# Preparation of Some 1,3-Selenazin-4-ones

Masataka YOKOYAMA,* Katsushi KUMATA, Hidekatsu HATANAKA, and Tadashi SHIRAISHI
Department of Chemistry, Faculty of Science, Chiba University,
Yayoi-cho, Chiba 260
(Received April 12, 1986)

**Synopsis.** 2-Cyano-3-hydroseleno-3-(methylthio)acrylamide reacts with carbonyl compounds in the presence of sulfuric acid and aroyl chlorides in the presence of pyridine to give the corresponding 2,3-dihydro-4*H*-1,3-selenazin-4-ones and 4*H*-1,3-selenazin-4-ones in moderate yields, respectively.

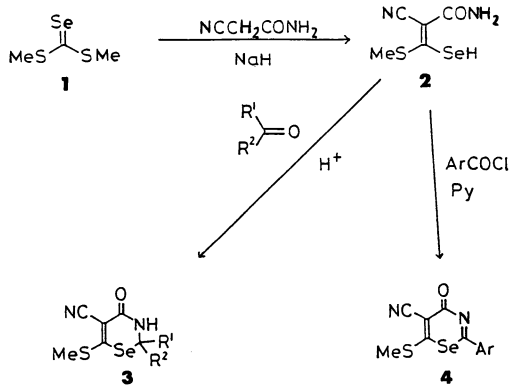
In the chemistry of heterocycles containing selenium and nitrogen atoms, many literatures concerning 1,3-selenazoles have appeared and their features have been well documented.[1] However, only some reports have been published on the synthesis of 4*H*-1,3-selenazines perhaps because of the synthetic difficulty.[2] During the course of studies on heteroatom rearrangements[3] we have fond a convenient preparative procedure for *S*,*S*-dimethyl dithioselenocarbonate (**1**).[4] As is synthetic application it was found that

Table Compounds **3** and **4** Prepared

| Product | Yield % | Mp $\theta_m$/°C | Molecular Formula[a] | IR cm$^{-1}$ | $^1$H NMR(solv./TMS) $\delta$(ppm) | MS[b] $m/z$(M$^+$) |
|---|---|---|---|---|---|---|
| **3a** | 53 | 189—190 | $C_8H_{10}N_2OSSe$ | 3120, 3020 (NH); 2200 (CN); 1640 (CO) | ($CDCl_3$) 1.89(s, 6H, $CH_3$); 2.65(s, 3H, $SCH_3$); 6.73 (br, 1H, NH) | 262 |
| **3b** | 90 | 204—205 | $C_{11}H_{14}N_2OSSe$ | 3120, 3020 (NH); 2200 (CN); 1640 (CO) | ($CDCl_3$) ca. 1.3(m, 6H, $CH_2$); ca. 2.0(m, 4H, $CH_2$); 2.7(s, 3H, $SCH_3$); 8.1(br, 1H, NH) | 302 |
| **3c** | 41 | 162—163 | $C_9H_{12}N_2OSSe$ | 3120, 3020 (NH); 2200 (CN); 1640 (CO) | ($CDCl_3$) ca. 1.0(m, 3H, $CH_3$); ca. 1.5(m, 2H, $CH_2$); ca. 2.0 (m, 2H, $CH_2$); 2.7(s, 3H, $SCH_3$); 5.16(d, 1H, CH, $J$=4 Hz); 6.14(br, 1H, NH) | 276 |
| **3d** | 51 | 214—215 | $C_{12}H_{10}N_2OSSe$ | 3120, 3020 (NH); 2200 (CN); 1640 (CO) | (Py-$D_5$) 2.7(s, 3H, $SCH_3$); 6.5 (br, 1H, CH); ca. 7.5(m, 5H, $C_6H_5$); 10.5(br, 1H, NH) | 310 |
| **3e** | 72 | 195—196 | $C_{10}H_8N_2O_2SSe$ | 3250(NH); 2200(CN); 1650(CO) | ($CDCl_3$) 2.7(s, 3H, $SCH_3$); 6.2 (br, 1H, CH); 6.26, 6.45, 6.53 (m, 3H, $C_4H_3O$); 7.5(br, 1H, NH) | 300 |
| **4a** | 59 | 188—189 | $C_{12}H_8N_2OSSe$ | 2220(CN); 1640(CO) | ($CDCl_3$) 2.8(s, 3H, $SCH_3$); 7.5, 7.7(m, 3H, $C_6H_5$); 8.0(m, 2H, $C_6H_5$) | 308 |
| **4b** | 70 | 235—236 | $C_{16}H_{10}N_2OSSe$ | 2220(CN); 1640(CO) | ($CDCl_3$-DMSO) 2.8(s, 3H, $SCH_3$); 7.4—8.0(m, 6H, $C_{10}H_7$); 8.4(s, 1H, $C_{10}H_7$) | 358 |
| **4c** | 48 | 137—138 | $C_{13}H_{10}N_2O_2SSe$ | 2210(CN); 1630(CO) | ($CDCl_3$-DMSO) 2.4(s, 3H, $CH_3$); 2.7(s, 3H, $SCH_3$); 5.8 (d, d, 2H, $C_6H_4$, $J$=8 Hz); 6.8(d, d, 2H, $C_6H_4$, $J$=8 Hz) | 338 |
| **4d** | 66 | 228—229 | $C_{12}H_7N_2OSSeCl$ | 2210(CN); 1640(CO) | ($CDCl_3$-DMSO) 2.8(s, 3H, $SCH_3$); 7.4(d, d, 2H, $C_6H_4$, $J$=8 Hz); 7.8(d, d, 2H, $C_6H_4$, $J$=8 Hz) | 342 |
| **4e** | 62 | 186—187 | $C_{11}H_7N_3OSSe$ | 2210(CN); 1640(CO) | (DMSO-$D_6$) 2.8(s, 3H, $SCH_3$); 7.4, 8.1, 8.6, 8.9(m, 4H, $C_5H_4N$) | 309 |

a) Satisfactory microanalyses obtained: C±0.30, H±0.22, N±0.28. b) M$^+$ based on $^{80}$Se isotope peak.

Scheme



**3a** $R^1=R^2=CH_3$ **4a** Ar=Phenyl
**3b** $R^1,R^2=-(CH_2)_5-$ **4b** Ar=2-Naphthyl
**3c** $R^1=n\text{-}C_3H_7$, $R^2=H$ **4c** Ar=*p*-Methoxyphenyl
**3d** $R^1=C_6H_5$, $R^2=H$ **4d** Ar=*p*-Chlorophenyl
**3e** $R^1$=Furyl, $R^2=H$ **4e** Ar=3-Pyridyl

several 4*H*-1,3-selenazin-4-ones could be easily synthesized starting from **1**. Herein we wish to report their preparations.

Compound **1** reacted with cyanoacetamide in the presence of sodium hydride under the oxygen-free conditions to give 2-cyano-3-hydroseleno-3-(methylthio)-acrylamide (**2**) (77% yield), which could be kept for two or three weeks in a refrigerator without decomposition. Compound **2** was allowed to react with various carbonyl compounds in the presence of sufuric acid and some aroyl chlorides in the presence of pyridine to afford the corresponding 2,3-dihydro-4*H*-1,3-selenazin-4-ones (**3**) and 4*H*-1,3-selenazin-4-ones (**4**) in moderate yields, respectively (see Table). In this reaction the use of acetophenone, benzophenone, and acyl chlorides did not give a satisfactory result.

## Experimental

Microanalyses were performed with a Perkin-Elmer 240 elemental analyser at the Analytical Center of Chiba University. IR spectra were recorded on a Hitachi 215 spectrometer. $^1H$ NMR spectra were determined with Japan Electron Optics Lab. (JEOL) JNM-FX-270 and MH-100. The chemical shifts are given in ppm with $(CH_3)_4Si$ as an internal standard. Mass spectra were measured on a Hitachi M-60 spectrometer at an ionizing energy at 70 eV. Chloroform and pyridine were purified by standard procedure, and tetrahydrofuran (THF) was distilled from benzophenone ketyl.

**2-Cyano-3-hydroxyseleno-3-(methylthio)acrylamide (2):** A 100 ml two-necked round flask equipped with a reflux condenser and a Teflon-coated magnetic bar, is dried in vacuo and then flushed with argon. In this flask are placed sodium hydride (60% dispersion, 1.6 g, 40 mmol) and THF (40 ml). To the resulting slurry solution is added cyanoacetamide (0.84 g, 10 mmol). After stirring at room temperature for 20 min, *S,S*-dimethyl dithioselenocarbonate (2.2 g, 12 mmol) solution in THF (10 ml) is added and the mixture is refluxed with stirring for 2.5 h until orange coloration is produced. The reaction is quenched with dropping of a degassed water under ice cooling, and a mixture of benzene (40 ml) and degassed water (40 ml) is added to the resulting solution. After shaking in a separatory funnel flushed with argon, an aqueous layer is transfered to a 100 ml Erlenmeyer flask containing hexane (20 ml). The aqueous solution is acidified with 6M-HCl (1 M=1mol $dm^{-3}$) under ice cooling. The obtained material is collected, washed with degassed water (20 ml×2), and dried in a vacuum desiccator; yellow powder of mp 102—104 °C; 1.7 g, yield 77% ; IR (KBr) 3380, 3280, 3200 (s), 2200 (vs), and 1650 $cm^{-1}$ (vs); $^1H$ NMR ($CDCl_3$) 2.72 (s, 3H, $SCH_3$), 7.26 (br, 2H, $NH_2$), and 16.38 (s, 1H, SeH).

Compound **2** thus obtained is used for the following procedures without purification because **2** decomposes to some extent on recrystallization.

**5-Cyano-6-methylthio-2-propyl-2,3-dihydro-4*H*-1,3-selenazin-4-one (3c). Typical Procedure:** A mixture of **2** (0.44 g, 2 mmol), *n*-butyraldehyde (0.2 g, 3 mmol)[3], 6M-$H_2SO_4$ (2 ml), and methanol (8 ml) is stirred for 4 h at room temperature. The reaction is quenched with water, thus obtained crystals are collected, and recrystallized from isopropyl alcohol to give **3c** as pale yellow needles; 0.22 g, yield 41%.

**5-Cyano-2-(*p*-chlorophenyl)-6-methylthio-4*H*-1,3-selenazin-4-one (4d). Typical Procedure:** A mixture of **2** (0.66 g, 3 mmol, *p*-chlorobenzoyl chloride (1.2 g, 7.6 mmol), pyridine (1.6 ml), and chloroform (10 ml) is shaken for 3 h at room temperature. The reaction is quenched with water and then ethanol, the obtained material is collected, dried in a vacuum desiccator; cream-colored powder (recry. from chloroform–hexane); 0.66 g, yield 66%.

Nicotinoyl chloride is prepared according to the literature.[5] The others are prepared from the reaction of the corresponding carboxylic acids with thionyl chloride in the usual way.

## References

1) E. Bulka, "Advances in Heterocyclic Chemistry," ed by A. R. Katritzky, Academic Press, (1963), Vol 2, p. 344.

2) M. Takahashi, S. Watanabe, and T. Kasai, *Heterocycles*, **14**, 1921 (1980); K. T. Potts, F. Huang, and R. K. Khattak, *J. Org. Chem.*, **42**, 1644 (1977); G. Simchen and G. Entenmann, *Justus Liebigs Ann. Chem.*, **8**, 1249 (1977); M. Dzurilla and P. Kristian, *Chem. Zvesti.*, **33**, 792 (1979); F. I. Luknitskii, D. O. Taube, and B. A. Vovsi, *Zh. Org. Khim.*, **5**, 1844 (1969); A. Shafiee, F. Assadi, and V. I. Cohen, *J. Heterocycl. Chem.*, **15**, 39 (1978); M. Dzurilla and P. Kristian, *Collect. Czech. Chem. Commun.*, **41**, 1388 (1976).

3) M. Yokoyama, T. Shiraishi, H. Hatanaka, and K. Ogata, *J. Chem. Soc., Chem. Commun.*, **1985**, 1704 and related references therein.

4) M. Yokoyama and H. Hatanaka, *Synthesis*, **9**, 891 (1985).

5) A. M. Grigorovskii and Z. M. Kimen *J. Gen. Chem.*, **18**, 171 (1948).