Reactions of Imidoyl Isoselenocyanates with Aromatic 2-Amino N-Heterocycles and 1-Methyl-1*H*-imidazole

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The reaction of *N*-phenylimidoyl isoselenocyanates **1** with 2-amino-1,3-thiazoles **10** in acetone proceeded smoothly at room temperature to give 4*H*-1,3-thiazolo[3,2-*a*][1,3,5]triazine-4-selones **13** in fair yields (*Scheme 2*). Under the same conditions, **1** and 2-amino-3-methylpyridine (**11**) underwent an addition reaction, followed by a spontaneous oxidation, to yield the 3*H*-4λ^4-[1,2,4]selenadiazolo[1′,5′:1,5][1,2,4]selenadiazolo[2,3-*a*]pyridine **14** (*Scheme 3*). The structure of **14** was established by X-ray crystallography (*Fig. 1*). Finally, the reaction of 1-methyl-1*H*-imidazole (**12**) and **1** led to 3-methyl-1-(*N*-phenylbenzimidoyl)-1*H*-imidazolium selenocyanates **15** (*Scheme 4*). In all three cases, an initially formed selenourea derivative is proposed as an intermediate.

Introduction. – The interest in Se-containing organic compounds is continuing, mainly because of their biological activities [1][2]. For this reason, convenient syntheses of selenaheterocycles and heterocyclic selones are much sought after. In recent years, the use of isoselenocyanates as easily accessible and safe building blocks has been demonstrated successfully [3]. Among them, the imidoyl derivatives of type **1**, which can be prepared conveniently from *N*-phenylimidoyl chlorides and potassium selenocyanate [4][5] are of special interest because of their bifunctional nature.

We have shown that the reaction of **1** with primary or secondary amines leads to selenourea derivatives, which, by subsequent reaction with activated bromomethylene compounds and treatment with a strong base, yield 2-amino-1,3-selenazoles **2** [5] (*Scheme 1*). Imidoyl isoselenocyanates **1**, R^1 = 2-(chloromethyl)phenyl, react with amines to give 6*H*-5,1,3-benzoselenadiazocines **3** [6]. In both cases, the initial reaction is a nucleophilic attack of the amine onto the isoselenocyanate, followed by an addition of the intermediate thiourea derivative with an electrophile in an inter- or intramolecular fashion. With amidines **4** and **6**, 1,3,5-triazineselones **5** and **7**, respectively, are formed smoothly at room temperature [7] (*Scheme 1*). Similarly, 2-amino-4,5-dihydro-1,3-thiazole (**8**) reacts with **1** to give the fused triazine-selones **9**. The formation of the triazine-selones **5**, **7**, and **9** has been rationalized by the initial formation of a selenourea derivative, followed by cyclization and elimination of aniline (Ar^2 = Ph).

The aim of the present study was the extension of the reaction of **1** with amidines to produce aromatic 2-amino azaheterocycles, such as 2-amino-1,3-thiazoles **10** and 2-

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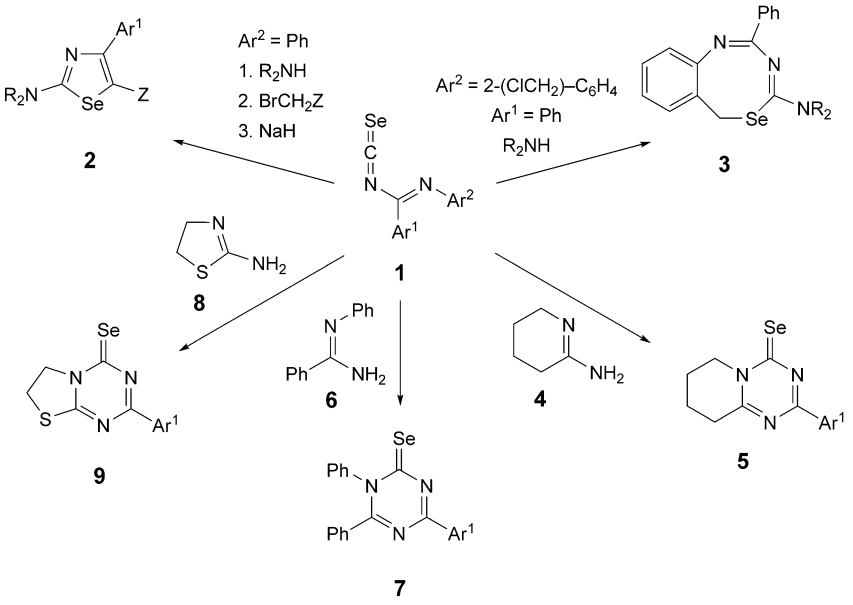
Scheme 1



aminopyridines **11**, *i.e.*, aromatic heterocycles with a formal amidine group, as well as to 1-methyl-1*H*-imidazole (**12**).

Results and Discussion. – The starting materials, *i.e.*, *N*-phenylbenzimidoyl isoselenocyanates **1a**–**1c** were prepared as described in [5]. In acetone at room temperature, they underwent a smooth reaction with equimolar amounts of 2-amino-1,3-thiazoles **10a** and **10b**, respectively, to give 4*H*-1,3-triazolo[3,2-*a*][1,3,5]triazine-4-selones **13** in 53–63% yield (*Scheme 2* and *Table 1*). The products precipitated from the reaction mixture as orange-yellow solids. Their structures were deduced from the spectroscopic data, the elemental analyses, and by analogy to the earlier described 6,7-dihydro derivative **9** ($Ar^1 = 4\text{-Cl–}C_6H_4$), the structure of which has been established by X-ray crystallography [7][2]). The formation of **13** can be rationalized as shown in *Scheme 2*: nucleophilic addition of the ring N-atom of **10** to the isoselenocyanate **1** leads to the intermediate selenourea derivative **B**, which spontaneously undergoes cyclization to give the fused ring system **C**. Elimination of aniline from the latter affords the product **13**.

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[2]) The analogous reaction of phenylbenzimidoyl isothiocyanate with **10a** has been described by *Barnikov* and *Ebeling* [8]. Furthermore, 2-aryl-4*H*-1,3-thiazolo[3,2-*a*][1,3,5]triazine-4-thiones have been obtained from the reaction of **10a** with aroyl isothiocyanates, which were prepared *in situ* from aroyl chlorides and NH_4SCN [9]. On the other hand, **10a** and alkoxycarbonyl isothiocyanates reacted in a non-selective manner *via* nucleophilic addition of either the NH_2 group or the ring N-atom [10].

Scheme 2

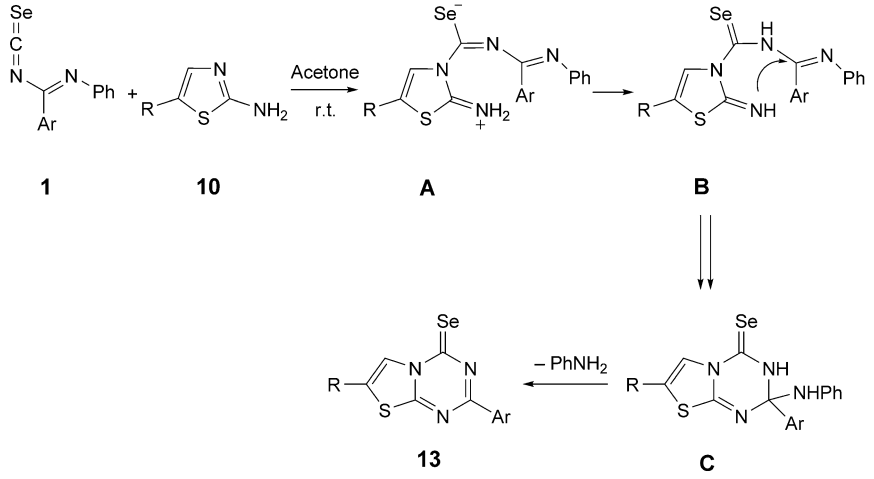


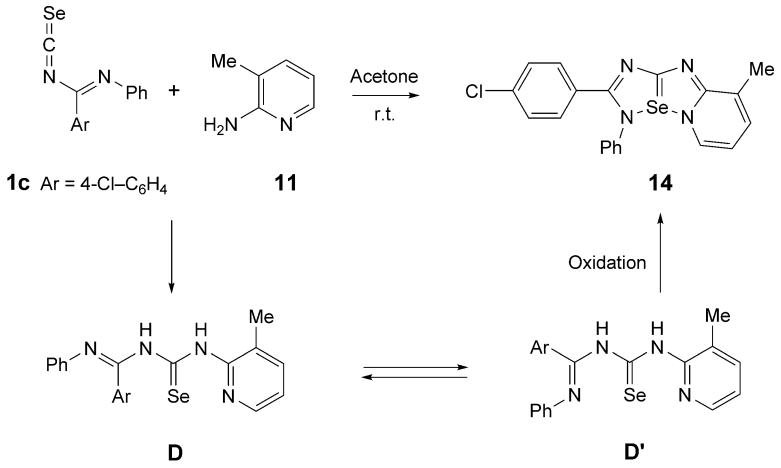
Table 1. *Prepared 2-Aryl-4*H*-1,3-thiazolo[3,2-*a*][1,3,5]triazole-4-selones* **13**

1	Ar	**10**	R	**13**	Yield [%]
1a	Ph	**10a**	H	**13a**	53
1b	4-Me–C_6H_4	**10a**	H	**13b**	60
1c	4-Cl–C_6H_4	**10a**	H	**13c**	60
1a	Ph	**10b**	Me	**13d**	57
1b	4-Me–C_6H_4	**10b**	Me	**13e**	63
1c	4-Cl–C_6H_4	**10b**	Me	**13f**	63

The next experiment was carried out with 2-amino-3-methylpyridine (**11**) and **1c**. It is worth mentioning that the reaction in acetone also occurred at room temperature. After stirring for 3 h, the mixture was poured into H_2O, leading to a yellowish, crystalline product in *ca.* 65% yield. The NMR spectra indicated clearly that no aniline was eliminated, and also the elemental analyses were in accordance with a 1:1 adduct. Therefore, the structure of the selenourea derivative **D** was proposed (*Scheme 3*). Surprisingly, the ^{1}H-NMR spectrum as well as the CI-MS (NH_3) data indicated that two H-atoms were missing. For this reason, a crystal-structure determination of the product was conducted to confirm that 2-(4-chlorophenyl)-9-methyl-3-phenyl-3*H*-4λ^4-[1,2,4]selenadiazolo[1′,5′:1,5][1,2,4]selenadiazolo[2,3-*a*]pyridine (**14**) was formed (*Fig. 1*).

The Se-atom appears to be three-coordinated in that it receives two dative bonds, one from the N-atom of the pyridine ring and the other from the N-atom adjacent to the unsubstituted Ph group. These N–Se bonds are asymmetric, differing by *ca.* 0.12 Å, and they are 0.08 – 0.20 Å longer than the C–Se bond. A normal N–Se bond is *ca.* 1.85 Å, which is in the range of 0.15 – 0.27 Å shorter than the N–Se bonds observed here. The C–Se bond (1.918(2) Å) is *ca.* 0.10 Å longer than the C=Se bond found in an analog of **13c** [7], which is consistent with the effect induced by the N–Se interactions and is

Scheme 3



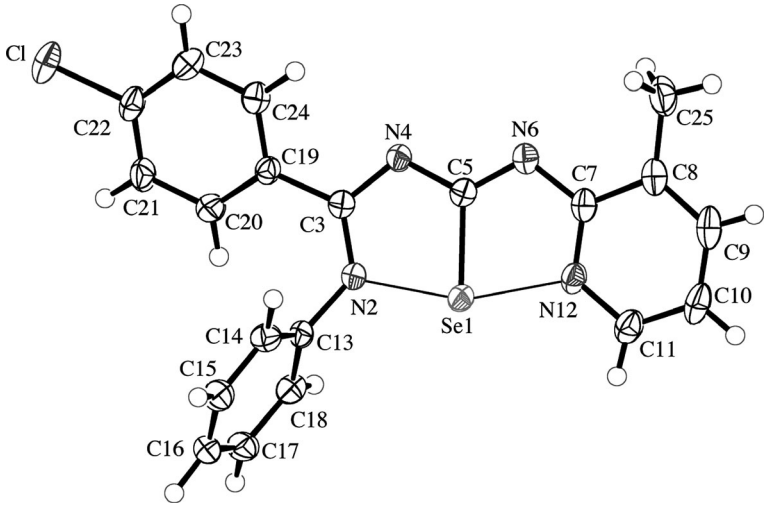


Fig. 1. *ORTEP Plot* [11] *of the molecular structure of* **14** (50% probability ellipsoids, arbitrary numbering of the atoms)

indicative of partial delocalization of the electron density in this bond. Similar C–Se bond lengths of *ca.* 1.90 Å have been observed in some related structures [12], where a formal C–Se bond is adjacent to a π-system. The dative bonds complete two fused five-membered rings. The bond lengths around these rings show considerable delocalization of all C–N bonds and the C–Se bond, which probably implies the existence of canonical forms of a resonance structure. None of the N-atoms in the structure are protonated, which is consistent with the NMR spectra.

The two five-membered rings are quite planar with the maximum deviation from the mean plane being 0.053(2) Å for C(7). This plane is nearly coplanar with that of the fused six-membered ring, the angle between the planes being only 5.09(9)°. If the three fused rings are considered together, the maximum deviation from the mean plane is 0.095(2) Å for N(2). The planes of the chlorophenyl ring and the remaining Ph ring make angles of 18.8(1)° and 75.39(9)°, respectively, with the mean plane of the two fused five-membered rings.

The unexpected formation of **14** may be explained by the initial addition of the amino N-atom of **11** onto the isoselenocyanate to yield the intermediate selenourea **D**. A spontaneous oxidation leads then to the isolated product. In contrast to the reactions with **10**, in which the ring N-atom was the most nucleophilic center, the NH_2 group of **11** acted as nucleophile. This observation may be rationalized by the higher aromaticity of the pyridine ring compared with that of the 1,3-thiazole ring.

Finally, 1-methyl-1*H*-imidazole (**12**), with a formal amidine structure integrated in the five-membered ring, was reacted with **1b** and **1c**, respectively, in acetone (*Scheme 4*). The reaction also proceeded at room temperature. After stirring the mixture overnight, it was poured into H_2O, and the formed precipitate was recrystallized from AcOEt. The elemental analyses showed that the molecular formulae of the products **15b** and **15c** correspond to the sum of the respective starting materials, *i.e.*, no elimination of aniline occurred. The NMR spectra also indicated clearly the presence of all expected H- and C-atoms, *e.g.*, in the case of **15b**, two signals for Me groups appeared at 4.19 and 37.7, and 2.36 and 21.5 ppm. Most remarkable was the appearance of a *singlet* at 9.30 ppm for the H-atom attached to C(2) of the imidazole ring (136.9 ppm). Furthermore, the most dominant absorption band in the IR spectrum (KBr) appeared at 2061 cm^{-1}. On the basis of extended NMR investigations (HSQC, $^1H/^{13}C$ and $^1H/^{15}N$ HMBC, TOCSY, and NOESY), the structures of 3-methyl-1-(*N*-phenylbenzimidoyl)-1*H*-imidazolium selenocyanates **15b** and **15c** were proposed (*Scheme 4*).

The resonances of the three N-atoms of the 1-(benzimidoyl)-1*H*-imidazolium moiety of **15c** were unambiguously localized at −202.4 (N(1)), −177.1 (N(3)), and −72.9 ppm (C=N) (*Fig. 2*). They showed the expected HMBC correlations with the H-atoms of the imidazolium ring as well as the *ortho*-H-atoms of the Ph ring; *e.g.*, N(1) exhibits correlations with H–C(2) at 9.35 ppm, H–C(4) at 7.81 ppm, H–C(5) at 7.67 ppm, and Me–N(1) at 4.18 ppm, whereas N(3) correlates with H–C(2), H–C(4), and H–C(5). The correlations of the imidoyl N-atom with the *ortho*-H-atoms of Ph and the imidoyl C-atom with the *ortho*-H-atoms of the 4-Cl–C_6H_4 moiety are indicative of the molecular structure. The H–C group absorbing at remarkably low field (9.35/137.1 ppm) is attributed to H–C(2) of the imidazolium ring. The characteristic chemical shifts for the selenocyanate ion are 117.8 (^{13}C) and −129.2 ppm (^{15}N). These as well as the IR absorption for the $NCSe^-$ ion are in very good agreement with the data of the recently studied ionic liquid 1-butyl-3-methyl-1*H*-imidazol-3-ium selenocyanate (**16**; *Fig. 2*) [13].

A reaction mechanism for the unexpected formation of **15** is proposed in *Scheme 4*. The first step, in analogy to the reaction of 2-amino-1,3-thiazoles **10** (*Scheme 2*), may be the nucleophilic addition of imidazole **12** to the isoselenocyanate **1** to give a zwitterionic intermediate **I**. The latter undergoes a cyclization to give the fused triazine-

Scheme 4

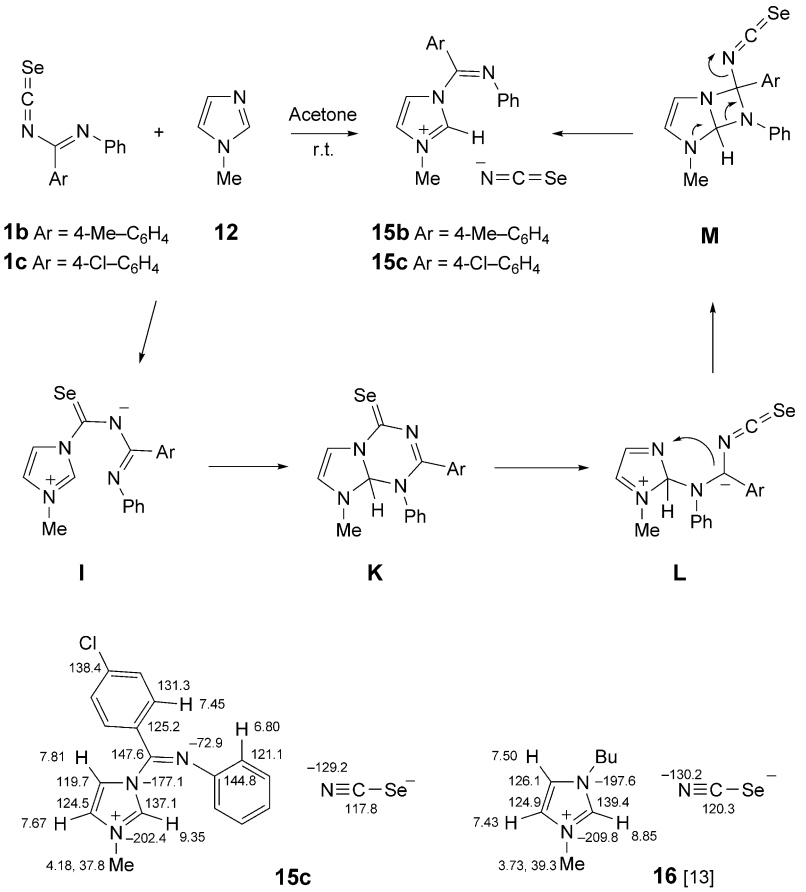


Fig. 2. *Selected ^{1}H-, ^{13}C-, and ^{15}N-NMR chemical shifts of* **15c** *in $CDCl_3$* (δ in ppm)

selone derivative **K**, which then forms a new zwitterion **L** *via* ring opening. Subsequent ring closure may form the fused 1,3-diazetidine **M**, which, *via* elimination of $NCSe^-$, leads to the isolated imidazolium salt.

Conclusions. – The presented results extend the knowledge on reactions of amidines with imidoyl isoselenocyanates **1** to heterocycles containing an 'amidine-like' moiety. The reaction of 2-amino-1,3-thiazoles **10** parallels those with amidines and, most likely, can be extended further to similar five-membered 2-amino heterocycles such as 2-amino-1,3-oxazoles, 2-aminoimidazoles, *etc.* We assume that all the reactions proceed *via* initial nucleophilic attack of the ring N-atom of the 2-amino heterocycle at the most electrophilic heterocumulene C-atom, in contrast to the mechanism formulated for the analogous reaction with aroyl isothiocyanates [9]. On the other hand, the NH_2 group of 2-aminopyridine (**11**) is the most nucleophilic center in the

reaction with **1**, leading to a selenourea derivative, which undergoes a spontaneous oxidation. Again a different type of product is formed in the reaction with 1-methyl-1*H*-imidazole (**12**), in which the initially formed adduct cannot stabilize and, therefore, undergoes a sequence of further reactions to give the imidazolium salts.

In conclusion, isoselenocyanates **1** are prone to react with various 'amidine-like' molecules leading to new Se-containing heterocycles, a reaction type, which deserves to be studied further.

We thank the analytical units of our institute for spectra and analyses, in particular, Dr. *G. Hopp-Rentsch*, for detailed NMR studies. Financial support of the work by the *Dr. Helmut Legerlotz-Foundation* and *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged.

Experimental Part

1. *General.* TLC: Silica gel *60* F_{254} plates (0.25 mm, *Merck*); hexane/AcOEt 1:1 or 2:1 as eluents. Column chromatography (CC): silica gel *60* (0.040–0.063 mm; *Merck*). M.p.: *Büchi B-540* apparatus; in capillary; uncorrected. IR Spectra: *Perkin-Elmer-Spektrum 1600 FT-IR* spectrophotometer; in KBr, in cm^{-1}. ^1H- (300 or 600 MHz), ^{13}C- (75 or 150 MHz), and ^{15}N-NMR (60.6 MHz) spectra: *Bruker ARX-300* or *AMX-600* instrument, in $CDCl_3$; chemical shifts in ppm (rel. to TMS (^1H and ^{13}C) or $MeNO_2$ (^{15}N)), coupling constants *J* in Hz; multiplicities of the ^{13}C signals were determined with DEPT spectra. EI- (70 eV) and CI-MS (NH_3 as carrier gas): *Finnigan MAT-95* or *Finnigan SSQ-700* instrument; ESI-MS: *Finnigan TSQ-700*. Elemental analyses: *Gerber Elementar Analysator EL* instrument.

2. *Starting Materials.* The preparation of *N*-phenylimidoyl isoselenocyanates **1a**–**1c** has been described in [5]. All other starting materials, **10a**, **10b**, **11**, and **12**, were commercially available (*Fluka*, *Sigma-Aldrich*) and were used without purification.

3. *Reactions of* **1** *with 2-Amino-1,3-thiazoles* **10**. To a stirred soln. of **1** (3–4.5 mmol) in acetone (20 ml) at r.t. was added the equivalent amount of **10**. Immediately, a yellow-to-orange precipitate formed. The mixture was stirred at r.t. for 1 h, the formed precipitate was filtered under vacuum, washed with some acetone, and dried in vacuum. The products were recrystallized from acetone or DMF.

*2-Phenyl-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13a**). From 878 mg (3.4 mmol) of **1a** and 340 mg (3.4 mmol) of **10a**. Yield: 0.53 g (53%). Orange crystals. M.p. 281.4–282.4° (acetone/DMF). IR (KBr): 3095*m*, 1548*m*, 1538*m*, 1513*s*, 1492*m*, 1456*s*, 1391v*s*, 1346*m*, 1325v*s*, 1296v*s*, 1279*m*, 1255*s*, 1164*w*, 1130*m*, 1093*m*, 1072*w*, 1022*w*, 999*w*, 978*w*, 942*w*, 892*m*, 848*s*, 800*w*, 756*w*, 716*s*, 693*s*. ^1H-NMR (300 MHz, $CDCl_3$): 8.93 (*d*, *J* = 4.9, 1 H); 8.61–8.57 (*m*, 2 arom. H); 7.64–7.57 (*m*, 1 arom. H); 7.53–7.48 (*m*, 2 arom. H); 7.32 (*d*, *J* = 4.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 179.4 (*s*, C=Se); 167.5, 160.3 (2*s*, C(2), C(8a)); 133.1 (*s*, 1 arom. C); 133.6, 130.5, 128.8 (3*d*, 5 arom. CH); 128.6, 112.9 (2*d*, C(5), C(6)). EI-MS: 295 (5), 294 (3), 293 (22, M^+), 291 (10), 290 (4), 289 (4), 188 (13), 187 (100), 104 (8), 103 (15), 84 (14), 77 (70). Anal. calc. for $C_{11}H_7N_3SSe$ (292.22): C 45.21, H 2.41, N 14.38, S 10.97; found: C 45.26, H 2.40, N 14.38, S 10.96.

*2-(4-Methylphenyl)-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13b**). From 987 mg (3.3 mmol) of **1b** and 330 mg (3.3 mmol) of **10a**. Yield: 0.60 g (59%). Yellow crystals. M.p. 295–296° (acetone). IR (KBr): 3131*w*, 3039*m*, 1604*w*, 1572*w*, 1536*s*, 1521v*s*, 1506*s*, 1422*s*, 1392v*s*, 1328*s*, 1300*s*, 1292*s*, 1254*s*, 1176*w*, 1166*m*, 1122*m*, 1016*w*, 892*m*, 845*s*, 790*w*, 772*m*, 740*s*, 711*w*. CI-MS: 310 (20), 309 (13), 308 (100, $[M+1]^+$), 307 (8), 306 (48), 305 (16), 304 (16). Anal. calc. for $C_{12}H_9N_3SSe$ (306.25): C 47.06, H 2.96, N 13.72, S 10.47; found: C 47.04, H 3.07, N 13.63, S 10.46.

*2-(4-Chlorophenyl)-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13c**). From 991 mg (3.1 mmol) of **1c** and 310 mg (3.1 mmol) of **10a**. Yield: 0.59 g (58%). Yellow crystals. M.p. 280° (dec.; acetone). ^1H-NMR (300 MHz, $CDCl_3$): 8.92 (*d*, *J* = 4.9, 1 H); 8.53, 7.47 (*AA'BB'*, J_{AB} = 8.9, 4 arom. H); 7.31 (*d*, *J* = 4.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 179.4 (*s*, C=Se); 167.6, 159.3 (2*s*, C(2), C(8a)); 140.2, 130.5 (2*s*, 2 arom. C); 131.7, 129.1 (2*d*, 4 arom. CH); 128.6, 113.0 (2*d*, C(5), C(6)). Anal. calc. for $C_{11}H_6ClN_3SSe$ (326.67): C 40.45, H 1.85, N 12.86, S 9.82; found: C 40.26, H 2.04, N 12.83, S 9.96.

*7-Methyl-2-phenyl-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13d**). From 878 mg (3.4 mmol) of **1a** and 388 mg (3.4 mmol) of **10b**. Yield: 0.60 g (58%). Orange crystals. M.p. 280–281° (acetone/DMF). IR (KBr): 3101*w*, 3053*w*, 3031*w*, 2967*w*, 1587*m*, 1518v*s*, 1492*m*, 1456*s*, 1401v*s*, 1384v*s*, 1341*s*, 1326*s*, 1298*m*, 1273*m*, 1256*s*, 1182*m*, 1137*m*, 1100*m*, 1080*m*, 1021*w*, 996*w*, 941*w*, 879*m*, 838*s*, 807*m*, 743*s*, 693*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.66 (*q*-like, $J = 1.4$, 1 H); 8.56–8.54 (*m*, 2 arom. H); 7.62–7.51 (*m*, 1 arom. H); 7.49–7.46 (*m*, 2 arom. H); 2.53 (*d*, $J = 1.4$, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 178.7 (*s*, C=Se); 167.1, 160.0 (2*s*, C(2), C(8a)); 133.9, 127.1 (2*s*, 1 arom. C, C(7)); 133.4, 130.4, 128.7 (3*d*, 5 arom. CH); 126.8 (*d*, C(6)); 13.5 (*q*, Me). EI-MS: 309 (12), 308 (8), 307 (55, M^+), 305 (27), 304 (10), 303 (9), 202 (13), 201 (100), 198 (15), 197 (14). Anal. calc. for $C_{12}H_9N_3SSe$ (306.25): C 47.06, H 2.96, N 13.72, S 10.47; found: C 46.99, H 2.83, N 13.85, S 10.63.

*7-Methyl-2-(4-methylphenyl)-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13e**). From 1.376 g (4.6 mmol) of **1b** and 524 mg (4.6 mmol) of **10b**. Yield: 0.93 g (63%). Orange-yellow crystals. M.p. 291° (dec.; DMF). IR (KBr): 3074*m*, 2933*w*, 1606*w*, 1589*m*, 1573*w*, 1530v*s*, 1508*s*, 1456*m*, 1420*s*, 1393v*s*, 1359*s*, 1333*s*, 1298*s*, 1275*s*, 1257*s*, 1179*m*, 1140*s*, 1111*m*, 1100*m*, 1018*w*, 992*w*, 877*m*, 848*s*, 852*w*, 836*s*, 764*s*. CI-MS: 324 (21), 323 (15), 322 (100, $[M+1]^+$), 321 (8), 320 (49), 319 (17), 318 (17), 258 (7). Anal. calc. for $C_{13}H_{11}N_3SSe$ (320.28): C 48.75, H 3.46, N 13.12, S 10.01; found: C 48.58, H 3.37, N 13.07, S 10.11.

*2-(4-Chlorophenyl)-7-methyl-4*H-*[1,3]thiazolo[3,2-*a*][1,3,5]triazine-4-selone* (**13f**). From 991 mg (3.1 mmol) of **1c** and 353 mg (3.1 mmol) of **10b**. Yield: 0.65 g (62%). Orange crystals. M.p. 282.0–282.5° (DMF). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.65 (*q*-like, $J = 1.4$, 1 H); 8.50, 7.46 (*AA′BB′*, $J_{AB} = 8.7$, 4 arom. H); 2.54 (*d*, $J = 1.4$, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 179.0 (*s*, C=Se); 168.0, 158.0 (2*s*, C(2), C(8a)); 140.2, 132.2, 127.5 (3*s*, 2 arom. C, C(7)); 131.5, 129.0 (2*d*, 4 arom. CH); 126.7 (*d*, C(6)); 13.4 (*q*, Me). EI-MS: 343 (17), 342 (6), 341 (38, M^+), 340 (5), 339 (17), 338 (6), 337 (6), 268 (23), 253 (45), 237 (37), 236 (12), 235 (100). Anal. calc. for $C_{12}H_8ClN_3SSe$ (340.69): C 42.31, H 2.37, N 12.33, S 9.41; found: C 42.10, H 2.29, N 12.26, S 9.27.

4. *Reaction of* **1c** *with 2-Amino-3-methylpyridine* (**11**). To a stirred soln. of **1c** (992 mg, 3.1 mmol) in acetone (20 ml) at r.t., 1 equiv. of **11** (335 mg, 3.1 mmol) was added, and the mixture was stirred for 3 h, until the starting materials were completely consumed (TLC). Then, the mixture was poured into H_2O and stirred for another 1 h. The yellowish precipitate was filtered under vacuum and recrystallized from Et_2O to give 0.85 g (64%) of *2-(4-chlorophenyl)-9-methyl-3-phenyl-3*H-*4λ⁴-[1,2,4]selenadiazolo-[1′,5′:1,5][1,2,4]selenadiazolo[2,3-*a*]pyridine* (**14**). M.p. 189.5–190.5. IR: 3041*w*, 2955*w*, 2948*w*, 1605*w*, 1592*w*, 1567*w*, 1511*s*, 1463*s*, 1445*m*, 1401*s*, 1367v*s*, 1319*m*, 1300*m*, 1286*s*, 1274*s*, 1223*m*, 1196*s*, 1125*m*, 1104*m*, 1089*m*, 1071*w*, 1015*m*, 992*w*, 951*m*, 892*w*, 838*m*, 778*m*, 765*w*, 748*m*, 734*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.24 (*dd*-like, $J = 8.7$, 0.8, 1 H); 7.63–7.54 (*m*, 3 H); 7.35–7.20 (*m*, 5 H); 7.08–7.04 (*m*, 2 H); 6.84 (*dd*-like, $J = 7.0$, 5.8, 1 H); 2.64 (*s*, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 174.4 (*s*, C=Se); 162.2, 156.4, 141.2, 136.2, 131.0, 130.5 (6*s*, 3 arom. C, 3 C); 137.0, 135.0, 126.2, 115.4 (4*d*, 1 arom. CH, 3 CH); 131.5, 129.3, 128.1, 125.5 (4*d*, 8 arom. CH); 17.5 (*q*, Me). CI-MS: 430 (5), 429 (38), 428 (19), 427 (100, $[M+1]^+$), 426 (13), 425 (46), 424 (15), 423 (15), 349 (14), 347 (25), 233 (13), 231 (41), 136 (7), 134 (12). Anal. calc. for $C_{20}H_{15}ClN_4Se$ (425.78): C 56.42, H 3.55, N 13.16, Cl 8.33; found: C 56.00, H 3.66, N 12.97, Cl 8.50.

Suitable crystals for the X-ray crystal-structure determination were obtained from Et_2O/AcOEt.

5. *Reactions of* **1** *with 1-Methyl-1*H-*imidazole* (**12**). To a soln. of **1b** (987 mg, 3.3 mmol) or **1c** (895 mg, 2.8 mmol) in acetone (30 ml), 1 equiv. of **12** (271 and 230 mg, resp.) was added, and the mixture was stirred at r.t. overnight. TLC indicated that the starting materials were completely consumed. Then, the mixture was poured into ice/H_2O and stirred for another 2 h. The yellowish precipitate was filtered under vacuum and recrystallized from AcOEt.

*3-Methyl-1-[(Z)-(4-methylphenyl)(phenylimino)methyl]-1*H-*imidazol-3-ium Selenocyanate* (**15b**). Yield: 0.66 g (52%). Pale yellow crystals. M.p. 116.5–117.5° (AcOEt). IR: 3181*w*, 3083*m*, 2061v*s*, 1654*s*, 1608*m*, 1583*s*, 1537*s*, 1509*w*, 1484*m*, 1449*w*, 1417*m*, 1333*s*, 1272*m*, 1233*s*, 1211*m*, 1189*m*, 1143*s*, 1088*m*, 1023*w*, 927*s*, 907*w*, 831*m*, 794*w*, 766*m*, 727*m*, 695*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 9.30 (br. *s*, H–C(2)); 7.78–7.76, 7.74–7.72 (2*m*, 2 H); 7.33–7.27 (*m*, 2 arom. H); 7.27–7.15 (*m*, 4 arom. H); 7.12–7.02 (*m*, 1 arom. H); 6.84–6.78 (*m*, 2 arom. H); 4.19 (*s*, MeN); 2.36 (*s*, Me). ^{13}C-NMR (150 MHz, $CDCl_3$): 148.7 (*s*, C=N); 145.2, 142.8, 123.8 (3*s*, 3 arom. C); 136.9 (*d*, C(2)); 130.2, 129.6, 129.0, 121.2 (4*d*, 2 arom. CH each); 125.5 (*d*, 1 arom. CH); 124.5, 119.8 (2*d*, C(4), C(5)); 117.6 (*s*, NCSe); 37.7 (*q* MeN); 21.5 (*q*, Me).

Table 2. *Crystallographic Data for Compound* **14**

Crystallized from	Et_2O/AcOEt
Empirical formula	$C_{20}H_{15}ClN_4Se$
Formula weight	425.72
Crystal color, habit	yellow, prism
Crystal dimensions [mm]	$0.30 \times 0.35 \times 0.45$
Temp. [K]	173(1)
Crystal system	triclinic
Space group	$P\bar{1}$
Z	2
Reflections for cell determination	25
2θ Range for cell determination [°]	39 – 40
Unit cell parameters:	
a [Å]	9.021(1)
b [Å]	9.503(1)
c [Å]	10.849(2)
α [°]	86.66(1)
β [°]	76.76(1)
γ [°]	89.33(1)
V [Å^3]	903.7(3)
D_x [g cm^{-3}]	1.564
$\mu(\mathrm{Mo}K_\alpha)$ [mm^{-1}]	2.235
Scan type	$\omega/2\theta$
$2\theta_{(\max)}$ [°]	60
Transmission factors (min; max)	0.867; 1.000
Total reflections measured	5584
Symmetry independent reflections	5290
Reflections with $I > 2\sigma(I)$	4284
Parameters refined	236
Final $R(F)$ ($I > 2\sigma(I)$ reflections)	0.0362
$wR(F^2)$ (all data)	0.0973
Weighting parameters: a, b[a])	0.053, 0.1553
Goodness-of-fit	1.056
Final $\Delta_{\max}/\sigma$	0.003
$\Delta\rho$ (max; min) [e Å^{-3}]	0.84; −0.79

[a]) $w^{-1} = [\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (F_o^2 + 2F_c^2)/3$.

^{15}N-NMR (60.6 MHz, $CDCl_3$): −205.3 (N(1)); −178.3 (N(3)); −78.6 (C=N)[3]). Anal. calc. for $C_{19}H_{18}N_4Se$ (381.34): C 59.84, H 4.76, N 14.69; found: C 59.71, H 4.76, N 14.61.

*1-[(4-Chlorophenyl)(phenylimino)methyl]-3-methyl-1*H*-imidazol-3-ium Selenocyanate* (**15c**). Yield: 0.62 g (55%). Pale yellow crystals. M.p. 144° (dec.; AcOEt). IR: 3140*m*, 3071*s*, 2060v*s*, 1672v*s*, 1594*s*, 1532*s*, 1489*s*, 1449*w*, 1415*m*, 1402*m*, 1359*m*, 1332*m*, 1274*m*, 1256*s*, 1214*w*, 1180*w*, 1142*s*, 1110*m*, 1089*s*, 1015*m*, 927*s*, 904*w*, 838*m*, 778*w*, 765*m*, 741*s*, 699*s*. ^{1}H-NMR (600 MHz, $CDCl_3$): 9.34 (br. *s*, H–C(2)); 7.82 – 7.80, 7.68 – 7.60 (2*m*, 2 H); 7.48 – 7.39 (*m*, 4 arom. H); 7.28 – 7.20 (*m*, 2 arom. H); 7.11 – 7.06 (*m*, 1 arom. H); 6.83 – 6.79 (*m*, 2 arom. H); 4.17 (*s*, MeN). ^{13}C-NMR (150 MHz, $CDCl_3$): 147.6 (*s*, C=N); 144.8, 138.4, 125.2 (3*s*, 3 arom. C); 137.1 (*d*, C(2)); 131.3, 129.8, 129.1, 121.1 (4*d*, 2 arom. CH each); 125.7 (*d*, 1 arom. CH); 124.5, 119.7 (2*d*, C(4), C(5)); 117.6 (*s*, NCSe); 37.7 (*q* MeN). ^{15}N-NMR (60.6 MHz,

[3]) The signal for $SeCN^-$ could not be detected.

$CDCl_3$): – 202.4 (N(1)); – 177.1 (N(3)); – 129.2 (NCSe); – 72.9 (C=N). Anal. calc. for $C_{18}H_{15}ClN_4Se$ (401.76): C 53.81, H 3.76, Cl 8.82, N 13.95; found: C 53.71, H 3.79, Cl 8.94, N 13.82.

X-Ray Crystal-Structure Determination of **14** (*Table 2* and *Fig. 1*)[4]). All measurements were performed on a *Rigaku AFC5R* diffractometer using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and a 12-kW rotating anode generator. The data collection and refinement parameters are given in *Table 2*, and a view of the molecule is shown in *Fig. 1*. The intensities were corrected for *Lorentz* and polarization effects. An empirical absorption correction based on azimuthal scans of several reflections [14] was applied. The structure was solved by direct methods using SIR92 [15], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent atom (1.5 U_{eq} for the Me group). Refinement of the structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was not applied. Neutral atom scattering factors for non-H-atoms were taken from [16a], and the scattering factors for H-atoms were taken from [17]. Anomalous dispersion effects were included in F_c [18]; the values for f' and f'' were those of [16b]. The values of the mass attenuation coefficients are those of [16c]. All calculations were performed using the SHELXL97 program [19].

REFERENCES

[1] J. Mlochowski, K. Kloc, R. Lisiak, P. Potaczek, H. Wojtowicz, *ARKIVOC* **2007**, *(vi)*, 14; M. Soriano-Garcia, *Curr. Med. Chem.* **2004**, *11*, 1657; C. W. Nogueira, G. Zeni, J. B. T. Rocha, *Chem. Rev.* **2004**, *104*, 6255; M. Koketsu, H. Ishihara, *Curr. Org. Chem.* **2003**, *7*, 175; G. Mugesh, W.-W. du Mont, H. Sies, *Chem. Rev.* **2001**, *101*, 2125.

[2] D. R. Garud, M. Makimura, M. Koketsu, *New J. Chem.* **2011**, *35*, 581; H. Tao, Y. Weng, R. Zhuo, G. Chang, I. L. Urbatsch, Q. Zhang, *ChemBioChem* **2011**, *12*, 868; E. Ibáñez, D. Plano, M. Font, A. Calvo, C. Prior, J. A. Palop, C. Sanmartín, *Eur. J. Med. Chem.* **2011**, *46*, 265; M. Kaname, M. Minoura, H. Sashida, *Tetrahedron Lett.* **2011**, *52*, 505; Y. Xie, J. Liu, J. Li, *Tetrahedron Lett.* **2011**, *52*, 932; D. Plano, Y. Baquedano, E. Ibáñez, I. Jiménez, J. A. Palop, J. E. Spallholz, C. Sanmartín, *Molecules* **2010**, *15*, 7292; E. H. Lee, Y.-J. Lim, S. K. Ha, T. H. Kang, M. Koketsu, C. Kang, S. Y. Kim, J.-H. Park, *J. Pharm. Pharmacol.* **2010**, *62*, 352; P. Suchocki, I. Misiewicz-Krzemińska, K. Skupińska, K. Niedźwiecka, K. Lubelska, Z. Fijałek, T. Kasprzycka-Guttman, *Pharmacol. Reports* **2010**, *62*, 352; C. Ling, Z. Zheng, X. C. Jiang, W. Zhong, S. Li, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5123; H. Sashida, C. Pan, M. Kaname, M. Minoura, *Synthesis* **2010**, 3091.

[3] M. Ninomiya, D. R. Garud, M. Koketsu, *Heterocycles* **2010**, *81*, 2027; H. Heimgartner, Y. Zhou, P. K. Atanassov, G. L. Sommen, *Phosphorus, Sulfur Silicon Relat. Elem.* **2008**, *183*, 840; D. R. Garud, M. Koketsu, H. Ishihara, *Molecules* **2007**, *12*, 504; M. L. Petrov, N. I. Zmitrovich, *Russ. J. Gen. Chem.* (Transl. of *Zh. Obshch. Khim.*) **1999**, *69*, 245.

[4] N. A. Kirsanova, G. I. Derkach, *Ukr. Khim. Zh.* **1970**, *36*, 372; *Chem. Abstr.* **1970**, *73*, 45417q.

[5] Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 1576.

[6] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2004**, *87*, 1452.

[7] Y. Zhou, A. Linden, H. Heimgartner, *Heterocycles* **2011**, *84*, accepted (DOI: 10.3987/COM-11-S(P)9).

[8] G. Barnikov, H. Ebeling, *Z. Chem.* **1973**, *13*, 468.

[9] S. Saeed, N. Rasid, P. G. Jones, U. Yunas, *J. Heterocycl. Chem.* **2010**, *47*, 908; U. Yunus, M. K. Tahir, M. H. Bhatti, S. Ali, M. Helliwell, *Acta Crystallogr., Sect. E* **2007**, *63*, o3690.

[10] M. Nagano, J. Tobitsuka, T. Matsui, K. Oyamada, *Chem. Pharm. Bull.* **1972**, *20*, 2618.

[11] C. K. Johnson, 'ORTEP II', Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, 1976.

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[4]) CCDC-827538 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* http://www.ccdc.cam.ac.uk/data_request/cif.

[12] Y. Zhou, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 539; *cf.* also P. K. Atanassov, A. Linden, H. Heimgartner, *J. Sulfur Chem.* **2006**, *27*, 181.
[13] A. Solangi, A. M. Bond, I. Burgar, A. F. Hollenkamp, M. D. Horne, T. Rüther, C. Zhao, *J. Phys. Chem. B* **2011**, *115*, 6843.
[14] A. C. T. North, D. C. Phillips, F. S. Mathews, *Acta Crystallogr., Sect. A* **1968**, *24*, 351.
[15] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.* **1994**, *27*, 435.
[16] a) E. N. Maslen, A. G. Fox, M. A. O'Keefe, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) D. C. Creagh, W. J. McAuley, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.6.8, p. 219; c) D. C. Creagh, J. H. Hubbell, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.4.3, p. 200.
[17] R. F. Stewart, E. R. Davidson, W. T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175.
[18] J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781.
[19] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112.

Received June 3, 2011