Preparation of Isoselenocyanate and Synthesis of Carbodiimide by Oxidation of Selenourea

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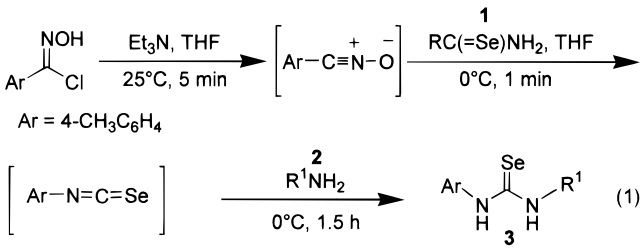
Isoselenocyanates have been shown to be susceptible to attack by nucleophilic reagents. And although many studies have reported the synthesis of isothiocyanates,[1,2] only limited numbers of studies on isoselenocyanates have been reported.[3,4] The few reported syntheses of isoselenocyanates[5−7] have included, for example, the reaction of isocyanides with selenium,[8] that of phenylimidolyl chloride with sodium selenide,[9] or that of isocyanates with phosphorus pentaselenide.[10] In the present study, we confirmed an interesting pathway to isoselenocyanate via cycloaddition by the reaction of nitrile oxides with primary selenoamide; in addition, we synthesized selenoureas from the isoselenocyanates with amines.

Carbodiimides are also very important for the construction of a wide variety of chemical structures. However, there currently exist only three practical syntheses of unsymmetric carbodiimides.[11−15] We describe here a synthesis of carbodiimides via oxidation of the corresponding selenoureas using $NaIO_4$.

Results and Discussion

The efficient synthesis of selenoureas **3** using isoselenocyanates was achieved by the following one-pot procedure (eq 1). To a THF solution of 4-tolylnitrile oxide



(1)

was added 4-tolylselenoamide **1a** (2 equiv), and the solution was stirred at 0 °C for 1 min. Then, *n*-propylamine **2a** (1.0 equiv) was added to the mixture, which was stirred at 0 °C for 1.5 h. *N*-*n*-Propyl-*N*′-4-tolylselenourea **3a** was obtained in a 60% yield as a yellow oil. In a similar manner, selenoureas **3** were obtained from a variety of amines **2**. The results of these syntheses are summarized in Table 1. When CH_2Cl_2 or Et_2O was used as a solvent instead of THF, the yield of **3a** was 55% or 50%, respectively. When 1 equiv of 4-tolylselenoamide **1a** was used in the reaction, the yield of **3a** was low, and urea was obtained as a byproduct. Even when the primary selenoamides bearing electron-withdrawing groups, such as 4-$CH_3OC_6H_5$ **1b** or 2-ClC_6H_5 **1c**, were used instead of 4-tolylselenoamide **1a**, the yields of the corresponding selenoureas were slightly lower than the yield when **1a** was used. The aliphatic selenoamide **1d** also gave the selenourea in high yield (78%). The yields of selenourea using arylamines **2f** and **2g** tended to decrease slightly compared with other amines because of the weak nucleophilicity of the aryl group.

Although the detailed mechanism of the above reaction has not yet been clarified, the formation of isoselenocyanate might be explained by the possible mechanism presented in Scheme 1. The thiocarbonyl group behaves as a dienophile toward dienes to afford a Diels−Alder adduct.[16,17] Similarly, the selenocarbonyl group of selenoamide would react with nitrile oxide (formed from hy-

Table 1. Selenourea 3 Synthesis of Amines with Isoselenocyanates Generated in Situ from Nitrile Oxide and RC(=Se)NH_2 1

selenoamide RC(=Se)NH_2 (**1**)	amine R^1NH_2 (**2**)		yield (%) of **3**	
4-$CH_3C_6H_4$ (**1a**)	$CH_3(CH_2)_2$	(**2a**)	60	(**3a**)
1a	$CH_3(CH_2)_3$	(**2b**)	74	(**3b**)
1a	$(CH_3)_2CHCH_2$	(**2c**)	68	(**3c**)
1a	$(CH_3)_3C$	(**2d**)	64	(**3d**)
1a	$C_6H_5CH_2$	(**2e**)	53	(**3e**)
1a	2-$CH_3C_6H_4$	(**2f**)	46	(**3f**)
1a	C_6H_5	(**2g**)	48	(**3g**)
4-$CH_3OC_6H_4$ (**1b**)	$CH_3(CH_2)_3$	(**2b**)	51	(**3b**)
2-ClC_6H_4 (**1c**)	$CH_3(CH_2)_3$	(**2b**)	46	(**3b**)
C_5H_{11} (**1d**)	$CH_3(CH_2)_3$	(**2b**)	78	(**3b**)

Scheme 1

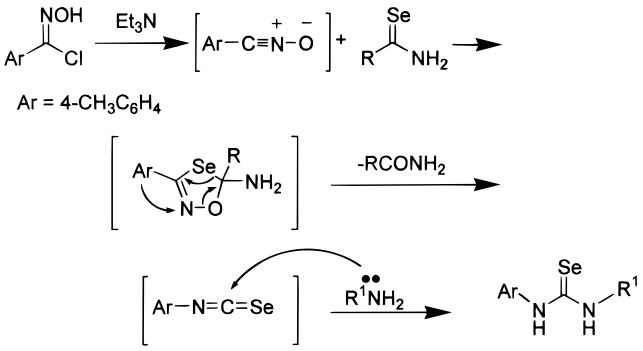


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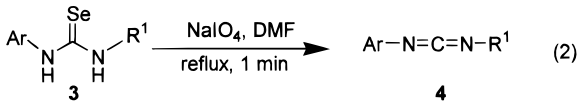
Table 2. Oxidation of Selenourea 3a with Various Oxidants

				yield (%)	
run	temp (°C)	time (min)	oxidant	**4a**	urea
1	25	45	$NaIO_4$[a]	38	18
2	25	45	$NaIO_4$	37	14
3	25	90	$NaIO_4$	46	5.0
4	reflux	1	$NaIO_4$	93	>1
5	reflux	10	$NaIO_4$	56	7.1
6	reflux	60	$NaIO_4$	>1	33
7	reflux	60	without	0	33
8	reflux	1	$NaClO_4$	0	48
9	reflux	1	$KMnO_4$	0	42
10	reflux	1	Na_2CrO_4	0	36

[a] Two milliliters of H_2O was added.

droximoyl chloride with amine) to afford an initial formation of intermediate 1,4,2-oxaselenazoline,[18] which could decompose into isoselenocyanate after rearrangement. Next, the amine attacks the carbon of the isoselenocyanate to give the corresponding selenourea (Scheme 1). Preisler and Scortia reported that the treatment of selenourea with oxidants, such as HCl and ferricyanide, produced the dimer of selenourea.[19] Further, Treppendahl[20] reported that the oxidation of *N*,*N*′-diphenylselenourea with H_2O_2 produced the benzoselenazolylguanidine, cyclic dimers, and trimers of the corresponding carbodiimides. The products would be distinguished from each other according to the oxidant used. We found that a brief oxidation of selenourea with $NaIO_4$ afforded the carbodiimide (eq 2). For example, to a refluxing DMF



3 **4** (2)

solution of $NaIO_4$ (1.1 equiv) was added **3a** (1.0 equiv) under an argon atmosphere. The reaction mixture was refluxed for 1 min and immediately poured into ice water. After the usual operations, *N*-*n*-propyl-*N*′-4-tolylcarbodiimide **4a** was afforded in 93% yield as a yellow oil. In these preparations of carbodiimides, at 25 °C the yields were low, and the corresponding urea was generated (runs 1−3). The longer the reflux time, the lower the yield of **4a** became. The corresponding urea, rather than **3a** or **4a**, was obtained (runs 5 and 6). Other oxidants, such as $NaClO_4$, $KMnO_4$, and Na_2CrO_4, could not yield the corresponding carbodiimide from selenourea (runs 8−10) (Table 2).

Some carbodiimides **4** were obtained in moderate to high yields by the oxidation of a variety of selenoureas with $NaIO_4$ (Table 3). The yields of carbodiimide using selenourea bearing R^1 = tertiary alkyl tended to decrease compared with those of R^1 = primary and secondary alkyl because of steric hindrance. Neither the dimer of selenourea nor the trimer of the carbodiimide[19,20] was obtained in this oxidation. In conclusion, although it is known that the dehydration or desulfurization of ureas and thioureas affords the corresponding carbodiimide,[11−14,20,21] few reports have been made on the preparation method

Table 3. Yields of Carbodiimides (4-$CH_3C_6H_4N$=C=NR^1) 4 Obtained by the Oxidation of Selenoureas

R^1	yield (%) of **4**
$CH_3(CH_2)_2$	93 (**4a**)
$CH_3(CH_2)_3$	90 (**4b**)
$CH_3CH_2(CH_3)CH$	95 (**4c**)
$(CH_3)_3C$	39 (**4d**)
2-$CH_3C_6H_4$	50 (**4e**)
C_6H_5	50 (**4f**)

of carbodiimides by the oxidation of selenoureas. The oxidation of selenourea by $NaIO_4$ is a facile method for preparing the carbodiimides.

Experimental Section

General. Tetrahydrofuran was distilled from sodium−benzophenone immediately prior to use. Primary selenocarboxamides were synthesized in accordance with the previously described procedure.[22] We also prepared 4-tolylnitrile oxide. The ^{77}Se chemical shifts were expressed in ppm deshielded with respect to neat Me_2Se in $CDCl_3$.

Synthesis of *N*-*n*-Propyl-*N*′-4-tolylselenourea 3a. To a THF solution of 4-tolylhydroximoyl chloride was added 1.1 equiv of Et_3N and the mixture stirred at 25 °C for 5 min. After cooling to 0 °C, 2 equiv of 4-tolylselenoamide **1a** was added to the reaction mixture and it was stirred at the same temperature for 1 min. Then, 1.0 equiv of *n*-propylamine **2a** was added to this, with stirring at 0 °C for 1.5 h. The mixture was concentrated in vacuo, and the residue was purified by column chromatography on silica gel using *n*-hexane: Et_2O (3:2) as eluent to give **3a** (60%). Mp: 97.3−98.8 °C. IR (KBr): 3336, 3182, 1541, 1521 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (3H, t, J = 7.2 Hz), 1.60 (2H, dt, J = 7.2 Hz), 2.36 (3H, s), 3.61−3.71 (2H, m), 6.24 (1H, br s), 7.11(2H, d, J = 8.0 Hz), 7.23 (2H, d, J = 8.0 Hz), 8.61 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.1, 20.9, 22.1, 49.5, 125.3, 130.7, 132.9, 137.7, 178.2 (C=Se). ^{77}Se NMR (76 MHz, $CDCl_3$): δ 198.0. MS (EI): m/z = 256. Anal. Calcd for $C_{11}H_{16}N_2Se$: C, 51.77; H, 6.32; N, 10.98. Found: C, 51.52; H, 6.26; N, 10.85.

***N*-*n*-Butyl-*N*′-4-tolylselenourea 3b.** IR (neat): 3371, 3196, 1545, 1513 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, J = 7.2 Hz), 1.30 (2H, dt, J = 7.2 Hz), 1.55 (2H, quintet, J = 7.2 Hz), 2.35 (3H, s), 3.67 (2H, q, J = 6.4 Hz), 6.26 (1H, br s), 7.11 (2H, d, J = 8.0 Hz), 7.23 (2H, d, J = 8.0 Hz), 8.93 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.3, 19.5, 20.6, 30.6, 47.2, 124.8, 130.2, 132.8, 137.0, 177.7 (C=Se). ^{77}Se NMR (76 MHz, $CDCl_3$): δ 193.3. HRMS: m/z = 269.24832, calcd for $C_{12}H_{18}N_2Se$, found 269.24841.

***N*-Isobutyl-*N*′-4-tolylselenourea 3c.** Mp: 76.0−77.9 °C. IR (KBr): 3375, 3180, 1543, 1522 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (6H, t, J = 6.4 Hz), 1.86−2.00 (1H, m), 2.35 (3H, s), 3.51 (2H, t, J = 5.7 Hz), 6.35 (1H, br s), 7.12 (2H, d, J = 8.0 Hz), 7.23 (2H, d, J = 8.0 Hz), 8.92 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 20.8, 27.8, 54.9, 125.1, 131.6, 132.9, 137.5, 178.1(C=Se). ^{77}Se NMR (76 MHz, $CDCl_3$): δ 196.6. MS (EI): m/z = 270. Anal. Calcd for $C_{12}H_{18}N_2Se$: C, 53.53; H, 6.74; N, 10.40. Found: C, 53.74; H, 6.66; N, 10.25.

***N*-*tert*-Butyl-*N*′-4-tolylselenourea 3d.** Mp: 128.8−131.8 °C. IR (KBr): 3166, 3006, 1558, 1537 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (9H, s), 2.34 (3H, s), 6.39 (1H, br s), 7.09 (2H, d, J = 8.2 Hz), 7.21 (2H, d, J = 8.2 Hz), 8.50 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 28.9, 54.6, 125.0, 128.8, 130.4, 137.2, 175.5 (C=Se). ^{77}Se NMR (76 MHz, $CDCl_3$): δ 255.2. HRMS: m/z = 269.24832, calcd for $C_{12}H_{18}N_2Se$, found 269.24828.

***N*-Benzyl-*N*′-4-tolylselenourea 3e.** Mp: 98.9−101.3 °C. IR (KBr): 3325, 3211, 1556, 1518 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (3H, s), 4.93 (2H, s), 6.50 (1H, br s), 7.11 (2H, d, J = 8.2 Hz), 7.17 (2H, d, J = 8.2 Hz), 7.26−7.33 (5H, m), 8.83 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 51.9, 125.3, 126.8, 127.6, 128.6, 129.0, 130.7, 132.8, 136.7, 179.0 (C=Se). ^{77}Se NMR

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(76 MHz, $CDCl_3$): δ 202.2. HRMS: m/z = 303.26544, calcd for $C_{15}H_{16}N_2Se$, found 303.26549.

***N*-2-Tolyl-*N*′-4-tolylselenourea 3f.** Mp: 141.8−143.7 °C. IR (KBr): 3351, 3146, 1548, 1508 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.21 (3H, s), 2.22 (3H, s), 7.02−7.22 (8H, m), 8.34 (2H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.0, 21.0, 125.9, 127.1, 127.9, 128.6, 130.0, 130.1, 131.3, 135.3, 179.3 (C═Se). HRMS: m/z = 303.26544, calcd for $C_{15}H_{16}N_2Se$, found 303.26536.

***N*-Phenyl-*N*′-4-tolylselenourea 3g.** Mp: 140.0−142.8 °C. IR (KBr): 3352, 3149, 1551, 1509 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.34 (3H, s), 6.50 (1H, br s), 7.16−7.39 (9H, m), 8.45 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 119.5, 125.6, 125.7, 127.4, 129.5, 130.2, 137.7, 178.6 (C═Se). ^{77}Se NMR (76 MHz, $CDCl_3$): δ 244.2. HRMS: m/z = 289.23856, calcd for $C_{14}H_{14}N_2Se$, found 289.23850.

Synthesis of *N*-*n*-Propyl-*N*′-4-tolylcarbodiimide 4a. To a refluxing DMF solution of $NaIO_4$ (1.1 equiv) was added a DMF solution of **3a** (1.0 equiv) under an argon atmosphere. The reaction mixture was refluxed for 1 min. After cooling with ice water immediately, the mixture was washed with saturated NaCl solution, and the organic layer was separated, dried over Na_2SO_4, and evaporated. The residue was subjected to column chromatography on silica gel using *n*-hexane:Et_2O (50:1) as eluent system, affording **4a** (90%) as a yellow oil. IR (neat): 2138 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.01 (3H, t, J = 7.2 Hz), 1.67 (2H, dt, J = 7.2 Hz), 2.31 (3H, s), 3.36 (2H, t, J = 6.8 Hz), 6.97 (2H, d, J = 8.1 Hz), 7.08 (2H, d, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.4, 20.9, 24.7, 48.6, 123.2, 129.9, 134.2, 136.6, 137.8. MS (EI): m/z = 174. Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C, 75.69; H, 8.30; N, 16.06.

***N*-*n*-Butyl-*N*′-4-tolylcarbodiimide 4b.** Yellow oil. IR (neat): 2128 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.93 (3H, t, J = 7.3 Hz), 1.43 (2H, dt, J = 7.3 Hz), 1.64 (2H, quintet, J = 6.8 Hz), 2.29 (3H, s), 3.37 (2H, t, J = 6.8 Hz), 6.97 (2H, d, J = 7.8 Hz), 7.06 (2H, d, J = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4, 19.8, 20.7, 33.3, 46.4, 123.1, 129.8, 134.0, 136.5, 137.7. HRMS: m/z = 188.27244, calcd for $C_{12}H_{16}N_2$, found 188.27248.

***N*-*sec*-Butyl-*N*′-4-tolylcarbodiimide 4c.** Yellow oil. IR (neat): 2132 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.00 (3H, t, J = 7.2 Hz), 1.32 (3H, d, J = 6.8 Hz), 1.53−1.66 (2H, m), 3.55 (1H, dt, J = 6.8 Hz), 6.98 (2H, d, J = 8.0 Hz), 7.09 (2H, d, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.7, 20.9, 22.5, 31.5, 56.0, 123.1, 130.0, 134.2, 136.6, 138.0. HRMS: m/z = 188.27244, calcd for $C_{12}H_{16}N_2$, found 188.27238.

***N*-*tert*-Butyl-*N*′-4-tolylcarbodiimide 4d.** Yellow oil. IR (neat): 2109 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.39 (9H, s), 2.31 (3H, s), 6.98 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 31.6, 57.2, 123.0, 129.9, 134.3, 138.0. HRMS: m/z = 188.27244, calcd for $C_{12}H_{16}N_2$, found 188.27236.

***N*-2-Tolyl-*N*′-4-tolylcarbodiimide 4e.** Yellow oil. IR (neat): 2137 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (3H, s), 2.37 (3H, s), 7.04−7.19 (8H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3, 20.9, 123.8, 124.6, 125.4, 126.8, 130.1, 130.8, 132.6, 134.6, 135.1, 136.1, 137.1. HRMS: m/z = 222.28956, calcd for $C_{15}H_{14}N_2$, found 222.28961.

***N*-Phenyl-*N*′-4-tolylcarbodiimide 4f.** Yellow oil. IR (neat): 2130 (N═C═N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (3H, s), 7.06−7.34 (9H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 124.0, 124.1, 125.5, 129.5, 130.1, 135.4, 138.8. HRMS: m/z = 208.26268, calcd for $C_{14}H_{12}N_2$, found 208.26260.

Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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