

Magnesium Amide-Induced Pummerer-Type Reactions of Cyclopropyl Sulfoxides. Synthesis of Cyclopropanone Dithioacetals

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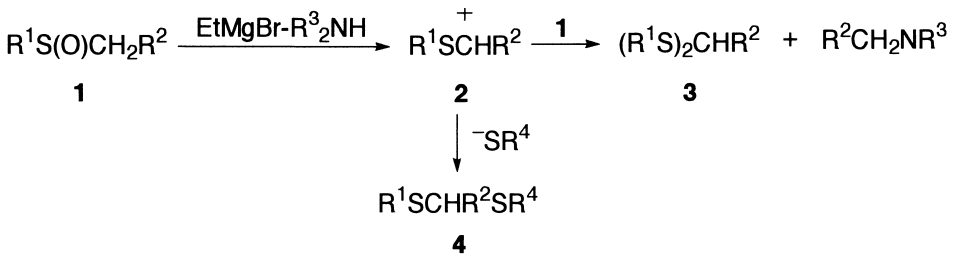
The reaction of cyclopropyl phenyl sulfoxide with a magnesium amide, generated from ethylmagnesium bromide and diisopropylamine, gave 1-(phenylthio)cyclopropanol in 72% yield. When the diisopropylmagnesium reagent was treated with a thiol prior to an interaction with cyclopropyl phenyl sulfoxides, symmetrical and unsymmetrical cyclopropanone dithioacetals were produced in fair yields along with small quantities of the corresponding 1-(phenylthio)cyclopropanols.

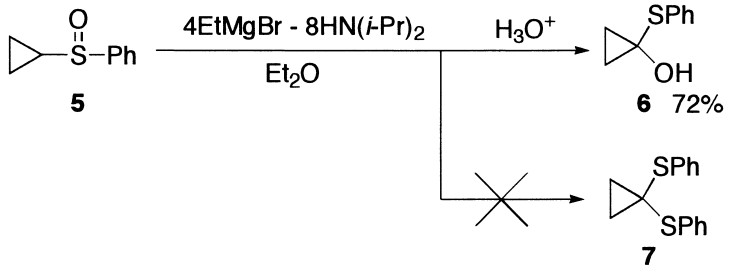
In our previous paper we described that the reactions of sulfoxides bearing α-hydrogens **1** with magnesium amides, generated in situ by a treatment of ethylmagnesium bromide with secondary amines, such as diisopropylamine or 2,2,6,6-tetramethylpiperidine in diethyl ether, afforded the corresponding symmetrical dithioacetals **3** via Pummerer-type carbonium ion intermediates **2** (Scheme 1).[1] We have also reported that the reaction of sulfoxides **1** with various thiols in the presence of a magnesium amide gave unsymmetrical dithioacetals **4** (Scheme 1).[2] As an extension of these studies, we examined the reactions of cyclopropyl phenyl sulfoxides with magnesium amides. In this paper, we describe the results of our investigation, which offer simple routes to 1-(phenylthio)cyclopropanol and cyclopropanone dithioacetals. Several reports on Pummerer-type reactions of cyclopropyl sulfoxides have been recorded previously.[3] However, to the best of our knowledge, no application to the preparation of cyclopropanone dithioacetals has been reported.

We began our investigation by first examining the reaction between cyclopropyl phenyl sulfoxide (**5**) with magnesium amides. Sulfoxide **5** was treated with a magnesium amide, generated from ethylmagnesium bromide (4 molar amounts) and diisopropylamine (8 molar amounts) overnight at room temperature.[1] After the usual workup, purification of the crude product by preparative TLC on silica gel afforded 1-(phenylthio)cyclopropanol (**6**) in good yield, and no trace amounts of bis(phenylthio)cyclopropane (**7**) could be detected (Scheme 2). It can be assumed that no production of **7** is due to the low stability of the cyclopropyl carbonium ion intermediate. de Boer et al. have reported on the preparation of 1-(alkylthio)cyclopropanols[4] and their transformation into 1-substituted cyclopropyl sulfides with a variety of nucleophiles. They synthesized 1-(alkylthio)cyclopropanols using cyclopropanones and thiols. Although this method appears to be convenient, cyclopropanones are unstable and difficult to handle.

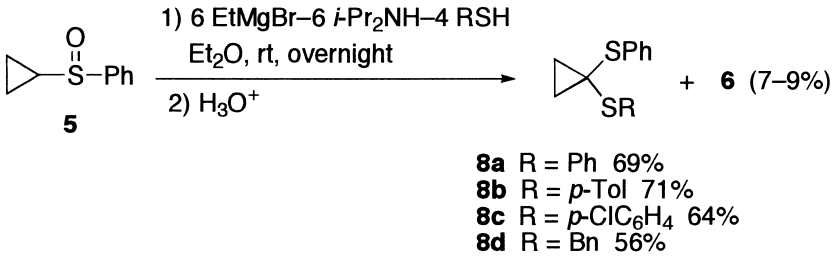
We next found that when the (diisopropylamino)magnesium reagent was treated with a thiol prior to an interaction with cyclopropyl phenyl sulfoxide (**5**), cyclopropane dithioacetals **8a–d** were obtained in fair yields along with small quantities of 1-(phenylthio)cyclopropanol (**6**), as shown in Scheme 3. Reactions of **5** with magnesium amide-thiol reagents, generated from various ratios of ethylmagnesium bromide, diisopropylamine, and a thiol, were initially examined. The use of 6 molar amounts each of ethylmagnesium bromide and diisopropylamine, and 4 molar amounts of thiols was found to be most effective for the production of **8**. Cyclopropanone dithioacetals have been synthesized by, for example, 1) the addition of dibromocarbene to olefins, followed by an exchange of the bromines of the resulting dibromocyclopropanes by RS groups;[5] 2) the base-induced cyclopropanation of 1,1,3-tris(phenylthio)alkanes[6] or 3) the reaction of sulfur-stabilized anions with ketene bis(phenylthio)acetal [1,1-bis(phenylthio)ethylene].[7]



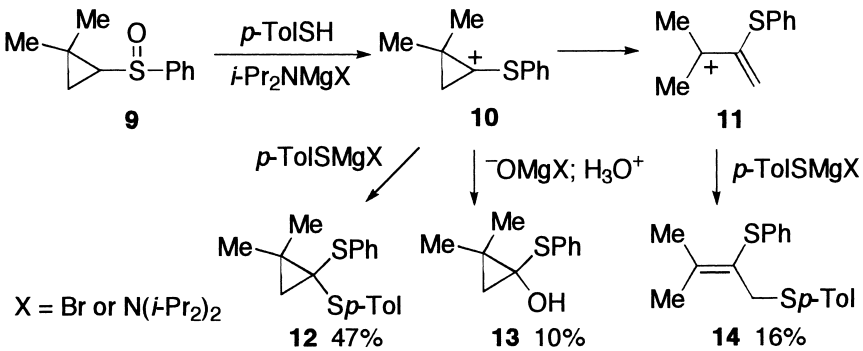
Scheme 1.



Scheme 2.



Scheme 3.



Scheme 4.

Transformations of cyclopropanone dithioacetals into other useful organic compounds have also been reported.[5,8]

Subsequently, a similar treatment of 2,2-dimethylcyclopropyl phenyl sulfoxide (**9**) with the magnesium amide in the presence of 4-methylbenzenethiol under the above-mentioned conditions gave the expected dithioacetal **12** along with 2,2-dimethyl-1-(phenylthio)cyclopropanol (**13**) and 2-methyl-4-(4-methylphenylthio)-3-phenylthio-2-butene (**14**), as illustrated in Scheme 4. The formation of **14** can be explained by a rearrangement of the cyclopropyl carbonium ion intermediate **10** to the stable allyl carbonium ion intermediate **11**.

In conclusion, the present magnesium amide-mediated Pummerer-type reactions can provide convenient methods for preparing 1-(phenylthio)cyclopropanol and cyclopropanone dithioacetals. The present methods may find some value in organic synthesis because of simple manipulations as well as the ready availability of the starting materials.

Experimental

General. The melting points were determined on a Laboratory Devices MEL-TEMP II melting point apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 1600 Series FT IR spectrometer. The ^{1}H NMR spectra were determined using $SiMe_4$ as an internal reference with a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz in $CDCl_3$. Low-resolution mass spectra were recorded on a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). High-resolution mass spectra were performed on a JEOL JMS-AX505 HA spectrometer (Faculty of Agriculture, this University). Thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 PF_{254}. All of the solvents used were dried over appropriate drying agents and distilled under argon prior to use.

Starting Materials. Cyclopropyl phenyl sulfoxide (**5**) and 2,2-dimethylcyclopropyl phenyl sulfoxide (**9**) were prepared following procedures reported by Oae et al.[3b] All other chemicals used in this study were commercially available.

1-(Phenylthio)cyclopropanol 6.[4] To a solution of EtMgBr (4.0 mmol) in Et_2O (5 mL) at 0 °C under argon was added *i*-Pr_2NH (0.81 g, 8.0 mmol); the mixture was heated at reflux temperature for 1 h. The turbid solution was cooled to 0 °C and cyclopropyl phenyl sulfoxide (**5**) (0.17 g, 1.0 mmol) was added. The temperature was raised to room temperature and the mixture was stirred overnight. The resulting mixture was quenched by adding aqueous NH_4Cl and extracted with Et_2O. The organic layer was

washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the crude product was purified by preparative TLC on SiO_2 to give **6** (0.12 g, 72%) as a pale-yellow oil: R_f 0.22 (1:5 EtOAc–hexane); bp 120 °C (bath temp)/26.7 Pa (lit.,[4] 90–93 °C/4.0 Pa); IR (neat) 3371 and 3059 cm^{-1}; ^1H NMR δ 1.1–1.3 (4H, m), 2.30 (1H, s), and 7.2–7.55 (5H, m); MS *m/z* (%) 166 (M^+, 3.0) and 110 (100).

1,1-Bis(phenylthio)cyclopropane 8a.[6a] **Typical Procedure for the Reactions of Cyclopropyl Phenyl Sulfoxides with Thiols in the Presence of a Magnesium Amide.** To a cooled (0 °C) turbid solution of a magnesium amide, generated from EtMgBr (6.0 mmol) and *i*-Pr_2NH (0.61 g, 6.0 mmol) in Et_2O (8 mL), as described above, benzenethiol (0.50 g, 4.0 mmol) was added under stirring. After the mixture was stirred for 20 min, cyclopropyl phenyl sulfoxide (**5**) (0.17 g, 1.0 mmol) was added. The resulting mixture was allowed to warm to room temperature, and stirring was continued overnight. A workup in a similar manner as described above gave a residue, which was purified by preparative TLC on SiO_2 (1:40 EtOAc–hexane) to give **8a** (0.18 g, 69%) along with 9% yield of **6** (15 mg). **8a**: a pale yellow oil; R_f 0.46; IR (neat) 3078, 3060, 1583, 1477, 1438, 1024, 889, 737, and 689 cm^{-1}; ^1H NMR δ 1.48 (4H, s), 7.27 (2H, t, J = 7.3 Hz), 7.33 (4H, t, J = 7.3 Hz), and 7.47 (4H, d, J = 7.3 Hz); MS *m/z* (%) 258 (M^+, 12) and 149 (100). Found: *m/z* 258.0537. Calcd for $C_{16}H_{16}S_2$: M, 258.0522.

1-(4-Methylphenylthio)-1-(phenylthio)cyclopropane (8b): a pale-yellow oil; R_f 0.29 (1:20 EtOAc–hexane); IR (neat) 3074, 3017, 1584, 1491, 1478, 1089, 802, 738, and 690 cm^{-1}; ^1H NMR δ 1.4–1.5 (4H, m), 2.34 (3H, s), and 7.1–7.5 (9H, m); MS *m/z* (%) 272 (M^+, 12), 163 (68), 149 (71), 105 (91), and 91 (100). Found: *m/z* 272.0692. Calcd for $C_{16}H_{16}S_2$: M, 272.0693. Found: C, 70.76; H, 5.85; S, 23.49%. Calcd for $C_{16}H_{16}S_2$: C, 70.54; H, 5.92; S, 23.54%.

1-(4-Chlorophenylthio)-1-(phenylthio)cyclopropane (8c): a pale-yellow oil; R_f 0.29 (1:40 EtOAc–hexane); IR (neat) 3058, 3003, 1583, 1438, 1415, 1296, 1177, and 889 cm^{-1}; ^1H NMR δ 1.45–1.5 (4H, m) and 7.25–7.5 (9H, m); MS *m/z* (%) 292 (M^+, 8.0), 183 (41), and 149 (100). Found: *m/z* 292.0142. Calcd for $C_{15}H_{13}ClS_2$: M, 292.0147. Found: C, 61.82; H, 4.73; S, 21.86%. Calcd for $C_{15}H_{13}ClS_2$: C, 61.52; H, 4.47; S, 21.90%.

1-(Benzylthio)-1-(phenylthio)cyclopropane (8d): a pale-yellow oil; R_f 0.50 (1:20 EtOAc–hexane); IR (neat) 3059, 3027, 1583, 1493, 1477, 1453, 1438, 1026, 738, and 687 cm^{-1}; ^1H NMR δ 1.05–1.1 (2H, m), 1.2–1.25 (2H, m), 4.00 (2H, s), and 7.2–7.55 (10H, m); MS *m/z* (%) 272 (M^+, 4.2), 181 (29), 167 (64), and 91 (100). Found: *m/z* 272.0674. Calcd for $C_{16}H_{16}S_2$: M, 272.0693.

1,1-Dimethyl-2-(4-methylyphenylthio)-2-(phenylthio)cyclopropane (12): a pale-yellow oil; R_f 0.30 (1:40 EtOAc–hexane); IR (neat) 3057, 3018, 1584, 1491, 1478, 1090, 800, and 690 cm^{-1}; ^1H NMR δ 1.19 (1H, d, J = 5.6 Hz), 1.22 (1H, d, J = 5.6 Hz), 1.49 (3H, s), 1.53 (3H, s), 2.32 (3H, s), and 7.1–7.35 (9H, m); MS *m/z* (%) 300 (M^+, 7.7), 177 (33), and 135 (100). Found: *m/z* 300.1009. Calcd for $C_{18}H_{20}S_2$: M, 300.1006. Found: C, 72.00; H, 6.80%. Calcd for $C_{18}H_{20}S_2$: C, 71.95; H, 6.71%.

2,2-Dimethyl-1-(phenylthio)cyclopropanol (13): a pale-yellow oil; R_f 0.05 (1:40 EtOAc–hexane); IR (neat) 3422 and 3058 cm^{-1}; ^1H NMR δ 0.90 (1H, d, J = 5.6 Hz), 0.94 (1H, d, J = 5.6 Hz), 1.30 (3H, s), 1.36 (3H, s), 2.32 (1H, s), and 7.1–7.45 (5H, m); MS *m/z* (%) 194 (M^+, 6.8) and 150 (100). Found: *m/z* 194.0764. Calcd for $C_{11}H_{14}OS$: M, 194.0765.

2-Methyl-4-(4-methylphenylthio)-3-phenylthio-2-butene (14): a pale-yellow oil; R_f 0.25 (1:40 EtOAc–hexane); IR (neat) 1625, 1583, 1491, 1478, and 738 cm^{-1}; ^1H NMR δ 1.75 (3H, s), 2.01 (3H, s), 2.30 (3H, s), 3.71 (2H, s), and 7.0–7.35 (9H, m); MS *m/z* (%) 300 (M^+, 8.1), 176 (33), and 135 (100). Found: *m/z* 300.1008. Calcd for $C_{18}H_{20}S_2$: M, 300.1006. Found: C, 71.84; H, 6.70%. Calcd for $C_{18}H_{20}S_2$: C, 71.95; H, 6.71%.

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