# Synthesis and Functionalization of 4-Halomethyl-1,3-selenazoles

Karlheinz Geisler,* Wolf-Diethard Pfeiffer, Cornelia Müller, Elvira Nobst, Ehrenfried Bulka, Peter Langer*

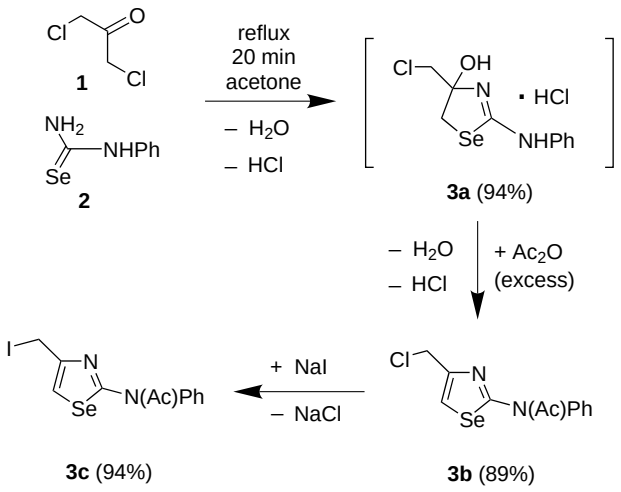
Institut für Chemie und Biochemie, Ernst-Moritz-Arndt-Universität Greifswald, Soldmannstr. 16, 17487 Greifswald, Germany
Fax +49(3834)964346; E-mail: peter.langer@uni-greifswald.de

*Received 5 March 2003; revised 31 March 2003*

**Abstract:** Double-functionalized, ionic and multivalent 1,3-selenazoles were prepared by nucleophilic displacement reactions of protected 4-halomethyl-2-amino-1,3-selenazoles.

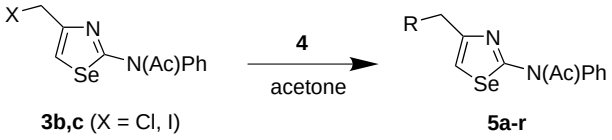
**Key words:** cyclizations, heterocycles, nucleophilic additions, selenium, halogens

1,3-Selenazoles are of considerable pharmacological relevance.[1] Synthetic approaches to these heterocycles mainly rely on the application of a selena-analogous Hantzsch procedure.[2,3] Double functionalized, multivalent and ionic 1,3-selenazole derivatives are of special pharmacological importance, due to their water solubility and physical properties. In addition, they are of interest in the field of material sciences (e.g. for solvatochromic effects). Interesting syntheses of highly functionalized 1,3-selenazoles have been reported for example by Banert and Hartmann.[4,5] Herein, we wish to report the synthesis of a great variety of double-functionalized and ionic 1,3-selenazoles by nucleophilic displacement reactions of 4-halomethyl-1,3-selenazoles.[6,7] Based on these results we also report the synthesis of novel multivalent 1,3-selenazole derivatives.




**Scheme 1** Synthesis of 4-halomethyl-1,3-selenazoles **3b**,**c**

Our starting point was the synthesis of the 4-halomethyl-2-amino-1,3-selenazoles **3b**,**c** which represent key intermediates for the synthesis of functionalized 1,3-selenazoles. After much synthetic effort, we have developed conditions for the efficient synthesis of **3b** and **3c**. The cyclization of α,α′-dichloroacetone (**1**) with phenylselenourea (**2**)[8] afforded semi-aminal **3a**. The isolation of **3a** by precipitation proved essential; however, an attempted purification resulted in a great loss in yield. Therefore, the crude material was used for transformation into **3b**. Treatment of **3a** with acetic anhydride resulted in elimination of water and protection of the amino group by acetylation to give, after thorough optimization of the reaction conditions (reaction time, concentration, stoichiometry, solvent for recrystallization), 4-chloromethyl-1,3-selenazole **3b** in 89% yield (Scheme 1). Treatment of **3b** with sodium iodide afforded the highly reactive 4-iodomethyl-1,3-selenazole **3c**.

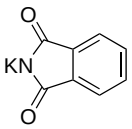
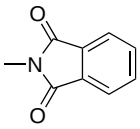
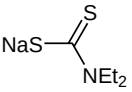
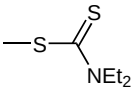
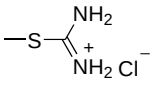
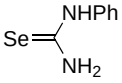
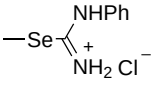
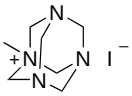
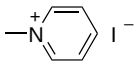
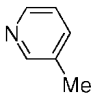
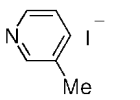
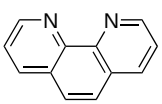
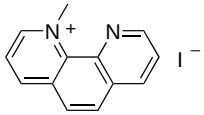



**Scheme 2** Nucleophilic displacement reactions of **3b**,**c**

The functionalization of protected 4-halomethyl-2-amino-1,3-selenazoles **3b**,**c** by nucleophilic displacement reactions was next studied. During the optimization of the reaction conditions, important parameters again proved to be the reaction time, concentration, stoichiometry and the solvent for recrystallization of the product. The reaction of **3c** with ammonium thiocyanate, potassium selenocyanate, sodium azide and potassium phthalimide afforded the functionalized 1,3-selenazoles **5a**–**d** in good yields (Scheme 2, Table 1). The *N*,*N*-diethyldithiocarbamate **5e** was prepared from **3c** and **4e** in good yield. A number of 1,3-selenazoles containing cationic side chains were prepared: selenazoles **5f**,**g**, containing the pharmacologically relevant isothiouronium and isoselenouronium moieties, were regioselectively prepared from **3b** and the corresponding thio- and selenoureas **4f**,**g**. The reaction of urotropine with **3c** gave the sterically encumbered ammonium salt **5h**. The reaction of tertiary amines **4i**–**k** with **3b**,**c** afforded the ammonium salts **5i**–**m** in quantitative yield. The reaction of **3c** with pyridine, 3-methylpyridine and phenanthroline gave the pyridinium salts **5n**–**p**. The reaction of triphenylphosphane (**4o**) with **3b** and **3c** afforded the phosphonium salts **5q** and **5r**, respectively, in quantitative yields. Heterocycles **5a**–**r** show only minor differences in their $^{77}$Se NMR shifts. This can be explained by the great distance between the selenium atom

Synthesis 2003, No. 8, Print: 05 06 2003.
Art Id.1437-210X,E;2003,0,08,1215,1220,ftx,en;T02403SS.pdf.

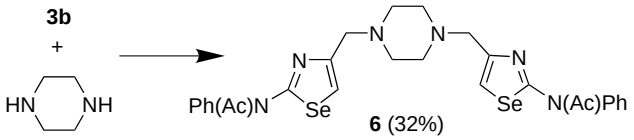
**Table 1** Synthesis of Substituted 2-(*N*-Acetylanilino)-1,3-selenazoles **5a**–**r**

| 5 | 4 | 3 | Reagent (**4**) | R | Yield (%)[a] | Mp (°C) |
|---|---|---|---|---|---|---|
| **a** | **a** | **c** | $NH_4SCN$ | —SCN | 92 | 154–155 |
| **b** | **b** | **c** | KSeCN | —SeCN | 95 | 162–164 |
| **c** | **c** | **c** | $NaN_3$ | —$N_3$ | 78 | 104–106 |
| **d** | **d** | **c** |  |  | 61 | 181–182 |
| **e** | **e** | **c** |  |  | 98 | 101–103 |
| **f** | **f** | **b** |  |  | 54 | 198–199 |
| **g** | **g** | **b** |  |  | 47 | 202–204 |
| **h** | **h** | **c** |  |  | 69 | 158–160 |
| **i** | **i** | **c** | $Me_3N$ | —$^{+}NMe_3\ I^-$ | 100 | 232–234 |
| **j** | **i** | **b** | $Me_3N$ | —$^{+}NMe_3\ Cl^-$ | 100 | 228–230 |
| **k** | **j** | **c** | $Et_3N$ | —$^{+}NEt_3\ I^-$ | 100 | 230–232 |
| **l** | **j** | **b** | $Et_3N$ | —$^{+}NEt_3\ Cl^-$ | 100 | 226–228 |
| **m** | **k** | **c** | $Et_2NPh$ | —$^{+}NEt_2Ph\ I^-$ | 100 | 152–153 |
| **n** | **l** | **c** |  |  | 90 | 223–224 |
| **o** | **m** | **c** |  |  | 92 | 214–215 |
| **p** | **n** | **c** |  |  | 68 | 194–196 |
| **q** | **o** | **c** | $PPh_3$ | —$^{+}PPh_3I^-$ | 100 | 204–203 |
| **r** | **o** | **b** | $PPh_3$ | —$^{+}PPh_3\ Cl^-$ | 100 | 244–246 |

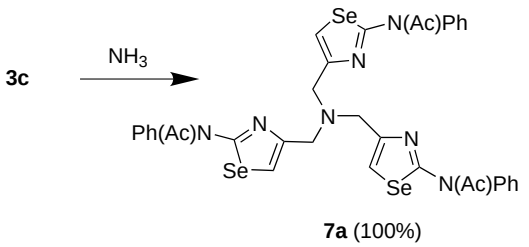
[a] Yields of isolated products

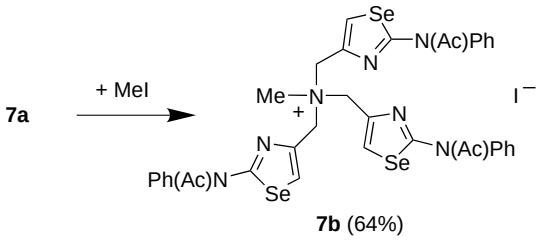
and the substituent R. Due to the electron withdrawing effect, a low field shift is observed for 1,3-selenazoles containing a cationic side-chain compared to electroneutral derivatives.

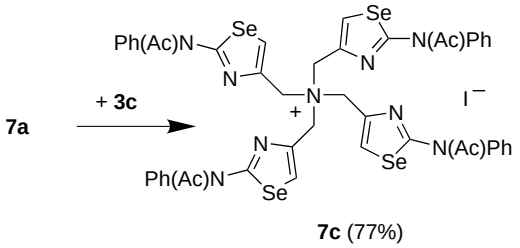
Multivalent selenazole derivatives are of special pharmacological interest, due to the amplification of the 1,3-selenazole presentation. The reaction of **3b** with piperazine afforded the divalent selenazole **6** (Scheme 3).




**Scheme 3** Synthesis of divalent selenazole **6**




**Scheme 4** Synthesis of multivalent selenazoles **7a**–**c**

The reaction of 4-iodomethyl-1,3-selenazole **3c** with $NH_3$ resulted in complete alkylation and formation of the tris-selenazole **7a** in quantitative yield (Scheme 4). Alkylation of **7a** with methyl iodide and **3c** afforded the interesting water soluble tris- and tetrakis-1,3-selenazoles **7b** and **7c**, respectively.

**2-(*N*-Acetylanilino)-4-halomethyl-1,3-selenazoles 3b and 3c**

An acetone solution (350 mL) of 1,3-dichloroacetone (14.0 g, 110 mmol) and *N*-phenylselenourea (11.4 g, 57.0 mmol) was refluxed for 20 min with exclusion of moisture. A grey solid precipitated. After cooling, the solid was filtered off and washed with acetone to give the salt **3a** as a grey solid (mp 130 °C, 17.5 g, 94%). To crude **3a** (7.00 g, 21.5 mmol) was added acetic anhydride (200 mL). The solution was refluxed for 15 min and subsequently concentrated to 80 mL. $H_2O$ (20 mL) was added and the solution was cooled to r.t. with stirring. A yellow oil precipitated which solidified upon standing. The solid was recrystallized from EtOH to give **3b**.

Yield: 6.01 g (89%); yellow crystals; mp 132–133 °C.

Anal. Calcd for $C_{12}H_{11}ClN_2OSe$ (313.7): C, 45.98; H, 3.54; N, 8.93. Found: C, 45.79; H, 3.55; N, 8.70.

A mixture of **3b** (3.14 g, 10.0 mmol) and NaI (1.90 g, 12.5 mmol) in dry acetone (50 mL) was refluxed for 5 min. After cooling to r.t., a crystalline precipitate formed which was washed with $H_2O$ and recrystallized (EtOH–$H_2O$) to give **3c**.

Yield: 3.82 g (94%); light brown prisms; mp 142 °C.

IR (KBr): 698 (s), 764 (m), 844 (w), 949 (w), 990 (w), 1114 (w), 1162 (m), 1282 (s), 1289 (s), 1301 (s), 1331 (m), 1372 (s), 1420 (m), 1490 (s), 1508 (m), 1594 (m), 1669 (s), 3052 (w), 3087 (w) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.97 (s, 3 H, $CH_3$), 4.38 (s, 2 H, $CH_2$), 7.43–7.59 (m, 5 H, ArH), 7.79 [s, 1 H, $^2J$ ($SeH_5$) = 42.3 Hz, $H_5$-selenazole].

$^{13}C$ NMR (DMSO-$d_6$, 75 MHz): δ = 4.11 ($CH_2$), 23.58 ($CH_3$), 117.77, 128.75, 128.86, 129.63 (CH), 139.90, 147.50 (C), 160.92 (C=O), 170.10 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 682.5.

MS (EI): *m*/*z* = 406 ($M^+$, 2), 316 (3), 314 (4), 279 (100), 277 (36), 272 (32), 237 (68), 93 (10), 77 (22).

Anal. Calcd for $C_{12}H_{11}N_2IOSe$ (405.09): C, 35.58; H, 2.74; N, 6.92. Found: C, 35.62; H, 2.81; N, 7.13.

**1,3-Selenazoles 5a–c,e,f; Typical Procedure**

An acetone solution of **3c** (2.03 g, 5.0 mmol) and $NH_4SCN$ (0.30 g, 5.0 mmol) was refluxed for 20 min. Potassium iodide was filtered off and the solution was cooled to r.t. A precipitate formed which was separated and recrystallized (EtOH–$H_2O$) to give **5a**.

Yield: 1.56 g (92%); colorless lamella.

**2-(*N*-Acetylanilino)-4-thiocyanatomethyl-1,3-selenazole (5a)**

Mp 154–155 °C.

IR (KBr): 965 (m), 998 (m), 1025 (w), 1105 (w), 11.45 (m), 1281 (s), 1290 (s), 1390 (s), 1425 (s), 1498 (s), 1600 (s), 1980 (s), 2155 (m), 2940 (w), 2995 (w), 3100 (w) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.85 (s, 3 H, $CH_3$), 4.05 (s, 2 H, $CH_2$), 7.43–751 (m, 5 H, ArH), 7.61 [s, 1 H, $^2J$ ($SeH_5$) = 42 Hz, $H_5$-selenazole].

Anal. Calcd for $C_{13}H_{11}N_3OSSe$ (338.27): C, 46.30; H, 3.28; N, 12.43. Found: C, 46.10; H, 3.50; N, 12.40.

**2-(*N*-Acetylanilino)-4-selenocyanatomethyl-1,3-selenazole (5b)**

This compounds was obtained by reaction of **3c** (2.03 g, 5.0 mmol) and KSeCN (0.72 g, 5.0 mmol) in acetone (30 mL) as described for **5a**.

Yield 1.82 g (95%); yellow prisms (EtOH–$H_2O$); mp 163 °C.

IR (KBr): 697 (m), 762 (m), 951 (w), 991 (m), 1131 (m), 1205 (m), 1284 (s), 1332 (m), 1375 (s), 1420 (m), 1489 (s), 1594 (s), 1594 (w), 1670 (s), 2146 (m), 3005 (w) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.97 (s, 3 H, $CH_3$), 4.16 (s, 2 H, $CH_2$), 7.43–7.54 (m, 5 H, ArH), 7.67 [s, 1 H, $^2J$ ($SeH_5$) = 42.1 Hz, $^2J$ ($SeH_{CH2}$) = 17.7 Hz), 5-H, selenazole].

$^{13}C$ NMR (DMSO-$d_6$, 75 MHz): δ = 23.66 ($CH_3$), 29.71 ($CH_2$), 104.73 (C), 118.64, 128.91, 128.98, 129.78 (CH), 140.14, 146.08 (C), 161.53 (C=O), 170.18 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 681.19 ($Se_1$), 281.51 ($Se_{SeCN}$).

MS (EI): *m*/*z* = 385, 383 ($M^+$, 4), 345 (6), 343 (20), 341 (19), 339 (12), 237 (100), 235 (60), 93 (16), 77 (38).

Anal. Calcd for $C_{13}H_{11}N_3OSe_2$ (383.16): C, 40.79; H, 2.93; N, 10.98. Found: C, 40.90; H, 3.20; N, 11.04.

**2-(*N*-Acetylanilino)-4-azidomethyl-1,3-selenazole (5c)**

Compound **5c** was prepared by reaction of **3c** (1.20 g, 3.0 mmol) and $NaN_3$ (0.20 g, 3.0 mmol) in acetone (20 mL) and $H_2O$ (5 mL). The mixture was refluxed for 30 min. Further purification was carried out as described for **5a**.

Yield: 0.75 g (78%); yellow prisms (ligroine); mp 105 °C.

IR (KBr): 759 (w), 992 (w), 1110 (w), 1170 (w), 1237 (m), 1256 (m), 1292 (s), 1333 (m), 1373 (m), 1449 (w), 1488 (s), 1594 (m), 1662 (s), 2093 (s), 2124 (s), 3099 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 300 MHz): δ = 2.05 (s, 3 H, $CH_3$), 4.10 (s, 2 H, $CH_2$), 7.25–7.55 (m, 6 H, ArH, $H_5$-selenazole).

$^{13}C$ NMR ($CDCl_3$, 75 MHz): δ = 23.70 ($CH_3$), 50.96 ($CH_2$), 116.87, 128.47, 128.96, 129.74 (CH), 139.93, 146.08 (C), 161.73 (C=O), 170.10 (C-2).

$^{77}Se$ NMR ($CDCl_3$, 60% $Me_2Se$ in $CDCl_3$): δ = 678.12.

MS (EI): *m*/*z* = 321 ($M^+$, 22), 319 (8), 279 (100), 277 (46), 250 (5), 237 (18), 235 (14), 197 (2), 184 (12), 184 (16), 170 (17), 143 (8), 133 (16), 104 (12), 93 (6), 77 (45), 65 (6), 43 (74).

Anal. Calcd for $C_{12}H_{11}N_5OSe$ (320.2): C, 45.01; H, 3.46; N, 21.87; Se, 24.66. Found: C, 45.20; H, 3.30; N, 21.98; Se, 24.43.

***N*-[2-(N-Acetylanilino)-1,3-selenazol-4-ylmethyl]phthalimide (5d)**

A DMF solution (20 mL) of phthalimide (2.94 g, 24.0 mmol) was heated at 80–90 °C. A MeOH solution (6.2 mL) of KOH was added dropwise with stirring. MeOH was evaporated by distillation to give a precipitate of potassium phthalimide. A DMF solution (20 mL) of selenazole **3b** (6.27 g, 20.0 mmol) was added dropwise to the mixture at 50 °C and the solution was stirred for 5 h. The mixture was allowed to stand overnight at 20 °C and poured into ice (50 g). An aq $Na_2CO_3$ solution (50%, 100 mL) of the product mixture was heated and the precipitated product was filtered off, washed with $H_2O$, and recrystallized (EtOH–$H_2O$, 1:1) to give **5d**.

Yield: 5.39 g (53%); light brown prisms; mp 181–182 °C.

IR (KBr): 965 (s), 997 (w), 1045 (w), 1085 (m), 1108 (s), 1186 (m), 1198 (m), 1270 (s), 1298 (s), 1320 (s), 1390 (s), 1398 (s), 1426 (s), 1491 (s), 1600 (m), 1672 (s), 1712 (s), 1780 (s), 2930 (w), 3180 (w) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 100 MHz): δ = 1.95 (s, 3 H, $CH_3$), 4.12 (s, 2 H, $CH_2$), 7.31–7.82 (m, 10 H, ArH, $H_5$-selenazole).

Anal. Calcd for $C_{20}H_{15}N_3O_3Se$ (424.33): C, 56.66; H, 3.56; N, 9.91; Se, 23.25. Found: C, 57.00, H, 3.10; N, 9.52; Se, 22.73.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]-*N*,*N*-diethyldithiocarbamate (5e)**

A mixture of **3c** (0.81 g, 2.0 mmol) and sodium diethyldithiocarbamate (2.0 mmol) in acetone (20 mL) was refluxed for 30 min. The work up was carried out as described for **5a**.

Yield: 98%; colorless lamella (ligroine); mp 102 °C.

IR (KBr): 700 (s), 768 (m), 826 (w), 915 (w), 986 (m), 1010 (m), 1142 (m), 1205 (s), 1273 (s), 1301 (s), 1331 (m), 1355 (m), 1370 (m), 1415 (m), 1452 (w), 1486 (s), 1596 (m), 1667 (s), 2977 (m) $cm^{-1}$.

$^1H$ NMR (300 MHz, DMSO-$d_6$): δ = 1.14 (s, 6 H, $CH_3$), 1.96 (s, 3, $CH_3$), 3.63–3.70 (q, 2 H, $CH_2$), 3.88–3.95 (q, 2 H, $CH_2$), 4.27 (s, 2 H, $SCH_2$), 7.42–7.58 (m, 5 H, ArH), 7.64 [s, 1 H, $^2J$ ($SeH_5$), 42.5 Hz, $H_5$-selenazole].

$^{13}C$ NMR (75 MHz, DMSO-$d_6$): δ = 11.25, 12.24 ($CH_2CH_3$), 23.57 ($CH_3$), 38.23 ($CH_2$), 46.36, 48.86 ($CH_2CH_3$), 117.43, 128.78,

128.85, 129.63 (CH), 140.05, 144.85 (C), 161.10 (C=O), 169.89 (C-2), 193.13 (C=S).

$^{77}$Se NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 678.66.

MS (EI): *m*/*z* = 427 ($M^+$, 20), 313 (22), 311 (100), 269 (38), 237 (22), 197 (3), 176 (4).

Anal. Calcd for $C_{17}H_{21}N_3OS_2Se$ (426.5): C, 47.88; H, 4.96; N, 9.85. Found: C, 47.90; H, 5.00; N, 9.76.

**_S_-[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyl]isothiuronium Chloride (5f)**

A mixture of **3b** (3.14 g, 10.0 mmol) and thiourea (0.76 g, 10.0 mmol) in acetone (65 mL) was refluxed for 35 min. The work up was carried out as described for **5a**.

Yield 2.10 g (54%); colorless prisms (EtOH–$H_2O$); mp 198–199 °C.

IR (KBr): 703 (m), 721 (w), 741 (w), 993 (w), 1164 (w), 1299 (s), 1335 (m), 1363 (m), 1435 (m), 1454 (m), 1477 (s), 1489 (s), 1523 (w), 1649 (s), 1677 (s), 2742 (m), 2958 (m), 3010 (m), 3077 (m), 3192 (m), 3261 (m), 3287 (m) $cm^{-1}$.

$^1$H NMR (300 MHz, DMSO-$d_6$): δ = 2.01 (s, 3 H, $CH_3$), 4.30 (s, 2 H, $CH_2$), 7.21–7.64 (m, 5 H, ArH), 7.75 [s, 1 H, $^2J$ ($SeH_5$) = 41.6 Hz, $H_5$-selenazole], 9.15 (s, 4 H, $H_2N$, $H_2N^+$).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 23.63 ($CH_3$), 31.59 ($CH_2$), 118.63, 128.61, 129.64, 130.12 (CH), 139.67, 144.39 (C), 163.08 (C=O), 170.12, 170.74 (C-2, $C=NH_2$).

$^{77}$Se NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 681.99.

MS (EI): *m*/*z* = 354 ($M^+$, 2), 314 (6), 312 (34), 310 (14), 272 (12), 270 (58), 268 (27), 237 (56), 235 (28), 197 (2), 189 (12), 166 (4), 156 (11), 118 (18), 93 (13), 77 (42), 71 (10), 51 (19), 43 (100).

Anal. Calcd for $C_{13}H_{15}N_4ClOSSe$ (389.77): C, 40.06; H, 3.88; N, 14.37; Cl, 9.09. Found: C, 39.70; H, 3.90; N, 14.38; Cl, 9.04.

**_Se_-[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyl]-_N_-phenylisoselenouronium Chloride (5g)**

A mixture of **3b** (0.95 g, 3.0 mmol) and *N*-phenylselenourea (0.60 g, 3.0 mmol) in PrOH (20 mL) was refluxed for 1 h. PrOH was distilled in vacuo. After cooling and addition of $Et_2O$, a crystalline precipitate formed which was recrystallized (EtOH–$Et_2O$, 1:1) to give **5g**.

Yield: 0.72 g (47%); slight brown prisms; mp 202–203 °C.

IR (KBr): 996 (w), 1080 (w), 1150 (w), 1180 (w), 1220 (w), 1285 (s), 1345 (m), 1380 (s), 1450 (s), 1480 (s), 1498 (s), 1585 (s), 1598 (s), 1645 (s), 1690 (s), 2930 (m), 3055 (w) $cm^{-1}$.

$^1$H NMR (DMSO-$d_6$, 100 MHz): δ = 2.11 (s, 3 H, $CH_3$), 4.32 (s, 2 H $CH_2$), 7.02–7.72 (m, 9 H, ArH, $H_5$-selenazole), 9.30 (s, 3 H, NH, $H_2N^+$).

Anal. Calcd for $C_{19}H_{19}N_4ClOSe_2$ (512.77): C, 44.51; H, 3.73; N, 10.92; Cl, 6.91. Found: C, 44.52; H, 3.78; N, 10.50; Cl, 6.83.

**[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyl]hexamethylenetetrammonium Iodide (5h)**

An EtOH solution (50 mL) of NaI (1.00 g, 5.0 mmol) was added to a mechanically stirred solution of urotropine (1.00 g, 7.5 mmol). An EtOH solution (15 mL) of **3c** (1.57 g, 5.0 mmol) was poured into the mixture. The solution was allowed to stand at 20 °C for 2 d. The precipitated product was collected by filtration and recrystallized (EtOH) to give **5h**.

Yield: 1.87 g (69%); colorless prisms; mp 158–160 °C.

IR (KBr): 702 (m), 783 (m), 807 (w), 826 (m), 934 (m), 1006 (s), 1042 (m), 1121 (m), 1121 (m), 1225 (w), 1268 (s), 1296 (s), 1311 (m), 1374 (m), 1455 (m), 1484 (s), 1493 (s), 1659 (m), 1675 (m), 2980 (w) $cm^{-1}$.

$^1$H NMR (DMSO-$d_6$, 300 MHz): δ = 2.00 (s, 3 H, $CH_3$), 3.89 (s, 2 H, $NCH_2$), 4.42 (d, 3 H, $NCH_2$), 4.56 (d, 3 H, $NCH_2$), 4.93 (s, 6 H, $NCH_2$), 7.48 (m, 5 H, ArH), 8.01 [s, 1 H, $^2J$ ($SeH_5$) = 40.64 Hz, $H_5$-selenazole].

$^{13}$C NMR (DMSO-$d_6$, 50 MHz): δ = 23.56 ($CH_3$), 55.34, 69.74, 77.88 ($CH_2$), 125.14, 128.73, 129.11, 129.67 (CH), 136.66, 140.09 (C), 162.90 (C=O), 170.15 (C-2).

$^{77}$Se NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 692.12.

MS (EI): *m*/*z* = 417/420 ($M^+$, 100/18), 415 (20), 306 (25), 280 (20), 238 (28), 184 (28), 140 (6), 119 (4), 91 (12), 77 (30), 58 (76), 43 (90).

Anal. Calcd for $C_{18}H_{23}N_6IOSe$ (545.26): C, 39.65; H, 4.25; N, 15.42. Found: C, 39.80; H, 4.40; N, 15.45.

**[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyl]trimethylammonium Iodide (5i)**

Compound **1c** (4.05 g, 10.0 mmol) was dissolved in $C_6H_6$ (35 mL) and $Me_3N$ (2 mL) was added dropwise. The mixture was gently heated and subsequently allowed to stand at 20 °C for 2 h to give a crystalline precipitate which was filtered off.

Yield: 4.64 g (100%); colorless prisms (DMF–$Et_2O$); mp 232–234 °C.

IR (KBr): 698 (m), 759 (w), 806 (w), 892 (m), 954 (m), 989 (m), 1139 (m), 1286 (s), 1304 (s), 1320 (m), 1382 (m), 1429 (w), 1453 (w), 1489 (s), 1596 (m), 1667 (s) $cm^{-1}$.

$^1$H NMR ($CDCl_3$, 100 MHz): δ = 1.96 (s, 3 H, $CH_3$), 3.13 (s, 9 H, Me), 4.58 (s, 2 H, $CH_2$), 7.17–7.52 (m, 5 H, ArH), 8.37 (s, 1 H, $H_5$-selenazole).

$^{13}$C NMR (DMSO-$d_6$): δ = 23.59 ($CH_3$), 52.02, 63.89 [$CH_2$, $N(CH_3)$], 126.40, 128.70, 129.02, 129.66 (CH), 139.17, 139.98 (C), 162.43 (C=O), 170.22 (C-2).

$^{77}$Se NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 696.98.

MS (EI): *m*/*z* = 336/338/339 ($M^+$, 50/100/60), 279 (12).

Anal. Calcd for $C_{15}H_{20}N_3IOSe$ (464.21). C, 38.81; H, 4.34; N, 9.05. Found: C, 39.10; H, 4.10; N, 8.97.

**[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyltrimethyl]ammonium Chloride (5j)**

The product was obtained by reaction of **3b** (3.14 g, 10.0 mmol) and $Me_3N$ (2 mL) in $C_6H_5$ (5 mL) as described for the preparation of **5i**.

Yield: 3.71 g (100%); colorless prisms (DMF–$Et_2O$); mp 228–230 °C.

Anal. Calcd for $C_{15}H_{20}N_2ClOSe$ (372.7): C, 48.34, H, 5.41; N, 11.27; Se, 21.18. Found: C, 48.40; H, 5.40; N, 10.86; Se, 21.07.

**[2-(_N_-Acetylanilino)-1,3-selenazol-4-ylmethyl]triethylammonium Iodide (5k)**

The product was obtained by reaction of **1c** (4.05 g, 10.0 mmol) and $Et_3N$ (2 mL) in $C_6H_6$ (50 mL). The mixture was allowed to stand at 20 °C for 2 d to give a precipitate, which was filtered off.

Yield: 5.06 g (100%); colorless prisms (DMF–$Et_2O$); mp 230–232 °C.

IR (KBr): 705 (m), 730 (w), 760 (m), 770 (s), 800 (m), 840 (w), 900 (w), 940 (w), 960 (w), 995 (m), 1015 (w), 1030 (w), 1080 (w), 1115 (w), 1130 (w), 1160 (w), 1180 (w), 1270 (m), 1300 (s), 1375 (s), 1455 (s), 1500 (s), 1525 (m), 1600 (s), 1670 (s), 3010 (w), 3050 (w) $cm^{-1}$.

$^1$H NMR ($CDCl_3$, 100 MHz): δ = 1.05 (t, 9 H, $CH_3$), 1.97 (s, 3 H, Me), 3.16 (q, 6 H, $CH_2$), 4.30 (s, 2 H, $CH_2$), 7.20–7.52 (m, 5 H, ArH), 8.28 (s, 1 H, $H_5$-selenazole).

Anal. Calcd for $C_{18}H_{26}NIOSe$ (506.3): C, 42.70; H, 5.18; N, 8.30. Found: C, 42.50; H, 5.10; N, 8.34.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]triethylammonium Chloride (5l)**

The product was obtained by reaction of **3b** (3.14 g, 10.0 mmol) and $Et_3N$ (2 mL) in $C_6H_6$ (50 mL). The mixture was allowed to stand at 20 °C for 1 month.

Yield: 4.15 g (100%); colorless prisms (DMF–$Et_2O$); mp 226–228 °C.

Anal. Calcd for $C_{18}H_{26}N_3ClOSe$ (414.84): C, 52.12; H, 6.32; N, 10.13; Se, 19.03. Found: C, 52.26; H, 6.45; N, 10.35; Se, 19.33.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]-*N*,*N*-diethylanilinium Iodide (5m)**

Compound **1c** (4.05 g, 10.0 mmol) was added portionwise to a DMF solution (10 mL) of $PhNEt_2$ (1 mL) with stirring. After stirring for 2 h, the mixture was treated with $Et_2O$ and the precipitated product was separated by filtration.

Yield: 5.54 g (100%); colorless lamella (EtOH); mp 151–153 °C.

IR (KBr): 700 (w), 800 (m), 835 (w), 850 (w), 980 (w), 940 (w), 960 (w), 1000 (w), 1090 (w), 1075 (w), 1115 (w), 1205 (m), 1260 (m), 1300 (s), 1380 (m), 1460 (m), 1495 (s), 1600 (m), 1675 (s), 3035 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 100 MHz): δ = 0.77 (t, 6 H, $CH_3$) 1.96 (s, 3 H, $CH_3$), 3.77 (m, 4 H, $CH_2$), 4.85 (s, 2 H, $CH_2$) 7.19–7.97 (m, 10 H, ArH, $H_5$-selenazole).

Anal. Calcd for $C_{22}H_{26}N_3IOSe$ (554.3): C, 47.67; H, 4.73; N, 7.58. Found: C, 47.60; H, 4.60; N, 7.56.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]pyridinium Iodide (5n)**

A mixture of **3c** (4.05 g, 10.0 mmol), pyridine (1 mL) and DMF (10 mL) was stirred at 20 °C for 3 h. The solution was treated with $Et_2O$ and the precipitated product was separated by filtration.

Yield: 4.45 g (90%); colorless prisms (EtOH); mp 223–224 °C.

IR (KBr): 705 (s), 742 (m), 774 (m), 991 (m), 1041 (w), 1169 (m), 1287 (s), 1313 (m), 1328 (m), 1340 (m), 1372 (s), 1444 (w), 1484 (s), 1596 (m), 1630 (m), 1666 (s), 3045 (m) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 2.05 (s, 3 H, $CH_3$), 5.64 (s, 2 H, $CH_2$), 7.32–8.78 (m, 11 H, ArH, $H_5$-selenazole and pyridine).

$^{13}C$ NMR (DMSO-$d_6$): δ = 23.56 ($CH_3$), 60.19 ($CH_2$), 120.23, 127.73, 128.58, 128.91, 129.55 (CH), 139.61, 142.54 (C), 144.67, 145.87 (CH), 162.63 (C=O), 170.06 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 691.99.

Anal. Calcd for $C_{17}H_{16}N_3IOSe$ (484.2): C, 41.91; H, 3.30; N, 8.62. Found: C, 41.82; H, 3.34; N, 8.67.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]-3-methylpyridinium Iodide (5o)**

The compound was obtained from **3c** (4.05 g, 10.0 mmol) and 3-methylpyridine (1 mL) in DMF (10 mL) as described for the preparation of **5n**.

Yield: 4.60 g (92%); colorless rods (EtOH); mp 214–215 °C.

IR (KBr): 707 (m), 758 (m), 992 (w), 1024 (w), 1155 (m), 1170 (m), 1247 (m), 1282 (s), 1303 (s), 1337 (m), 1375 (s), 1487 (s), 1505 (s), 1595 (m), 1633 (w), 1667 (s), 2981 (m), 3001 (m), 3035 (m), 3048 (m) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.99 (s, 3 H, $CH_3$), 2.46 (s, 3 H, $CH_3$), 5.63 (s, 2 H, $CH_2$), 7.31–8.71 (m, 10 H, ArH, $H_5$-selenazole, pyridine).

$^{13}C$ NMR (DMSO-$d_6$, 50 MHz): δ = 17.88 ($CH_3$ to pyridine), 23.55 ($CH_3$), 59.90 ($CH_2$), 120.18, 127.04, 128.54, 128.87, 129.81 (CH), 138.05, 139.62 (C), 141.79 (CH), 142.35 (C), 144.22, 146.05 (CH), 162.55 (C=O), 169.98 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 699.86.

MS (EI): *m*/*z* = 368/369/370/372/374 ($M^+$, 19/20/58/100/20), 279 (30), 237 (18), 176 (4).

Anal. Calcd for $C_{18}H_{18}N_3IOSe$ (498.2): C, 43.39; H, 3.64; N, 8.43. Found: C, 43.40; H, 3.70; N, 8.61.

**[2-(*N*-Acetylanilino)selenazol-4-ylmethyl]-1,10-phenanthrolinium Iodide (5p)**

A mixture of **3c** (4.05 g, 10.0 mmol) and 1,10-phenanthroline (1.8 g, 10 mmol) in DMF (10 mL) was heated for 1 min at 40 °C. After cooling and addition of $Et_2O$, a crystalline precipitate was formed. The product was collected by filtration.

Yield: 4.00 g (68%); yellow prisms (DMF–$Et_2O$); mp 194–196 °C.

IR (KBr): 698 (w), 727 (w), 758 (w), 852 (w), 991 (m), 1155 (w), 1241 (w), 1284 (s), 1371 (m), 1486 (s), 1527 (m), 1591 (w), 1668 (s), 2991 (w), 3050 (w) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.80 (s, 3 H, $CH_3$), 6.94 (s, 2 H, $NCH_2$), 7.31–9.40 (m, 13 H, ArH, phenanthroline), 7.82 [s, 1 H, $^2J$ ($SeH_5$) = 41.91 Hz, $H_5$-selenazole].

$^{13}C$ NMR (DMSO-$d_6$, 50 MHz): δ = 23.44 ($CH_3$), 62.78 ($CH_2$), 117.50, 124.06, 125.24, 126.78, 128.15, 128.69, 129.30, 130.51 (CH), 131.38, 132.11, 136.47 (C), 137.68 (CH), 139.45, 139.51, 144.10 (C), 147.45, 149.36, 151.52 (CH), 161.42 (C=O), 169.74 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 696.14.

Anal. Calcd for $C_{24}H_{19}N_4IOSe$ (585.3): C, 49.25; H, 3.27; N, 9.57. Found: C, 49.30; H, 3.10; N, 9.60.

**[2-(*N*-Acetylanilino)-1,3-selenazol-4-ylmethyl]triphenylphosphonium Iodide (5q)**

A $CDCl_3$ solution (5 mL) of **1c** (0.40 g, 1.0 mmol) and $Ph_3P$ (0.26 g, 1.0 mmol) was stirred for 1 h at 20 °C. The mixture was allowed to stand for 3 d to give a crystalline precipitate.

Yield: 0.67 g, (100%); colorless prisms (EtOH–$H_2O$); mp 204–205 °C.

IR (KBr): 635 (w), 694 (m), 751 (m), 846 (w), 993 (w), 1110 (m), 1156 (w), 1296 (s), 1330 (w), 1372 (m), 1483 (m), 1519 (w), 1591 (w), 1670 (s), 2847 (w), 3053 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 300 MHz): δ = 1.95 (s, 3 H, $CH_3$), 5.23–5.27 (d, 2 H, *J* = 13.8 Hz), 6.95–8.17 (m, 20 H, ArH), 8.17–8.18 (d, *J* = 3.37 Hz, 1 H), $^2J$ ($SeH_5$) = 43.34 Hz, $H_5$-selenazole.

$^{13}C$ NMR (75 MHz, DMSO-$d_6$): δ = 23.42 ($CH_3$), 27.02 (d, $CH_2$), 118.34, 119.48 (Ar), 120.99 (d, Ph to P), 128.34, 129.0 (Ar), 129.66 (d, Ph to P), 133.52 (d, Ph to P), 134.34 (Ar), 137.65 (d, Ph to P), 139.56 (Ar), 162.03 (C=O), 170.01 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 683.99.

MS: *m*/*z* = 539/540/541/542/543 ($M^+$, 13/65/100/32/20).

Anal. Calcd for $C_{30}H_{26}N_2IOPSe$ (667.4): C, 53.99; H, 3.93; N, 4.20. Found: C, 53.70; H, 4.00; N, 4.45.

**[2-(*N*-Acetylanilino)selenazol-4-ylmethyl]triphenylphosphonium Chloride (5r)**

Compound **3b** (0.31 g, 1.0 mmol) and $Ph_3P$ (0.26 g, 1.0 mmol) in $CDCl_3$ (5 mL) was allowed to stand at 20 °C for 6 d. The precipitated product was collected by filtration.

Yield: 0.50 g (100%); colorless prisms (EtOH–$Et_2O$); mp 244–246 °C.

IR (KBr): 1110 (m), 1250 (m), 1308 (s), 1430 (m),1480 (s), 1560 (s), 2961 (s) $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$, 300 MHz): δ = 1.89 (s, 3 H, $CH_3$), 5.10–5.15 (d, $CH_2$, *J* = 13.8 Hz), 7.13–7.89 (m, 21 H, ArH, $H_5$-selenazole).

Anal. Calcd for $C_{30}H_{26}N_2ClOPSe$ (575.94): C, 62.56; H, 4.55; N, 4.86. Found: C, 62.61; H, 4.65; N, 4.69.

**1,4-[Bis-2-(*N*-acetylanilino)-1,3-selenazol-4-ylmethyl]piperazine (6)**

Compound **3b** (6.30 g, 20.0 mmol) and piperazine hexahydrate (2.80 g, 20.0 mmol) were dissolved in acetone (20 mL). The mixture was allowed to stand for 2 d. During this time a crystalline precipitate formed which was filtered off.

Yield: 0.70 g (32%); colorless lamella (PrOH); mp 211 °C.

$^1H$ NMR (DMSO-$d_6$, 100 MHz): δ = 1.97 (s, 6 H, $CH_3$), 4.07–4.12 (t, 8 H, $NCH_2$), 7.43–8.01 (m, 12 H, ArH, $H_5$-selenazole).

Anal. Calcd for $C_{28}H_{30}N_6O_2Se_2$ (640.5): C, 52.51; H, 4.72; N, 13.12. Found: C, 52.48; H, 4.70; N, 12.92.

**Tris[2-(*N*-acetylanilino)-1,3-selenazol-4-ylmethyl]amine (7a)**

To a DMF solution (50 mL) of **3c** was added $NH_3$ for 15 min with stirring. The precipitated product was collected by filtration.

Yield: 2.83 g (100%); colorless prisms (DMF); mp 244–246 °C.

IR (KBr): 705 (w), 745 (w), 765 (w), 835 (m), 950 (m), 995 (m), 1040 (m), 1060 (m), 1080 (m), 11.30 (m), 1165 (m), 1180 (m), 1240 (m), 1292 (s), 1320 (m), 1375 (s), 1430 (m), 1460 (m), 1490 (s), 1530 (m), 1600 (m), 1675 (s), 28.30 (w), 3080 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 100 MHz): δ = 1.89 (s, 9 H, $CH_3$), 3.29 (s, 6 H, $CH_2$), 7.10–7.54 (m, 18 H, ArH, $H_5$-selenazole).

$^{13}C$ NMR (50 MHz, DMSO-$d_6$): δ = 23.56 ($CH_3$), 58.89 ($CH_2$), 127.24, 128.82, 129.25, 129.98 (CH), 138.27, 140.19 (C), 162.08 (C=O), 170.16 (C-2).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 692.79.

Anal. Calcd for $C_{26}H_{33}N_7O_3Se_3$ (848.6): C, 50.95; H, 3.92; N, 11.35; Se, 27.91. Found: C, 50.80; H, 4.10; N, 11.51; Se, 28.33.

**Tris[2-(*N*-acetylanilino)selenazol-4-ylmethyl]methylammonium Iodide (7b)**

To a stirred DMF solution (70 mL) of **7a** (2.55 g, 3.0 mmol) MeI (1.14 g, 8.0 mmol) was added dropwise at 60 °C. After cooling, $Et_2O$ was added to give a colorless precipitate.

Yield: 1.90 g (64%); colorless prisms (DMF–$Et_2O$); mp 184–186 °C.

IR (KBr): 700 (m), 759 (w), 994 (w), 1117 (w), 1164 (w), 1291 (s), 1373 (m), 1429 (w), 1455 (w), 1488 (s), 1599 (w), 1672 (s), 3012 (w), 3058 (w), 3093 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 100 MHz): δ = 2.11 (s, 9 H, $CH_3$), 2.55 (s, 3 H, $CH_3$), 4.21 (s, 6 H, $CH_2$), 7.59–7.75 (m, 18 H, ArH, $H_5$-selenazole).

$^{77}Se$ NMR (DMSO-$d_6$, 60% $Me_2Se$ in $CDCl_3$): δ = 692.79.

MS (EI): *m*/*z* = 860/862/864/866 ($M^+$, 46, 38, 69, 78, 62), 602 (96), 468 (10), 406 (40), 379 (95), 278 (100), 236 (29), 207 (18).

Anal. Calcd for $C_{37}H_{36}N_7IO_3Se_3$ (990.5): C, 44.86; H, 3.66; N, 9.90; I, 12.65. Found: C, 45.10; H, 3.90; N, 10.03; I, 12.65.

**Tetrakis[2-(*N*-acetylanilino)-1,3-selenazol-4-ylmethyl]ammonium Iodide (7c)**

A DMF solution (70 mL) of **7a** (2.55 g, 3.0 mmol) and **3c** (1.20 g, 3.0 mmol) was heated at 100 °C. Further preparation was carried out as described for **7a**.

Yield: 2.90 g (77%); yellow prisms (DMF–$Et_2O$); mp 185–187 °C.

IR (KBr): 701 (s), 724 (w), 741 (w), 760 (m), 825 (w), 843 (w), 953 (w), 990 (m), 1102 (w), 1175 (w), 1296 (s), 1428 (m), 1437 (m), 1452 (m), 1490 (m), 1494 (m), 1673 (s), 3006 (w), 3099 (w) $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 300 MHz): δ = 2.06 (s, 12 H, $CH_3$), 3.92, (s, 8 H, $CH_2$), 6.80 [s, 1 H, $^2J$ ($SeH_5$) = 42.73 Hz, $H_5$-selenazole], 7.39–8.02 (m, 24 H, ArH, $H_5$-selenazole).

$^{13}C$ NMR (50 MHz, DMSO-$d_6$): δ = 23.71 ($CH_3$), 57.84 ($CH_2$), 127.83, 128.93, 129.63, 130.61 (CH), 138.10, 140.38 (C), 162.06 (C=O), 170.15 (C-2).

$^{77}Se$ NMR ($CDCl_3$, 60% $Me_2Se$ in $CDCl_3$): δ = 681.99.

Anal. Calcd for $C_{48}H_{44}N_9IO_4Se_4$ (1253.4): C, 45.99; H, 3.54; N, 10.05; I, 10.12. Found: C, 45.60; H, 3.80; N, 10.11; I, 9.93.

## Acknowledgment

Financial support from the Deutsche Forschungsgemeinschaft (Heisenberg-scholarship for P. L. and Normalverfahren) is gratefully acknowledged.

## References

(1) For the antibiotically active *C*-glycosyl selenazole selenazofurin, see: Goldstein, B. M.; Kennedy, S. D.; Hennen, W. J. *J. Am. Chem. Soc.* **1990**, *112*, 8265; and references cited therein.

(2) (a) Larsen, R. *1,3-Selenazoles, In Comprehensive Heterocyclic Chemistry II*, Vol. 3; Shinkai, I.; Katritzky, A.; Rees, C. W.; Scriven, E. F. V., Eds.; Elsevier Science: Oxford, **1996**, Chapt. 8:. (b) Wirth, T. *Organoselenium Chemistry. Modern Developments in Organic Synthesis*; Springer: Berlin, **2000**.

(3) (a) Koketsu, M.; Nada, F.; Ishihara, H. *Synthesis* **2002**, 195. (b) Geisler, K.; Jacobs, A.; Künzler, A.; Mattes, M.; Girrleit, I.; Zimmermann, B.; Bulka, E.; Pfeiffer, W.-D.; Langer, P. *Synlett* **2002**, 1983. (c) Lai, L.-L.; Reid, D. H. *Synthesis* **1993**, 870. (d) Ishihara, H.; Koketsu, M.; Fukuta, Y.; Nada, F. *J. Am. Chem. Soc.* **2001**, *123*, 8408. (e) Koketsu, M.; Fukuta, Y.; Ishihara, H. *Tetrahedron Lett.* **2001**, *42*, 6333. (f) Zhang, P.-F.; Chen, Z.-C. *Synthesis* **2000**, *9*, 1219. (g) Maeda, H.; Kambe, N.; Sonoda, N.; Fujiwara, S.-I.; Sinike, T. *Tetrahedron* **1997**, *53*, 13667. (h) Ogawa, A.; Miyaka, J.; Karasaki, Y.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1985**, *50*, 384. (i) Kaminski, R.; Glass, R. S.; Skowronska, A. *Synthesis* **2001**, 1308. (j) Cohen, V. J. *Synthesis* **1978**, 668.

(4) Banert, K.; Toth, C. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1627; *Angew. Chem.* **1995**, *107*, 1776, and references cited therein.

(5) (a) Hartmann, H.; Eckert, K.; Schröder, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 556; *Angew. Chem.* **2000**, *112*, 567, and references cited therein. (b) Keil, D.; Hartmann, H.; Zug, I.; Schröder, A. *J. Prakt. Chem.* **2000**, *342*, 169.

(6) For 4-halomethyl-1,3-thiazoles, see: Simiti I., Farkas M., Silberg S.; *Chem. Ber.;* **1962**, *95:* 2672.

(7) (a) For a preliminary communication, see: Geisler, K.; Meinke, H.-J.; Müller, C.; Nobst, E.; Bulka, E. *Wiss. Z. Univ. Greifswald* **1988**, *37*, 1. (b) for reactions of 4-chloromethyl-1,3-selenazoles, see: Kumar, Y.; Green, R.; Borysko, K. Z.; Wise, ; Wotring, L. L.; Townsend, L. B. *J. Med. Chem.* **1993**, *36* , 3843. (c) Hanson, R. N.; Davis, A. M. *J. Heterocycl. Chem.* **1981**, *18*, 205. (d) Shafiee, A.; Kiaeay, G.; Vosooghi, M. *J. Heterocycl. Chem.* **1981**, *18*, 789.

(8) For the synthesis of **2**, see: Bulka, E.; Ahlers, K.-D.; Tucek, E. *Chem. Ber.* **1967**, *10*, 1367.