

A Novel Selenium-Containing Heterocycle. Lewis Acid-Assisted Reaction of Selenoamides
with Aldehydes Leading to 6*H*-1,3,5-Oxaselenazines

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New selenium-containing heterocyclic compounds, 6*H*-1,3,5-oxaselenazines, have been synthesized stereoselectively by the reaction of selenoamides with aldehydes in the presence of boron trifluoride etherate complex.

Selenoamides hold great promise as useful precursors for synthesis of selenium-nitrogen heterocyclic compounds,^{1,2)} since they have a highly reactive carbon-selenium double bond as well as an intrinsic Se-C-N unit. Nonetheless, practical use of selenoamides for the synthesis of heterocycles has been limited to some examples³⁾ owing to the difficulty in preparing selenoamides.⁴⁾ Recently, we have developed a convenient method for synthesis of selenoamides by the reaction of nitriles with selenium, carbon monoxide, and water.⁵⁾ Herein we report the Lewis acid-assisted condensation of selenoamides with aliphatic aldehydes, leading to novel heterocyclic compounds containing a Se-C-N unit in the ring with high stereoselectivity.⁶⁾

Boron trifluoride etherate complex (10 mmol) was added dropwise over 2-min period to a magnetically stirred mixture of selenobenzamide (5 mmol) and acetaldehyde (12 mmol) in chloroform (20 mL) at 0 °C. The resultant solution was warmed to 20 °C and stirring was continued for 1 h. The reaction mixture was poured

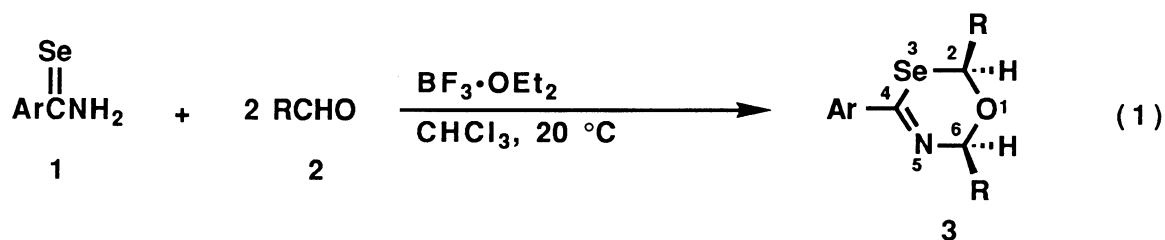
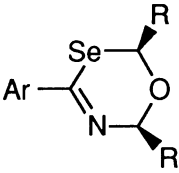


Table 1. Synthesis of 6H-1,3,5-Oxaselenazines **3**^{a)}

Entry	Selenoamide 1	Aldehyde 2	Product 3	Yield/% ^{b)}	Mp $\theta_m/^{\circ}\text{C}$
	$\begin{array}{c} \text{Se} \\ \\ \text{ArCNH}_2 \end{array}$	RCHO			
1	Ar = Ph	R = CH ₃	3a	82	oil
2	Ar = Ph	R = <i>n</i> -C ₇ H ₁₅	3b	69	oil
3	Ar = Ph	R = <i>t</i> -C ₄ H ₉	3c	86	98.0 ~ 98.5
4	Ar = Ph	R = 	3d	97	78.0 ~ 79.0
5	Ar = <i>m</i> -ClC ₆ H ₄	R = 	3e	83	70.0 ~ 71.0
6	Ar = <i>p</i> -CH ₃ OC ₆ H ₄	R = 	3f	97	80.5 ~ 81.0

a) Reaction time: 20 h except for entries 1 and 2 (1 h). b) Isolated yield of *cis*-isomer.

into 30 mL of saturated aqueous NaHCO₃ and extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried over MgSO₄, and concentrated *in vacuo*. The residual oil was purified by flash chromatography on silica gel (eluted with hexane/Et₂O = 100/1) to afford 2,6-dimethyl-6H-1,3,5-oxaselenazine (**3a**) in 82% yield.

Results are summarized in Table 1. The method is successful with aliphatic aldehydes, and provided oxaselenazines **3** in good yields. In contrast, the reaction of aromatic aldehydes with selenoamides resulted in the formation of a complex mixture with deposition of elemental selenium. As for the Lewis acids, TiCl₄ and AlCl₃ were less effective than BF₃•OEt₂. FeCl₃ and ZnCl₂ exerted no effect on this reaction.

Spectral data of oxaselenazines **3** are listed in Table 2. In ¹³C NMR, the underlined signals can be assigned to the α -carbon of selenium (C2) on the basis of satellite caused by ⁷⁷Se. By a similar reason, H^a can also be distinguished clearly from H^b in ¹H NMR. In ⁷⁷Se NMR, the signals of **3** appeared at δ 340 $\pm$ 40.⁷⁾

Isolated oxaselenazines **3** are all single stereoisomers with *cis*-configuration,⁸⁾ which was confirmed by the observed NOE enhancements of the integral of H^a by 7-10% and no increment

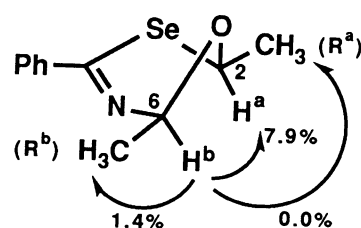
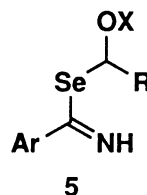
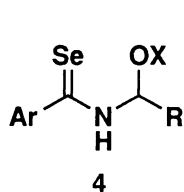


Fig. 1.

Table 2. Spectral Data of Oxaselenazines **3**^{a)}

	IR ν/cm^{-1} ($\nu_{\text{C=N}}$)	MS m/e (CI, $M^+ + 1$)	^1H NMR ^{b)} δ/ppm (H^{a}) (H^{b})	^{13}C NMR ^{c)} δ/ppm (C_n , $^1J_{\text{SeC}}$)	^{77}Se NMR ^{d)} δ/ppm ($^2J_{\text{SeH}}$, $^3J_{\text{SeH}}/\text{Hz}$)
3 a	1611 (neat)	255 (M^+) ^{e)}	<u>5.65</u> (q, $J = 6.1$ Hz) 5.17 (q, $J = 6.1$ Hz)	<u>73.3</u> (C_2 , 56.8 Hz) 157.8 (C_4), 89.5 (C_6)	381 (12.5, 16.3)
3 b	1620 (neat)	424	<u>5.59</u> (dd, $J = 5.6, 6.9$ Hz) 4.98 (dd, $J = 5.4, 6.8$ Hz)	<u>78.5</u> (C_2 , 56.8 Hz) 157.6 (C_4), 92.7 (C_6)	362 (11.0, 11.0)
3 c	1622 (KBr)	240	<u>5.42</u> (s) 4.62 (s)	<u>84.2</u> (C_2 , 61.0 Hz) 156.6 (C_4), 96.1 (C_6)	315 (12.6)
3 d	1618 (KBr)	392	<u>5.41</u> (d, $J = 7.0$ Hz) 4.74 (d, $J = 5.2$ Hz)	<u>89.0</u> (C_2 , 58.6 Hz) 157.9 (C_4), 99.0 (C_6)	343 (12.6, 6.1)
3 e	1615 (KBr)	426	<u>5.41</u> (d, $J = 6.1$ Hz) 4.72 (d, $J = 5.2$ Hz)	<u>84.6</u> (C_2 , 59.0 Hz) 157.7 (C_4), 96.0 (C_6)	348 (12.0, 6.5)
3 f	1609 (KBr)	- ^{f)}	<u>5.39</u> (d, $J = 6.7$ Hz) 4.72 (d, $J = 5.5$ Hz)	<u>84.2</u> (C_2 , 59.6 Hz) 161.6 (C_4), 96.0 (C_6)	336 (12.4, 6.0)

a) All products gave satisfactory analytical data ($\text{C} \pm 0.35$, $\text{H} \pm 0.21$, $\text{N} \pm 0.18\%$). b) ^1H - ^{77}Se couplings were observed for H^{a} . c) ^{13}C - ^{77}Se couplings were observed for C_2 . d) External Me_2Se (neat) was used as the standard ($\delta = 0$). e) The value for M^+ was obtained by EI. f) The value ($M^+ + 1 - \text{RCO} = 310$) was obtained.



of the integrated intensity on the protons of R^{a} , upon irradiation of H^{b} (see, Fig. 1).⁹⁾

A possible reaction path may involve the initial formation of **4** ($\text{X} = \text{Lewis acid}$) and/or **5** ($\text{X} = \text{Lewis acid}$) by the reaction of selenoamides with one equivalent of aldehydes in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$. The reaction of a selenoamide **1** ($\text{Ar} = \text{Ph}$) with an aldehyde **2** ($\text{R} = \text{cyclohexyl}$) was carried out in a shorter time (10 min) at 0°C , and quenched immediately with water. After a usual workup, **4** ($\text{Ar} = \text{Ph}$, $\text{R} = \text{cyclohexyl}$, $\text{X} = \text{H}$)¹⁰⁾ was obtained together with an oxaselenazine **3d**, but **5** ($\text{Ar} = \text{Ph}$, $\text{R} = \text{cyclohexyl}$, $\text{X} = \text{H}$) was not detected. This observation suggests the intermediacy of **4** ($\text{X} = \text{Lewis acid}$).

In summary, a new selenium-nitrogen heterocycle **3** was easily synthesized by using selenoamide as the key starting material.

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- 6) For the sulfur analogue, see: C. Giordano and A. Belli, *Synthesis*, **1975**, 789.
- 7) The ^{77}Se NMR spectra of **3** were taken on a Bruker AM 600 spectrometer (sweep width = 2000 Hz, 65 K data points, pulse width = 45° , acquisition time = 1.024s).
- 8) In all cases examined, signals assigned to the *trans*-isomer (<7%) were detected in a crude mixture by 1H NMR. Isomerization of the *trans*-oxaselenazine into the more stable *cis*-isomer seems to take place during the purification by column chromatography on silica gel.
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- 10) Spectral data of **4** are as follows: IR (KBr) 3200-3400 cm^{-1} ; 1H NMR ($CDCl_3$) δ 5.12 (d, OH , $J_{CHOH} = 3.4$ Hz, exchangeable), 5.49 (ddd, $NHCH(OH)CH$, $J_{NHCH} = 6.1$, $J_{CHOH} = 3.4$, $J_{CHCH} = 6.1$ Hz); ^{13}C NMR ($CDCl_3$) δ 84.4 ($NHCH$), 206.1 ($C=Se$), MS (CI, m/e) 298 ($M^+ + 1$).

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