Structure of *N*-Aryl Selenoacetamides in Solutions and in the Solid State

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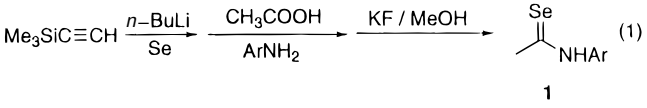
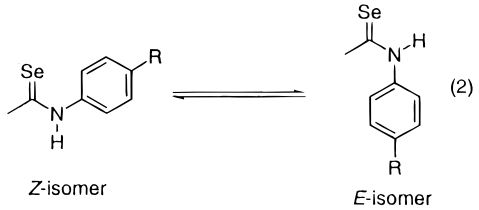
Synthesis and synthetic applications of selenium counterparts of amides, i.e., selenoamides, have been widely developed in recent years.[1,2] On the contrary, little is known about their structures. There has been several reports on the X-ray molecular structure analyses of only tertiary selenoamides[3−5] and selenoformamides.[6] No structural studies have been reported on secondary selenoamides except for one case[7] despite their potential importance related to those on well-known ordinary amides[8] and thioamides.[9] Herein we report the structure of *N*-aryl selenoacetamides in solutions and in the solid state.

N-Aryl selenoamides **1** were synthesized from the reactions of (trimethylsilyl)acetylene, *n*-butyllithium, selenium, acetic acid, and arylamines followed by the reactions with potassium fluoride in moderate to good yields (eq 1).[2o] The selenoamides **1** existed as a stereoisomeric mixture (eq 2). The yields of **1** and the ratios





of two isomers are listed in Table 1. The structures of major isomers were determined by the comparison of the chemical shifts of **1** with those of *N*-aryl thioamides.[10] In the ^{1}H NMR spectra the signals corresponding to N−H proton of *E*-isomers were observed in the lower fields than those of *Z*-isomers. On the other hand, the signals due to a methyl group attached to the selenocarbonyl group in *E*-isomers were upfield of those in *Z*-isomers. The ratios of the isomers were determined by the relative intensities of these methyl signals. *N*-Aryl selenoamides **1** were found to exist predominantly as *Z*-isomers in THF-d_8, acetone-d_6, CD_3OD, and CD_3CN. As for amides, secondary *N*-aryl amides have been reported to exist only as *Z*-isomers.[11] The predominance of *Z*-isomers in thioamides has been explained by the steric repulsion between ortho-protons of the aromatic ring and an alkyl group at the position α to the thiocarbonyl group in *E*-isomers.[10] A similar steric repulsion clearly exists in selenoamides, and this seemed to explain the results of entries 4−7 in Table 1. However, this does not explain

Table 1. Synthesis of *N*-Aryl Selenoamides 1 and the Ratio of *E*- and *Z*-Isomers[a]

entry	Ar	compd	yield[b] (%)	ratio of *E*:*Z* isomers[c]	ratio of *E*:*Z* isomers of $CH_3C(S)NHAr$[c,d]
1	C_6H_5	**1a**	59	61:39	36.5:63.5
2[e]	C_6H_4-CH_3-4	**1b**	31	65:35	42.5:57.5
3	C_6H_4-OCH_3-4	**1c**	71	64:36	44:56
4				23:77[f]	
5				17:83[g]	
6				14:86[h]	
7				17:83[i]	
8[j]	C_6H_4-Cl-4	**1d**	19	49:51	30:70
9	C_6H_4-Br-4	**1e**	34	48:52	28.5:71.5

[a] Synthesis of **1** was carried out as follows: (trimethylsilyl)-acetylene (2 mmol), *n*-BuLi (2 mmol), Se (2 mmol), CH_3CO_2H (2 mmol), arylamine (2 mmol), KF (2 mmol), CH_3OH (5 mL), and THF (5 mL). [b] Isolated yield. [c] In $CDCl_3$, ref 9c. [d] The Ar group is identical to that of **1** in each entry. [e] 4-$CH_3C_6H_4NH_2$·HCl was used instead of CH_3CO_2H and 4-$CH_3C_6H_4NH_2$. [f] In THF-d_8. [g] In acetone-d_6. [h] In CD_3OD. [i] In CD_3CN. [j] 4-$ClC_6H_4NH_2$·HCl was used instead of CH_3CO_2H and 4-$ClC_6H_4NH_2$.

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Table 2. Crystal Data and Data Collection Parameters of 1c

formula	$C_9H_{11}NOSe$
formula weight	228.15
crystal system	monoclinic
space group	$P2_1$(No. 4)
a/Å	5.552(1)
b/Å	7.673(2)
c/Å	10.912(1)
β/deg	96.51(1)
V/Å^3	461.8(1)
Z value	2
d_{calcd}/g cm^{-3}	1.641
μ(Mo Kα)/cm^{-1}	40.16
radiation, λ/Å	Mo Kα, 0.71069
temp/°C	−80.0
residuals: R,[a] R_ω[b]	0.026, 0.031

[a] $R = \Sigma(||F_o| - |F_c||)/\Sigma|F_o|$. [b] $R_\omega = [\Sigma\omega(|F_o| - |F_c|)^2/\Sigma\omega F_o^2]^{1/2}$, $\omega = [\sigma^2(F_o) + p^2F_o^2/4]^{-1}$.

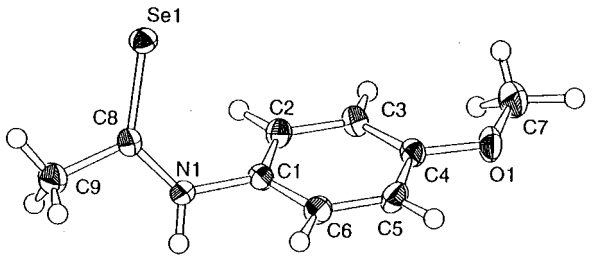
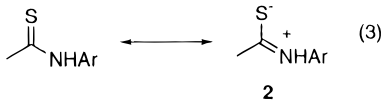


Figure 1. An ORTEP drawing of the molecular structure of **1c**. Selected bond distances (Å), bond angles (deg), and twisted angles (deg): Se1−C8 1.776(5), N1−C8 1.315(6), N1−C1 1.448(5), C8−C9 1.503(6), Se1−C8−N1 125.1(3), Se1−C8−N1−C1 −0.2(7), C2−C1−N1−C8 −63.8(7).

the ratios of the isomers since *E*-isomers predominate over *Z*-isomers in the case of selenoamides **1a**−**c** in $CDCl_3$ (entries 1−3). The ratios of *E*- and *Z*-isomers of **1** were also compared with those of *N*-aryl thioamides. The introduction of electron-withdrawing groups such as chlorine and bromine on aromatic rings increased the ratio of *Z*-isomers of both seleno- and thioamides in $CDCl_3$ (entries 8 and 9).

The molecular structure of the *N*-(4-methoxyphenyl)selenoacetamide (**1c**) was determined by the X-ray diffraction study. The crystal data and data collection parameters are listed in Table 2.[12] The X-ray molecular structure of **1c** is shown in Figure 1 with selected bond distances, angles, and twisted angles. The bond distance in the selenocarbonyl group C═Se is 1.776(5) Å, which is shorter than those of the reported tertiary selenoamides[3−5] and selenoformamides.[6] The C(Se)−N single bond (1.315(6) Å) is similar to those of the reported selenoamides.[3−6] These bond distances are also shorter than those of selenoformamide ($HC(Se)NH_2$) (C═Se, 1.783 Å; C−N, 1.345 Å) determined by molecular orbital calculations.[13] Noteworthy is that the aromatic ring on the nitrogen atom is deviated from the plane of Se═C−N by 63.8(7)°. Molecular orbital calculations have indicated the phenyl ring of the *N*-phenylacetamide are in the same plane of O═C−N.[8b] Likewise, the torsion angle of C−N−C−C of the *N*-(4-methoxyphenyl)acetamide was reported to be 20.3°.[14] Accordingly, the resonance stabilizing effect of the aromatic ring works well in the ordinary amides. On the contrary, the aromatic ring and the Se═C−N group do not appear to be in conjugation in the selenoamide **1c**. This also has suggested the importance of the steric and/or electronic repulsion between the selenium atom of the selenocarbonyl group and the aromatic ring. Nevertheless, **1c** existed as a *Z*-isomer in the solid state.

To confirm if two isomers of **1c** interconvert within the NMR time scale, a spin saturation transfer ^{1}H NMR experiment was performed.[15] When the signal for ortho-protons of the aromatic ring of *E*-isomer was irradiated, the spectrum exhibited negative NOE effect in the signal due to ortho-protons of the *Z*-isomer. This observation has suggested that the interconversion of two isomers clearly occurs at room temperature in $CDCl_3$, although the rotational barrier around C−N bond is believed to become higher when the oxygen atom of amides is replaced with the sulfur and selenium atoms.[16] This was further supported by phase-sensitive 2-D ^{1}H NOESY spectroscopy. Positive cross peaks were observed for methyl, aryl, and NH protons between two isomers. Then, the ^{1}H NMR spectrum of **1c** dissolved in $CDCl_3$ at −40 °C was measured. The *Z*- and *E*-isomers existed in a 50:50 ratio at this temperature. When the temperature was raised to 0 °C, the ratio of two isomers ended up as a 35:65 ratio, and this did not change even when it was cooled to −40 °C again. Consequently, *E*-isomers of **1** were thermodynamically more stable than *Z*-isomers of **1** in $CDCl_3$. The higher rotational barriers between *E*- and *Z*-isomers of *N*-aryl thioamides have been observed[8a,16] and accounted for by the preference for polar resonance structures such as **2** compared with the case of ordinary amides (eq 3).[17] The present results have suggested that a similar argument should not necessarily be applied to the selenoamides.[18]



(3)

2

Experimental Section

All reactions were carried out under an argon atmosphere. Melting points were uncorrected. IR spectra were recorded in KBr pellets. ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. As for **1c**, NOE difference and phase-sensitive 2-D ^{1}H NOESY spectra were also measured at 400 MHz. Diethyl ether was distilled from sodium benzophenone ketyl prior to use.

General Procedure for Synthesis of *N*-Aryl Selenoacetamides 1. To an Et_2O solution (5 mL) of lithium alkyneselenolate generated from (trimethylsilyl)acetylene (0.28 mL, 2 mmol), *n*-butyllithium (1.6 M hexane solution, 1.25 mL, 2 mmol), and selenium (0.158 g, 2 mmol) was added acetic acid (0.11 mL, 2 mmol) at −78 °C, and the solution was stirred for 5 min. Then, to the solution was added arylamine (2 mmol) at this temperature. After the mixture was stirred for 0.5−1 h at room temperature, methanol (5 mL) and potassium fluoride (0.116 g, 2 mmol) were added, and the solution was further stirred for 30 min. The mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with Et_2O three times. The combined organic layers were dried over $MgSO_4$ and concentrated. The

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residue was purified by silica gel column chromatography using *n*-hexane−CH_2Cl_2 as eluent to afford the *N*-aryl selenoacetamides **1**.

***N*-Phenylethaneselenoamide (1a):** yellow solid, mp 82−84 °C; IR (KBr) 3108, 1492, 1445, 1381, 1136, 968, 767, 713, 570, 506 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.51, 2.73 (s, 3H), 7.10−7.70 (m, 5H), 10.25 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 33.8, 40.2, 124.4, 124.5, 127.5, 128.1, 128.9, 129.6, 138.3, 139.7, 205.3, 207.3; MS *m*/*z* 199 (M^+). Anal. Calcd for C_8H_9NSe: C, 48.50; H, 4.58. Found: C, 48.36; H, 4.38.

***N*-(4-Methylphenyl)ethaneselenoamide (1b):**[19] yellow solid, mp 103−106 °C; IR (KBr) 3142, 3103, 2959, 2361, 2344, 1534, 1507, 1376, 1133, 812, 706, 586, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30, 2.33 (s, 3H), 2.47, 2.71 (s, 3H), 7.00−7.50 (m, 4H), 10.51 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 21.1, 21.2, 33.7, 40.2, 124.4, 129.6, 130.2, 136.0, 138.4, 205.3, 207.4; MS *m*/*z* 213 (M^+). Anal. Calcd for $C_9H_{11}NSe$: C, 50.95; H, 5.23. Found: C, 51.22; H, 5.25.

***N*-(4-Methoxyphenyl)ethaneselenoamide (1c):** yellow solid, mp 127−128 °C; IR (KBr) 3167, 3010, 1612, 1534, 1510, 1376, 1300, 1255, 1171, 1133, 1030, 827, 684, 588 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46, 2.75 (s, 3H), 3.80, 3.81 (s, 3H), 6.80−7.60 (m, 4H), 9.21, 10.29 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 33.6, 39.9, 55.4, 55.5, 114.1, 114.7, 116.5, 126.0, 131.5, 132.8, 158.6, 159.2, 205.3, 207.6; MS *m*/*z* 229 (M^+). Anal. Calcd for $C_9H_{11}NOSe$: C, 47.38; H, 4.86. Found: C, 47.21; H, 4.74.

***N*-(4-Chlorophenyl)ethaneselenoamide (1d):** yellow solid, mp 105−108 °C; IR (KBr) 3140, 3099, 2968, 2366, 1534, 1487, 1375, 1136, 1091, 1013, 858, 822, 740, 588, 511 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27, 2.50 (s, 3H), 6.80−7.50 (m, 4H), 9.73 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 34.0, 40.7, 125.7, 126.0, 129.3, 129.9, 132.9, 134.1, 136.9, 138.2, 206.1, 208.4; MS *m*/*z* 233 (M^+). Anal. Calcd for C_8H_8ClNSe: C, 41.32; H, 3.47. Found: C, 41.40; H, 3.51.

***N*-(4-Bromophenyl)ethaneselenoamide (1e):**[19] yellow solid, mp 138−141 °C; IR (KBr) 3136, 3092, 2966, 1531, 1482, 1376, 1137, 1066, 1010, 854, 813, 587, 516 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.48, 2.72 (s, 3H), 7.00−7.70 (m, 4H), 9.26, 10.55 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 34.0, 40.9, 125.9, 126.2, 132.3, 133.0, 137.3, 206.0, 208.7; MS *m*/*z* 277 (M^+). Anal. Calcd for C_8H_8BrNSe: C, 34.69; H, 2.91. Found: C, 34.61; H, 3.00.

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Supporting Information Available: Complete tables of crystallographic data, final atomic coordinates, and equivalent isotropic thermal parameters, bond distances, bond angles, and torsion angles (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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