1]hept-2-ene 7-exoxide with lithium triethylborohydride and treatment of the resulting dithiolate with N, N'-carbonyldiimidazole *in situ* furnished 6,7-di-*tert*-butyl-2,4,8-trithia-3-oxobicyclo[3.2.1]oct-6-ene 8-endoxide in 89% yield. Thioxo analog, 6,7-di-*tert*-butyl-2,4,8-trithia-3-thioxobicyclo[3.2.1]oct-6-ene 8-endoxide was also prepared by the reaction of dithiolate with N, N'-thiocarbonyldiimidazole in 79% yield.

Keywords: 2,4,8-trithiabicyclo[3.2.1]oct-6-ene; dihydrothiophene; sulfur heterocycles; trithiocarbonate; phosphonate

1. Introduction

We have been investigating small molecules of sulfur such as sulfur monoxide (SO) (*1*), diatomic sulfur (S_2) (*2–4*), disulfur monoxide (S_2O) (*4–7*), and triatomic sulfur (S_3) (*4–7*). Recently, we have reported that the reaction of thiophene 1-oxide **1** with disulfur dichloride, followed by treatment with aqueous sodium hydrogen carbonate, furnishes bicyclic compound **2** in good yield (*4*). If the oxygen atom of the sulfinyl group of **2** can be removed, the resulting **4** would undergo retro Diels–Alder reaction to generate singlet S_2 with driving force of the formation of hetero aromatic **5**. However, attempted deoxygenation of **2** did not provide clear experimental evidence for the formation of singlet S_2 (*4*). Therefore, we now examine the preparation of **4** by reduction of **2** to dihydrothiophenedithiol **3** followed by oxidative recyclization (Scheme 1). This study, though different from our initial intentions, led us to the synthesis of a new bicylic system of sulfur, as described below.

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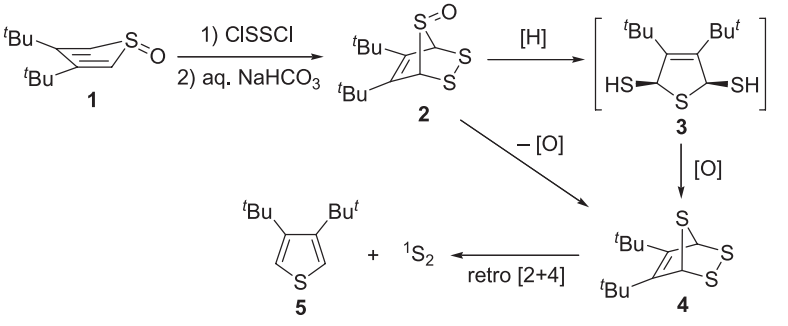
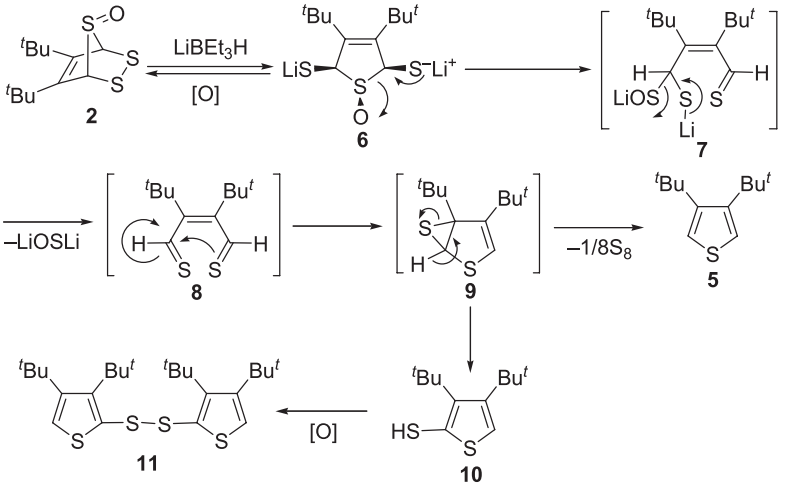


Scheme 1.

2. Results and discussion

Reduction of **2** with lithium triethylborohydride ($LiBEt_3H$) (*8*) was examined repeatedly at room temperature changing the molar ratio of $LiBEt_3H$ and/or reaction time with the expectation of obtaining **3**. The reactions furnished the starting material **2**, thiophene **5**, and thiophenethiol **10** as the principal products (Scheme 2). For example, one of these afforded **2**, **5**, and **10** in 26%, 17%, and 13% yields, respectively. Thiol **10** was labile and was readily oxidized to disulfide **11** during purification (*9*). The structure of **11** was determined unambiguously by X-ray diffraction analysis (Figure 1). When the above reduction was quenched by addition of ice water, the three compounds were isolated from the aqueous layer, though **2** was not for all the cases. Thus, the reduction probably affords dithiolate **6** initially, but seemingly further reduction that leads to the expected **3** does not occur. Dithiolate **6** is soluble in water and is taken up in the aqueous layer. Then, during the workup of the aqueous layer, some part of **6** is oxidized to give the starting material **2**, and the other part provides dithial **8** by elimination of LiOSLi. Electrocyclization of **8** gives thiirane **9** (*9–11*), from which **5** and **10** are produced by loss of sulfur and by ring opening, respectively (*9*).

Although the above results are disappointing from a viewpoint of the generation of singlet S_2, the proposed intermediate **6** is a promising starting material for the synthesis of new sulfur-containing



Scheme 2.

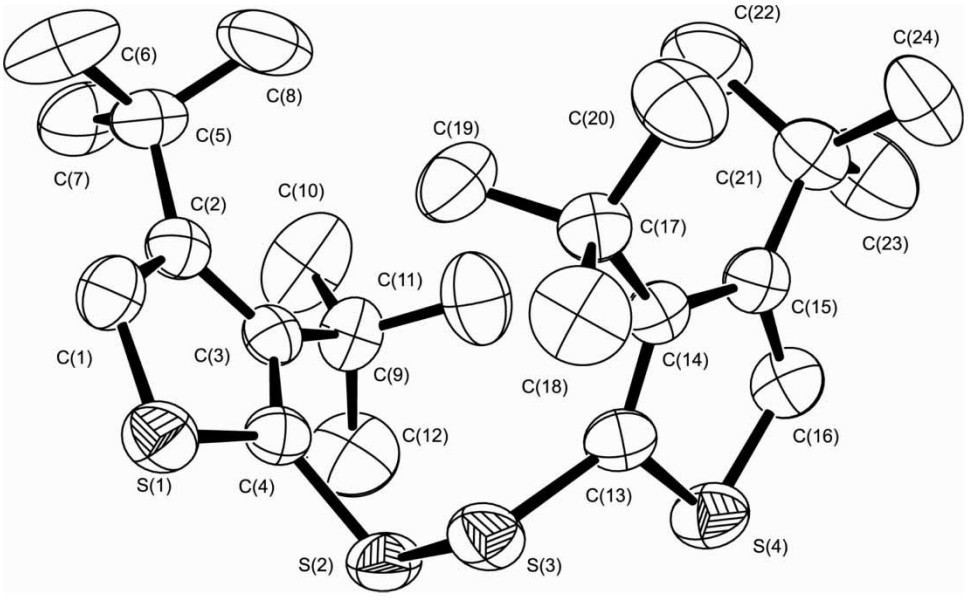
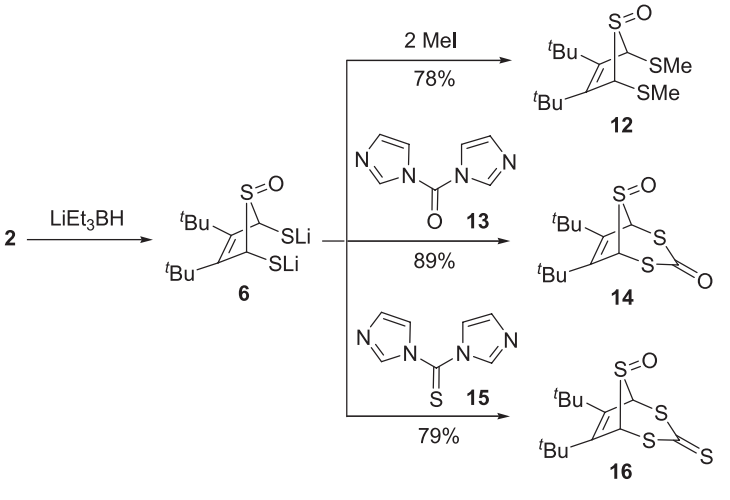
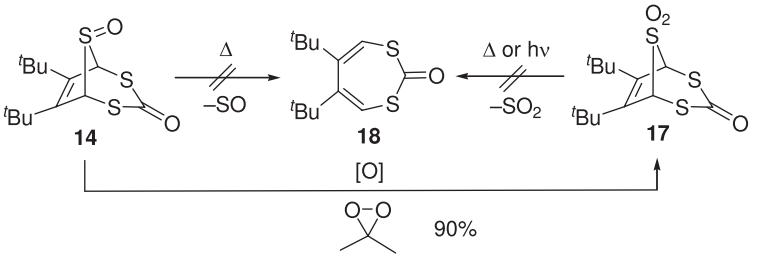


Figure 1. ORTEP diagram for **11** showing atom labeling scheme. Thermal ellipsoids are drawn at the 50% probability level and the hydrogen atoms are omitted for clarity.

heterocycles. Therefore, as a beginning, the reaction of **6** with methyl iodide was examined in order to obtain more rigid evidence for the formation of **6** (Scheme 3). Thus, **2** was treated with excess $LiBEt_3H$ in THF and then with excess methyl iodide, which gave the expected product **12** in 78% yield. Reduction of **2** with $LiBEt_3H$ followed by treatment with *N*, *N*′-carbonydiimidazole **13** furnished a new sulfur-containing bicylic compound **14** in 89% yield. The use of *N*, *N*′-thiocarbonydiimidazole **15**, in place of **13**, provided a sulfur analog **16** in 79% yield. Incidentally, carbon disulfide cannot react with **6** to give **16**, although the 1,2-dithiol obtained by reduction of 3,4-di-(1-adamantyl)-1,2-dithiete reacted with carbon disulfide to give the corresponding 2-thioxo-1,3-dithiole (*8*).



Scheme 3.

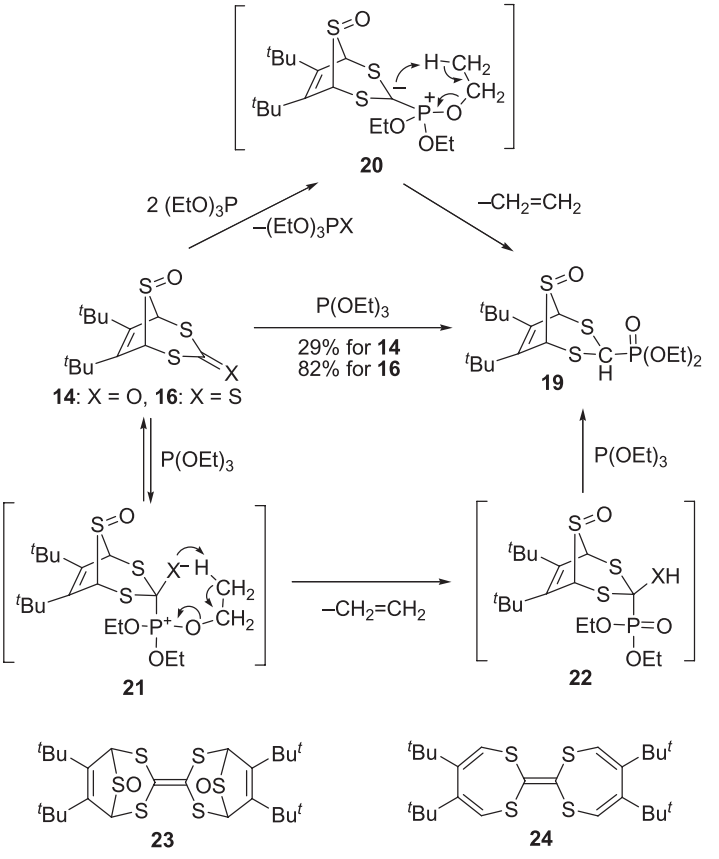


Scheme 4.

Although **14** was expected to undergo thermal extrusion of SO to give 1,3-dithiepin-2-one **18**, a higher analog of 1,3-dithiol-2-one, it was thermally stable and did not show any tendency to extrude SO. Therefore, **14** was converted to sulfone **17** in 90% yield by oxidation with dimethyldioxirane (Scheme 4). However, **17** was also thermally stable and did not undergo SO_2 extrusion to give **18**, although **17** possesses a unit of 2,5-dihydrothiophene-1,1-dioxide, and it is well known that 2,5-dihydrothiophene-1,1-dioxides undergo thermal extrusion of SO_2 to give 1,3-butadienes in good yields (*12,13*). Sulfone **17** was also inert to photochemical extrusion of SO_2. Irradiation of 254 nm light to a dichloromethane solution of **17** in a Pyrex test tube resulted in the recovery of **17**.

Next we have examined dechalogenation of **14** and **16** by phosphorus reagents with the expectation of obtaining **23** (*14–16*) from which **24**, a higher analog of tetrathiafulvalene, might be derived. This study led us to the unexpected product. Thus, heating **14** with triethyl phosphite at 110–115 °C for 24 h furnished phosphonate **19** in 29% yield (Scheme 5). The same compound was also obtained in 82% yield by the reaction of **16** with triethyl phosphite under the same conditions. Since we thought that methine hydrogen of **19** originated from β-hydrogen of triethyl phosphite and thus the reactions with phosphorus reagents having no β-hydrogen might furnish the desired product **23**, the reactions with trimethyl phosphite and triphenyl phosphite were examined. However, **16** was inert to these reagents under the same conditions and was recovered unchanged. The methine proton of $CHP(O)(OEt)_2$ part of **19** appeared at δ 4.46 in $CDCl_3$ as doublet with $J = 15.4$ Hz due to coupling with ^{31}P. However, the stereochemistry of this part could not be determined, though we have examined aromatic solvent-induced shifts (*17*) and $Eu(tfc)_3$-induced shifts [$Eu(tfc)_3$ = tris(3-trifluoroacetyl-d-camphorato)europium(III)]; for example, the methine proton described above appeared at δ 4.67 in C_6D_6 and δ 2.09 in $CDCl_3$ in the presence of an equimolar amount of $Eu(tfc)_3$ (downfield shift of 0.21 ppm and upfield shift of 2.35 ppm, respectively) (see Experimental).

The most probable mechanism for the formation of **19** involves dechalcogenation by triethyl phosphite, addition of triethyl phosphite that produces phosphorus ylide **20** (*18*), and intramolecular elimination of **20** that furnishes **19** and ethylene (Scheme 5). However, this mechanism cannot explain the fact that reactions of **16** with trimethyl and triphenyl phosphites resulted in the recovery of **16** without the formation of the expected **23**. An alternative mechanism involves reversible addition of triethyl phosphite to the carbonyl carbon of **14** or thiocarbonyl carbon of **16** that forms **21**, although addition to thiocarbonyl sulfur is the mechanism previously proposed for desulfurization (*18*). Then, intramolecular elimination of **21** forms **22** and ethylene. Finally **22** might be reduced to **19** by triethyl phosphite, a trivalent phosphorus reagent. Reportedly, thiols are desulfurized to give the corresponding hydrocarbons and triethyl thionophosphate, both in good yields (*19*).



Scheme 5.

3. Experimental

3.1. *Reduction of (2) with lithium triethylborohydride ($LiBEt_3H$)*

Reduction of **2** with $LiBEt_3H$ was examined repeatedly at room temperature, changing the molar ratio of $LiBEt_3H$ and/or reaction time. The reaction afforded the starting material **2**, thiophene **5**, and thiophenethiol **10** as the principal products. The following is a representative example. To a stirred solution of 50 mg (0.18 mmol) of **2** in 2 ml of THF was added 1.0 ml (1.1 mmol) of a 1.06 M THF solution of $LiBEt_3H$ at $-18\,^{\circ}C$ under argon through a rubber septum. After the mixture had been stirred for 2.5 h at $-18\,^{\circ}C$ and then at room temperature for 2 days, the reaction was quenched by addition of ice water. The mixture was extracted with ether to give 13 mg (26%) of the starting material **2**. The aqueous layer was acidified by 2 M HCl and then extracted with ether. The ether extract was purified by silica gel column chromatography to give 6 mg (17%) of **2** and 6 mg (13%) of **10**: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.43 (s, 9H), 1.48 (s, 9H), 1.66 (s, 1H), 7.22 (s, 1H); singlet at δ 1.66 that originated from SH disappeared by addition of D_2O. During further purification, **10** was oxidized to bis(3,4-di-*tert*-butyl-2-thienyl) disulfide (**11**) : mp 173–174 °C; yellow crystals; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.9, 34.4, 36.0, 37.2, 126.2, 132.1, 152.0, 154.4. Anal. calcd for $C_{24}H_{38}S_4$: C, 63.38, H, 8.42. Found: C, 63.31: H, 8.49.

3.2. *cis-cis-2,5-Bis(methylthio)-2,5-dihydrothiophene 1-oxide (12)*

To a stirred solution of 50 mg (0.18 mmol) of **2** in 2 ml of THF was added 1.0 ml (1.1 mmol) of a THF solution of $LiBEt_3H$ at −18 °C under argon through a rubber septum. After the mixture had been stirred for 0.5 h at −18 °C and then for 3 h at room temperature, 110 mg (0.78 mmol) of methyl iodide was added. The resulting mixture was stirred for 1 h and the reaction was quenched by addition of ice water. The mixture was extracted with ether and the ether extracts were dried over anhydrous magnesium sulfate and evaporated. The resulting solid residue was purified by silica gel column chromatography to give 40 mg (78%) of **12**: mp 122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 18H), 2.26 (s, 6H), 4.30), (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.5, 32.3, 35.4, 72.5, 141.7; IR (KBr) 1082 cm^{-1} (S=O). Anal. calcd for $C_{14}H_{26}OS_3$: C, 54.85; H, 8.55. Found: C, 54.75; 8.51.

3.3. *6,7-Di-tert-butyl-2,4,8-trithia-3-oxobicyclo[3.2.1]oct-6-ene 8-endoxide (14)*

To a stirred solution of 100 mg (0.36 mmol) of **2** in 5 ml of THF was added 0.76 ml (0.72 mmol) of a THF solution of $LiBEt_3H$ at −0 °C under argon through a rubber septum. After the mixture had been stirred for 0.5 h at −0 °C and then for 3 h at room temperature, a solution of 172 mg (1.08 mmol) of *N*, *N*′-carbonyldiimidazole (**13**) in 4 ml of *N*, *N*-dimethylformamide was added. After the resulting mixture had been stirred for 3 h, the reaction was quenched by addition of ice water. The mixture was extracted with ether and the ether extracts were dried over anhydrous magnesium sulfate and evaporated. The solid residue was chromatographed on a column of silica gel with dichloromethane as the eluent to furnish 98 mg (89%) of **14**: mp 215.0–215.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 18H), 5.00 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 32.5, 35.6, 68.8, 144.3, 181.8; IR (KBr) 1633 (C=O), 1090 cm^{-1} (S=O). Anal. calcd for $C_{13}H_{20}O_2S_3$: C, 51.28; H, 6.62. Found: C, 51.48; H, 6.57.

3.4. *6,7-Di-tert-butyl-2,4,8-trithia-3-thioxobicyclo[3.2.1]oct-6-ene 8-endoxide (16)*

To a stirred solution of 100 mg (0.36 mmol) of **2** in 5 ml of THF was added 0.72 ml (0.72 mmol) of a THF solution of lithium $LiBEt_3H$ at 0 °C under argon through a rubber septum. After the mixture had been stirred for 2 h at −0 °C and then for 2 h at room temperature, a solution of 200 mg (1.12 mmol) of *N*, *N*′-thiocarbonyldiimidazole (**15**) in 3 ml of THF was added. After the resulting mixture had been stirred for 3 h, the reaction was quenched by addition of ice water. The mixture was extracted with ether and the ether extracts were dried over anhydrous magnesium sulfate and evaporated. The resulting residue was chromatographed on a column of silica gel with dichloromethane as the eluent to furnish 91 mg (79%) of **16**: mp 238.5–239.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 18H), 4.89 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.5, 35.6, 69.0, 144.3, 212.3; IR (KBr) 1020 (C=S), 1092 cm^{-1} (S=O). Anal. calcd for $C_{13}H_{20}OS_4$: C, 48.71; H, 6.29. Found: C, 48.89; H, 6.28.

Carbon disulfide failed to react with **6** to give **16**. Thus, reduction of **2** by an equimolar amount of $LiBEt_3H$ followed by treatment with excess carbon disulfide resulted in the recovery of **2** in 58% yield.

3.5. *6,7-Di-tert-butyl-2,4,8-trithia-3-oxobicyclo[3.2.1]oct-2-ene 8,8-dioxide (17)*

To a stirred solution of 50 mg (0.16 mmol) of **14** in 2 ml of dichloromethane was added a dilute solution of dimethyldioxirane (3.75 ml, 0.30 mmol) in acetone at 0 °C. The mixture was stirred for 1.5 h and then evaporated. The residue was purified by silica gel column chromatography to

give 3 mg (6%) of the starting material **14** and 46 mg (90%) of the dioxide **17** as colorless crystals: mp 215–217 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 18H), 4.74 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 32.3, 36.2, 64.9, 146.9, 179.8; IR (KBr) 1123, 1316 (SO_2), 1633 cm^{-1} (C=O).

3.6. *6,7-Di-tert-butyl-3-diethoxyphosphinyl-2,4,8-trithiabicyclo[3.2.1]oct-6-ene 8-endoxide (19)*

3.6.1. *Preparation from **14***

A mixture of 20 mg (0.067 mmol) of **14** and 1 ml (5.8 mmol) of triethyl phosphite was heated at 110–115 °C for 24 h under argon. The mixture was evaporated to dryness under reduced pressure and the residue was chromatographed on a column of silica gel with AcOEt as the eluent to give 8 mg (29%) of **19**: mp 145 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (t, $J = 7.0$ Hz, 6H), 1.45 (s, 18H), 4.25–4.40 (m, 4H), 4.46 (d, $J = 15.4$ Hz, 1H), 4.50 (s, 2H); ^{1}H NMR (C_6D_6, 300 MHz) δ 1.02 (s, 18H), 1.13 (t, $J = 7.0$ Hz, 6H), 3.87 (d, $J = 3.8$ Hz, 2H), 4.10–4.24 (m, 4H), 4.67 (d, $J = 15.4$ Hz, 1H); ^{1}H NMR ($CDCl_3$, additive: equimolar amount of (+)Eu(tfc)$_3$, 300 MHz) δ 1.49 (broad s, 24H), 2.09 (broad s, 1H), 4.46–4.62 (m, 4H), 4.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 16.3, 16.4, 32.5, 35.8, 36.1 (d, $^2J_{13C-31P} = 144.0$ Hz), 64.3 (d, $^3J_{13C-31P} = 6.5$ Hz), 64.9 (d, $^3J_{13C-31P} = 8.0$ Hz), 79.4, 139.5; IR (KBr) 1013 (S=O), 1263 cm^{-1} (P=O). Anal. calcd for $C_{17}H_{31}O_4PS_3$: C, 47.86; H, 7.32. Found: C, 47.59; H.7.25.

3.6.2. *Preparation from **16***

A mixture of 20 mg (0.062 mmol) of **16** and 1 ml (5.8 mmol) of triethyl phosphite was heated at 110–115 °C for 24 h under argon. The mixture was evaporated to dryness under reduced pressure and the residue was chromatographed on a column of silica gel with AcOEt as the eluent to give 22 mg (82%) of **19**.

Heating 20 mg (0.062 mmol) of **16** in 1 ml of trimethyl phosphite at 110–115 °C for 24 h under argon resulted in the 80% recovery of **16**. Heating 20 mg (0.062 mmol) of **16** in 1 ml of triphenyl phosphite at 110–115 °C for 24 h under argon also resulted in the recovery of **16**.

3.7. *X-ray crystallographic analysis of (11)*

Crystal data for **11** were recorded on a Bruker SMART APEX CCD area detector by using 0.30°-wide ω scans and graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å). Frame data (4 s, 0.30°-wide ω scans) were collected using the Bruker SMART software package. Peak integration was performed by the Bruker SAINT-Plus software package. Absorption correction was made by SADABS software. Space group determination was done by XPREP software. All calculations were performed by the Bruker SHELXTL-NT software package. The structure was solved by direct methods and refined with full-matrix least-squares by all independent reflections. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were placed at calculated positions.

11: $C_{24}H_{38}S_4$, $M_w = 454.78$, triclinic, space group $\bar{P}1$; $a = 10.7070(15)$, $b = 11.0825(16)$, $c = 11.2034(17)$ Å, $\alpha = 93.275(10)$, $\beta = 93.275(10)$, $\gamma = 93.275(10)$ deg; $Z = 2$; $V = 1259.2(3)$ Å^3; $D_c = 1.199$ g/cm^3, $\mu = 0.386$ mm^{-1}; measured reflections 9319, independent reflections 5985 [R(int) = 0.0360], $R1 = 0.0806$, w$R2 = 0.1956$, GOF = 1.042.

Crystallographic data for the structural analysis have been deposited at the Cambridge Crystallographic Data Center, CCDC No. 717766.[1]

Note

1. Copies of this information can be obtained from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; Email: deposit@ccdc.ac.uk or http://www.ccdc.cam.ac.uk).

Supporting information

This material (the CIF file for X-ray diffraction analysis of compound **11** and the selected bond length, bond angle, and dihedral angle data) is available with the online version of this article.

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