Synthesis and characterization of novel 1,3-selenazine derivatives. $BF_3 \cdot Et_2O$-assisted reaction of primary selenoamides with α,β-unsaturated ketones

Mamoru Koketsu,* Takayuki Senda, Katsuhiro Yoshimura and Hideharu Ishihara *

Department of Chemistry, Faculty of Engineering, Gifu University, 1-1 Yanagido, Gifu, 501-1193, Japan

Received (in Cambridge) 23rd November 1998, Accepted 8th January 1999

Reaction of primary selenoamides with α,β-unsaturated ketones in the presence of $BF_3 \cdot Et_2O$ provided 5,6-dihydro-4*H*-1,3-selenazine derivatives in high yields. Among the 1,3-selenazine diastereomers bearing two asymmetric carbons at the C4 and C6 positions, the *cis* form is predominant.

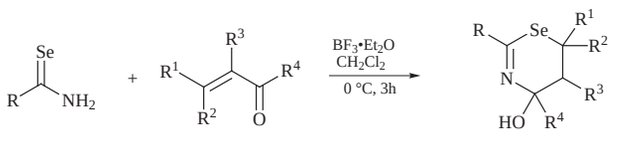
Introduction

Many syntheses of heterocyclic compounds containing sulfur or selenium[1] have been reported because of their various interesting biological activities. For example, 1,3-thiazine or thiazole derivatives possess antitumor activity,[2] antibacterial activity,[3] human immunodefiency virus (HIV) inhibition,[4] and other notable activities. On the other hand, only a few reports have been published on both selenium- and nitrogen-containing heterocyclic compounds.[5] This is mainly due to the fact that the essential selenium-containing starting materials are less readily available than the sulfur analogue intermediates. Only a few practical applications of primary selenoamides[6] to the synthesis of heterocycles have been made owing to the difficulty in preparing the primary selenoamides.

We have previously investigated the synthesis and characterization of selenocarbonyl compounds[7] and developed a convenient method for the synthesis of potassium selenocarboxylates.[8] It was found that the selenobenzoates function for a reagent of introducing selenium to nitriles to give primary selenoamides under mild conditions.[9] Here, we describe a convenient preparation and the spectroscopic characteristics of novel 5,6-dihydro-4*H*-1,3-selenazine derivatives from primary selenoamides.

Results and discussion

Because the selenoamide is considered to contain a selenoamide–selenoimidate tautomerism and bear two reactive sites, its reactivity is of interest. The reaction of primary selenoamides with 2 equiv. of aldehydes is initiated by nucleophilic addition of the nitrogen of the selenoamide to the carbonyl carbon to give 1,3,5-oxaselenazines.[5g] On the other hand, the reaction of the selenoamide with halomethyl ketone afforded 1,3-selenazole with attack of selenium on the ketone.[5a,6d] The reaction of primary selenoamide **1** with α,β-unsaturated ketone **2** gives 1,3-selenazine derivative **3** in good yields under mild conditions (Scheme 1). The results are summarized in Table 1. The structure of **3** was confirmed by studies of IR, UV, ^1H, ^{13}C, and ^{77}Se NMR, HRMS, and/or elemental analysis. Because



1 + **2** → **3**

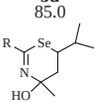
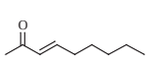
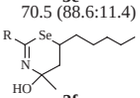
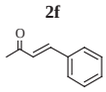
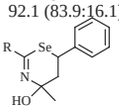
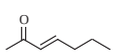
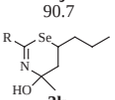
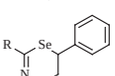
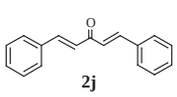
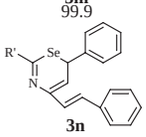
Scheme 1

$^1J(^{77}Se–^{13}C)$ values were observed at the C6 carbon of **3a**, it was confirmed that **3a** was formed by the nucleophilic addition of the selenium atom of selenoamide not to the carbonyl carbon of **2a** but to the β-position of the carbonyl carbon of **2a**. Similarly, the one step reaction of other α,β-unsaturated ketones with primary selenoamides gave 5,6-dihydro-4*H*-1,3-selenazine derivatives in good to high yields (entries 1–13). There was no difference in yield of 5,6-dihydro-4*H*-1,3-selenazine derivatives from the corresponding aromatic (entries 1–8) and aliphatic (entries 9–13) selenoamides. Even cyclohexenone (entries 8 and 13) afforded the 5,6-dihydro-4*H*-1,3-selenazine derivatives in good yield without steric hindrance. However, the reaction of selenoamide with 1,5-diphenylpenta-1,4-dien-3-one gave 6*H*-1,3-selenazine **3n**, and its yield was low (31.5%). 4-Methylselenobenzamide was recovered in 60% yield (entry 14).

As for spectroscopic data for the obtained 1,3-selenazine derivatives, in the IR spectra of 5,6-dihydro-4*H*-1,3-selenazine derivatives, the absorption of the C=N bond of **3a**–**3h** was observed at 1594.1 ± 3.2 cm^{-1} and that of **3i**–**3m** was 1643.2 ± 39.4 cm^{-1}. In the mass spectra of 5,6-dihydro-4*H*-1,3-selenazine derivatives, the corresponding nitrile is observed as the most stable fragment ion peak together with molecular peak. For example, the CIMS spectrum of **3c** showed peaks at *m*/*z* (%, fragment) 118 (100.0, $[p$-toluonitrile + 1$]^+$), 180 (34.7, $[M - p$-toluonitrile$]^+$), 280 (12.1, $[M + 1 - H_2O]^+$), 296 (7.9, $[M + 1$ ^{78}Se isotope$]^+$), and 298 (16.0, $[M + 1]^+$). In the ^{77}Se NMR spectra of 1,3-selenazine derivatives, ^{77}Se signals were observed in the range of δ 334.6 ± 60.0, which are at a higher field compared with ^{77}Se signals of dihydroselenophenes (δ 480.0 ± 96.4)[10] and selenocarbonyl compounds (δ 1420–2131).[11] The ^{77}Se signals of **3d**, **3g**, **3h**, **3l**, and **3m** are deshielded by approximately 50–100 ppm by the effect of the substituent at C6 compared with other 1,3-selenazines. $^1J(^{77}Se–^{13}C)$ values of **3**, which were observed for the C6 carbon, were 54.2 ± 1.7 Hz. These values are typical for a C–Se single bond with an sp^3 carbon but not for a C–Se double bond with an sp^2 carbon.[12]

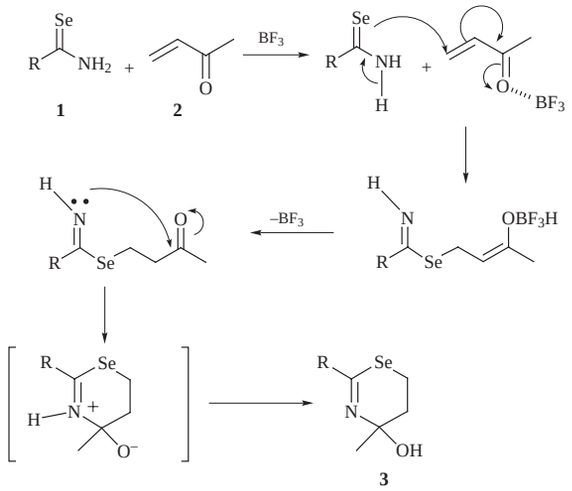
Selenazines **3c**, **3e**–**3g**, and **3j**–**3l** consist of diastereomers containing two or three asymmetric centers at the C4, C6 and/or C5 positions of the selenazine ring. NOE irradiation techniques confirmed that the major diastereomer has a *cis* relationship between the OH group at C4 and the substituent at C6. The NOE spectra indicated the presence of diastereomers in a ratio of approximately 74–90% (*cis*): 26–10% (*trans*). Irradiation of the methyl group of C4 produced a positive NOE effect on the hydrogen atoms at C6 and C5. The NOE effect between CH_3 at C4 and the hydrogen at C6 of **3f** was 9.8%, and that for **3g** was 14.2%, respectively.

Table 1 Preparation of 1,3-selenazines

Entry	Selenoamide **1**	α,β-Unsaturated ketone **2**	Yield, % (*cis*/*trans*)[a]
1	R = 4-$CH_3C_6H_4$ **1a**	 **2a**	 **3a** 73.4
2	**1a**	 **2b**	 **3b** 87.9
3	**1a**	 **2c**	 **3c** 93.3
4	**1a**	 **2d**	 **3d** 85.0
5	**1a**	 **2e**	 **3e** 70.5 (88.6:11.4)
6	**1a**	 **2f**	 **3f** 92.1 (83.9:16.1)
7	**1a**	 **2g**	 **3g** 99.9 (74.2:25.8)
8	**1a**	 **2h**	 **3h** 81.1
9	R = n-C_5H_{11} **1b**	**2b**	 **3i** 99.9
10	**1b**	**2c**	 **3j** 90.7
11	**1b**	 **2i**	 **3k** 91.3 (83.5:16.5)
12	**1b**	**2g**	 **3l** 86.2 (89.6:10.4)
13	**1b**	**2h**	 **3m** 99.9
14	**1a**	 **2j**	 **3n** 31.5

[a] Calculated from ^{1}H NMR spectra.

Though the detailed mechanism of the above reaction has not been clarified yet, the 5,6-dihydro-4*H*-1,3-selenazine formation could be explained by the possible mechanism presented in Scheme 2. The Michael adduct was detected by ^{13}C NMR spectroscopy.[13]



Scheme 2

Experimental

General methods

Primary selenoamides were synthesized in accordance with a previously described procedure.[9] The ^{77}Se NMR (76 MHz) spectra were obtained from a JEOL α-400 spectrometer, and ^{77}Se chemical shifts are expressed in ppm deshielded with respect to neat Me_2Se in $CDCl_3$. $^1J(^{77}Se–^{13}C)$ values are the ^{77}Se satellites of the proton-decoupled ^{13}C NMR spectra.

4-Hydroxy-4-methyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine (3a)

4-Hydroxy-4-methyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine **3a** was synthesized as follows: to a solution of 4-methylselenobenzamide (0.20 g, 1 mmol) in dry dichloromethane (10 mL) was added methyl vinyl ketone (0.070 g, 1 mmol) at 0 °C under an argon atmosphere. To this solution was added $BF_3{\cdot}Et_2O$ (1.2 mmol). The reaction mixture was stirred for 3 h, quenched with saturated sodium carbonate solution (40 mL), and extracted with dichloromethane (40 mL × 3). The extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by column chromatography on silica gel using dichloromethane as the eluent to give 0.203 g (73.4%) of **3a** as a yellow powder. When the temperature of the reaction was raised to 25 °C or lowered to −25 °C, the yields of **3a** were 46.8% and 49.0%, respectively. Further, when $CHCl_3$, ether or THF was used as a solvent instead of CH_2Cl_2, the yield of **3a** was low. Mp 89.0–89.6 °C; IR (KBr) 3160, 1594 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 341 (2.42), 255 (3.98); ^{1}H NMR ($CDCl_3$) δ 1.28 (3H, s), 1.46–1.62 (1H, m), 1.88 (1H, dt, J = 4.2, 9.6 Hz), 2.25 (3H, s), 2.99–3.07 (2H, m), 3.81 (1H, br s), 7.07 (2H, d, J = 8.2 Hz), 7.54 (2H, d, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 18.3, 21.4, 24.9, 30.0, 85.1, 126.5, 129.1, 137.5, 141.0, 156.8; ^{77}Se NMR ($CDCl_3$) δ 245.0; Anal. Calc. for $C_{12}H_{15}NOSe$: C, 53.53; H, 5.62; N, 5.20. Found: C, 53.49; H, 5.61; N, 5.03%).

4-Ethyl-4-hydroxy-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine (3b)

3b–**n** were prepared following the same procedure as **3a**. Mp 60.6–61.3 °C; IR (KBr) 3150, 1593 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 345 (3.17), 260 (3.94); ^{1}H NMR ($CDCl_3$) δ 1.02 (3H, t, J = 5.86 Hz, CH_3), 1.62–1.74 (3H, m), 2.01–2.05 (1H, m), 2.36 (3H, s, CH_3Ph), 2.86 (1H, br s, OH), 3.08–3.19 (1H, m), 7.17 (2H, d, J = 8.4 Hz, Ar), 7.64 (2H, d, J = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 7.1, 17.7, 21.3, 27.6, 30.3,

86.6, 126.5, 129.0, 137.6, 140.9, 156.4; ^{77}Se NMR ($CDCl_3$) δ 250.4; HRMS: m/z = 283.04748, calc. for $C_{13}H_{17}NOSe$, found 283.04745.

4-Hydroxy-4,5,6-trimethyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine (3c)

Mp 110.0–111.8 °C; IR (KBr) 3288, 1594 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 343 (2.25), 260 (3.96); ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, d, J = 6.6 Hz, CH_3), 1.37 (3H, s, CH_3), 1.46 (3H, d, J = 7.0 Hz, CH_3), 1.64–1.77 (1H, m, CH), 2.36 (3H, s, $PhCH_3$), 3.05 (1H, br s, OH), 3.88–4.01 (1H, m, CH), 7.17 (2H, d, J = 8.2 Hz, Ar), 7.65 (2H, d, J = 8.2 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 7.4,19.1, 21.3, 25.8, 36.8, 38.3, 90.3, 126.4, 129.0, 137.1, 140.9, 158.4; ^{77}Se NMR ($CDCl_3$) δ 299.3; HRMS: m/z = 297.06312, calc. for $C_{14}H_{19}NOSe$, found 297.06309.

4-Hydroxy-4,6,6-trimethyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine (3d)

Mp 92.0–93.3 °C; IR (KBr) 3316, 1590 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 340 (2.07), 260 (3.96); ^{1}H NMR ($CDCl_3$) δ 1.51 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.64 (3H, s, CH_3), 1.79 (1H, d, J = 14.0 Hz), 1.84 (1H, d, J = 14.0 Hz), 2.36 (3H, s, CH_3Ph), 2.88 (1H, br s, OH), 7.18 (2H, d, J = 7.8 Hz, Ar), 7.68 (2H, d, J = 7.8 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 21.3, 28.9, 33.0, 34.7, 41.7, 46.9, 88.7, 127.0, 129.0, 137.6, 141.0, 158.6; ^{77}Se NMR ($CDCl_3$) δ 439.4; Anal. Calc. for $C_{14}H_{19}NOSe$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.27; H, 6.47; N, 4.63%.

***cis*-4-Hydroxy-6-isopropyl-4-methyl-2-(4-methylphenyl)-5,6-dihydro-4*H*-1,3-selenazine (3e)**

Mp 79.5–80.6 °C; IR (KBr) 3261, 1599 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 349 (1.68), 257 (4.02); ^{1}H NMR ($CDCl_3$) δ 1.01 (6H, d, J = 6.8 Hz, C6-C(CH_3)$_2$), 1.34 (3H, s, CH_3), 1.35 (1H, t, J = 13.4 Hz), 1.85 (1H, q, J = 6.4 Hz), 1.97 (1H, dd, J = 6.4, 13.4 Hz), 2.34 (3H, s, CH_3Ph), 3.37–3.49 (1H, m, C6), 4.01 (1H, br s, OH), 7.15 (2H, d, J = 8.1 Hz, Ar), 7.65 (2H, d, J = 8.1 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 19.8, 20.4, 21.2, 24.0, 33.7, 36.4, 45.3, 88.4, 126.5, 128.9, 137.2, 140.6, 157.6; ^{77}Se NMR ($CDCl_3$) δ 306.5; Anal. Calc. for $C_{15}H_{21}NOSe$: C, 57.87; H, 6.80; N, 4.50. Found: C, 57.92; H, 6.78; N, 4.30%).

***cis*-4-Hydroxy-4-methyl-2-(4-methylphenyl)-6-pentyl-5,6-dihydro-4*H*-1,3-selenazine (3f)**

Mp 66.9–67.7 °C; IR (KBr) 3178, 1590 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 342 (2.37), 258 (4.01); ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, t, J = 6.8 Hz), 1.30–1.33 (6H, m, $(CH_2)_3$), 1.33 (3H, s, CH_3), 1.34–1.42 (2H, m), 1.62–1.68 (1H, m), 1.77–1.84 (1H, m), 1.98 (1H, dd, J = 4.4, 13.6 Hz), 2.33 (3H, s, CH_3Ph), 3.48–3.53 (1H, m, C6), 4.02 (1H, br s, OH), 7.13 (2H, d, J = 8.1 Hz, Ar), 7.63 (2H, d, J = 8.1 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 13.8, 21.2, 22.3, 24.2, 26.7, 31.4, 37.4, 37.4, 39.1, 87.8, 126.5, 128.8, 137.1, 140.5, 157.1; ^{77}Se NMR ($CDCl_3$) δ 339.4; HRMS: m/z = 339.11007, calc. for $C_{17}H_{25}NOSe$, found 339.11003.

***cis*-4-Hydroxy-4-methyl-2-(4-methylphenyl)-6-phenyl-5,6-dihydro-4*H*-1,3-selenazine (3g)**

Mp; 105.3–106.3 °C; IR (KBr) 3260, 1597 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 342 (2.59), 259 (4.08); ^{1}H NMR ($CDCl_3$) δ 1.49 (3H, s, CH_3), 1.96 (1H, t, J = 13.6 Hz), 2.19 (1H, dd, J = 4.4, 13.6 Hz), 2.36 (3H, s, CH_3Ph), 3.13 (1H, br s, OH), 4.69 (1H, dd, J = 4.4, 13.6 Hz, C6), 7.18 (2H, d, J = 7.8 Hz, Ar), 7.24–7.29 (1H, m, Ar), 7.33–7.38 (4H, m, Ar), 7.66 (2H, d, J = 7.8 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 21.4, 24.9, 38.6, 40.2, 88.4 (C4), 126.6, 127.7, 127.9, 128.9, 129.1, 136.9, 140.9, 141.1, 157.6; ^{77}Se NMR ($CDCl_3$) δ 387.4; Anal. Calc. for $C_{18}H_{19}NOSe$: C, 62.60; H, 5.55; N, 4.06. Found: C, 62.32; H, 5.47; N, 3.99%).

5-Hydroxy-3-(4-methylphenyl)-4-aza-2-selenabicyclo[3.3.1]non-3-ene (3h)

Mp 115.1–117.0 °C; IR (KBr) 3264, 1596 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 300 (2.82), 263 (3.93); ^{1}H NMR ($CDCl_3$) δ 1.60–1.65 (2H, m), 1.77–1.811 (2H, m), 1.93 (1H, d, J = 10.6 Hz), 1.99 (2H, s), 2.07 (1H, d, J = 12.5 Hz), 2.34 (3H, s, CH_3Ph), 3.49–3.53 (1H, m), 3.90 (1H, br s, OH), 7.16 (2H, d, J = 7.9 Hz, Ar), 7.64 (2H, d, J = 7.9 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 18.9, 21.2, 33.3, 34.1, 36.2, 39.4, 82.9, 126.4, 128.9, 137.3, 140.6, 158.0; ^{77}Se NMR ($CDCl_3$) δ 380.2; HRMS: m/z = 295.04555, calc. for $C_{14}H_{17}NOSe$, found 295.04745.

4-Ethyl-4-hydroxy-2-pentyl-5,6-dihydro-4*H*-1,3-selenazine (3i)

IR (Neat) 3408, 1713 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 305 (3.34), 245 (3.34); ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 6.6 Hz, CH_3), 0.97 (3H, t, J = 7.5 Hz, CH_3), 1.32 (4H, t, J = 3.6 Hz), 1.47–1.57 (1H, m), 1.58–1.65 (4H, m), 1.98 (1H, dt, J = 4.2, 13.9 Hz), 2.34–2.42 (2H, m), 2.99–3.03 (2H, m), 3.95 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ 7.09, 13.9, 17.2, 22.3, 27.5, 27.7, 29.8, 31.0, 43.5, 86.2, 160.7; ^{77}Se NMR ($CDCl_3$) δ 252.9; HRMS: m/z = 263.07877, calc. for $C_{11}H_{21}NOSe$, found 263.07871.

4-Hydroxy-4,5,6-trimethyl-2-pentyl-5,6-dihydro-4*H*-1,3-selenazine (3j)

IR (Neat) 3246, 1624 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 302 (2.31), 242 (3.42); ^{1}H NMR ($CDCl_3$) δ 0.81 (3H, d, J = 6.8 Hz, CH_3), 0.89 (3H, t, J = 7.1 Hz, CH_3), 1.29 (3H, s, C4-CH_3), 1.22–1.37 (4H, m, $(CH_2)_2$), 1.40 (3H, d, J = 7.0 Hz, CH_3), 1.54–1.67 (3H, m), 2.42 (2H, t, J = 7.5 Hz), 3.78–3.91 (1H, m), 3.88 (br, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 7.2, 13.9, 19.1, 22.3, 26.1, 27.7, 31.0, 36.3, 38.3, 43.0, 89.6, 162.9; ^{77}Se NMR ($CDCl_3$) δ 303.6; HRMS: m/z = 277.09442, calc. for $C_{12}H_{23}NOSe$, found 277.09437.

***cis*-4-Hydroxy-4-methyl-2-pentyl-6-propyl-5,6-dihydro-4*H*-1,3-selenazine (3k)**

IR (Neat) 3242, 1626 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 301 (2.46), 244 (3.45); ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 6.4 Hz, CH_3), 0.94 (3H, t, J = 7.1 Hz, CH_3), 1.29 (3H, s, C4-CH_3), 1.29–1.48 (6H, m), 1.51–1.69 (4H, m), 1.73–1.86 (1H, m), 1.96 (1H, dt, J = 4.1, 13.5 Hz), 2.41 (2H, t, J = 7.0 Hz), 3.41–3.56 (1H, m, C6), 4.30 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ 13.8, 13.9, 20.3, 22.3, 24.8, 27.7, 31.0, 36.6, 39.3, 39.7, 43.0, 87.3, 161.4; ^{77}Se NMR ($CDCl_3$) δ 345.1; HRMS: m/z = 291.11007, calc. for $C_{13}H_{25}NOSe$, found 291.11001.

***cis*-4-Hydroxy-4-methyl-2-pentyl-6-phenyl-5,6-dihydro-4*H*-1,3-selenazine (3l)**

IR (Neat) 3198, 1634 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 292 (3.41), 241 (3.95); ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 6.8 Hz, CH_3), 1.32–1.34 (4H, m, $(CH_2)_2$), 1.43 (3H, s, CH_3), 1.61–1.66 (2H, m, CH_2), 1.92 (1H, t, J = 13.7 Hz), 2.12 (1H, dd, J = 4.0,13.7 Hz), 2.46 (2H, t, J = 7.1 Hz), 4.61 (1H, dd, J = 4.0, 13.7 Hz, C6), 4.63 (br, 1H, OH), 7.24–7.34 (5H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.3, 25.2, 27.6, 31.0, 38.7, 39.4, 42.7, 87.7, 127.5, 127.7, 128.8, 140.9, 162.1; ^{77}Se NMR ($CDCl_3$) δ 395.6; HRMS: m/z = 325.09442, calc. for $C_{16}H_{23}NOSe$, found 325.09437.

5-Hydroxy-3-pentyl-4-aza-2-selenabicyclo[3.3.1]non-3-ene (3m)

IR (Neat) 3214, 1619 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 304 (3.14), 236 (3.43); 1 H NMR ($CDCl_3$) δ 0.90 (3H, t, J = 7.1 Hz), 1.33–1.37 (5H, m), 1.54–1.67 (3H, m), 1.73–1.80 (2H, m), 1.88–2.02 (4H, m), 2.45 (2H, q, J = 7.6 Hz), 3.80–3.83 (1H, m), 4.58 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ 13.8, 18.9, 22.3, 27.9, 31.0, 33.2, 34.4, 35.9, 39.5, 43.5, 82.4, 163.3;

^{77}Se NMR ($CDCl_3$) δ 385.7; HRMS: m/z = 275.07877, calc. for $C_{12}H_{21}NOSe$, found 275.07873.

2-(4-Methylphenyl)-4-(2-phenylvinyl)-6-phenyl-6*H*-1,3-selenazine (3n)

Mp 54.5–56.0 °C; IR (KBr) 1599 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log (ε/dm^3 mol^{-1} cm^{-1})) 292 (4.33), 243 (4.13); ^{1}H NMR ($CDCl_3$) δ 2.39 (3H, s, CH_3Ph), 4.97 (1H, d, J = 6.0 Hz), 5.23 (1H, d, J = 1.1 Hz), 5.34 (1H, d, J = 6.0 Hz), 6.93 (1H, d, J = 15.8 Hz), 7.20–7.45 (6H, m, Ar), 7.54 (2H, dd, J = 1.3, 7.0 Hz, Ar), 7.93 (2H, dd, J = 1.3, 7.0 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ 21.4, 38.0, 108.8, 126.8, 127.6, 127.7, 128.2, 128.6, 128.8, 129.0, 129.3, 129.5, 136.9, 137.3, 141.8, 142.3, 148.4, 161.5; ^{77}Se NMR ($CDCl_3$) δ 350.1; HRMS: m/z = 415.08386, calc. for $C_{25}H_{21}NOSe$, found 415.08381.

References

1 (*a*) J. Goerdeler and H. Horstman, *Chem. Ber.*, 1960, **93**, 671; (*b*) J. E. Jansen and R. A. Mathes, *J. Am. Chem. Soc.*, 1955, **77**, 2866; (*c*) J. L. Garraway, *J. Chem. Soc.*, 1964, 4008; (*d*) T. Kappe and W. Golser, *Synthesis*, 1972, 312; (*e*) S. Hoff and A. P. Blok, *Rec. Trav. Chim.*, 1973, **92**, 631; (*f*) W. Hanefeld, *Arch. Pham.* (*Weinheim*), 1977, **310**, 273; (*g*) W. Schroth, R. Spitzner, B. Koch, S. Freitag and D. Mielke, *Tetrahedron*, 1982, **38**, 937; (*h*) W. Hanefeld, *Arch. Pham.* (*Weinheim*), 1984, **317**, 297; (*i*) T. Okawara, H. Kashihara and M. Furukawa, *Chem. Pharm. Bull.*, 1985, **33**, 3479; (*j*) P. Perjési, D. Szabó, G. Batta and A. Földesi, *Tetrahedron Lett.*, 1987, **28**, 571; (*k*) P. Perjési, D. Szabó, G. Batta and A. Földesi, *Acta Chim. Hung.*, 1986, **122**, 119; (*l*) D. Briel, J. Sieler, G. Wagner and W. Schade, *Phosphorus and Sulfur*, 1988, **35**, 55; (*m*) A. D. Shutalev, M. T. Pagaev and L. A. Ignatova, *Zh. Org. Khim.*, 1991, **27**, 1274; (*n*) N. Yasuda, M. Karikomi and T. Toda, *Chem. Lett.*, 1995, 1141; (*o*) A. Katritzky, C. W. Rees and E. F. V. Scriven, *Comprehensive Heterocyclic Chemistry II. A Review of the Literature 1982–1995*, Elsevier Science, Oxford, 1996, vol. 1–11; (*p*) H. Gröger, D. Tehranfar, J. Martens, J. R. Goerlich, H. Thönnessen, P. G. Jones and R. Schmutzler, *Heteroatom Chem.*, 1997, **8**, 1997; (*q*) T. Toda, M. Karikomi and N. Yasuda, *Reviews on Heteroatom Chemistry*, ed. S. Oae, MYU, Tokyo, 1997, vol. 16, p. 119.

2 (*a*) P. C. Srivastava and R. K. Robins, *J. Med. Chem.*, 1983, **26**, 445; (*b*) Y. Kumar, R. Green, D. S. Wise, L. L. Wotring and L. B. Townsend, *J. Med. Chem.*, 1993, **36**, 3849; (*c*) Y. Kumar, R. Green, K. Z. Borysko, D. S. Wise, L. L. Wotring and L. B. Townsend, *J. Med. Chem.*, 1993, **36**, 3843.

3 (*a*) R. M. Kedar, N. N. Vidhale and M. M. Chincholkar, *Orient. J. Chem.*, 1996, **12**, 301; (*b*) A. W. Raut and A. G. Doshi, *Orient. J. Chem.*, 1995, **11**, 205; (*c*) J. L. Vennerstrom, M. T. Makler, C. K. Angerhofer and J. A. Williams, *Antimicrob. Agents Chemother.*, 1995, **39**, 2671.

4 R. Jansen, B. Kunze, H. Reichenbach, E. Jurkiewicz, G. Hunsmann and G. Höfle, *Liebigs Ann. Chem.*, 1992, 357.

5 (*a*) V. I. Cohen, *Synthesis*, 1979, 66; (*b*) V. I. Cohen, *J. Heterocycl. Chem.*, 1979, **16**, 13; (*c*) A. Shafiee, A. Mazloumi and V. I. Cohen, *J. Heterocycl. Chem.*, 1979, **16**, 1563; (*d*) M. Takahashi, S. Watanabe and T. Kasai, *Heterocycles*, 1980, **14**, 1921; (*e*) C. Bochu, A. Couture and P. Grandclaudon, *J. Org. Chem.*, 1988, **53**, 4852; (*f*) A. Shafiee, A. Shafaati and B. Habibi-Khameneh, *J. Heterocycl. Chem.*, 1989, **26**, 709; (*g*) M. Sekiguchi, A. Ogawa, S. Fujiwara, N. Kambe and N. Sonoda, *Chem. Lett.*, 1990, 913; (*h*) V. S. Brovarets and R. N. Vydzhak, *Russ. J. Gen. Chem.*, 1993, **63**, 733; (*i*) D. Dubreuil, J. P. Pradère, N. Giraudeau, M. Goli and F. Tonnard, *Tetrahedron Lett.*, 1995, **36**, 237; (*j*) A. Shafiee and M. Etebari, *J. Sci.*, *Islamic Repub. Iran*, 1995, **6**, 166; (*k*) K. Shimada, Y. Matsuda, S. Hikage, Y. Takeishi and Y. Takikawa, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 1037.

6 (*a*) A. Ogawa, J. Miyake, N. Kambe, S. Murai and N. Sonoda, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 1448; (*b*) V. I. Cohen, *Synthesis*, 1978, 768; (*c*) K. Shimada, S. Hikage, Y. Takeishi and Y. Takikawa, *Chem. Lett.*, 1990, 1403; (*d*) L.-L. Lai and D. H. Reid, *Synthesis*, 1993, 870; (*e*) X.-R. Zhao, M.-D. Ruan, W.-Q. Fan and X.-J. Zhou, *Synth. Commun.*, 1994, **24**, 1761.

7 (*a*) H. Ishihara, M. Yoshimi, N. Hara, H. Ando and S. Kato, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 835; (*b*) H. Ishihara, M. Yoshimi and S. Kato, *Angew. Chem.*, *Int. Ed. Engl.*, 1990, **29**, 530; (*c*) S. Kato, H. Kageyama, Y. Kawamura, T. Murai and H. Ishihara, *Chem. Ber.*, 1992, **125**, 417; (*d*) S. Kato, T. Komuro, T. Kanda, H. Ishihara and T. Murai, *J. Am. Chem. Soc.*, 1993, **115**, 3000; (*e*) Y. Kawahara, S. Kato, T. Kanda, T. Murai and H. Ishihara, *J. Chem. Soc.*, *Chem. Commun.*, 1993, **3**, 277; (*f*) S. Kato, T. Kawachi, K. Ibi, S. Nakaiida, K. Kawai, T. Kanda, T. Murai and H. Ishihara, *Heteroatom Chem.*, 1995, **6**, 215.

8 H. Ishihara and Y. Hirabayashi, *Chem. Lett.*, 1976, 203.

9 H. Ishihara, K. Yoshimura and M. Koketsu, *Chem. Lett.*, 1998, 1287.

10 M. Koketsu, Y. Miyajima and H. Ishihara, *Chem. Lett.*, 1998, 645.

11 (*a*) E. R. Cullen, F. S. J. Guziec, C. J. Murphy, T. C. Wong and K. K. Andersen, *J. Am. Chem. Soc.*, 1981, **103**, 7055; (*b*) T. C. Wong, F. S. J. Guziec and C. A. Moustakis, *J. Chem. Soc.*, *Perkin Trans. 2*, 1983, 1471; (*c*) T. Murai, K. Kakami, K. Hayashi, T. Komura, H. Takada, M. Fujii, T. Kanda and S. Kato, *J. Am. Chem. Soc.*, 1997, **119**, 8592.

12 (*a*) M. Garreau, G. J. Martin, M. L. Martin, J. Morel and C. Paulmier, *Org. Magn. Reson.*, 1974, **6**, 648; (*b*) J. R. Bartels-Keiith, M. T. Burgess and J. M. Stevenson, *J. Org. Chem.*, 1977, **42**, 3725; (*c*) T. C. Wong and E. M. Engler, *J. Mol. Struct.*, 1980, **67**, 279.

13 In ^{13}C NMR ($CDCl_3$), the Michael adduct, *Se*-3-oxobutyl 4-methylbenzenecarboselenoimidate, as intermediate was observed. Two peaks were observed at δ = 193.7 and 207.0, which were assigned to the $^{13}C{=}NH_2$ and the carbonyl carbon resonance of the Michael adduct, respectively. ^{13}C NMR ($CDCl_3$) δ 18.4, 21.7, 29.8, 44.1, 128.3, 129.8, 140.0, 143.6, 193.7 (SeC=NH) and 207.0 (C=O).

Paper 8/09131E