  Bull. Chem. Soc. Jpn., 58, 1448—1451 (1985) [Vol. 58, No. 5

Synthesis Utilizing Reducing Ability of Carbon Monoxide. New Methods for Synthesis of *N*-Substituted Selenoamides

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(Received November 12, 1984)

Convenient one-pot syntheses of *N*-substituted selenoamides (**2**) from nitriles, metallic selenium, carbon monoxide, water, and amines have been developed on the basis of an amino-group-exchange reaction of *in situ* formed *N*-unsubstituted selenoamides (**1**) with primary or secondary amines. The reactions consist of two processes, *i.e.*, the formation of selenoamides **1** by the reaction of nitriles and H_2Se formed from selenium, carbon monoxide and water, and the subsequent amino-group-exchange reaction of **1** with aliphatic amines. The obtained **2** are generally stable enough to be kept for several weeks under the atmosphere of nitrogen at 0 °C without any appreciable degradation. In the cases of primary amines, the corresponding selenoamides were also obtained from nitriles, selenium, carbon monoxide, and primary amines by a single-step mixing at the beginning of the reaction.

The development of new synthetic reactions using carbon monoxide has been the subject of continuing interest.[1] One of the fascinating applications of carbon monoxide to organic synthesis is as reducing agent.[2] Recently, we reported that elemental selenium is readily reduced to hydrogen selenide by carbon monoxide and water under mild conditions,[3] and that a variety of *N*-unsubstituted selenoamides (**1**) can be synthesized in high yields from the corresponding nitriles by use of this reaction system (Eq. 1).[4]

$$RCN + Se + CO + H_2O \xrightarrow{base} \underset{\mathbf{1}}{R\text{-}\overset{\overset{Se}{\|}}{C}\text{-}NH_2} + CO_2 \qquad (1)$$

Selenoamides are not only useful for the synthesis of selenium–nitrogen heterocycles such as 1,3-selenazoles,[5] but also synthetically promising because they can be expected to react with various organic or inorganic reagents owing to the high reactivity of their carbon–selenium double bond. But the development of their chemistry has been greatly restricted by the lack of general procedures for the formation of selenoamides. The hitherto known procedures for synthesis of *N*-substituted selenoamides (**2**) were limited to the following three methods: (i) The reaction of amides with phosphorus selenide,[6] (ii) the substitution reaction of selenoesters with amines,[7] and (iii) the addition of secondary amines to alkyneselenols.[8] However, these methods are not general, and in some cases the yields are very low.

Now we wish to describe new efficient methods for the synthesis of selenoamides **2**, which were developed by the modification of the reaction system of Eq. 1.

Results and Discussion

Our strategy for the synthesis of **2** is the amino-group-exchange reaction of **1** formed *in situ* from the reaction of Eq. 1 with primary or secondary amines (Eq. 2).

$$RCN + Se + CO + H_2O \xrightarrow[-CO_2]{base} [\mathbf{1}] \xrightarrow[-NH_3]{R^1NH_2} \underset{\mathbf{2}}{R\text{-}\overset{\overset{Se}{\|}}{C}\text{-}NHR^1} \qquad (2)$$

The reaction of benzonitrile with selenium, carbon monoxide, and water in the presence of triethylamine in THF at 100 °C for 5 h, followed by treatment of the resulting mixture with butylamine at 100 °C for 3 h successfully afforded *N*-butylbenzenecarboselenoamide (**2b**) (81%) [Method A].

The representative results are shown in Table 1. The reaction appears general with respect to the substituents of selenoamides: Both aromatic and aliphatic, and both *N*-mono- and *N,N*-disubstituted selenoamides were all easily synthesized in moderate to high yields. But the yields of aromatic selenoamides (**2a—2g**) differed depending on the bulkiness of the alkyl groups of amines (R=primary alkyl group: >80%; secondary: 30—50%; tertiary: 0%). In the cases of *N*-(*s*-alkyl) derivatives (**2a**, **2c**, and **2f**), better yields were obtained when the amino-group-exchange reaction was conducted for a longer reaction time (20h). On the other hand, the amino-group-exchange reaction with aromatic amines did not take place under these reaction conditions.

Structural assignments of selenoamides were based on spectral analyses (IR, ^{1}H-NMR, and Mass spectrum: see Table 1) and elemental analyses after purification of the products by column chromatography on silica gel.

N-Substituted selenoamides are yellow crystalline or red oil, and are generally stable enough to be kept for several weeks under an atmosphere of nitrogen at about 0 °C without degradation. Upon exposure to air, however, they gradually decomposed along with the deposition of elemental selenium.

In addition to Method A, a more facile procedure (Method B) became available for the preparation of

Table 1. Synthesis of *N*-substituted Selenoamides[a)]

Entry	Selenoamide		Yield/%[b,c)] Method A	Yield/%[b,c)] Method B	IR cm^{-1}	^{1}H-NMR, δ (CCl_4)	Mass (M^+)	Mp θ_m/°C
1	Ph-C(=Se)-NHC$_3$H$_7^i$	**2a**	41 (74)	36 (77)	3180 1525	1.42(d, 6H), 4.85(m, 1H), 7.00—7.70(m, 5H), 8.20 (brs, 1H)	227	68
2	Ph-C(=Se)-NHC$_4$H$_9^n$	**2b**	81	93	3180 1530	0.84(t, 3H), 1.00—1.90(m, 4H), 3.53(m, 2H), 6.70—7.70 (m, 5H), 8.40(brs, 1H)	241	Oil
3	Ph-C(=Se)-NHC$_4$H$_9^s$	**2c**	34 (77)	27 (61)	3180 1530	0.98(t, 3H), 1.28(d, 3H), 1.70 (m, 2H), 4.64(m, 1H), 6.80—7.85(m, 5H), 8.00(brs, 1H)	241	Oil
4	Ph-C(=Se)-NHC$_4$H$_9^t$	**2d**	(0)	(0)	—	—	—	—
5	Ph-C(=Se)-NHCH$_2$Ph	**2e**	87	94	3155 1520	4.84(d, 2H), 7.00—7.80 (m, 10H), 8.20(brs, 1H)	275	76—78
6	Ph-C(=Se)-NH- 	**2f**	47 (75)	42 (82)	3135 1530	0.50—2.50(m, 10H), 4.52 (m, 1H), 7.00—7.80(m, 5H), 7.95(brs, 1H)	267	95
7	Ph-C(=Se)-NHC$_8$H$_{17}^n$	**2g**	88	95	3180 1530	0.60—2.00(m, 15H), 3.57 (m, 2H), 6.80—7.70(m, 5H), 8.50(brs, 1H)	297	Oil
8	Ph-C(=Se)-NMe$_2$	**2h**	46	0	1525	2.98(s, 3H), 3.52(s, 3H) 7.14(s, 5H)	213	46—46.5
9	Ph-C(=Se)-N 	**2i**	45	0(0)	1500	1.74(m, 6H), 3.46(m, 2H), 4.38(m, 2H), 7.18(m, 5H)	253	89—89.5
10	*n*-C$_3$H$_7$-C(=Se)-NHC$_4$H$_9^n$	**2j**	54	18	3200 1540	0.87—1.17(m, 6H), 1.17—2.09(m, 6H), 2.66(t, 2H), 3.62(q, 2H), 8.70(brs, 1H)	207	Oil
11	*n*-C$_3$H$_7$-C(=Se)-NHCH$_2$Ph	**2k**	74	31	3125 1530	0.93(t, 3H), 1.80(t-q, 2H), 2.62(t, 2H), 4.75(d, 2H), 7.26(s, 5H), 8.10(brs, 1H)	241	53.5—54
12	CH$_3$-C(=Se)-NHCH$_2$Ph	**2l**	48	30	3155 1550	2.59(s, 3H), 4.80(d, 2H), 7.33(s, 5H), 8.00(brs, 1H)	213	88—89
13	PHCH$_2$-C(=Se)-NHCH$_2$Ph	**2m**	71	74	3145 1545	4.13(s, 2H), 4.81(m, 2H), 7.20(s, 5H), 7.25(s, 5H), 7.70(brs, 1H)	289	94.5—95.5

a) All reactions were performed on 5 mmol scale according to the procedures described in the text. b) Isolated yield. c) The yields in the parentheses refer to that obtained by the reaction conducted for prolonged reaction periods in the amino-group-exchange reaction (20 h).

N-monosubstituted selenoamides (Eq. 3). For example, *N*-benzylbenzenecarboselenoamide (**2e**) was obtained in 94% yield by heating the mixture of benzonitrile, selenium, and benzylamine under CO pressure in THF.

$$RCN + Se + CO + 3R^1NH_2 \longrightarrow \mathbf{2} + (R^1NH)_2C{=}O + NH_3 \quad (3)$$

As shown in Eq. 3, Method B affords the corresponding urea derivative as a by-product concomitantly, which is easily separable from **2**. A suggested reaction path is illustrated in Eq. 4.

$$2R^1NH_2 + Se + CO \xrightarrow[-(R^1NH)_2C=O]{} H_2Se \xrightarrow{RCN} \mathbf{1} \xrightarrow[-NH_3]{R^1NH_2} \mathbf{2} \quad (4)$$

This method is inapplicable to synthesis of *N,N*-disubstituted selenoamides probably because the reaction of secondary amines with carbon monoxide and selenium does not give hydrogen selenide but the ammonium salts of selenocarbamic *Se*-acids.[9)]

In summary, general and convenient methods for the synthesis of selenoamides using carbon monoxide and selenium have been developed. The present

methods offer several advantages against hitherto known methods: (i) A wide range of applicability to a variety of selenoamides (aromatic and aliphatic; *N*-monosubstituted, and *N,N*-disubstituted); (ii) satisfactory yields of a variety of selenoamides; (iii) one-pot syntheses with simple operations without troublesome handling of hydrogen selenide.

Experimental

General. The instruments used were as follows: Melting points, Yanagimoto micro melting point apparatus; ^{1}H-NMR, Hitachi R-24B; IR, Shimadzu IR-400; MS, Hitachi RMU-6A.

All reactions were carried out using a 50-mL stainless-steel autoclave (SUS-304) purchased from Taiatsu Scientific Glass Co., Ltd.

Metallic selenium (99.99%) from Nakarai Chem. Co., Ltd. and carbon monoxide (99.99%) from Neriki Gas Co. Ltd. were used as purchased. Nitriles (benzonitrile, butyronitrile, acetonitrile, and phenylacetonitrile), amines (isopropylamine, butylamine, *s*-butylamine, *t*-butylamine, benzylamine, cyclohexylamine, octylamine, dimethylamine, piperidine, and triethylamine), and solvent (tetrahydrofuran) were all purchased from commercial sources, and purified by distillation or recrystallization. CO pressures mentioned in the paper refer to those at 25 °C.

General Experimental Procedure for Synthesis of **2** *(Method A).* In an autoclave were placed benzonitrile (0.52 g, 5 mmol), selenium (0.43 g, 5.5 mmol), water (1 mL, 56 mmol), triethylamine (1 mL), THF (5 mL), and a magnetic stirring bar. The autoclave was flushed with carbon monoxide three times, charged at 5 kg/cm^2, and set in an oil bath maintained at 100 °C. The reaction was carried out for 5 h with magnetic stirring. Then the autoclave was cooled to room temperature, and the carbon monoxide was purged in a well-ventilated hood. Butylamine (1.0 mL, 10 mmol) was immediately added to the reaction mixture under an atmosphere of nitrogen, and the reaction was continued at 100 °C for 3 h under nitrogen. After the reaction was complete, the resulting mixture was transferred to a 100 mL flask, dried overnight ($MgSO_4$), and then filtered. Evaporation of the filtrate, followed by purification by the column chromatography on silica gel (hexane–Et_2O) gave 0.97 g (4.0 mmol, 81%) of **2b**: Found: C, 55.39; H, 6.58; N, 5.85. Calcd for $C_{11}H_{15}NSe$: C, 55.00; H, 6.29; N, 5.83.

Similarly prepared were the followings.

2a: Found: C, 53.38; H, 5.85; N, 6.18%. Calcd for $C_{10}H_{13}NSe$: C, 53.10; H, 5.79; N, 6.19.

2c: Found: C, 55.38; H, 6.51; N, 5.72. Calcd for $C_{11}H_{15}NSe$: C, 55.00; H, 6.29; N, 5.83.

2e: Found: C, 61.36; H, 4.76; N, 5.01. Calcd for $C_{14}H_{13}NSe$: C, 61.32; H, 4.78; N, 5.11.

2f: Found: C, 58.66; H, 6.29; N, 5.15. Calcd for $C_{13}H_{17}NSe$: C, 58.65; H, 6.44; N, 5.26.

2g: Found: C, 60.97; H, 8.05; N, 4.87. Calcd for $C_{15}H_{23}NSe$: C, 60.80; H, 7.82; N, 4.73.

2h: Found: C, 50.98; H, 5.34; N, 6.57. Calcd for $C_9H_{11}NSe$: C, 50.95; H, 5.23; N, 6.60.

2i: Found: C, 57.21; H, 6.08; N, 5.50. Calcd for $C_{12}H_{15}NSe$: C, 57.15; H, 5.99; N, 5.55.

2j: Found: C, 47.09; H, 8.71; N, 6.81. Calcd for $C_8H_{17}NSe$: C, 46.60; H, 8.31; N, 6.79.

2k: Found: C, 55.13; H, 6.34; N, 5.72. Calcd for $C_{11}H_{15}NSe$: C, 55.00; H, 6.29; N, 5.83.

2l: Found: C, 51.18; H, 5.18; N, 6.55. Calcd for $C_9H_{11}NSe$: C, 50.95; H, 5.23; N, 6.60.

2m: Found: C, 62.60; H, 5.24; N, 4.82. Calcd for $C_{15}H_{15}NSe$: C, 62.50; H, 5.25; N, 4.86.

(Method B). Benzonitrile (0.52 g, 5 mmol), selenium (0.43 g, 5.5 mmol), butylamine (2.0 mL, 20 mmol), and THF (5 mL) were placed in an autoclave with a magnetic stirring bar. The reaction was carried out under the pressure of CO (5 kg/cm^2) at 80 °C for 5 h in a similar manner to that described in Method A. After the reaction was complete, the autoclave was cooled to room temperature and the carbon monoxide was purged. The reaction mixture was trasferred to a 100 mL flask and left overnight under the atmosphere of air in order to decompose benzenecarboselenoamide (**1**) and the remaining hydrogen selenide. The depositing metallic selenium was filtered off, and the solvent was removed from the filtrate under reduced pressure. The resulting residue was chromatographed on silica gel to give 1.12 g (4.7 mmol, 93%) of **2b** and 0.86 g (5.0 mmol) of *N,N'*-dibutylurea.

This work was supported in part by a Grant-in-Aid for Scientific Research No. 57470061 from the Ministry of Education, Science, and Culture of Japan.

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