Efficient one-pot preparation of 6-methylsulfanyl-5-phenyl-2,3-dihydro-1*H*-pyrrolizine from 2-*tert*-butylsulfanyl-3-phenyl- or pyrrolidin-1-yl-cyclopropenethiones

COMMUNICATION

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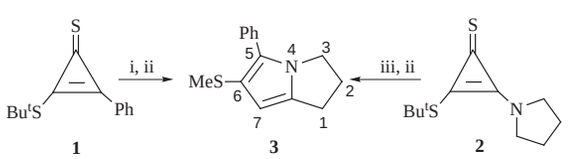
The one-pot reaction of 2-*tert*-butylsulfanyl-3-phenyl- or pyrrolidin-1-yl-cyclopropenethiones 1 and 2 with lithium pyrrolidinide or phenyllithium at −70 °C, followed by methylation with methyl iodide, gives 6-methylsulfanyl-5-phenyl-2,3-dihydro-1*H*-pyrrolizine 3 in a high yield.

Although cyclopropenethiones are of interest as a reactive unsaturated small-ring system accessible for organic synthesis, their reaction modes remain ambiguous. In this respect, it is worthwhile to explore the reactions of cyclopropenethiones having different substituents, because it may provide information about the selectivity of nucleophilic addition and the reactivity of the intermediates. Accordingly we investigated recently the reaction of 2-*tert*-butylsulfanyl-3-phenyl cyclopropenethione **1** with phenyllithium at room temperature, followed by treatment with methyl iodide, and reported that the reaction proceeds *via* the regioselective addition of the phenyl anion to the 3-position, followed by the selective cleavage of the C_1–C_3 bond, to give 1-*tert*-butylsulfanyl-1-methylsulfanyl-3,3-diphenylallene in high yield.[1] We now report a novel reaction of cyclopropenethiones with lithium pyrrolidinide or phenyllithium, followed by treatment with methyl iodide, giving 6-methylsulfanyl-5-phenyl-2,3-dihydro-1*H*-pyrrolizine **3** in high yield, as shown in Scheme 1.

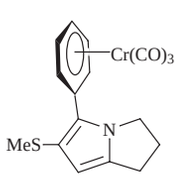


1 **3** **2**

Scheme 1 *Reagents and conditions*: i, lithium pyrrolidinide, THF, −70 °C, 1 h; ii, MeI, −70 °C, 30 min; iii, phenyllithium, THF, −70 °C, 1 h

The reactions were carried out as follows. A solution of lithium pyrrolidinide, prepared from pyrrolidine and *n*-butyllithium, in THF was added under argon to a solution of **1** in THF at −70 °C, and the solution was stirred at −70 °C for 1 h. Methyl iodide was added, and then the solution was stirred at −70 °C for 30 min. The reaction of 2-*tert*-butylsulfanyl-3-(pyrrolidin-1-yl)cyclopropenethione **2** with phenyllithium also was carried out in a similar manner as above. The isolation of the products from the reaction mixture, using column chromatography on silica gel, gave **3** in 90 and 81% isolated yield from **1** and **2**, respectively. When the reaction of **2** with phenyllithium was carried out at room temperature, as described in the reaction of **1** with phenyllithium,[1] many components, which could not be isolated, were produced without the formation of **3**. Furthermore, after the reaction of **2** with phenyllithium at −70 °C, the addition of silica gel instead of methyl iodide resulted in the formation of **1** in 72% yield, *via* substitution of the pyrrolidinyl group with a phenyl group.

The ^{1}H NMR spectrum of **3** in $CDCl_3$ showed a singlet at δ_H 2.27 due to the methylsulfanyl group, three multiplets at δ_H 2.38–2.49, 2.85–2.91 and 3.93–3.98 due to three CH_2 groups, a singlet at δ_H 6.02 due to the proton in the 7-position, and a multiplet at δ_H 7.23–7.50 due to the phenyl protons. The ^{13}C NMR spectrum of **3** in $CDCl_3$ showed three signals at δ_C 20.6, 24.6 and 27.3 for three methylene carbons, a signal at δ_C 46.8 for the methylsulfanyl carbon, and eight signals at δ_C 103.8, 115.7, 126.6, 127.7, 128.2, 128.6, 132.3 and 137.1 for the carbons in the 5-, 6-, 7- and 8-positions and the phenyl group. The X-ray structure of **3** could not be obtained, as it was difficult to prepare a suitable single crystal. Therefore, **3** was converted into complex **4** by reaction with hexacarbonylchromium[2] and the



4

X-ray structure was measured. The ORTEP drawing of **4** is shown in Fig. 1,† and indicates that the benzene ring of **3** forms the complex with tricarbonylchromium, the phenyl and methylsulfanyl groups are attached to the 5- and 6-positions respectively, the plane of the benzene ring is inclined at about 40° to the 2,3-dihydro-1*H*-pyrrolizine ring, and the tricarbonylchromium group is placed in the N-atom side of the 2,3-dihydro-1*H*-pyrrolizine ring. The IR spectrum of **4** showed absorptions due to three carbonyl groups at 1961, 1905 and 1883 cm^{-1}. The ^{1}H and ^{13}C NMR spectra of **4** indicated that the signals due to the phenyl group are shifted to higher field compared with those of **3**.

A possible pathway for the formation of **3** is proposed in Scheme 2. Efficient formation of **3** from both **1** and **2** indicates that the addition of the pyrrolidin-1-yl and phenyl anions to the cyclopropenethione ring occurs regioselectively at the 3-position with the phenyl or pyrrolidinyl group to give the adduct **5**. This is consistent with the reaction of **1** with phenyllithium, followed by methylation with methyl iodide.[1] The fact that **1** is converted into **2** by treatment with silica gel indicates that the ring-opening of **5** does not occur under these condi-

† The atom numbering used in Fig. 1 is not that referred to in the text. The correct IUPAC numbering is shown in Scheme 1.

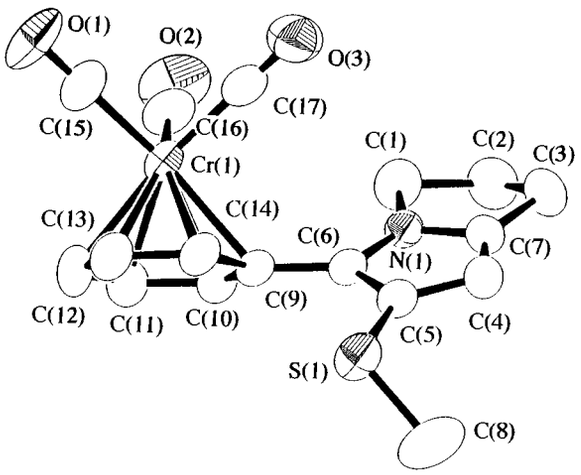
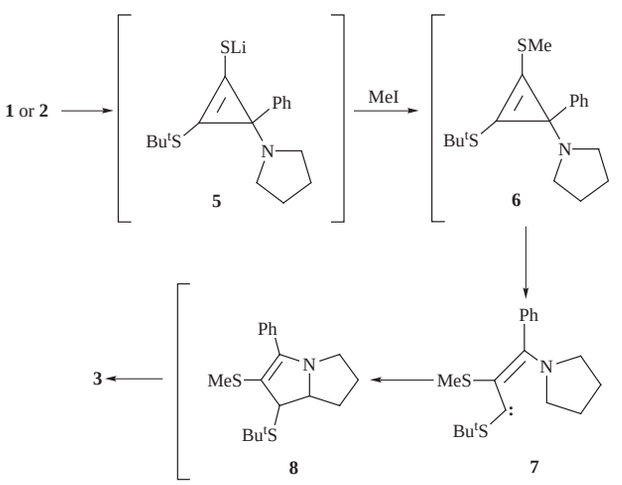


Fig. 1 ORTEP drawing and atomic numbering of **4**. Selected bond lengths (Å) and angles (°): Cr(1)–C(9) 2.244(1), Cr(1)–C(10) 2.217(1), Cr(1)–C(11) 2.209(2), Cr(1)–C(12) 2.210(2), Cr(1)–C(13) 2.201(2), Cr(1)–C(14) 2.203(1), Cr(1)–C(15) 1.835(2), Cr(1)–C(16) 1.834(2), Cr(1)–C(17) 1.837(2), O(1)–C(15) 1.148(2), O(2)–C(16) 1.147(2), O(3)–C(17) 1.147(2), N(1)–C(1) 1.456(2), N(1)–C(6) 1.379(2), N(1)–C(7) 1.361(2), C(1)–C(2) 1.543(5), C(2)–C(3) 1.490(5), C(3)–C(7) 1.494(2), C(4)–C(5) 1.413(2), C(4)–C(7) 1.362(2), C(5)–C(6) 1.389(2), C(6)–C(9) 1.460(2); Cr(1)–C(9)–C(6) 130.54(10), C(9)–Cr(1)–C(10) 36.55(5), C(1)–N(1)–C(6) 136.4(1), C(1)–N(1)–C(7) 113.5(1), N(1)–C(1)–C(2) 100.8(2), C(1)–C(2)–C(3) 107.6(2), C(2)–C(3)–C(7) 102.6(2), N(1)–C(6)–C(5) 105.9(1), C(4)–C(5)–C(6) 108.4(1), C(5)–C(4)–C(7) 106.8(1).



Scheme 2

tions. The adduct **5** is methylated with methyl iodide to give the cyclopropene **6**. The ring-opening of **6** leads to the formation of the vinylcarbene intermediate **7**, in which the carbenic carbon is stabilized by the more electron-donating *tert*-butylsulfanyl group, as described in our previous paper.[3] The carbenic carbon undergoes intramolecular cyclization with the pyrrolidinyl group to give **8**, which is converted into **3** by the elimination of *tert*-butanethiol.

Experimental

Melting points were determined on a Yanaco MP-S3 melting point apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer model 1600 FT spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX270 FT spectrometer for solutions in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Elemental analyses were performed by a Yanaco CHN CORDER MT-3. Column chromatography was performed on silica gel (Wakogel C-300).

Preparation of 3

From 1. A solution of *n*-butyllithium (1.1 mmol) in hexane was added under argon to a solution of pyrrolidine (1.1 mmol) in dry THF (10 ml) and the solution was stirred under argon at −70 °C for 30 min. The solution was added under argon to a solution of **1**[4] (1 mmol) in dry THF (10 ml) and the mixture was stirred at −70 °C for 1 h. After methyl iodide (2 mmol) was added, the solution was stirred at −70 °C for 30 min. After addition of diethyl ether (100 ml), the ethereal layer was washed with water (50 ml × 2), dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2–hexane (7 : 3 v/v) as eluent to give **3** in 90% yield.

From 2. A diethyl ether–cyclohexane solution (1.07 ml) of phenyllithium (1.1 mmol) was added under argon to a solution of **2**[1] (1 mmol) in dry THF (20 ml) at −70 °C, the solution was stirred at −70 °C for 1 h and treated in the analogous manner to that described above to give **3** in 81% yield.

6-Methylsulfanyl-5-phenyl-2,3-dihydro-1*H*-pyrrolizine 3. Colorless crystals, mp 75–76 °C (from dichloromethane–hexane) (Found: C, 73.29; H, 6.79; N, 5.96%. $C_{14}H_{15}NS$ requires C, 73.32; H, 6.59; N, 6.11%); ν_{max}(KBr)/cm^{-1} 3061, 2974, 2950, 2914, 2897, 1601, 1573, 1543, 1510, 1480, 1458, 1444, 1412, 1290, 1074, 958, 755, 697, 682 and 667; δ_H 2.27 (s, 3 H, SMe), 2.38–2.49 (m, 2 H, CH_2), 2.85–2.91 (m, 2 H, CH_2), 3.93–3.98 (m, 2 H, CH_2), 6.02 (s, 1 H, 7-H) and 7.23–7.50 (m, 5 H, phenyl H); δ_C 20.6, 24.6, 27.3, 46.8, 103.8, 115.7, 126.6, 127.7, 128.2, 128.6, 132.3 and 137.1.

Preparation of the tricarbonylchromium complex 4

Hexacarbonylchromium (2.6 mmol) was added to a solution of **3** (2 mmol) in di-*n*-butyl ether (100 ml)–THF (10 ml) and the mixture was refluxed under argon with stirring at 140 °C for 16 h. After the solvent was evaporated under reduced pressure, diethyl ether (100 ml) was added to the residue and the ethereal layer was filtered with Celite. The filtrate was evaporated to dryness under reduced pressure and the residue was purified by column chromatography on silica gel with CH_2Cl_2–hexane (7 : 3 v/v) as eluent to give **4** in 85% yield.

Tricarbonylchromium complex 4. Yellow crystals, mp 97–99 °C (from dichloromethane–hexane) (Found: C, 55.75; H, 4.39; N, 3.61%. $C_{17}H_{15}CrNO_3S$ requires C, 55.88; H, 4.14; N, 3.83%); ν_{max}(KBr)/cm^{-1} 3080, 2983, 2917, 1961 (C=O), 1905 (C=O), 1883 (C=O), 1552, 1527, 1476, 1442, 1286, 1148, 1080, 826, 797, 658, 633 and 530; δ_H 2.32 (s, 3 H, SMe), 2.48–2.56 (m, 2 H, CH_2), 2.83–2.88 (m, 2 H, CH_2), 4.10–4.15 (m, 2 H, CH_2), 5.31–5.33 (m, 1 H, phenyl H), 5.43–5.48 (m, 2 H, phenyl H), 5.68–5.70 (m, 2 H, phenyl H) and 5.97 (s, 1 H, 7-H); δ_C 20.3, 24.4, 27.5, 47.6, 91.2, 92.5, 92.9, 103.2, 104.4, 119.8, 122.4, 139.6 and 233.3 (C=O).

Crystal structure determination for 4.‡ Data were collected on a Rigaku AFC-5R diffractometer, $C_{17}H_{15}CrNO_3S$, FW = 365.37, prismatic, space group $P\bar{1}$ (#2), a = 9.371(1), b = 11.044(2), c = 8.918(1) Å, α = 101.29(1), β = 111.877(9), γ = 76.75(1)°, V = 827.5(2) Å^3, F = 398.00, Z = 2, D = 1.559 g cm^{-3}, μ(Mo-Kα) = 8.36 cm^{-1}. The structure was solved by direct methods and refined on F by full-matrix least-squares using TEXSAN,[5] converging with unweighted and weighted agreement factors of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.032$ and $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2]^{\frac{1}{2}} = 0.049$ with GOF of 1.97 for 3444 observed reflections [$I > 3.00\ \sigma(I)$] and 237 variable parameters.

‡ Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web pages (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/197.

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