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LETTERS

Preparation of *N*,*N*-unsubstituted selenoureas and thioureas from cyanamides

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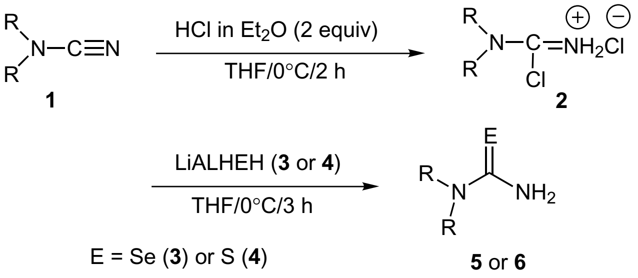
Abstract—Reaction of cyanamides with LiAlHSeH and LiAlHSH in the presence of HCl in diethyl ether provided the corresponding *N*,*N*-unsubstituted selenoureas and thioureas in moderate to high yields, respectively. © 2001 Elsevier Science Ltd. All rights reserved.

The syntheses of many selenocarbonyl compounds have been reported and the recent reviews detail the studies.[1] Selenoureas are used as the precursors for the syntheses of selenium–nitrogen heterocyclic compounds[2] and their activities have received increasing attentions.[3] There is only a few reports of preparation of *N*,*N*-unsubstituted selenourea by the reaction of hydrogen selenide with cyanamide.[2d] The preparation of *N*,*N*-unsubstituted selenourea without using poisonous hydrogen selenide has rarely been reported.[1b] In this study, we investigated the synthesis of *N*,*N*-unsubstituted selenourea using LiAlHSeH.[4] Herein, we report the facile preparation of *N*,*N*-unsubstituted selenoureas and thioureas by the reaction of cyanamides with the introduction reagent of selenium and sulfur.

In a typical procedure, 1N HCl (2 equiv.) in diethyl ether was added to *N*,*N*-dimethylcyanamide **1a** (1 equiv.) of THF solution. The reaction mixture became a milky white suspension from colorless solution in less than 30 seconds and then was stirred at 0°C for 2 h. The compound **2** was formed in situ.[5] Subsequently, LiAlHSeH **3** (1 equiv.)[4,6] was added to the reaction mixture. The reaction mixture was further stirred at 0°C for 3 h. After usual workup, **5a** was obtained in a 70% yield as a yellow crystal[7] (Scheme 1). The results of reactions of various cyanamides **1** with LiAlHSeH **3** or LiAlHSH **4** are summarized in Table 1. The reactions of cyanamides **1** with **3** gave the corresponding *N*,*N*-unsubstituted selenoureas in 70–91% yields. Similarly, the reactions using LiAlHSH **4** gave the corresponding *N*,*N*-unsubstituted thioureas in 52–89% yields. In the present reaction, the selection of chlorinating reagent of cyanamides was of importance. The combination of LiAlHSeH with phosphorus oxychloride, oxalyl chloride or hydrogen chloride in diethyl ether was examined for the chlorination of cyanamides and the synthesis of urea. Previously, we have confirmed *N*,*N*-disubstituted selenourea can be obtained by the reaction of the corresponding amide with LiAlHSeH and oxalyl chloride.[8] However, in the present reaction, only the combination with hydrogen chloride in diethyl ether gave a satisfactory result. The formation of *N*,*N*-unsubstituted selenourea and thiourea could be explained by the possible mechanism presented in Scheme 2.

The reaction of chloro(methylthio)iminonium salt chloride, prepared by the reaction of methyl thiocyanate **7** with hydrogen chloride in ether, with LiAlHSeH afforded *S*-methyl selenothiocarbamate **8** in a 51% yield (Table 1, entry 9, Scheme 3).[9]

In conclusion, LiAlHSeH and LiAlHSH, as an introduction reagent of selenium and sulfur atom, reacted with **2** giving the corresponding *N*,*N*-unsubstituted selenoureas and *N*,*N*-unsubstituted thioureas, respectively.



Scheme 1.

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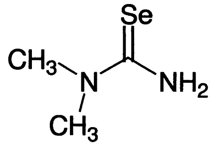
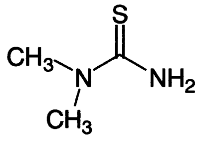
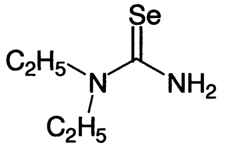
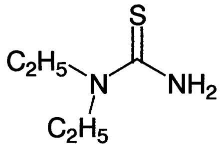
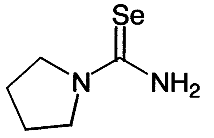
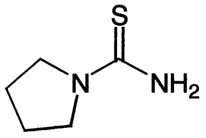
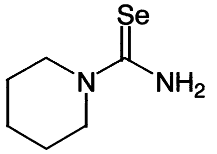
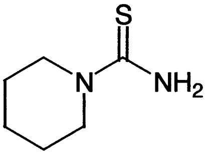
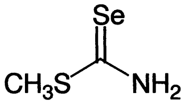
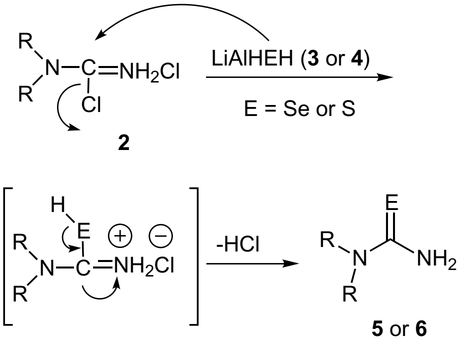
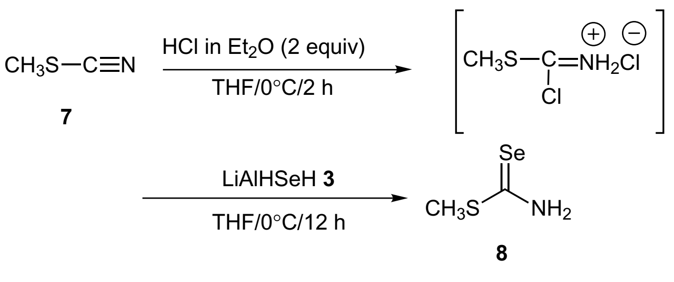
Table 1. Syntheses of *N*,*N*-unsubstituted selenoureas, *N*,*N*-unsubstituted thioureas and *S*-methyl selenocarbamate

entry	Product	Yield (%)[a]	entry	Product	Yield (%)[a]
1	 **5a**	70	5	 **6a**	52
2	 **5b**	76	6	 **6b**	55
3	 **5c**	88	7	 **6c**	84
4	 **5d**	91	8	 **6d**	89
			9	 **8**	51

[a] Isolated yield (%).



Scheme 2.



Scheme 3.

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4. Ishihara, H.; Koketsu, M.; Fukuta, Y.; Nada, F. *J. Am. Chem. Soc.*, in press.
5. Intermediate **2a** was isolated quantitatively. ^{1}H NMR ($CDCl_3$): δ 3.40 (3H, s, CH_3), 3.76 (3H, s, CH_3), 10.65 (1H, br s, NH), 11.14 (1H, br s, NH), ^{13}C NMR ($CDCl_3$): δ 42.8, 43.0, 195.9, MS (CI): $m/z=107$ [M^++1-HCl].
6. The preparation of LiAlHSeH **2**: to a solution of selenium powder (0.80 g, 10.0 mmol) in dry THF (100 mL) was added lithium aluminium hydride **1** (0.38 g, 10.0 mmol) at 0°C under an argon atmosphere. The mixture was stirred for 30 min. The black selenium powder was consumed in less than 10 min. The reaction mixture became a heterogeneous grayish suspension. The **2** is formed in situ and is then ready for further reaction.
7. Spectral data of selected compounds. *N*,*N*-Dimethylselenourea **5a**: Mp 172.2–172.8°C; IR (KBr) 3366, 3162, 1551 cm^{-1}, ^{1}H NMR ($CDCl_3$): δ 3.18 (6H, br s, CH_2), 7.60 (2H, br s, NH), ^{13}C NMR ($CDCl_3$): δ 37.9, 45.3, 177.7, ^{77}Se NMR ($CDCl_3$): δ 230.4, MS (CI) $m/z=153$ [M^++1], HRMS (EI) calcd for $C_3H_8N_2Se$ 151.98522, found 151.98346. *N*,*N*-Diethylselenourea **5b**: Mp 121.8–122.7°C; IR (KBr) 3340, 3176, 1534 cm^{-1}, ^{1}H NMR ($CDCl_3$): δ 1.27 (6H, t, $J=6.8$ Hz, CH_3), 3.49 (2H, br s, CH_2), 3.97 (2H, br s, CH_2), 6.48 (2H, br s, NH), ^{13}C NMR ($CDCl_3$): δ 12.2, 42.9, 51.1, 176.6, ^{77}Se NMR ($CDCl_3$): δ 209.8, MS (CI) $m/z=181$ [M^++1], HRMS (EI) calcd for $C_5H_{12}N_2Se$ 180.0165, found 180.0147. 1-Selenocarbamoylpiperidine **5d**: Mp 145.0–146.2°C; IR (KBr) 3303, 3169, 1522 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.47 (4H, m, CH_2), 1.59 (2H, m, CH_2), 3.76 (4H, br s, CH_2), 7.75 (2H, br s, NH), ^{13}C NMR (DMSO-d_6): δ 23.6, 25.3, 176.0, ^{77}Se NMR (DMSO-d_6): δ 218.5, MS (CI) $m/z=193$ [M^++1]. HRMS (EI) calcd for $C_6H_{12}N_2Se$ 192.0165, found 192.01499. *N*,*N*-Diethylthiourea **6b**: Mp 99.2–100.6°C; IR (KBr) 3376, 3192, 1522 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.06 (6H, t, $J=6.8$ Hz, CH_3), 3.53 (4H, br s, CH_2), 7.10 (2H, br s, NH), ^{13}C NMR (DMSO-d_6): δ 12.6, 44.5, 179.8, MS (CI) $m/z=133$ [M^++1]. 1-Thiocarbamoylpiperidine **6d**: Mp 127.4–129.1°C; IR (KBr) 3334, 3188, 1510 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.45 (4H, m, CH_2), 1.56 (2H, m, CH_2), 3.69 (4H, br s, CH_2), 7.25 (2H, br s, NH), ^{13}C NMR (DMSO-d_6): δ 23.7, 25.3, 48.2, 180.2, MS (CI) $m/z=145$ [M^++1].
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9. *S*-Methyl selenothiocarbamate **8**: Mp 58.9–59.5°C; IR (KBr) 3275, 3122, 1636 cm^{-1}, ^{1}H NMR (acetone-d_6): δ 2.61 (3H, s, CH_3), 9.19 (1H, br s, NH), 9.53 (1H, br s, NH), ^{13}C NMR (aceton-d_6): δ 22.0, 204.9, ^{77}Se NMR (acetone-d_6): δ 554.2, MS (CI): $m/z=156$ [M^++1], HRMS (EI) calcd for C_2H_5NSSe 154.93076, found 154.93083.