Tetrahedron 65 (2009) 4775–4780

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of 2-selenoxoperhydro-1,3-selenazin-4-ones via diselenocarbamate intermediates

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ARTICLE INFO

Article history:
Received 26 January 2009
Received in revised form 31 March 2009
Accepted 1 April 2009
Available online 9 April 2009

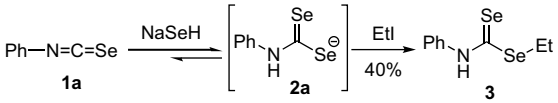
Keywords:
Selenium
Selenocarbamate
Isoselenocyanate
1,3-Selenazine

ABSTRACT

The reactions of the diselenocarbamates, generated from isoselenocyanates and sodium hydroselenide, with acryloyl chlorides afforded 2-selenoxoperhydro-1,3-selenazin-4-ones. The structure of the product was confirmed by X-ray diffraction analysis.

1. Introduction

In recent years, interest in synthesis of selenium-containing compounds has increased because of their interesting reactivities[1] and their potential biological activity. The biological and medicinal properties of selenium and organoselenium compounds are increasingly appreciated, mainly due to their antioxidant, antitumor, antimicrobial, and antiviral properties.[2] For example, 1,3-selenazine derivatives have been reported to show antibacterial and antitumor effects.[3] The results of the investigation of the structure–biological activity relationship studies indicate that the 1,3-selenazine skeleton bearing specific substituent groups strongly influences their activity. Therefore the preparation of many substituted variety of 1,3-selenazines is desired for the development of potential agents. In recent years, our group has reported the synthesis of variety of 1,3-selenazines from the selenoureas[4] or selenoamides.[5] Recently, isoselenocyanates have been emerged as a powerful tool for the synthesis of the selenium-containing heterocycles.[6] However, we have reported the synthesis of 1,3-selenazines from the acylisoselenocyanates via diselenocarbamate intermediate.[7] In continuation of the above investigations, we were interested to find out a new synthetic strategy for the preparation of the novel 1,3-selenazines from isoselenocyanates via diselenocarbamate intermediates. Only a few examples on the reactivity of diselenocarbamate have been described in literature.[7,8] For example, the treatment of phenyl isoselenocyanate **1a** with selenating reagent NaSeH resulted in the formation of the diselenocarbamate **2a**, which on in situ reaction with the ethyl iodide resulted in the formation of compound **3** (Scheme 1). The first step in the reaction is reversible and formed diselenocarbamate intermediate **2a** converts back into the starting isoselenocyanates, which is the main reason for the low yield of the product **3**.[7] These results stimulated us to study the reactivity of diselenocarbamate intermediates **2** in detail, in order to synthesize 1,3-selenazines **4** via intramolecular Michael addition. Herein we describe the new synthesis of 1,3-selenazines **4** via diselenocarbamate intermediates **2**.



Scheme 1.

2. Results and discussion

Substituted alkyl and arylisoselencyanates **1** for our approach were prepared by reactions of *N*-substituted formamides with an excess of triphosgene, selenium and triethylamine according to the previous literature.[9] First, the treatment of selenating reagent

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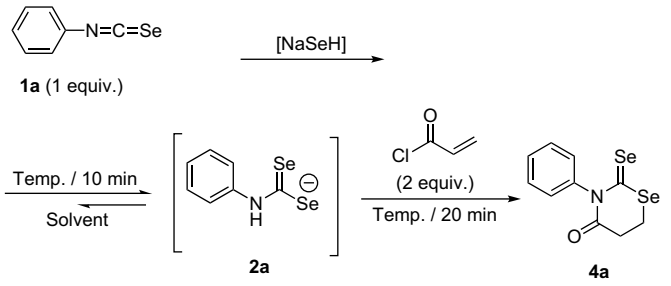
doi:10.1016/j.tet.2009.04.004

NaSeH, generated by the reaction of $NaBH_4$ and Se, with phenylisoselencyanate **1a** and further with acryloyl chloride at room temperature was examined (Scheme 2, Table 1, entry 2). To our delight the reaction took place readily at room temperature and the cyclization product **4a** was obtained by the intramolecular cyclization reaction in 44% yield after work-up of the reaction mixture (entry 2). The structure of **4a** was elucidated by studies of IR, ^{1}H-, ^{13}C-, ^{77}Se NMR, COSY, HMQC, HMBC, MS, and elemental analysis.



Scheme 2.

Table 1
Optimization of the reaction conditions for **4a**

Entry	Solvent	Temp (°C)	Yield[a] (%)
1	THF	+40	42
2	THF	rt	44
3	THF	0	46
4	THF	−20	52
5	THF	−40	67
6	THF	−60	71
7	THF	−80	68
8	DMF	−60	63
9	CH_3CN	−60	52
10	Toluene	−60	52
11	DCM	−60	75
12	Chloroform	−60	47
13	Acetone	−60	46

[a] Isolated yields.

The reactions using NaSeH afforded a slightly higher yield of product **4a** than yield of reaction using LiAlHSeH.[10] Therefore, to improve the yield of cyclization, various conditions using NaSeH were then screened (Table 1). At 40 °C and room temperature isoselenocyanate **1a** was recovered (entries 1 and 2). As shown in Table 1, −60 °C was the suitable temperature for the cyclization reaction (entry 6). Furthermore, the reaction was influenced by the solvent used and the best result was obtained when reaction was carried out in CH_2Cl_2 (entry 11). Longer reaction time resulted in the decomposition of the product **4a**.

Under the optimized conditions (Table 1, entry 11), the reactions of other substituted isoselenocyanates **1** with various acryloyl chlorides were investigated and the results are summarized in Table 2. First, the effect of the substitution on isoselenocyanate was examined (entries 1–8). In most cases isoselenocyanates gave the corresponding 1,3-selenazines **4** in moderate to high yields (entries 1–3, 6 and 7). However, reactions of *o*-chlorophenyl- and *o*-tolylisoselenocyanates gave the corresponding **4** in low yields because of steric hindrance (entries 4 and 5). The reaction was strongly influenced by the substitution pattern on the isoselenocyanate skeleton (entries 1–6). The benzyl isoselenocyanate (**1g**) afforded 1,3-selenazine **4g** in 72% yield (entry 7). In the case of cyclohexyl isoselenocyanate the reaction was complicated and the corresponding product **4h** was isolated in low yield 4% (entry 8). Next, the effect on the acryloyl chloride part was examined (entries 9–13). The β-monosubstituted aromatic acryloyl chlorides afforded 1,3-selenazines **4i** and **4j** in low yields (entries 9 and 10). Bulky groups such as Ph and *p*-$NO_2C_6H_4$ at β-carbon may block the attack of selenium and make the yield lower. α,β-Dimethyl acryloyl chloride gave good yields of 1,3-selenazine **4l** (entry 12). The β-dimethyl- and cyclohexyl acryloyl chlorides afforded 1,3-selenazines **4k** and **4m** in 9% and 19% yield, respectively (entries 11 and 13).

The structures of the products were established on the basis of their spectroscopic data. The ^{1}H NMR spectra of **4** in $CDCl_3$, protons of *C*6 carbon, show the selenium coupling at ^2J (^{77}Se–^{1}H)=35.8±11.0 Hz, the values are for the protons on the carbon which is directly attached to selenium. The ^{13}C NMR of the product shows two carbonyl peaks for the C=O at δ 168.7±1.9 and for the C=Se at δ 203.4±2.0, respectively. In the ^{77}Se NMR spectra of the 1,3-selenazines **4**, two ^{77}Se signals were observed for C–Se and C=Se bonds in the range of δ 614.7±56.5 and δ 1180.4±48.6, respectively. The values δ 1180.4±48.6 are typical for a C=Se single bond with an sp^2 selenium atom, i.e., for selenocarbonyl compounds.[11] The values δ 614.7±56.5 are at a higher field compared with ^{77}Se signals of selenocarbonyl compounds. The values are typical for a C–Se single bond with an sp^3 selenium atom not for a C=Se double bond with an sp^2 selenium atom.[12] These values confirm the presence of diselenocarbamate linkage in the structure of **4**.

In order to confirm the structure of **4c**, we carried out the X-ray analysis of this compound. An ORTEP drawing, depicted in Figure 1, shows the molecular structure of **4c**.[13] The bond angle of the selenium atom C1–Se1–C4 was 101.3(4)°. The length of Se1–C1 bond in **4c** is 1.857(9) Å, which is shorter than a typical C–Se single bond (1.94 Å).[14] The bond angle of the nitrogen atom C1–N1–C2 was 126.9(3)°. The two C–N bond lengths of both N1–C1 (1.366(5) Å) and N1–C2 (1.420(5) Å) in **4c** are shorter than the usual single bond length of 1.47 Å.[15]

The formation of the 1,3-selenazine derivatives **4** can be explained by the reaction mechanism shown in Scheme 3. In the presence of NaSeH, diselenocarbamate **2** was generated. The reaction proceeds via intermediate **5** or **7**. The intermediate **5**, which is formed by the nucleophilic substitution of the acryloyl chloride by the Se-atom of **2** undergoes a base catalyzed 1,3-acyl shift to give the rearranged intermediate **6**. Similar Se→N[7,16] or S→N migrations of the acetyl group are known and S→N migrations of the acetyl group have been studied in depth kinetically[17] and were described recently by Pihlaja and co-workers.[18] Finally, the Se-atom attacks the β-carbon of the acrylamide group **6** and the 1,3-selenazines **4** are formed by intramolecular Michael addition.

3. Conclusion

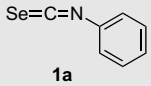
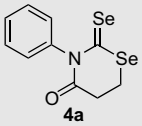
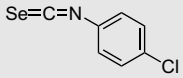
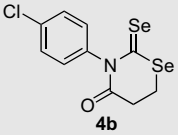
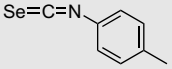
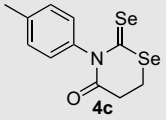
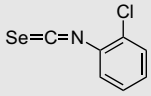
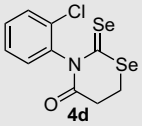
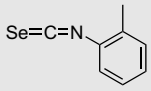
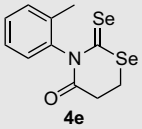
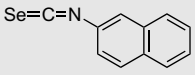
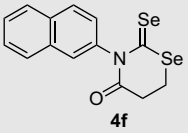
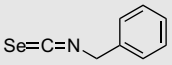
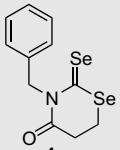
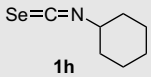
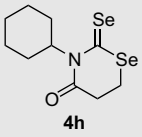
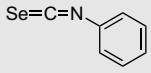
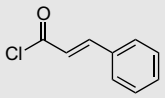
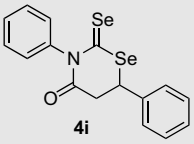
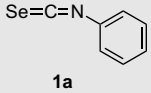
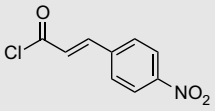
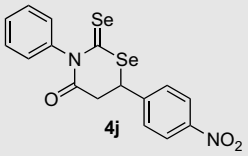
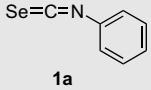
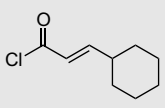
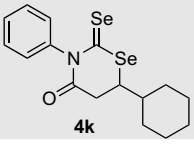
In conclusion, we report the one pot synthesis of 2-selenoxoperhydro-1,3-selenazin-4-ones **4** by the reaction of the diselenocarbamates, generated from isoselenocyanates and sodium hydroselenide, with acryloyl chlorides. The structure of product **4c** was confirmed by X-ray diffraction analysis. Further investigation into the scope and limitations of this reaction is underway.

4. Experimental

4.1. General

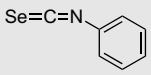
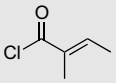
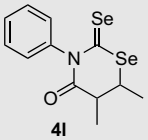
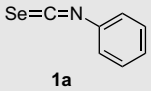
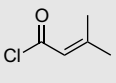
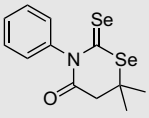
All solvents and reagents were purchased from the suppliers and used without further purification. All reactions were performed in round-bottom flask fitted with balloon filled with argon, otherwise specified. Transfer of air- and moisture-sensitive liquids was performed via cannula under a positive pressure of argon. TLC analysis was performed on Merck TLC (silica gel 60F_{254} on glass

Table 2
Synthesis of 2-selenoxoperhydro-1,3-selenazin-4-one **4**

Entry	Isoselenocyanate	Acryloyl chloride	Time	Product	^{77}Se NMR (δ)		Yield (%)
					C–Se	C=Se	
1	 **1a**		20 min	 **4a**	578.4	1208.2	75
2	 **1b**		20 min	 **4b**	582.3	1225.5	70
3	 **1c**		20 min	 **4c**	577.2	1197.5	60
4	 **1d**		20 min	 **4d**	581.1	1206.2	15
5	 **1e**		20 min	 **4e**	574.6	1195.8	8
6	 **1f**		20 min	 **4f**	580.3	1213.0	68
7	 **1g**		20 min	 **4g**	574.7	1109.3	72
8	 **1h**		20 min	 **4h**	576.3	1051.3	4
9	 **1a**		1 h	 **4i**	678.9	1186.0	11
10	 **1a**		40 min	 **4j**	675.0	1216.7	10
11	 **1a**		1 h	 **4k**	631.3	1181.4	9

(*continued on next page*)

Table 2 (*continued*)

Entry	Isoselenocyanate	Acryloyl chloride	Time	Product	^{77}Se NMR (δ)		Yield (%)
					C–Se	C=Se	
12	 **1a**		20 min	 **4l**	627.4	1167.1	48
13	 **1a**		50 min	 **4m**	753.6	1187.2	19

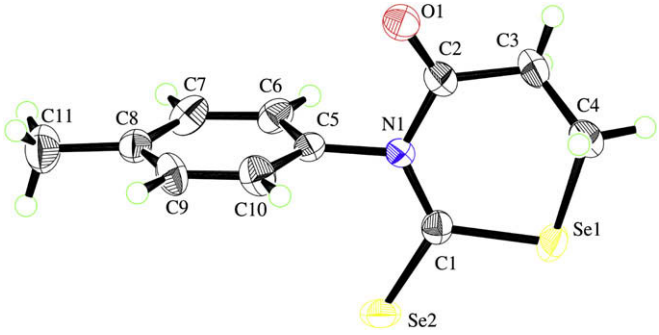
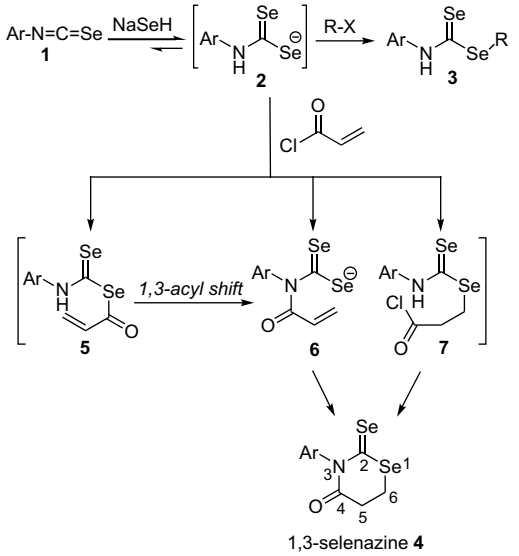


Figure 1. Crystal structure of 3-(*p*-tolyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4c**).



Scheme 3.

plate). Melting points were measured by a Yanagimoto micro-melting point apparatus (uncorrected). IR spectra were measured on JASCO FT/IR-410 Fourier Transform Infrared Spectrometer. The ^{1}H NMR, ^{13}C NMR spectra and ^{77}Se NMR spectra were measured on JEOL:JNM ECX-400 P, JEOL:JNM ECA-600 spectrometers in $CDCl_3$. Chemical shifts of protons are reported in δ values referred to TMS as an internal standard, and the following abbreviations were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. The ^{77}Se chemical shifts were expressed in δ values deshielded with respect to neat Me_2Se. ^{2}J (^{77}Se–^{1}H) and ^{1}J (^{77}Se–^{13}C) values are observed as ^{77}Se satellites of the ^{1}H NMR and ^{13}C NMR spectra. MS were measured on a JEOL JMS-700.

4.2. Representative experimental procedure

A NaSeH solution was prepared by the reaction of $NaBH_4$ (62.3 mg, 1.65 mmol) with elemental selenium (65.1 mg, 0.82 mmol) in anhyd EtOH (2 mL) at 0 °C for 30 min under an argon atmosphere. To a stirred solution of phenylisoselenocyanate (100 mg, 0.55 mmol) in CH_2Cl_2 (5 mL) was added NaSeH solution at −60 °C and stirring was continued for additional 10 min at this temperature. Acryloyl chloride (98.2 μL, 1.10 mmol) was added to the reaction mixture at −60 °C. After stirring at this temperature for 20 min, the reaction mixture was extracted with Et_2O and washed with water. The organic phase was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was chromatographed on silica gel using ether/hexane (3:2→1:1) as eluent to give compound **4a** (127 mg, 75%).

*4.2.1. 3-Phenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4a**)*

Red crystals. Mp 185–186 °C. IR (KBr): 1709, 1590, 1302, 1239, 1134 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.15 (2H, t, J=6.9 Hz, ^{2}J (^{77}Se-^{1}H)=28.4 Hz, Se–CH_2), 3.55 (2H, t, J=6.9 Hz, O=C–CH_2), 7.15 (2H, d, J=7.8 Hz, Ar–H), 7.40–7.49 (3H, m, Ar–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (^{1}J (^{77}Se–^{13}C)=63.3 Hz), 35.4, 128.5, 128.8, 129.4, 141.1, 167.2, 203.1. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 578.4, 1208.2. MS (EI): m/z=319 [M^{+}]. Anal. Calcd for $C_{10}H_9NOSe_2$: C, 37.88; H, 2.86; N, 4.42. Found: C, 37.86; H, 3.20; N, 4.49.

*4.2.2. 3-(p-Chlorophenyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4b**)*

Red crystals. Mp 143–144 °C. IR (KBr): 1720, 1710, 1653, 1487, 1237, 1118 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.16 (2H, t, J=6.7 Hz, ^{2}J (^{77}Se–^{1}H)=28.4 Hz, Se=CH_2), 3.56 (2H, t, J=6.7 Hz, O=C–CH_2), 7.09 (2H, d, J=8.7 Hz, Ar), 7.43 (2H, d, J=8.7 Hz, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (^{1}J (^{77}Se–^{13}C)=63.6 Hz), 35.4, 129.7, 130.0, 134.8, 139.4, 167.1, 203.0. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 582.3, 1225.5. MS (EI): m/z=353 [M^{+}]. Anal. Calcd for $C_{10}H_8ClNOSe_2$: C, 34.17; H, 2.29; N, 3.98. Found: C, 34.03; H, 2.54; N, 3.95.

*4.2.3. 3-(p-Tolyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4c**)*

Red crystals. Mp 170–171 °C. IR (KBr): 1714, 1677, 1509, 1235, 1126 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.39 (3H, s, Ar–CH_3), 3.14 (2H, t, J=6.9 Hz, ^{2}J (^{77}Se–^{1}H)=27.9 Hz, Se–CH_2), 3.55 (2H, t, J=6.6 Hz, O=C–CH_2), 7.03 (2H, d, J=8.2 Hz, Ar–H), 7.27 (2H, d, J=8.2 Hz, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 21.6 (^{1}J

(^{77}Se–^{13}C)=55.6 Hz), 35.4, 128.1, 130.1, 138.9, 138.7, 167.2, 203.3. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 577.2, 1197.5. MS (EI): m/z=333 [M^+]. Anal. Calcd for $C_{11}H_{11}NOSe_2$: C, 39.90; H, 3.35; N, 4.23. Found: C, 39.68; H, 3.43; N, 4.19.

4.2.3.1. ***4c**: X-ray crystallographic data*[13]. Single-crystal X-ray diffraction: Rigaku AFC7R Mercury CCD area-detector diffractometer using graphite monochromated Mo Kα radiation (λ=0.71069 Å). The structures were solved by direct methods (SIR97, Altomare, A., Burla, M., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A., Polidori, G., Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115) and refined by full-matrix least-squares on F^2 (SHELEX-97, Program for Crystal Structure Refinement, G. M. Sheldrick, Universitat Göttingen, 1997). All non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined by a riding model. Empirical absorption corrections were applied. Single crystal was grown from Et_2O–hexane: $C_{11}H_{11}NOSe_2$, M_r=331.13, Red color crystal (0.29×0.20×0.10 mm^3), Crystal system: trigonal, space group: '$P3_2$', a=11.4194(9), b=11.4194(9), c=7.7246(8) Å, γ=120°, V=872.35(13) Å^3, Z=3, μ=6.330 mm^{-1}, D_{calcd}=1.891 Mg/m^3, Reflections collected: 7120, independent reflections: 2104 unique (R_{int}=0.0431), 183 parameters, θ range for data collection 3.35–27.49°. Limiting indices −14h14, −14k14, −7l10, largest max./min. in the final difference Fourier synthesis 0.312 e Å^{-3}/−0.247 e Å^{-3}, max./min. transmission 0.5702/0.2611, T=296(2) K, R_1=0.0293 [$I>2\sigma(I)$], wR_2=0.0595. R indices (all data) R_1=0.0323, wR_2=0.0607.

*4.2.4. 3-(o-Chlorophenyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4d**)*

Red oil. IR (neat): 1716, 1473, 1234, 1129 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.18 (2H, td, J=2.3, 6.4 Hz, ^2J (^{77}Se–^{1}H)=29.8 Hz, Se=CH_2), 3.55 (2H, t, J=6.4 Hz, O=C–CH_2), 7.23–7.27 (1H, m, Ar), 7.35–738 (2H, m, Ar), 7.50 (1H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (^1J (^{77}Se–^{13}C)=60.4 Hz), 35.3, 127.9, 130.3, 130.4, 130.6, 132.1, 138.7, 166.7, 202.0. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 581.1, 1206.2. MS (EI): m/z=353 [M^+], 318 [M^+−Cl]. Anal. Calcd for $C_{10}H_8ClNOSe_2$: C, 34.17; H, 2.29; N, 3.98. Found: C, 33.99; H, 2.42; N, 3.98.

*4.2.5. 3-(o-Tolyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4e**)*

Red crystals. Mp 115–116 °C. IR (KBr): 1712, 1234, 1130 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (3H, s, Ar–CH_3), 3.09–3.23 (2H, m, Se–CH_2), 3.48–3.62 (2H, m, O=C–CH_2), 7.06 (1H, d, J=7.8 Hz, Ar–H), 7.25–7.36 (3H, m, Ar–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 21.7 (^1J (^{77}Se–^{13}C)=56.6 Hz), 35.5, 127.3, 128.4, 129.3, 131.2, 135.4, 140.2, 167.0, 202.0. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 574.6, 1195.8. MS (EI): m/z=333 [M^+]. Anal. Calcd for $C_{11}H_{11}NOSe_2$: C, 39.90; H, 3.35; N, 4.23. Found: C, 40.24; H, 3.47; N, 4.09.

*4.2.6. 3-(2-Naphtyl)-2-selenoxoperhydro-1,3-selenazin-4-one (**4f**)*

Red crystals. Mp 187–188 °C. IR (KBr): 1714, 1653, 1598, 1508, 1234, 1128 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.07–3.27 (2H, m, Se–CH_2), 3.52–3.65 (2H, m, O=C–CH_2), 7.24 (1H, dd, J=1.9, 6.4 Hz, Ar–H), 7.46–7.55 (2H, m, Ar–H), 7.66 (1H, d, J=1.9 Hz, Ar–H), 7.81–7.94 (3H, m, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.7 (^1J (^{77}Se–^{13}C)=63.3 Hz), 35.4, 126.1, 126.5, 126.9, 127.3, 127.9, 128.2, 129.2, 133.0, 133.5, 138.4, 167.3, 203.1. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 580.3, 1213.0. MS (EI): m/z=369 [M^+]. Anal. Calcd for $C_{14}H_{11}NOSe_2$: C, 45.80; H, 3.02; N, 3.81. Found: C, 45.72; H, 3.14; N, 3.76.

*4.2.7. 3-Benzyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4g**)*

Red crystals. Mp 108–109 °C. IR (KBr): 1714, 1603, 1341, 1324, 1133 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.98 (2H, t, J=6.9 Hz, ^2J (^{77}Se–^{1}H)=28.0 Hz, Se–CH_2), 3.41 (2H, t, J=6.9 Hz, O=C–CH_2), 5.85 (2H, s, N–CH_2), 7.30–7.35 (5H, m, Ar–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3 (^1J (^{77}Se–^{13}C)=63.3 Hz), 35.7, 52.5, 127.6, 128.0, 128.4 135.9, 166.8, 203.8. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 574.7, 1109.3. MS (EI): m/z=333 [M^+]. Anal. Calcd for $C_{11}H_{11}NOSe_2$: C, 39.90; H, 3.35; N, 4.23. Found: C, 39.85; H, 3.42; N, 4.25.

*4.2.8. 3-Cyclohexyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4h**)*

Orange crystals. Mp 87–89 °C. IR (KBr): 2929, 1723, 1523, 1297, 1220, 1127 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15–1.45 (4H, m, cyclohexyl), 1.60–1.90 (4H, m, cyclohexyl), 2.21–2.34 (2H, m, cyclohexyl), 2.96 (2H, t, J=6.9 Hz, ^2J (^{77}Se–^{1}H)=28.0 Hz, Se–CH_2), 3.36 (2H, t, J=6.9 Hz, O=C–CH_2), 5.70 (1H, tt, J=3.2, 11.9 Hz, cyclohexyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3 (^1J (^{77}Se–^{13}C)=63.3 Hz), 25.2, 26.3, 29.3, 37.7, 66.4, 167.1, 205.4. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 576.3, 1051.3. MS (EI): m/z=325 [M^+]. Anal. Calcd for $C_{10}H_{15}NOSe_2$: C, 37.17; H, 4.68; N, 4.33. Found: C, 37.28; H, 5.03; N, 4.22.

*4.2.9. 3,6-Diphenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4i**)*

Purple crystals. Mp 195–196 °C. IR (KBr): 1706, 1591, 1231, 1209, 1194, 1121 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.77–3.90 (2H, m, O=C–CH_2), 4.90 (1H, dd, J=3.4, 12.2 Hz, Se–CH), 7.19 (2H, d, J=7.6 Hz, Ar–H), 7.33–7.39 (3H, m, Ar–H), 7.41 (2H, d, J=7.6 Hz, Ar–H), 7.45 (1H, t, J=7.6 Hz, Ar–H), 7.49 (2H, t, J=7.6 Hz, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 41.8 (^1J (^{77}Se–^{13}C)=60.7 Hz), 42.3, 127.3, 128.4, 128.8, 128.9, 129.4, 129.6, 136.2, 141.0, 167.9, 203.6. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 678.9, 1186.0. MS (EI): m/z=395 [M^+]. Anal. Calcd for $C_{16}H_{13}NOSe_2$: C, 48.87; H, 3.33; N, 3.56. Found: C, 48.52; H, 3.47; N, 3.54.

*4.2.10. 6-(p-Nitrophenyl)-3-phenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4j**)*

Purple crystals. Mp 202–203 °C. IR (KBr): 1706, 1598, 1522, 1349, 1236, 1198, 1114 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.82–3.92 (2H, m, O=C–CH_2), 4.98 (1H, dd, J=4.0, 11.0 Hz, ^2J (^{77}Se–^{1}H)=24.8 Hz, Se–CH), 7.18 (2H, d, J=8.2 Hz, Ar–H), 7.44–7.52 (3H, m, Ar–H), 7.56 (2H, d, J=8.2 Hz, Ar–H), 8.29 (2H, d, J=8.2 Hz, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 40.9 (^1J (^{77}Se–^{13}C)=63.6 Hz), 41.6, 124.7, 128.3, 128.6, 129.1, 129.6, 140.5, 143.7, 147.9, 166.9, 201.4. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 675.0, 1216.7. MS (EI): m/z=440 [M^+]. Anal. Calcd for $C_{16}H_{12}N_2O_3Se_2$: C, 43.85; H, 2.76; N, 6.39. Found: C, 43.91; H, 3.09; N, 6.40.

*4.2.11. 6-Cyclohexyl-3-phenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4k**)*

Pink crystals. Mp 205–207 °C. IR (KBr): 1705, 1222, 1132 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03–1.31 (5H, m, cyclohexyl), 1.68–1.92 (6H, m, cyclohexyl), 3.40–3.48 (5H, m, cyclohexyl), 3.40–3.48 (2H, m, O=C–CH_2), 3.57–3.62 (1H, m, Se–CH_2), 7.13 (2H, d, J=6.8 Hz, Ar–H), 7.40–7.49 (3H, m, Ar–H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 26.0, 30.8, 39.8, 41.8 (^1J (^{77}Se–^{13}C)=60.4 Hz), 45.9, 128.6, 128.9, 129.5, 141.3, 168.4, 202.5. ^{77}Se NMR (75 MHz, $CDCl_3$): δ 631.3, 1181.4. MS (EI): m/z=401 [M^+]. Anal. Calcd for $C_{11}H_{11}NOSe_2$: C, 48.13; H, 4.80; N, 3.51. Found: C, 48.32; H, 5.03; N, 3.24.

*4.2.12. 5,6-Dimethyl-3-phenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4l**)*

Red crystals. Mp 138–139 °C. IR (KBr): 1719, 1587, 1305, 1211, 1124 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.53 (3H, d, J=6.9 Hz, CH_3), 1.67 (3H, d, J=6.9 Hz, CH_3), 3.25 (1H, quin., J=6.9 Hz, O=C–CH), 3.33 (1H, quin., J=6.9 Hz, ^2J (^{77}Se–^{1}H)=46.7 Hz, Se–CH), 7.12 (2H, d, J=8.3 Hz, Ar–H), 7.40–7.48 (3H, m, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 15.7, 20.4, 40.2 (^1J (^{77}Se–^{13}C)=62.1 Hz), 46.1, 128.5, 128.7, 129.3, 141.7, 170.5, 202.1. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 627.4, 1167.1. MS (EI): m/z=347 [M^+]. Anal. Calcd for $C_{12}H_{13}NOSe_2$: C, 41.76; H, 3.80; N, 4.06. Found: C, 41.68; H, 3.94; N, 4.05.

*4.2.13. 6,6-Dimethyl-3-phenyl-2-selenoxoperhydro-1,3-selenazin-4-one (**4m**)*

Red crystals. Mp 170–171 °C. IR (KBr): 1712, 1590, 1257, 1224, 1203 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 1.70 (6H, s, 2×CH_3), 3.40 (2H, s, O=C–CH_2), 7.15 (2H, d, J=8.2 Hz, Ar–H), 7.43 (1H, t, J=8.2 Hz, Ar–H), 7.48 (2H, t, J=8.2 Hz, Ar–H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 29.0, 44.1 (^1J (^{77}Se–^{13}C)=60.7 Hz), 50.8, 128.6, 128.8, 129.5, 141.1, 168.0, 203.3. ^{77}Se NMR (95 MHz, $CDCl_3$): δ 753.6, 1187.2. MS (EI): m/z=347 [M^+]. Anal. Calcd for $C_{12}H_{13}NOSe_2$: C, 41.76; H, 3.80; N, 4.06. Found: C, 41.71; H, 3.94; N, 4.06.

Acknowledgements

This work was supported by a Grant-in-Aid for Science Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Nos. 20590005 and 17550099) to which we are grateful.

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