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Synthesis of 1,2,4-Trithiolanes from Thione *S*-Oxides and Lawesson Reagent at Room Temperature

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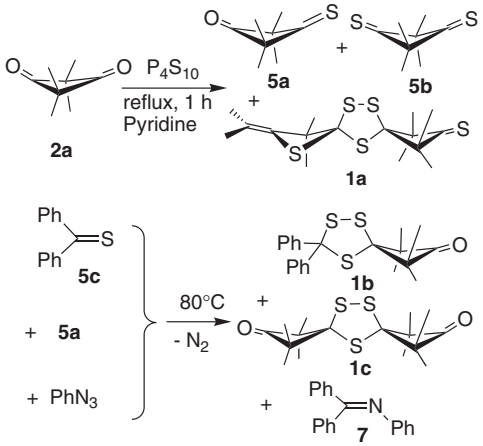
The reaction of 2,2,4,4-tetramethyl-3-thioxocyclobutanone *S*-oxide with Lawesson reagent (L. R.) afforded the corresponding 1,2,4-trithiolane. Thiopivalophenone and thiopivalophenone *S*-oxides reacted with L. R. at rt to give the corresponding *S*-sulfide, which further reacted with thiones to afford the corresponding *cis*-1,2,4-trithiolanes.

1,2,4-Trithiolanes (**1**) are well-known heterocycles, some of which are obtained from natural products.[1] Although many methods for the formation of **1** have been reported,[2] there are a few reports on the direct synthesis of **1** from ketones (**2**) by using thiation reagents.[3] We have reported on the isolation of *cis*- and *trans*-**1** from pivalophenone and P_4S_{10} in refluxing pyridine.[4] While the intermediacy of the thiosulfines (**3**) and the dithiiranes (**4**) has been proposed to explain the reaction mechanisms leading to **1**, Huisgen and Rapp have clearly shown that the reaction of **3** prepared from tetraaryl-1,2,4-trithiolanes with acetylenes or thiones (**5**) gave the corresponding cycloadducts.[5] The isolation of a series of stable **4** was accomplished by Ishii and Nakayama.[6] Recently, Shimada et al. reported the synthesis of sterically crowded **4** by the reaction of thioketone *S*-oxides (**6**) with Lawesson reagent (L. R.).[7] These results prompted us to investigate the synthesis of **1** from ketones **2** via thiosulfine **3** or dithiirane **4** under mild conditions.

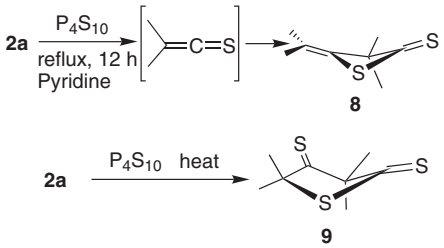
Elam and Davis reported the synthesis of 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**5a**) and 1,3-dithione (**5b**) by the reaction of 2,2,4,4-tetramethyl-1,3-cyclobutanedione (**2a**) with P_4S_{10}. They isolated trithiolane (**1a**) as a side product (2.8%).[8] Mloston and Heimgartner reported that the reaction of thiobenzophenone (**5c**) with PhN_3 in the presence of **5a** gave 1,2,4-trithiolanes (**1b**, **1c**) and imine (**7**) (Scheme 1).[9]

When dione **2a** was treated with P_4S_{10} in refluxing pyridine for 12 h, the corresponding dithioester (**8**) was produced almost quantitatively, whereas the reaction of **2a** with P_4S_{10} up to 200 °C under reduced pressure resulted in the formation of 3,3,5,5-tetramethyl-4-thioxothiolane-2-thione (**9**) in 72% yield (Scheme 2). Since **9** was previously prepared by the irradiation of dithione **5b** in methanol via radical species,[10] the reaction might proceed through a similar radical intermediate.

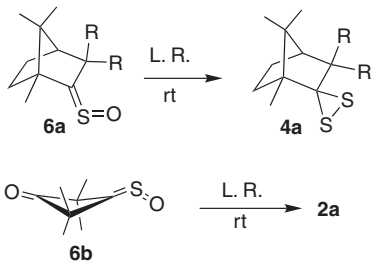
Recently, Shimada et al. reported the synthesis of sterically crowded dithiirane (**4a**) by the reaction of thioketone *S*-oxide (**6a**) with L. R.[7] Mloston et al. have reported that the attempted



Scheme 1.



Scheme 2.



Scheme 3.

formation of trithiolane **1c** by the reaction of 2,2,4,4-tetramethyl-3-thioxocyclobutanone *S*-oxide (**6b**) with L. R. was unsuccessful, and only desulfurated product **2a** could be detected (Scheme 3).[11] We have been interested in this reaction because a possible formation of trithiolane **1** or dithiirane **4** at room temperature. When sulfine **6b** was treated with L. R. in the presence of monothione **5a** at room temperature for 7 days, 1,1,3,3,7,7,9,9-octamethyl-5,10,11-trithiadispiro[3.1.3.2]undecane-2-thione-8-one (**1d**) was obtained in 7% yield along with monothione **5a** and dione **2a**, suggesting that the intermediates should be thiosulfine **3a** or dithiirane **4b** (Scheme 4).

Since the yield of **1d** was low, we then applied this method to the synthesis of **1** from thiopivalophenone *S*-oxides. The treatment of *p*-methylthiopivalophenone *S*-oxide (**6c**) with L. R., followed by the addition of *p*-methylthiopivalophenone (**5d**) for 72 h, resulted in the formation of *cis*-trithiolane **1e**[4] in 79% yield. Another isomer (*trans*-trithiolane **1e**) was not obtained. When thione **5d** was treated with L. R. at rt for 19 days, *cis*-**1e** was obtained in 26% yield, suggesting that a prolonged reaction time was required for completion. Additionally, the re-

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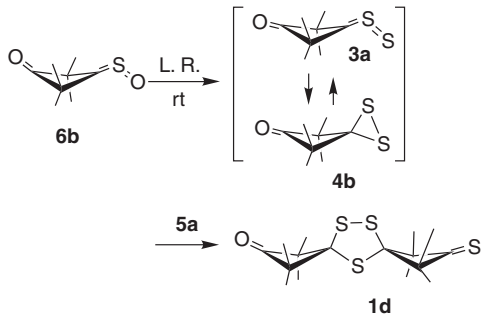
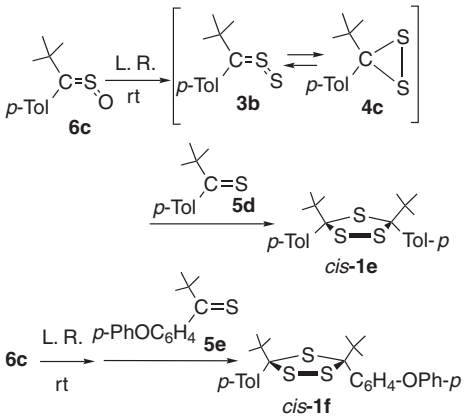


Scheme 4.



Scheme 5.

action of *S*-oxide **6c** with L. R., followed by addition of *p*-phenoxythiopivalophenone (**5e**), gave unsymmetrical *cis*-trithiolane (**1f**) in 42% yield (Scheme 5).

Experimental

Reaction of Dione 2a with P_4S_{10}. A mixture of **2a** (280 mg, 2.0 mmol) and P_4S_{10} (445 mg, 1.0 mmol) was gradually heated up to 200 °C under reduced pressure (3 Torr) for 1 h. The resulting mixture was cooled to rt and chromatographed over silica gel by elution from hexane–dichloromethane (3:1) to afford an orange-yellow oil of 4-thioxothiolane-2-thione **9** (279 mg, 1.44 mmol). Bp 55–60 °C/3 Torr (lit.[12] bp 122 °C/15 Torr).

Reaction of *S*-Oxide 6b with L. R. at Room Temperature. To a solution of **6b** (69 mg, 0.4 mmol) in dichloromethane (2 mL) was added L. R. (242 mg, 0.6 mmol). After being stirred for 10 min, thioxocyclobutanone **5a** (94 mg, 0.6 mmol) was added in one portion. After being stirred for 7 d at rt, the reaction mixture was evaporated to give dark-purple oily crystals, which were chromatographed over silica gel by elution with hexane–dichloromethane (1:1) to afford reddish-purple crystals of trithiolane **1d** (10 mg, 0.028 mmol). Mp 72–74.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 3H, Me), 1.49 (s, 3H, Me), 1.50 (s, 3H, Me), 1.56 (s, 3H, Me). ^{13}C NMR ($CDCl_3$) δ 21.45 (Me), 25.25 (Me), 26.07 (Me), 30.18 (Me), 66.76 (quaternary C), 69.72 (quaternary C), 85.67 (S–C–S), 89.59 (S–C–S), 218.73 (C=O), 278.89 (C=S). Found: C, 53.88; H, 7.03%. Calcd for $C_{16}H_{24}OS_4$: C, 53.29; H, 6.71%. A correct elemental analysis of **1d** was not obtained, but its ^{13}C NMR clearly shows the trithiolane structure. Thioxocyclobutaone **5a** (55 mg, 0.35 mmol) and **2a** (35 mg, 0.25 mmol) were also isolated.

Reaction of *S*-Oxide 6c with L. R. in the Presence of 5d at Room Temperature. To a solution of *S*-oxide **6c** (208 mg, 1.0 mmol) in dichloromethane (15 mL) was added a solution of L. R. (136 mg, 3.4 mmol) at rt. After stirring for 1 h, **5e** (192 mg, 1.0 mmol) was added to this solution. After stirring for 72 h, the reaction mixture was evaporated to give pale-blue oily crystals. The resulting mixture was chromatographed over silica gel by elution from hexane, hexane–dichloromethane (2:1), and hexane–dichloromethane (1:1) to give *cis*-trithiolane **1e** (328 mg, 0.79 mmol), **5d** (29 mg, 0.14 mmol), and *p*-methylpivalophenone (**2b**) (12 mg, 0.07 mmol). *cis*-Trithiolane **1c**; mp 134–135 °C. The spectral data were identical with the reported value.[4] Found: C, 68.82; H, 7.52%. Calcd for $C_{24}H_{32}OS_3$: C, 69.17; H, 7.74%. Similarly, reaction of *S*-oxide **6c** (30 mg, 0.14 mmol) with L. R. (68 mg, 0.17 mmol) in the presence of thione **5e** (38 mg, 0.14 mmol) was carried out. Unsymmetrical *cis*-trithiolane **1f** (28 mg, 0.059 mmol, 42%) and a mixture of *p*-methyl- and *p*-phenoxythiopivalophenone (**5d**:**5e** = 1:1 by ^{1}H NMR, 16 mg, 0.07 mmol) were obtained. *cis*-3,5-Di-*tert*-butyl-3-*p*-methylphenyl-5-*p*-phenoxyphenyl-1,2,4-trithiolane **1f**: colorless crystals. Mp 124–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 9H, *tert*-Bu), 1.24 (s, 9H, *tert*-Bu), 2.23 (s, 3H, Me), 6.65 (d, 2H, J = 9 Hz, Ar), 6.81 (d, 2H, J = 8 Hz, Ar), 6.85 (d, 2H, J = 7 Hz, Ar), 7.05 (t, 1H, J = 7 Hz, Ph), 7,29 (d, 2H, J = 8 Hz), 7.40. ^{13}C NMR (100 M Hz, $CDCl_3$) δ 20.90, 26.65, 29.44, 34.97, 36.53, 37.73, 38.78, 39.71, 40.20, 90.68 (S–C–S), 98.81 (S–C–S), 126.87, 130.52, 136.04, 139.37. Found: C, 70.03; H, 6.99%. Calcd for $C_{29}H_{34}OS_3$: C, 70.40; H, 6.93%.

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