Synthesis and Characterization of 2-Iminoperhydro-1,3-selenazin-4-ones by Reaction of *N*,*N*'-Disubstituted Selenoureas with Acryloyl Chloride

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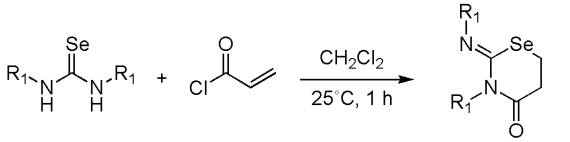
There are many selenium-containing heterocyclic compounds found in the literature [1]. Of these many are potential pharmaceutical agents [2]. The use of selenoureas as the precursors is one of the most efficient methods for the synthesis of heterocyclic compounds containing selenium [3]. We describe here the synthesis of 2-imino perhydro-1,3-selenazin-4-ones by the reaction of selenoureas with acryloyl chloride.

Various reactions were investigated to establish the optimal conditions for the synthesis of 3-isopropyl-2-isopropyliminoperhydro-1,3-selenazin-4-one (**3a**). The reaction of *N*,*N*'-diisopropylselenourea (**1a**) with acryloyl chloride (**2**) was carried out in dichloromethane under an argon atmosphere. When reaction was carried out at 0 °C, 25 °C and at reflux, the yield of **3a** was 48, 88 and 63%, respectively. Next, the optimal molar ratio of reagents was investigated at 25 °C. When 1, 2 and 3 equiv. of **1a** were used with respect to **2**, the yield of **3a** was 70, 88 and 48%, respectively.

Scheme 1



1a-d **2** **3a-d**

1	R_1	3	Yield (%)
a	$(CH_3)_2CH_2$-	a	88
b	C_6H_{11} -	b	73
c	C_6H_5-	c	74
d	2-$CH_3C_6H_4$-	d	47

Using the optimal reaction conditions, four kinds of 2-iminoperhydro-1,3-selenazin-4-ones **3a-d** were prepared from the reaction of corresponding *N*,*N*'-disubstituted selenoureas **1a-d** with acryloyl chloride **2** (Scheme 1). The structures of **3a-d** were confirmed by studies of IR, MS, ^{1}H, ^{13}C, ^{77}Se, 2D NMR spectra and elemental analysis. The crystal and molecular structure of **3a** was determined using X-ray diffraction analysis (Figure 1) [4]. The bond length of C2-N10 in **3a** is 1.262(3) Å and is clearly a double bond [5]. The sum of the three angles around each of the C2 and N3 atoms is 359.9(3)° and 358.7(3)°, respectively. The torsion angles of Se1-C2-N3-C4, C2-N3-C4-C5, N3-C4-C5-C6, C4-C5-C6-Se1, C2-Se1-C6-C5 and C6-Se1-C2-N3 are 39.7(3), -16.9(3), -42.9(3), 69.3(2), -40.2(2) and -8.2(2)°, respectively. The two C-N bond lengths of both N3-C4 (1.382(3) Å) and C2-N3 (1.426(3) Å) in **3a** also are shorter than the usual value of 1.47 Å [5,6]. These results can be attributed to the delocalization of the two π electrons and lone pair electrons on N3. To the best of our knowledge, there are hardly any reports regarding crystal structures of 1,3-selenazine thus far [7], while crystal structures of 1,3-selenazoles have been reported [8]. Both methylene protons at the C5 and C6 of **3a** are the same chemical shift (δ 3.01) and singlet peak on the ^{1}H NMR spectrum as it happens, cross peaks between the methylene protons and the carbons at the C5 (δ 15.7) and C6 (δ 38.1) were clearly observed on the HMQC spectrum. The ^1J (^{77}Se-^{13}C) values (in the case of **3a**, J = 30.0 Hz) at the C6 carbon and the ^2J (^{77}Se-^{1}H) values (in the case of **3a**, J = 11.7 Hz) at the C6 proton of **3** were observed on the proton-decoupled ^{13}C NMR and ^{1}H NMR spectra. Though the 3-alkyl-2-alkyliminoperhydro-

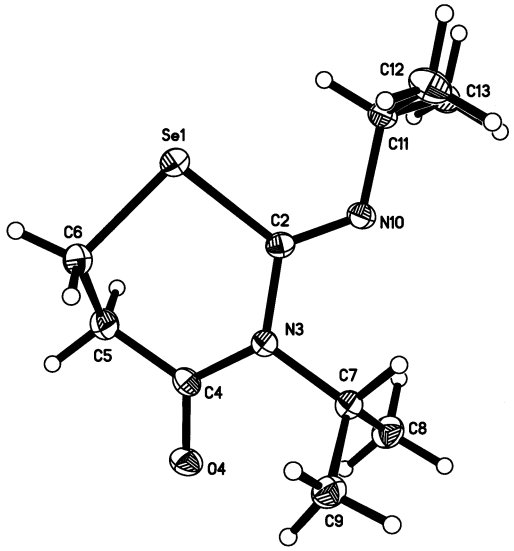


Figure 1. ORTEP diagram (50% thermal ellipsoids) of compound **3a**.

1,3-selenazin-6-one is a possible product, the possibility of its formation was ruled out by the observation of the ^2J (^{77}Se-^{1}H) and ^1J (^{77}Se-^{13}C) values at the C6 carbon of **3**. Previously, though it was reported that the reaction of selenoureas with α-haloacyl halides led the formation of a 5-memberd ring 2-amino-1,3-selenazol-4-one [8,9], in the present study, it was confirmed that the reactions using *N*,*N*'-disubstituted selenoureas and α,β-unsaturated acyl chlorides give the corresponding 6-membered ring 1,3-selenazine **3** without the presence of activator.

EXPERIMENTAL

Selenoureas were synthesized according to previously described procedures [10]. The ^{77}Se chemical shifts are expressed in ppm deshielded with respect to near Me_2Se in $CDCl_3$. ^2J (^{77}Se-^{1}H) values and ^1J (^{77}Se-^{13}C) values are the ^{77}Se satellites of the ^{1}H NMR spectra and proton-decoupled ^{13}C NMR spectra.

General Procedure for Synthesis of 3-Isopropyl-2-isopropylimino-perhydro-1,3-selenazin-4-one (**3a**).

Acryloyl chloride (0.5 mmol) was added to stirred solution of *N*,*N*'-diisopropylselenourea (1.0 mmol) in dry dichloromethane (25 mL) at 25 °C under an argon atmosphere. The reaction mixture was stirred for 1 h at 25 °C. The mixture was extracted with diethyl ether (50 mL) and washed with saturated sodium chloride solution (30 mL). The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel with dichloromethane:diethyl ether (40:1) to give **3a** (0.23 g, 88% yield) as white crystals. Mp: 55.0–56.0 °C; IR (KBr): 1605, 1672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (6H, d, J = 5.9 Hz), 1.38 (6H, d, J = 6.8 Hz), 3.01 (4H, s, ^2J (^{77}Se-^{1}H) = 11.7 Hz), 3.41-3.50 (1H, m), 4.83-4.93 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7 (^1J (^{77}Se-^{13}C) = 30.0 Hz), 20.3, 23.4, 38.1, 50.1, 55.6, 140.2, 170.8; ^{77}Se NMR (78.2 MHz, $CDCl_3$): δ 367.3; MS (CI): m/z = 263 [M$^+$ + 1]; HRMS calcd. for $C_{10}H_{18}N_2OSe$: 262.0583; found: 262.0591. X-ray Crystallographic Data: Single crystals were grown from CH_2Cl_2-hexane. Crystal system Monoclinic; Space group $P2_1/c$; T = 190(2) K; a = 14.4860(14) Å, b = 10.2630(10) Å, c = 8.2880(8) Å, β = 105.840(5)°, V = 1185.4(2) Å^3, Z = 4; D_c = 1.464 g cm^{-3}; Crystal size 0.40 x 0.30 x 0.08 mm; Mo Kα (0.71073 Å); Diffractometer KappaCCD; θ range for data collection 2.9 to 27.5°, Limiting indices -18≤h≤18, -12≤k≤13, -10≤l≤10; Reflections collected: 20391, Independent reflections: 2702 [R_{int} = 0.0357]; Refinement method: Full-matrix least-squares on F^2, Goodness of fit on F^2: 1.042, Final least squares cycle included non-hydrogen atoms with anisotropic thermal parameters and hydrogen atoms at fixed positions with isotropic thermal parameters. Final R indices [I>2σ(I)] $R1$ = 0.0326, $wR2$ = 0.0784 R indices (all data) $R1$ = 0.0443, $wR2$ = 0.0839, Largest diff. peak and hole 0.484 and -0.740 e. Å^{-3} for all data [4].

3-Cyclohexyl-2-cyclohexyliminoperhydro-1,3-selenazin-4-one (**3b**).

This compound was obtained as a white solid. Mp: 84.8 – 86.0 °C; IR (KBr): 1610, 1665 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 - 1.80 (20H, m), 2.97 – 3.04 (4H, m), 3.16 – 3.21 (1H, m), 4.40 – 4.50 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0, 24.2, 25.7, 26.4, 30.0, 33.2, 38.2, 58.4, 63.3, 140.1, 170.7; ^{77}Se NMR (76 MHz, $CDCl_3$): δ 376.7; MS (CI): m/z = 343 [M$^+$+1].

Anal. Calcd for $C_{16}H_{26}N_2OSe$: C, 56.30; H, 7.68; N 8.21. Found: C, 56.36; H, 7.63; N, 8.09.

3-Phenyl-2-phenyliminoperhydro-1,3-selenazin-4-one (**3c**).

This compound was obtained as a white solid. Mp: 156.0 – 158.0 °C; IR (KBr): 1579, 1697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.07 (2H, dd, J = 5.8, 7.5 Hz), 3.33 (2H, dd, J = 5.7, 6.9 Hz), 6.47 – 7.47 (10H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.3 (^1J (^{77}Se-^{13}C) = 56.2 Hz), 37.3, 120.1, 124.5, 127.9, 128.5, 129.0, 129.2, 139.2, 149.0, 149.1, 170.6; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 357.1; MS (CI): m/z = 331 [M$^+$+1]; HMRS calcd. for $C_{16}H_{14}N_2OSe$: 330.0271; found 330.0290.

3-(2-Methylphenyl)-2-(2-methylphenyl)iminoperhydro-1,3-selenazin-4-one (**3d**).

This compound was obtained as a red solid. Mp: 40.0 – 42.0 °C; IR (KBr): 1611, 1697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.99 (3H, s), 2.26 (3H, s), 3.03 – 3.15 (2H, m), 3.28 – 3.40 (2H, m), 6.65-7.37 (8H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.1, 17.6, 18.0, 37.2, 119.5, 124.5, 126.3, 126.9, 128.3, 128.5, 128.6, 130.5, 130.8, 135.5, 138.5, 147.5, 147.6, 170.2; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 357.5; MS (CI): m/z = 359 [M$^+$+1]; HMRS calcd. for $C_{18}H_{18}N_2OSe$: 358.0583; found 358.0562.

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[4] CCDC 229583 contains the supplementary crystallographic data for **3a**. This data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge

Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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