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Original article

One-pot synthesis of selenocarbamates from isocyanates and diselenides using the Zn/$AlCl_3$ system

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ABSTRACT

Several *N*-alkyl/aryl-*Se*-alkyl/(aryl)selenocarbamates were prepared from various isocyanates and diselenides by reductive cleavage of Se–Se bond with the Zn/$AlCl_3$ system in dry acetonitrile at 80 °C.

1. Introduction

Over the last three decades, organoselenium chemistry has not only been of constant scientific interest but also used intensively [1]. Recently, many synthetic methods for the compounds containing selenium have been studied and reported due to their interesting reactivity [2] and potential pharmaceutical importance [3]. Among the selenium compounds, selenocarbamates are an important class of compounds whose biological, especially antiviral activity, have been investigated [4]. These compounds have also been employed as an efficient source of acyl radicals by homolytic cleavage of the Se–CO bond [5], and for the construction of α-alkylidene lactams [6]. There are a limited number of reports of selenocarbamate synthesis including treatment of a *N*-tosylamine with triphosgene followed by addition of phenylselenol [7], reaction of an amine and carbon monoxide with elemental selenium followed by treatment with an alkyl halide [8], treatment of diselenides with lithium triethylborohydride followed by a reaction with diethylcarbamyl chloride [9], reactions of selenocarboxylic acids with aryl isocyanates [10], and treatment of bis[*N*,*N*-dimethylcarbamoyl] diselenides with NaH or $NaBH_4$, followed by reacting with various alkylating agents [11]. However, some disadvantages such as synthetic inconvenience, unavailability of starting materials and reagents, needs of an inert atmosphere and low temperatures encountered in the reported methodologies necessitate the development of more convenient methods. Ishihara and co-workers reported the synthesis of *N*-alkyl-*Se*-alkylselenocarbamates by the reaction of isocyanates with LiAlHSeH, followed by addition of alkyl halides [12], This method, however, requires an argon atmosphere, and also the reagent, LiAlHSeH, has to be made *in situ* prior to the reaction. It was also limited to the preparation of *Se*-alkylselenocarbamates.

2. Experimental

Chemicals were purchased from Merck or Aldrich. Yields referred to the yields of isolated products. IR spectra were obtained using an ABB FTLA 2000 instrument. NMR spectra were recorded using a Bruker DRX-500 Avance spectrometer with a nominal frequency of 500 MHz for proton and 125 MHz for carbon (^{13}C), respectively, in $CDCl_3$ using TMS as an internal standard. Mass spectra were recorded with a Hewlett-Packard model 5973 instrument.

2.1. Typical procedure for the preparation of N-cyclohexyl-Se-phenylselenocarbamate (**3a**)

A mixture of diphenyl diselenide (0.20 g, 0.64 mmol), Zn dust (0.23 g, 3.5 mmol), finely ground anhydrous $AlCl_3$ (0.43 g, 3.2 mmol), and dry CH_3CN (10 mL) was stirred at 80 °C for 1 h until the zinc powder had almost disappeared. Then, cyclohexyl isocyanate (0.20 g, 1.6 mmol) was added in one portion to the solution and stirring was continued at that temperature for 0.5 h in

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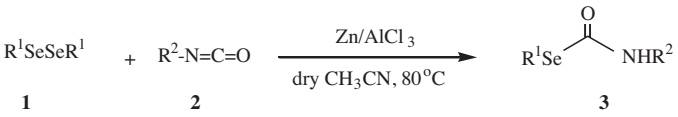
air atmosphere. After completion of the reaction as indicated by TLC analysis, the solution was filtered, and the filtrate was evaporated, EtOAc (20 mL) was added and washed with water (3 × 10 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated to give the crude product, which upon addition of petroleum ether (30 mL), the pure *N*-cyclohexyl-*Se*-phenylselenocarbamate (**3a**, 0.23 g, 64%) solidified as colorless crystals. Mp 95–97 °C; IR (KBr, cm^{-1}): ν_{max} 1660, 3297; ^1H NMR ($CDCl_3$): δ 1.11–1.19 (m, 3H), 1.33–1.39 (m, 2H), 1.56–1.62 (m, 3H), 1.88–1.92 (m, 2H), 3.72–3.79 (m, 1H), 5.27 (br s, 1H), 7.41–7.46 (m, 3H), 7.72–7.75 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 24.8, 25.7, 33.1, 51.3, 127.6, 129.7, 130.1, 131.9, 136.9, 161.9; MS: *m*/*z* (%) 284 $[M+2]^+$ (100), 282 $[M^+]$ (52), 225 (20), 158 (68), 156 (75), 83 (54), 55 (61), 41 (38).

Selective data: **3c**: Colorless crystals, mp 116–118 °C; IR (KBr, cm^{-1}): ν_{max} 1674, 3260; ^1H NMR ($CDCl_3$): δ 7.15 (br s, 1H), 7.23–7.28 (m, 4H), 7.43–7.50 (m, 3H), 7.75 (d, 2H, *J* = 6.2 Hz); ^{13}C NMR ($CDCl_3$): δ 120.9 (br), 126.8, 129.6, 130.38, 130.43, 136.3, 137.2, 161.9; MS: *m*/*z* (%) 314 $[M+4]^+$ (3), 312 $[M+2]^+$ (6), 310 $[M^+]$ (4), 158 (88), 156 (42), 155 (32), 153 (100), 125 (45), 90 (34), 78 (78), 63 (17), 51 (16). **3d**: Colorless crystals, mp 93–95 °C; IR (KBr, cm^{-1}): ν_{max} 1669, 3282; ^1H NMR ($CDCl_3$): δ 2.34 (s, 3H), 7.10–7.14 (m, 3H), 7.23 (d, 2H, *J* = 8.3 Hz), 7.46–7.51 (m, 3H), 7.78 (d, 2H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$): δ 21.3, 119.5 (br), 127.2, 130.04, 130.12, 130.3, 134.9 (br), 137.1, 162.2; MS: *m*/*z* (%) = 292 $[M+2]^+$ (68), 290 $[M^+]$ (35), 158 (100), 156 (51), 133 (58), 106 (48), 91 (30), 77 (52), 51 (30). **3e**: Light pink crystals, mp 116–118 °C; IR (KBr, cm^{-1}): ν_{max} 1653, 3323; ^1H NMR ($CDCl_3$): δ 1.12–1.22 (m, 3H), 1.33–1.41 (m, 2H), 1.62–1.69 (m, 3H), 1.93–1.95 (m, 2H), 3.77–3.79 (m, 1H), 5.25 (br s, 1H), 7.39 (d, 2H, *J* = 8.3 Hz), 7.63 (d, 2H, *J* = 8.3 Hz); ^{13}C NMR ($CDCl_3$): δ 24.9, 25.7, 33.2, 51.6, 125.5, 130.2, 136.1, 138.1, 160.9; MS: *m*/*z* (%) 320 $[M+4]^+$ (13), 318 $[M+2]^+$ (30), 316 $[M^+]$ (15), 194 (49), 192 (100), 190 (50), 156 (24), 112 (45), 83 (90), 67 (39), 55 (47), 41 (43). **3f**: Pale yellow crystals, mp 110–112 °C; IR (KBr, cm^{-1}): ν_{max} 1658, 3304; ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H), 7.12–7.16 (m, 3H), 7.27 (d, 2H, *J* = 8.4 Hz), 7.42 (d, 2H, *J* = 8.4 Hz), 7.67 (d, 2H, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$): δ 21.3, 119.9 (br), 125.1, 130.1, 130.3, 135.1 (br), 136.5, 138.2; MS: *m*/*z* (%) 328 $[M+4]^+$ (1), 326 $[M+2]^+$ (2), 324 $[M^+]$ (1), 194 (31), 192 (62), 190 (34), 133 (100), 112 (23), 104 (38), 91 (15), 77 (25), 51 (21). **3i**: Pale yellow crystals, mp 100–102 °C; IR (KBr, cm^{-1}): ν_{max} 1652, 3239; ^1H NMR ($CDCl_3$): δ 2.46 (s, 3H), 7.12–7.15 (m, 2H), 7.29–7.34 (m, 6H), 7.68 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$): δ 21.8, 119.7 (br), 123.6, 125.2 (br), 129.5, 131.3, 137.2, 137.8, 140.7, 161.8; MS: *m*/*z* (%) 291 $[M+2]^+$ (3), 289 $[M^+]$ (1), 172 (71), 170 (36), 119 (44), 91 (100), 77 (19), 65 (25), 51 (11).

3. Results and discussion

Recently, transition-metal selenolates or complexes have been widely used in the synthesis of organoselenium compounds [13], but reports exploring zinc selenolates are rare [14]. As a part of our interest in zinc chemistry, we are constantly searching for novel applications of zinc selenolates in chemical reactions. In the present study we describe the use of zinc metal–aluminum chloride (Zn/$AlCl_3$) system for the cleavage of diselenides and *in situ* addition of selenolate anion to isocyanates to give the corresponding *N*-alkyl(aryl)-*Se*-alkyl(aryl)selenocarbamates (Scheme 1).

The experiments were initially conducted using cyclohexyl isocyanate and diphenyl diselenide, as a model reaction, at various molar ratios, solvents, and temperatures under an aerial atmosphere. It was found that the reaction proceeded quantitatively with a molar ratio of diselenide:Zn:$AlCl_3$:isocyanate = 1:5.5:5:2.5 in dry acetonitrile at 80 °C. The presence of aluminum chloride is essential in both steps (Se–Se bond cleavage and addition to isocyanate). In the absence of this Lewis acid, the reaction slows down considerably. This Lewis acid acts as a catalyst by its coordination with the oxygen atom in isocyanates, hence,

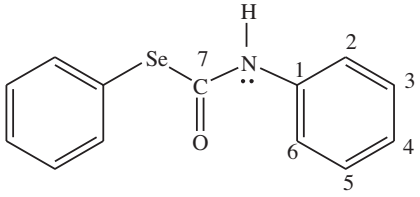


Scheme 1. Reaction of diselenides **1** and isocyanates **2** in the presence of Zn/$AlCl_3$ system.

Table 1
Synthesis of various *N*-alkyl(aryl)-*Se*-alkyl(aryl)selenocarbamates.

Entry	R^1	R^2	Time (h)	Product	Yield (%)[a,b]
1	Ph	*c*-C_6H_{11}	3.5	**3a**	64
2	Ph	Ph	0.5	**3b**	89 [15]
3	Ph	4-ClC_6H_4	0.5	**3c**	35
4	Ph	4-MeC_6H_4	0.5	**3d**	56
5	4-ClC_6H_4	*c*-C_6H_{11}	1	**3e**	68
6	4-ClC_6H_4	4-MeC_6H_4	0.75	**3f**	32
7	$PhCH_2$	*c*-C_6H_{11}	2	**3g**	22 [12b]
8	$PhCH_2$	Ph	2	**3h**	48 [12b]
9	4-MeC_6H_4	Ph	0.5	**3i**	65

[a] Isolated yield.
[b] References for known compounds.



Scheme 2. *s-Trans* form of compound **3b**.

facilitates the attack by the selenolate anion. The disappearance of zinc powder during the preliminary treatment of diselenides with Zn/$AlCl_3$ is attributed to the formation of zinc selenolate intermediate [14a–e], which further undergoes nucleophilic attack to the isocyanate to afford the selenocarbamates. The structures of all the products were established by analyzing their analytical and spectral (IR, ^1H and ^{13}C NMR, and Ms) data. Reactions of four diselenides with four different isocyanates gave various *N*-alkyl(aryl)-*Se*-alkyl(aryl)selenocarbamates (Table 1). The highest yield was obtained for *N*-phenyl-*Se*-phenylselenocarbamate **3b** (89%, entry 2, Table 1), and the lowest for *N*-cyclohexyl-*Se*-benzylselenocarbamate **3g** (22%, entry 7, Table 1).

In the ^{13}C NMR spectrum of **3b** in $CDCl_3$, an interesting spectral feature was observed. A significant line broadening was observed for the peaks of C_1, C_2, C_4, C_6, and C_7 at δ 137.7, 119.8, 125.2, 119.8, and 161.6, respectively, while those of C_3 and C_5 (both at δ 129.6) were, as usual, observed as sharp peaks at +25 °C (Scheme 2). The broad signals became sharper when the spectrum was measured at −25 °C. As reported earlier by Koketsu *et al.* [12b], the full conjugation of the nitrogen lone pair electrons with the entire π-system of the phenyl ring of the major *s-trans* form led to these interesting observations in the ^{13}C NMR spectrum. As a result of this conjugation, some alterations in the chemical shifts of the carbon atoms in the phenyl ring were observed especially for C_2, C_4, and C_6.

4. Conclusion

In conclusion, we have developed a novel, efficient and simple protocol for the synthesis of selenocarbamates. This method has the advantages of operational simplicity, mild reaction conditions, fast reaction rates, simple reaction work-up, lack of toxicity, and low costs.

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