FULL PAPER

Synthesis of 1,3,5-Triazepineselone Derivatives from Acyl Isoselenocyanates and Benzene-1,2-diamine

by **Issa Yavari*** and **Shabnam Mosaferi**

Department of Chemistry, Tarbiat Modares University, P.O. Box 14115 – 175, Tehran, Iran
(phone: + 98-21-82883465; fax: + 98-21-82883455; e-mail: yavarisa@modares.ac.ir)

Tandem reaction between acyl isoselenocyanates, generated from acyl chlorides and KSeCN, and benzene-1,2-diamine in acetone at room temperature, gave 1,3,5-triazepineselone derivatives in moderate to good yields.

Introduction. – Triazepines are seven-membered heterocycles with three N-atoms at various positions. Recently, triazepine derivatives with a wide range of bioactivities have been synthesized [1]. Selenium is a trace element, essential for efficient operation of the human body. Originally, selenium was considered as a poison and dangerous component, until 1957 it was identified as an essential nutrient for bacteria, mammals, and birds [2]. In recent years, increasing attention has been paid to organoselenium compounds because of their diverse pharmaceutical and synthetic applications [3 – 11].

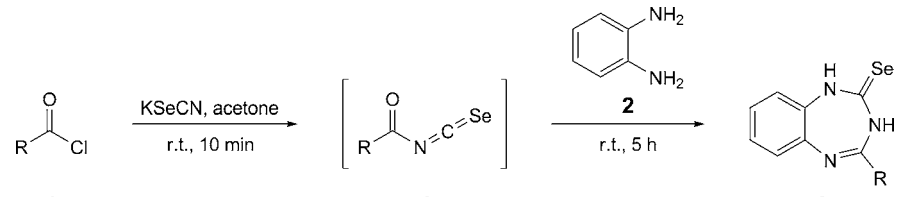
Acyl isoselenocyanates are useful intermediates, which were prepared by the reaction of acyl chlorides with KSeCN [12]. The acyl isoselenocyanates were never isolated. The existence of these intermediates was confirmed by their reactions with nucleophiles [13 – 15].

As part of our current studies on the synthesis of organoselenium compounds [16], we report a simple and efficient procedure for the synthesis of 4-substituted 1,3-dihydro-2*H*-1,3,5-benzotriazepine-2-selone derivatives **3** *via* tandem reaction of acyl isoselenocyanates, generated from acyl chlorides and KSeCN, and benzene-1,2-diamine (**2**) in acetone at room temperature (*cf. Table*).

Results and Discussion. – Initially, BzCl (**1a**) was selected as the model substrate. Among several solvents screened, acetone was the best. When the reaction was performed in acetone at room temperature for 5 h, product **3a** was obtained in 74% yield (*Table*). Thus, the optimized reaction conditions used were acyl chloride (1 mmol), KSeCN (1 mmol), and benzene-1,2-diamine (1 mmol), in acetone at room temperature.

The structures of compounds **3a** – **3g** were assigned on the basis of their IR, ^{1}H- and ^{13}C-NMR, and MS data. The ^{1}H-NMR spectrum of **3a** exhibited two *singlet*s for NH H-atoms (δ(H) 9.55 and 12.77 ppm), along with characteristic *multiplet*s for the aromatic H-atoms. The ^{13}C-NMR spectrum of **3a** exhibited twelve signals in agreement with the proposed structure. The MS spectrum of **3a** displayed the molecular-ion peak at *m*/*z* 300. The NMR spectra of compounds **3b** – **3g** are similar to those of **3a**, except for the substituents, which showed characteristic signals in the appropriate regions of the spectra.

Table. *Formation of 4-Substituted 1,3-Dihydro-2*H*-1,3,5-benzotriazepine-2-selones* **3**



1 **4** **3**

Entry	R	Product	Yield [%]
1	Ph	**3a**	74
2	4-Cl–C_6H_4	**3b**	80
3	4-O_2N–C_6H_4	**3c**	84
4	2-Cl–C_6H_4	**3d**	78
5	4-Me–C_6H_4	**3e**	67
6	Bn	**3f**	73
7	2-Me–C_6H_4	**3g**	60

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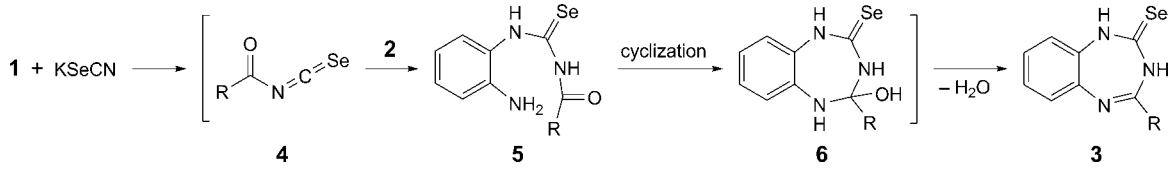
Scheme



A plausible mechanism for the formation of compounds **3** is given in the *Scheme*. The acyl isoselenocyanate **4**, formed from **1** and KSeCN, undergoes nucleophilic attack by **2** to afford intermediate **5**. This intermediate is converted to product **3** *via* cyclization and elimination of H_2O.

In conclusion, acyl isoselenocyanate intermediates, generated from acyl chlorides and KSeCN, are trapped by benzene-1,2-diamine to afford 1,3,5-triazepineselone derivatives. The potential diversity of this type of reaction and available starting materials are the main advantages of this methodology.

Experimental Part

General. All chemicals were obtained commercially and used without further purification. IR Spectra: *Shimadzu-IR-460* spectrometer; in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker DRX-500 Avance* instrument at 500.1 and 125.7 MHz, resp.; δ in ppm, *J* in Hz. EI-MS: *Finnigan-MAT-8430EI-MS* mass spectrometer; at 70 eV; in *m/z* (rel. %). Elemental analyses: *Vario EL III CHNOS* elemental analyzer.

General Procedure for the Preparation of Compounds **3**. To a stirred soln. of KSeCN (0.144 g, 1 mmol) in acetone (2 ml), a soln. of acyl chloride **1** (1 mmol) in acetone (2 ml) was added at r.t. After 10 min, a soln. of benzene-1,2-diamine (**2**; 0.108 g, 1 mmol) in acetone (2 ml) was added. After completion of the reaction (*ca.* 5 h; TLC (AcOEt/hexane 1:3) monitoring), the precipitate was filtered and washed with Et_2O to give the product.

*1,3-Dihydro-4-phenyl-2*H*-1,3,5-benzotriazepine-2-selone* (**3a**). Yield: 0.22 g (74%). Cream powder. M.p. 193° (dec.). IR (KBr): 3426, 1654, 1525. ^1H-NMR: 6.97 – 6.98 (*m*, 1 arom. H); 7.21 (*t*, $^3J = 7.2$, 1 arom. H); 7.47 – 7.52 (*m*, 3 arom. H); 7.64 (*t*, $^3J = 7.3$, 1 arom. H); 7.84 – 7.88 (*m*, 3 arom. H); 9.55 (*s*, NH); 12.77 (*s*, NH). ^{13}C-NMR: 121.7 (C); 125.9 (C); 127.4 (CH); 127.8 (2 CH); 128.9 (CH); 129.3 (2 CH); 131.2 (CH); 134.0 (CH); 134.5 (CH); 140.3 (C); 166.8 (C=N); 182.2 (C=Se). EI-MS: 300 (4, M^+), 223 (9), 210 (27), 194 (100), 179 (21), 121 (7), 106 (68), 90 (18), 77 (56). Anal. calc. for $C_{14}H_{11}N_3Se$ (300.22): C 56.01, H 3.69, N 14.00; found: C 56.46, H 3.74, N 14.08.

*4-(4-Chlorophenyl)-1,3-dihydro-2*H*-1,3,5-benzotriazepine-2-selone* (**3b**). Yield: 0.27 g (80%). Green powder. M.p. 196° (dec.). IR (KBr): 3422, 1668, 1519. ^1H-NMR: 7.49 – 7.53 (*m*, 4 arom. H); 7.80 – 7.87 (*m*, 4 arom. H); 9.47 (*s*, NH); 12.67 (*s*, NH). ^{13}C-NMR:125.9 (C); 127.5 (CH); 128.1 (C); 129.2 (2 CH); 129.7 (2 CH); 130.4 (C); 131.6 (CH); 134.5 (CH); 136.9 (C); 140.9 (CH); 165.6 (C=N); 182.1 (C=Se). EI-MS: 334 (3, M^+), 258 (20), 244 (78), 223 (18), 196 (8), 138 (100), 111 (43), 90 (16), 76 (23). Anal. calc. for $C_{14}H_{10}ClN_3Se$ (334.66): C 50.24, H 3.01, N 12.56; found: C 50.56, H 3.05, N 12.67.

*1,3-Dihydro-4-(4-nitrophenyl)-2*H*-1,3,5-benzotriazepine-2-selone* (**3c**). Yield: 0.29 g (84%). Pale-brown powder. M.p. 194° (dec.). IR (KBr): 3433, 1625, 1534, 1337. ^1H-NMR: 7.16 – 7.54 (*m*, 3 arom. H); 7.96 – 8.32 (*m*, 5 arom. H); 10.66 (*s*, NH); 12.62 (*s*, NH). ^{13}C-NMR: 122.5 (CH); 123.4 (2 CH); 123.6 (CH); 125.9 (C); 129.2 (CH); 129.7 (2 CH); 129.9 (C); 135.3 (C); 140.2 (C); 149.0 (CH); 167.9 (C=N); 182.4 (C=Se). EI-MS: 345 (2, M^+), 255 (20), 239 (81), 223 (11), 196 (95), 149 (16), 122 (21), 106 (100), 90 (9). Anal. calc. for $C_{14}H_{10}N_4O_2Se$ (345.21): C 48.71, H 2.92, N 16.23; found: C 49.16, H 2.89, N 16.32.

*4-(2-Chlorophenyl)-1,3-dihydro-2*H*-1,3,5-benzotriazepine-2-selone* (**3d**). Yield: 0.26 g (78%). Pale-green powder. M.p. 191° (dec.). IR (KBr): 3436, 1634, 1520. ^1H-NMR: 7.36 – 7.49 (*m*, 3 arom. H); 7.51 – 7.56 (*m*, 3 arom. H); 7.88 – 7.97 (*m*, 2 arom. H); 11.89 (*s*, NH); 12.63 (*s*, NH). ^{13}C-NMR: 123.8 (CH); 128.1 (CH); 130.5 (CH); 130.9 (CH); 131.2 (CH); 131.3 (C); 131.5 (CH); 131.7 (CH); 132.3 (C); 132.4 (C); 133.1 (C); 133.5 (CH); 167.5 (C=N); 182.6 (C=Se). EI-MS: 334 (3, M^+), 258 (12), 244 (15), 228 (8), 223 (9), 111 (20), 106 (39), 90 (53), 76 (100). Anal. calc. for $C_{14}H_{10}ClN_3Se$ (334.66): C 50.24, H 3.01, N 12.56; found: C 50.69, H 3.07, N 12.69.

*1,3-Dihydro-4-(4-methylphenyl)-2*H*-1,3,5-benzotriazepine-2-selone* (**3e**). Yield: 0.21 g (67%). Pale-green powder. M.p. 188° (dec.). IR (KBr): 3429, 1632, 1505. ^1H-NMR: 2.49 (*s*, Me); 7.10 – 7.13 (*m*, 2 arom. H); 7.33 (*d*, $^3J = 7.2$, 2 arom. H); 7.43 – 7.46 (*m*, 2 arom. H); 8.01 – 8.04 (*m*, 2 arom. H); 10.21 (*s*, NH); 12.13 (*s*, NH). ^{13}C-NMR: 21.6 (Me); 127.3 (C); 127.6 (CH); 128.2 (CH); 128.5 (C); 129.1 (2 CH); 129.4 (2 CH); 134.8 (C); 135.2 (CH); 143.9 (C); 144.3 (CH); 168.5 (C=N); 182.3 (C=Se). EI-MS: 314 (8, M^+), 238 (100), 223 (11), 208 (7), 196 (9), 118 (43), 106 (24), 91 (35), 76 (52). Anal. calc. for $C_{15}H_{13}N_3Se$ (314.24): C 57.33, H 4.17, N 13.37; found: C 57.68, H 4.22, N 13.48.

*4-Benzyl-1,3-dihydro-2*H*-1,3,5-benzotriazepine-2-selone* (**3f**). Yield: 0.23 g (73%). Brown powder. M.p. 186° (dec.). IR (KBr): 3412, 1673, 1519. ^1H-NMR: 3.74 (*s*, CH_2); 7.23 – 7.29 (*m*, 4 arom. H); 7.31 – 7.34 (*m*, 4 arom. H); 7.71 – 7.73 (*m*, 1 arom. H); 11.98 (*s*, NH); 12.47 (*s*, NH). ^{13}C-NMR: 42.2 (CH_2); 125.3 (C); 126.5 (CH); 127.0 (CH); 127.6 (C); 128.2 (CH); 128.4 (2 CH); 129.1 (CH); 129.4 (2 CH); 134.1 (C); 135.6 (CH); 169.6 (C=N); 181.5 (C=Se). EI-MS: 314 (9, M^+), 237 (43), 223 (17), 208 (10), 196 (21), 118 (38), 106 (29), 91 (100), 77 (34). Anal. calc. for $C_{15}H_{13}N_3Se$ (314.24): C 57.33, H 4.17, N 13.37; found: C 57.62, H 4.22, N 13.49.

*1,3-Dihydro-4-(2-methylphenyl)-2*H*-1,3,5-benzotriazepine-2-selone* (**3g**). Yield: 0.19 g (60%). Pale-yellow powder. M.p. 189° (dec.). IR (KBr): 3425, 1625, 1545. ^1H-NMR: 2.31 (*s*, Me); 7.20 – 7.40 (*m*, 6 arom. H); 7.90 – 7.95 (*m*, 2 arom. H); 12.10 (*s*, NH); 12.82 (*s*, NH). ^{13}C-NMR: 20.2 (Me); 125.9 (C); 126.3 (CH); 127.8 (C); 128.5 (CH); 128.9 (CH); 129.7 (C); 131.4 (CH); 131.9 (CH); 132.7 (C); 134.6 (CH); 135.3 (CH); 136.9 (CH); 171.3 (C=N); 182.4 (C=Se). EI-MS: 314 (9, M^+), 238 (100), 223 (13), 208 (10), 196 (6), 118 (26), 106 (7), 91 (20), 76 (48). Anal. calc. for $C_{15}H_{13}N_3Se$ (314.24): C 57.33, H 4.17, N 13.37; found: C 57.67, H 4.22, N 13.46.

REFERENCES

[1] M. A. Ibrahim, N. M. El-Gohary, *Heterocycles* **2014**, *89*, 1125.
[2] K. Schwarz, C. M. Foltz, *J. Am. Chem. Soc.* **1957**, *79*, 3292.
[3] C. F. Bortolatto, P. M. Chagas, E. A. Wilhelm, G. Zeni, C. W. Nogueira, *J. Enzyme Inhib. Med. Chem.* **2013**, *28*, 677.
[4] P. M. Chagas, C. F. Bortolatto, E. A. Wilhelm, J. A. Roehrs, C. W. Nogueira, *Behav. Pharmacol.* **2013**, *24*, 37.
[5] D. R. Garud, M. Koketsu, H. Ishihara, *Molecules* **2007**, *12*, 504.
[6] H. Heimgartner, Y. Zhou, P. K. Atanassov, G. L. Sommen, *Phosphorus, Sulfur Silicon Relat. Elem.* **2008**, *183*, 840.
[7] M. Ninomiya, D. R. Garud, M. Koketsu, *Heterocycles* **2010**, *81*, 2027.

[8] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2010**, *93*, 395.
[9] Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2011**, *94*, 1575.
[10] K. Kobayashi, Y. Yokoi, *Helv. Chim. Acta* **2012**, *95*, 761.
[11] A. M. Pieczonka, K. Ciepielowski, Z. Cebulska, G. Mlostoń, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2013**, *96*, 397.
[12] I. B. Douglass, *J. Am. Chem. Soc.* **1937**, *59*, 740.
[13] Y. Zhou, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 539.
[14] M. Koketsu, Y. Yamamura, H. Aoki, H. Ishihara, *Phosphorus, Sulfur Silicon Relat. Elem.* **2006**, *181*, 2699.
[15] F. Mohr, *J. Heterocycl. Chem.* **2014**, *51*, 1435.
[16] I. Yavari, Z. Taheri, M. Nematpour, A. Sheikhi, *Helv. Chim. Acta* **2015**, *98*, 343.

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