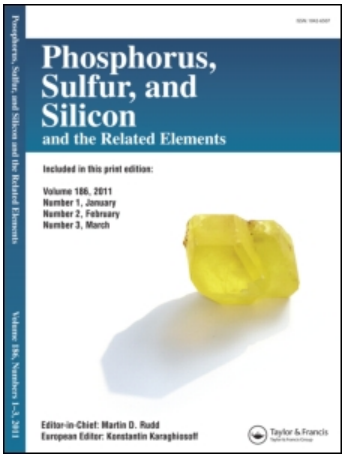

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SYNTHESIS OF DITHIOCARBAMATES AND SELENOTHIOCARBAMATES

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SYNTHESIS OF DITHIOCARBAMATES AND SELENOTHIOCARBAMATES

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Several dithiocarbamates and selenothiocarbamates were synthesized by the reaction of N,N-*dimethylthiocarbamoyl chloride with the corresponding thiolates and selenolates.*

Keywords: Dithiocarbamate; selenothiocarbamate; thiocarbamoyl chloride

Dithiocarbamates have received considerable interest because of key intermediates of materials for high-density information storage and for miniaturization of switching devices, applications in inorganic and organic synthesis,[1] and medicinal purposes.[2] For example, pyrrolidine dithiocarbamate blocks influenza virus-induced apoptosis via the inhibition of viral gene replication and transcription at an early stage of infection. In spite of the growing interest in applications of these compounds, preparative methods available for their synthesis are still limited.[3] Their methods work only for either alkyl esters of thiocarbamates[4] or aryl esters of thiocarbamates,[5] not for both esters of thiocarbamates. A facile method for the preparation of the dithiocarbamates would certainly be very useful.[6] Herein, we report a procedure for preparation of the both esters of dithiocarbamates by the reaction of *N*,*N*-dimethylthiocarbamoyl chloride with the corresponding thiolates and selenolates.

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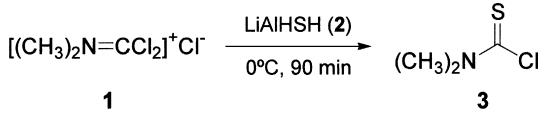
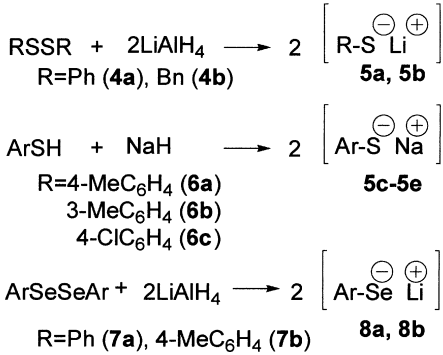
RESULTS AND DISCUSSION

The key reagent used in this study was *N*,*N*-dimethylthiocabamyl chloride (**3**). The commercially available chloride (**3**) has been prepared by the reaction of a limited amount of chlorine on the precursor tetramethylthiuram disulfide.[7] We have found that the conversion of dichloromethylenedimethyliminium chloride $[Cl_2C=N(CH_3)_2]^+Cl^-$ (**1**) into **3** can be carried out quantitatively under mild conditions by the use of LiAlHSH (**2**), which we have recently developed as a novel reagent for the introduction of sulfur atom,[8] as shown in Scheme 1.



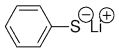
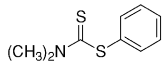
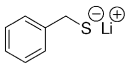
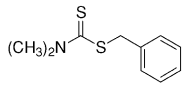
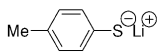
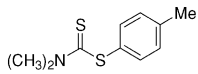
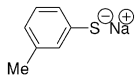
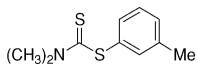
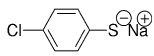
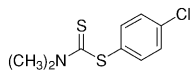
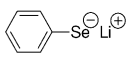
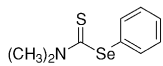
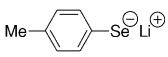
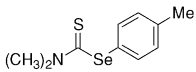
SCHEME 1

We carried out a procedure for the preparation of the dithiocarbamates and selenothiocarbamates using reactions of **3** with the corresponding thiolates **5** and selenolates **8**. A solution of PhS^-Li^+ **5a** and BnS^-Li^+ **5b** was prepared by the reaction of lithium aluminum hydride (2 equiv.) with the corresponding diphenyl disulfide **4a** and dibenzyl disulfide **4b** respectively. A solution of three kinds of ArS^-Na^+ **5c–e** was prepared by the reaction of sodium hydride (1 equiv.) with the corresponding thiols **6a–c** respectively. A solution of $PhSe^-Li^+$ **7a** and $4\text{-}MeC_6H_4Se^-Li^+$ **7b** was prepared by the reaction of lithium aluminum hydride (2 equiv.) with the corresponding diphenyl diselenide **8a** and di-*p*-tolyl diselenide **8b** respectively (Scheme 2).

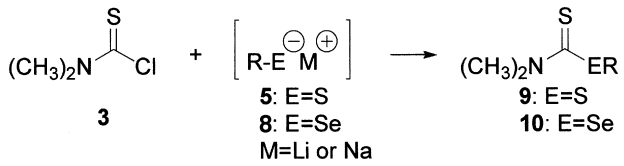


SCHEME 2

TABLE I Synthesis of Dithiocarbamates (**9**) and Selenothiocarbamates (**10**)

Thiolates (**5**) Selenolates (**8**)		Products (**9**, **10**)		Yield (%)
	**5a**		**9a**	81
	**5b**		**9b**	67
	**5c**		**9c**	73
	**5d**		**9d**	71
	**5e**		**9e**	65
	**8a**		**10a**	55
	**8b**		**10b**	49

The solution of RS^-Li^+ **5a–b** and RS^-Na^+ **5c–e** (1.0 equiv.), respectively, was added to the solution of **3** (2.0 equiv.) at room temperature under an argon atmosphere. After workup, *S*-alkyl *N*,*N*-dimethyldithiocarbamates **9a–e** were obtained as white crystals in moderate yields (Scheme 3, Table I). Reactions of **3** with the lithium arylselenolates **8** also gave the corresponding *Se*-aryl *N*,*N*-dimethylselenothiocarbamates **10** (Table I).



SCHEME 3

Experimental

Melting points were determined by use of Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were measured on Perkin-Elmer 1600 spectrometer. ^{1}H, ^{13}C, and ^{77}Se spectra were recorded on a JEOL-JNM-α400 (400 MHz) spectrometer. Mass spectra were obtained on a Shimadzu 9020-DF mass spectrometer. Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use.

N,N-*Dimethylthiocarbamoyl*

^{1}H NMR ($CDCl_3$) δ 3.43 (3H, s), 3.53 (3H, s); ^{13}C NMR ($CDCl_3$) δ 44.0, 45.0, 187.3; MS (CI): $m/z = 124$ [$M^+ + 1$].

S-Phenyl N,N-*Dimethyldithiocarbamate 9a*

To anhydrous THF solution (10 mL) of LiAlHSH **2** (2.0 mmol), was added dichloromethylenedimethyliminium chloride **1** (0.32 g, 2.0 mmol) at 0°C under an argon atmosphere. The reaction mixture was stirred at 0°C for 1.5 h. This solution was added to the solution of PhS^-Li^+ **5a** (1.0 mmol), which was prepared by the reaction of lithium aluminum hydride (0.046 g, 1.2 mmol) with diphenyl disulfide **4a** (0.11 g, 0.5 mmol) in dry THF (10 mL) at 0°C for 30 min under an argon atmosphere. The reaction mixture was stirred at 0°C for 2 h. The mixture was extracted with dichloromethane (100 mL) and washed with water (30 mL). The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel with dichloromethane:hexane (3:1) to yield **9a** of 0.16 g (81%) as white crystals; m.p. 90.5–92.7°C, IR (KBr): 1474 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.55 (3H, s), 7.41–7.50 (5H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 42.0, 45.6, 129.1, 130.0, 131.7, 136.9, 197.6; MS (CI): $m/z = 198$ [$M^+ + 1$] Lit.[5]

S-Benzyl N,N-*Dimethyldithiocarbamate 9b*

White crystals; m.p. 39.0–39.8°C, IR (KBr): 1499 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 3.29 (3H, s), 3.51 (3H, s), 4.53 (2H, s), 7.23 (1H, t, $J = 7.2$ Hz, Ar), 7.28 (2H, t, $J = 7.2$ Hz, Ar), 7.36 (2H, d, $J = 7.2$ Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 41.2, 42.3, 45.1, 127.2, 128.3, 129.1, 135.9, 196.4; MS (CI): $m/z = 212$ [$M^+ + 1$] Lit.[9]

S-(4-Methylphenyl) N,N-*Dimethyldithiocarbamate 9c*

White crystals; m.p. 107.9–111.0°C, IR (KBr): 1491 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 2.40 (3H, s), 3.49 (3H, s), 3.56 (3H, s), 7.25 (2H, d, $J = 8.0$ Hz, Ar), 7.35 (2H, d, $J = 8.0$ Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 21.5, 41.9, 45.7, 128.2, 130.0, 136.8, 140.4, 198.1; MS (CI): $m/z = 212$ [$M^+ + 1$] Lit.[5]

S-(3-Methylphenyl) N,N-*Dimethyldithiocarbamate 9d*

White crystals; m.p. 31.1–32.8°C, IR (KBr): 1497 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2.33 (3H, s), 3.40 (3H, s), 3.47 (3H, s), 7.18–7.30 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 21.1, 41.8, 45.4, 128.7, 130.6, 131.1, 133.7, 137.1, 138.6, 197.4; MS (CI): $m/z = 212$ $[M^+ + 1]$ Lit.[10]

S-(4-Chlorophenyl) N,N-*Dimethyldithiocarbamate 9e*

White crystals; m.p. 93.3–95.5°C, IR (KBr): 1473 cm^{-1}, ^1H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.55 (3H, s), 7.36–7.43 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 42.0, 45.7, 129.4, 130.1, 136.5, 138.2, 196.8; MS (CI): $m/z = 232$ $[M^+ + 1]$ Lit.[5]

Se-Phenyl N,N-*Dimethylselenothiocarbamate 10a*

White crystals; m.p. 118.1–119.3°C, IR (KBr): 1498 cm^{-1}, ^1H NMR ($CDCl_3$) δ 3.46 (3H, s), 3.54 (3H, s), 7.39–7.58 (5H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 43.4, 45.6, 129.3, 129.6, 130.7, 137.7, 195.3; ^{77}Se NMR δ 702.9; MS (CI): $m/z = 246$ $[M^+ + 1]$ Lit.[11]

Se-(4-Methylphenyl) N,N-*Dimethylselenothiocarbamate 10b*

White crystals; m.p. 104.8–107.1°C, IR (KBr): 1487 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2.40 (3H, s), 3.46 (3H, s), 3.54 (3H, s), 7.23 (2H, d, $J = 7.7$ Hz, Ar), 7.45 (2H, d, $J = 7.7$ Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 21.5, 43.3, 45.6, 127.3, 130.2, 137.6, 139.9, 195.8; ^{77}Se NMR δ 693.8; MS (CI): $m/z = 260$ $[M^+ + 1]$; Anal. Calcd for $C_{10}H_{13}NSSe$: C, 46.51; H, 5.07; N, 5.42. found: C, 46.53; H, 5.01; N, 5.41%.

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