Synthesis and Structure of Thia and Selena Heterocycles Containing Cycloamidine Substructures

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Abstract: Cyclization of a bis-arylimidoyl chloride with an acylselenourea leads to the construction of a 1,3-selenazolidine with a heteroradialene structure. Another reaction of the bis-arylimidoyl chloride (hydrazinolysis) leads to the formation of Δ^2-1,2-diazetines, which we have shown previously to be reactive precursors for ring transformation reactions that yield unusual heterocycles. We now demonstrate that the reaction of these Δ^2-1,2-diazetines with various isothio- or isoselenocyanates affords an efficient entry to highly substituted 1,3,4-thia- or -selenadiazines. The structures of these novel derivatives were confirmed by NMR and mass spectroscopy, elemental analysis, and X-ray structural analysis. Detailed multidimensional ^{77}Se NMR experiments as well as density functional theory (DFT) calculations show structural specifics of these compounds.

Key words: ring expansion, heterocycles, selenium, sulfur, noncovalent chalcogen interactions

Selenium is an essential trace element and is incorporated in organisms via the non-proteinogenic amino acid selenocysteine and in the active site of redox enzymes such as glutathione peroxidase.[1] Ever since this discovery, there has been increasing scientific interest in the synthesis of selenium compounds and investigation of their pharmacological potential. This has led to quite a few pharmaceutical compounds and agricultural chemicals based on selenium- or sulfur-containing organic compounds. Examples of this interest are the compounds selenazofurine and thiazofurine, which are potent antitumor and antiviral drugs.[2] The antithyroid activity of pharmaceuticals in the methimazol series, based also on the thiazole/selenazole substructure, should be mentioned in this context.[2g]

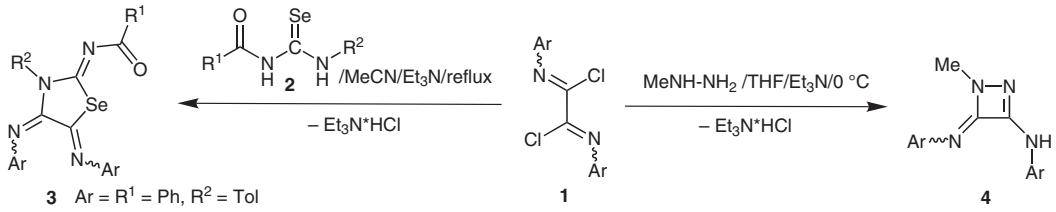
Organic compounds containing selenium are much less stable than their sulfur analogues. Classical synthetic procedures for thioderivatives thus often fail when applied to their seleno counterparts. This is offset by the increasing demand for stable and nontoxic organic compounds containing selenium, especially for potential pharmaceuticals. This dilemma requires a continuous expansion of preparative strategies.[3] In this context we now present two novel strategies for the synthesis of 1,3-selenazolidines and 1,3,4-thia- or -selenadiazines containing highly variable substituent patterns.

During the course of our past work, it has become increasingly clear that bis-arylimidoyl chlorides **1** of oxalic acid are excellent (and selective) biselectrophilic C2-synthons that can be employed in a wide range of heterocyclizations as well as carbocyclizations.[4]

We are now investigating the potential of **1** for providing further entry points for obtaining novel selenium- and sulfur-containing heterocycles (Schemes 1 and 2).

A bis-imidoyl chloride **1** condenses easily with an acylselenourea **2** to give a 1,3-selenazolidine (Scheme 1). Heating a mixture of **1** and **2** in acetonitrile in the presence of triethylamine thus leads to a red product **3** in acceptable yield (Table 1).

Elemental analysis and mass spectroscopy data of **3** indicated a 1:1 cyclization product. A C=Se signal (ca. δ = 185.5)[5] was missing in the ^{13}C NMR spectrum and only one signal at δ = 762.1 was detected in the ^{77}Se NMR spectrum. A single-crystal X-ray analysis showed that selenium had been incorporated into the ring (Figure 1). The



Scheme 1 Synthesis of 1,3-selenazolidines **3** and Δ^2-1,2-diazetines **4a–c** [Ar = 4-*n*-BuC_6H_4 (**4a**), 4-*t*-BuC_6H_4 (**4b**), 4-EtO_2CC_6H_4 (**4c**)]

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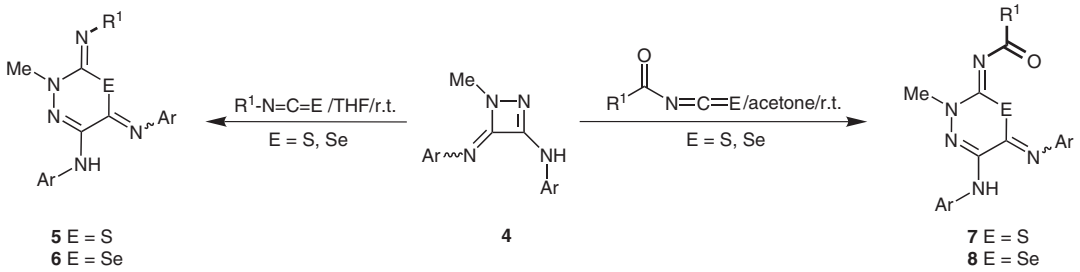

Scheme 2 Synthesis of 1,3,4-thiadiazines **5** and **7** and 1,3,4-selenadiazines **6** and **8** from **4**

unambiguous structural assignment of **3** is shown in Figure 1. The acyl moiety shows a *cis* arrangement with respect to the chalcogen atom (d_{Se-OAc} = 2.591 Å), and the C1–Se–C3 bond angle is 86.6°. 1,3-Selenazolidines such as **3** cannot be obtained by classical synthetic routes. Until now, access to **3** as well as analogous 1,3,4-thia- or -selenadiazines has been limited mainly to the cyclization of α-halo ketones with thio- or selenoureas or thio- or selenosemicarbazides.[3b,6]

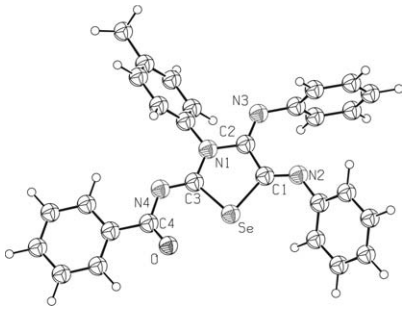

Figure 1 Solid-state structure (X-ray analysis) of derivative **3**

We have previously shown that a controlled hydrazinolysis of **1** conveniently yields Δ^2-1,2-diazetines[7] **4** (Scheme 1), which are quite useful in a number of versatile ring-transformation reactions due to their inherent ring strain.[8] Compounds **4** react with isocyanates to yield semicyclic urea derivatives.[9] In contrast to this, isothiocyanates immediately lead to ring-transformed products, e.g. 1,3,4-thiadiazines **5** (Scheme 2).[9] Animated by this different reactivity, we have now extended our investigations to include acylisothiocyanates, isoselenocyanates, and acylisoselenocyanates.

There are very few existing procedures for obtaining isoselenocyanates.[10] We used the protocol of Barton et al. in which gray selenium is added to in situ generated isocyanides.[10b] The isoselenocyanates obtained in this manner were unstable towards column chromatography and were thus used directly, without further purification, in ring-transformation reactions according to Scheme 2. Upon workup of the reaction mixtures by repetitive crystallization (MeOH–H_2O), the 1,3,4-selenadiazines **6a–c** were obtained in good yields. The selenadiazine structure was confirmed by elemental analysis, mass spectra, and NMR experiments.

Table 1 Synthesis of Sulfur- and Selenium-Substituted Heterocycles **3** and **5–8**[a]

Compound	E (in **5–8**)	Ar	R^1	δ (^{77}Se NMR) (ppm)	Yield (%)
3	–	Ph	Ph	762.1	68
5	S	Tol	PMP	–	89
6a	Se	Tol	PMP	499.72	80
6b	Se	Tol	4-BrC_6H_4	497.52	63
6c	Se	Tol	4-*t*-BuC_6H_4	596.28	84
7a	S	Tol	Me	–	92
7b	S	Tol	Et	–	96
7c	S	Tol	*i*-Pr	–	49
7d	S	Tol	*t*-Bu	–	95
7e	S	Tol	cyclopropyl	–	89
7f	S	Tol	cyclobutyl	–	51
7g	S	Tol	$CHPh_2$	–	80
7h	S	Tol	Ph	–	83
7i	S	Tol	Tol	–	62
7j	S	Tol	PMP	–	90
7k	S	Tol	4-PhC_6H_4	–	86
8b	Se	Tol	Et	594.09	79
8c	Se	Tol	*i*-Pr	501.26	81
8d	Se	Tol	Cyclobutyl	594.41	57
8e	Se	Tol	*t*-Bu	596.05	97
8f	Se	4-BrC_6H_4	*t*-Bu	598.20	92
8g	Se	4-*n*-BuC_6H_4	*t*-Bu	497.52	88
8h	Se	4-*t*-BuC_6H_4	*t*-Bu	597.19	83
8i	Se	4-$EtO_2CC_6H_4$	*t*-Bu	609.10	90
8j	Se	Tol	$CHPh_2$	597.73	86
8k	Se	Tol	Tol	594.30	54
8l	Se	Tol	PMP	595.32	81

[a] See Schemes 1 and 2 for the reactions.

We then explored the reactivity of **4** towards acylheterocumulenes such as $R^1CON{=}C{=}E$ (R^1 = alkyl, aryl; E = S, Se) (Scheme 2). The acylheterocumulenes were generated in situ by addition of the corresponding carboxylic chlorides to a solution of sodium thiocyanate or potassium selenocyanate in dry acetone at 0 °C.[11] Addition of **4** to the solution and stirring for one hour at room temperature yielded the corresponding 1,3,4-thiadiazines **7** or 1,3,4-selenadiazines **8**. The success of this reaction depends significantly on the purity of the carboxylic acid chloride employed. The in situ generated isoselenocyanates decompose rapidly in the presence of traces of hydrochloric acid under extrusion of red amorphous selenium. When the carboxylic acid chlorides were purged by distillation and immediately used, good to excellent yields of the acyl derivatives **7** or **8** were obtained (50–96%; not optimized).

To test the scope and limitations of this reaction, a variety of Δ^2-1,2-diazetines **4** as well as acylheterocumulenes were employed. Table 1 demonstrates that we could vary the chalcogen atom E, the aryl groups Ar, and substituents R^1 widely within this synthetic route. In addition, we succeeded in expanding the pool of accessible Δ^2-1,2-diazetines **4** to include the 4-*n*-butylphenyl-, 4-*tert*-butylphenyl-, and 4-(ethoxycarbonyl)phenyl-substituted derivatives **4a**, **4b**, and **4c**, respectively.

Compounds **5**–**8** are yellow crystalline solids that are remarkably stable in solution. Even after standing in deuterated chloroform for longer periods, decomposition of the selenacycles **6** and **8** could not be detected by NMR-spectroscopy. Mass spectra of **5**–**8** show characteristic fragmentation patterns independent of the identity of the chalcogen. The structures shown in Scheme 2 could be confirmed by single-crystal X-ray structural analyses of compounds **7g** and **8j** (Figure 2).

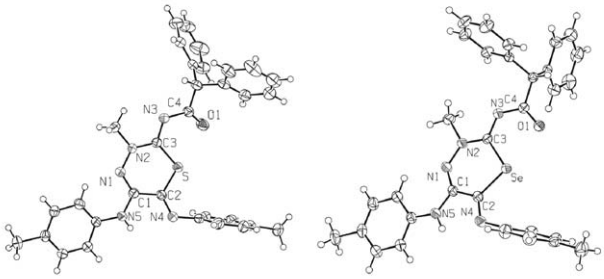

Figure 2 Solid-state structures (X-ray analysis) of derivatives **7g** (left) and **8j** (right)

In both **7g** and **8j**, the proton is located on the exocylic N5 and forms an intramolecular hydrogen bond to N4 [N4–H, 2.298 Å (**7g**) and 2.156 Å (**8j**)] (Figure 2). The central ring in 1,3,4-thiadiazine **7g** is very slightly twisted in a boat conformation in which the sulfur atom juts out ca. 10° more than N1 (Figure 3). In contrast, the ring in 1,3,4-selenadiazine **8j** is nearly planar (Figure 3).

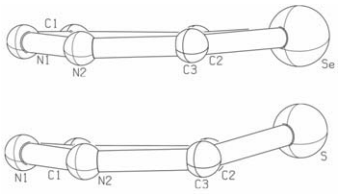

Figure 3 Perspective drawings of the ring planes in **7g** and **8j**

The ring-bonding angles are significantly influenced by the chalcogen atom. A relatively small C3–E–C2 angle (**7g**, 101.93°; **8j**, 97.72°) is compensated by a widening of the C1–C2–N1 and N1–N2–C3 angles (Figure 2). As in **3**, the acyl moiety shows a *cis* arrangement with respect to the chalcogen. The distance between E and O1 is shorter than expected when compared to classical van der Waals radii [d_{EO1} = 2.603 Å (**7g**), 2.560 Å (**8j**)]. This noncovalent interaction has been rationalized by a simple p→σ* model between the chalcogen centers. The lone pair on the donor chalcogen (occupied p orbital on O1) interacts 'through space' with a properly positioned σ* orbital on the acceptor (S/Se).[12] Newer theoretical studies (Bleiholder et al.) show that noncovalent chalcogen interactions can be described as the sum of several interactions: electrostatics, induction, electronic dispersion, and exchange correlation energies.[13] Thus, electrostatics and 'through space' hyperconjugation could possibly play a major bonding role in acceptor-substituted systems such as these 1,3,4-thia- or -selenadiazines **7** and **8**.

Animated by these results, we performed calculations of the smallest system **7a/8a**, in which R^1 = Me. We optimized both the *cis* and the *trans* isomers of these systems at the TPSS(RI)/def2-TZVP (density functional) level of theory (Figure 4).

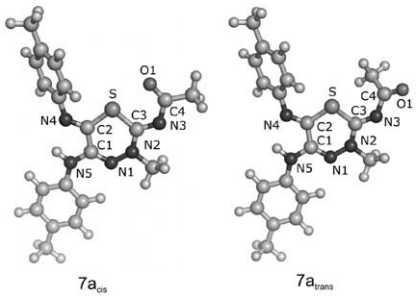

Figure 4 Optimal structures of the *cis* and *trans* isomers of **7a**, calculated at the TPSS(RI)/def2-TZVP level of theory

In accord with experiment, the *cis* isomer is with ΔE = 33.9 kJ/mol for **7a** (S) and 41.8 kJ/mol for **8a** (Se) clearly energetically favored (Table 2). An NBO analysis carried out at the B3LYP/6-31++G(d,p) level of theory shows that the 'through space' $p_{O1}\rightarrow\sigma^*_{C3-E}$ interaction between the divalent chalcogen centers plays a major role and provides ca. 28 (S) or 50 (Se) kJ/mol of stabilization energy. It is quite interesting that this interaction energy doubles upon exchanging S for Se, although the O1–E distance is somewhat less affected [2.535 Å (S) vs 2.516 Å

Table 2 Selected Structural and Electronic Interactions in Compounds **7a** and **8a**, Calculated at the TPSS(RI)/TZVP Level of Theory (B3LYP/6-31++G(d,p) Densities for the NBO Properties)

	E	ΔE[a] (kJ/mol)	δ[b] (°)	d_{E-O1}[c] (Å)	$E_{p\rightarrow\sigma^*}$[d] (kJ/mol)	E_{π}[e] (kJ/mol)
7a$_{cis}$	S	0.0	0.2	2.535	28	129
7a$_{trans}$	S	33.9	139.7	–	–	65
8a$_{cis}$	Se	0.	0.0	2.516	50	151
8a$_{trans}$	Se	41.8	114.4	–	–	16
7a′$_{cis}$[f]	S	0.	0.3	2.572	25	149
7a′$_{trans}$[f]	S	18.9	166.9	–	–	124

[a] Energy difference between the *cis* and *trans* isomers.
[b] Optimal O1–C4–N4–C3 dihedral angle.
[c] E–O1 bond distance.
[d] Energy (NBO) of the p→σ* hyperconjugative interaction.
[e] Energy (NBO) of the $\pi_{C3=N3}\rightarrow\pi^*_{C4=O1}\times\ \pi_{C4=O1}\rightarrow\pi^*_{C3=N3}$ delocalization interaction.
[f] Modified model: R^1 = H instead of R^1 = Me.

(Se)] This can be attributed to both the higher polarizability of Se (increased transferability of accepted σ* density to other atomic orbitals) as well as a much larger σ_{C3-Se}* lobe which increases the spatial overlap with p_{O1}.

A second factor, which stabilizes the *cis* isomer, is steric repulsion between R^1 (Me) and E in the *trans* conformation as observed from the fact that the optimal $d_{O1-C4-N4-C3}$ dihedral angle strongly deviates from the ideal value of 180° [139.7° (S) vs 114.4° (Se)]. Replacement of the methyl group by hydrogen (model **7a′** in Table 2) relieves this steric strain, and the dihedral angle relaxes to 166.9°. Because the acyl functionality is turned out of the ring plane, π-delocalization into the ring as measured by the $\pi_{C3=N3}\rightarrow\pi^*_{C4=O1}\times\ \pi_{C4=O1}\rightarrow\pi^*_{C3=N3}$ hyperconjugative interaction (E_{π}) is, especially in the *trans* isomer of the selenium derivative **8a**, disrupted.

^{1}H NMR spectra of compounds **5**–**8** show no evidence for possible prototropic forms of the semicyclic amidine substructure. ^{13}C NMR spectra provide evidence for the acyl functionality in **7** and **8** ($\delta_{C=O}$ = 170–190). Two resonance groups of the selenium nuclei could be detected at δ = 500 and 600 in the ^{77}Se NMR spectra (Table 1).

Quite surprisingly, we detected fine coupling (J = 2–3 Hz) in the selenium signals due to proton coupling in the ^{77}Se NMR spectra. This coupling is eliminated when the spectra are obtained in the proton-decoupled mode. This observation is in direct contrast to our proposed structures, which contain no protons in the positions α or β to the selenium nucleus. However, [^{1}H,^{77}Se]-HMBC correlation experiments showed this to be due to the *ortho* protons of the *N*4-aryl substituents (see Figure 2), which are close enough to the selenium nucleus for through-space coupling to occur (Figure 5).

In summary, we have described two new synthetic routes for the preparation of selenacycles. Furthermore, we have enlarged the pool of available ring transformations starting from Δ^2-1,2-diazetines **4**. We expect that the new

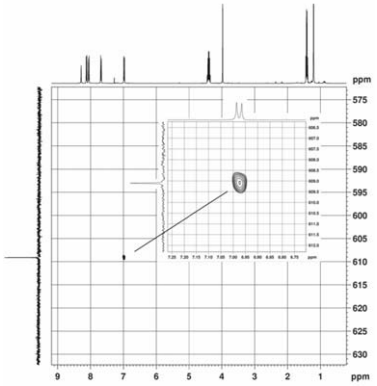

Figure 5 [^{1}H,^{77}Se]-HMBC correlation spectrum of **8i** (Ar = 4-$EtO_2CC_6H_4$; R^1 = *t*-Bu), showing a cross peak between selenium and the *ortho* protons of the *N*4-aryl substituents

compounds presented in this article would show interesting follow-up chemistry; e.g., pyrazoles could possibly be obtained by a ring-contraction reaction.[6c,e,14] The feasibility of these reactions will be topics of further articles. Finally, we would like to point out the structural relationship of these new compounds with pharmaceuticals based on thiadiazines (potent matrix-metalloproteinase inhibitors).[15] We are now investigating the biological potential of these compounds.

All solvents were dried and purified by standard techniques. The reagents employed were of commercial quality (Aldrich, Lancaster, Fluka, Merck). Reactions were monitored by TLC (aluminum plates coated with alumina or silica, from Fluka). Melting points were measured on a KSPS 1000 digital detector system from Krüss and a B-545 (Boetius system) from Büchi and are uncorrected. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 250 (250 MHz) or Bruker DRC-400 (400 MHz) spectrometer. ^{77}Se NMR spectra (76 MHz) were obtained on a Bruker DRC-400 spectrometer, with Me_2Se used as external (^{77}Se) standard. Mass spectra were measured on a Trio 2000 spectrometer from Fisons. Elemental analyses were carried out with a Varion EL III automatic analyzer from Elementar Analysensysteme GmbH.

Quantum Chemical Methodology

The density functional programs provided by the ORCA[16] suite were used for all calculations except the NBO[17] analyses. Geometry optimizations were carried out employing the TPSS[18] functional with the def2-TZVP[19] basis set featuring a split valence triple-ζ basis set with polarization functions on all atoms. For the TPSS calculations the split resolution of identity approximation (Split-RI-J[20]) was employed. NBO analyses were carried out using an NBO5.0[17] augmented Gaussian03[21] version employing the B3LYP[22] functional with the 6-31++G(d,p)-Basis set.[23]

Crystal Structure Determination[24]

Intensity data for the compounds were collected on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-K_α radiation. The data were corrected for Lorentz and polarization effects but not for absorption effects.[25,26] The structures were solved using direct methods (SHELXS[27]) and refined by full-matrix least-squares techniques against Fo^2 (SHELXL-97[28]). For the amine group N5 of compounds **7g** and **8i** the hydrogen atoms were located by difference Fourier synthesis and refined isotropically. The other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.[28] The program XP[29] was used for structure representations.

N-[4,5-Bis(phenylimino)-3-*p*-tolyl-1,3-selenazolidin-2-ylidene]benzamide (3)

A soln of **1** (2.77 g, 10 mmol), **2** (3.17 g, 10 mmol), and Et_3N (5 mL) in MeCN (80 mL) was heated under reflux for 4 h. Et_3N·HCl was removed by filtration, the solvent was removed in vacuo, and the residue was purified by recrystallization ($CHCl_3$–heptane).

Yield: 68%; red crystals; mp 197.0–199.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.7 Hz, 2 H, CH), 7.60–6.88 (m, 13 H, CH), 6.86 (d, *J* = 7.6 Hz, 2 H, CH), 6.81 (d, *J* = 7.6 Hz, 2 H, CH), 2.46 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6 (C=O), 166.8, 151.9, 150.7, 149.1, 147.6, 139.1, 135.9, 135.6, 133.7, 130.6, 130.3, 129.9, 129.7, 128.8, 128.7, 128.5, 128.1, 127.5, 123.4, 120.0, 119.7, 119.3, 119.1, 109.5 (CH, C_{quat}), 21.0 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 762.1 (s).

Anal. Calcd for $C_{29}H_{22}N_4OSe$: C, 66.79; H, 4.25; N, 10.74. Found: C, 66.67; H, 4.16; N, 10.60.

X-ray crystallography data for **3**:[24] $C_{29}H_{22}N_4OSe$, *M* = 521.5 g·mol^{-1}, red plate, size 0.08 × 0.08 × 0.06 mm^3, monoclinic, space group $P2_1/n$, *a* = 13.9378(12), *b* = 13.7489(20), *c* = 14.2802(12) Å, β = 116.460(6)°, *V* = 2450.0(1) Å^3, *T* = –90 °C, *Z* = 4, ρ_{calcd} = 1.414 g·cm^{-3}, μ (Mo-K_α) = 15.32 cm^{-1}, *F*(000) = 656, 7365 reflections in *h*(–13/13), *k*(–13/13), *l*(–14/14), measured in the range 2.10° ≤ Θ ≤ 27.42°, completeness Θ_{max} = 99.5%, 2425 independent reflections, R_{int} = 0.033, 1600 reflections with $F_o > 4\sigma(F_o)$, 152 parameters, 0 restraints, $R1_{obs}$ = 0.0445, $wR2_{obs}$ = 0.146, $R1_{all}$ = 0.0465, $wR2_{all}$ = 0.174, GOOF = 1.025, largest difference peak and hole: 0.441/–0.401 e·Å^{-3}.

Δ^2-1,2-Diazetines 4a–c; General Procedure

A THF soln (60 mL) of the appropriate **1** (5 mmol) and Et_3N (3 mL, 20 mmol) was cooled to 0 °C and a soln of $MeNHNH_2$ (5 mmol) in THF (20 mL) was added dropwise. After complete conversion of **1** (by TLC), the reaction mixture was filtered to remove the Et_3N·HCl. The solvent was then removed in vacuo at r.t. and the residue was purified by recrystallization (MeOH–H_2O).

1-Methyl-3-(4-*n*-butylphenylamino)-4-(4-*n*-butylphenylimino)-Δ^2-1,2-diazetine (4a)

Yield: 58%; yellow crystals; mp 110.5–115.7 °C.

^{1}H NMR (250 MHz, THF-d_8): δ = 9.03 (s, 1 H, NH), 7.42 (d, *J* = 8.4 Hz, 2 H, CH), 7.26–6.96 (m, 6 H, CH), 2.68–2.48 (m, 7 H, CH_3N, CH_2), 1.68–1.49 (m, 4 H, CH_2), 1.45–1.25 (m, 4 H, CH_2), 1.00–0.84 (m, 6 H, CH_3).

^{13}C NMR (63 MHz, THF-d_8): δ = 155.1, 154.1, 139.3, 138.6, 135.6, 134.2, 126.8, 126.7, 121.8, 115.7 (CH, C_{quat}), 37.8 (CH_3N), 33.1, 32.9, 31.9, 31.7, 20.3, 20.2 (CH_2), 11.4 (CH_3).

MS (DEI): *m*/*z* = 362 [M$^+$], 319, 263, 214, 203, 188, 131, 106, 91, 77.

Anal. Calcd for $C_{23}H_{30}N_4$: C, 76.20; H, 8.34; N, 15.46. Found: C, 76.16; H, 8.46; N, 15.45.

1-Methyl-3-(4-*tert*-butylphenylamino)-4-(4-*tert*-butylphenylimino)-Δ^2-1,2-diazetine (4b)

Yield: 64%; yellow crystals; mp 136.3 °C (dec).

^{1}H NMR (250 MHz, THF-d_8): δ = 9.04 (s, 1 H, NH), 7.50–7.30 (m, 6 H, CH), 7.14 (d, *J* = 8.4 Hz, 2 H, CH), 2.61 (s, 3 H, CH_3N), 1.33, 1.31 [2 s, 18 H, $(CH_3)_3C$].

^{13}C NMR (63 MHz, THF-d_8): δ = 155.2, 154.2, 146.8, 142.4, 139.1, 135.3, 123.7, 123.6, 121.6, 115.4 (CH, C_{quat}), 37.9 (CH_3N), 32.3, 32.0 [$(CH_3)_3C$], 28.9, 28.8 [$(CH_3)_3C$].

MS (DEI): *m*/*z* = 362 [M$^+$], 337, 214, 203, 188, 173, 159, 131, 115, 91, 77.

Anal. Calcd for $C_{23}H_{30}N_4$: C, 76.20; H, 8.34; N, 15.46. Found: C, 75.99; H, 8.36; N, 14.95.

1-Methyl-3-[4-(ethoxycarbonyl)phenylamino]-4-[4-(ethoxycarbonyl)phenylimino]-Δ^2-1,2-diazetine (4c)

Yield: 50%; orange crystals; mp 128.4–130.8 °C (dec).

^{1}H NMR (250 MHz, THF-d_8): δ = 9.60 (s, 1 H, NH), 8.08–7.91 (m, 4 H, CH), 7.56 (d, *J* = 8.9 Hz, 2 H, CH), 7.22 (d, *J* = 8.2 Hz, 2 H, CH), 4.39–4.25 (m, 4 H, CH_2), 2.61 (s, 3 H, CH_3N), 1.40–1.31 (m, 6 H, CH_3).

^{13}C NMR (63 MHz, THF-d_8): δ = 163.2, 163.1 (C=O), 155.0, 145.8, 141.5, 128.7, 128.4, 126.0, 122.3, 120.7, 115.2 (CH, C_{quat}), 58.5, 58.2 (CH_2), 37.8 (CH_3N), 11.8, 11.7 (CH_3).

MS (DEI): *m*/*z* = 394 [M$^+$], 366, 351, 349, 338, 321, 293, 265, 230, 219, 204, 190, 165, 159, 120.

Anal. Calcd for $C_{21}H_{22}N_4O_4$: C, 63.95; H, 5.62; N, 14.20. Found: C, 63.82; H, 5.80; N, 14.10.

Heterodiazines 5 and 6a–c; General Procedure

A THF soln (60 mL) of Δ^2-1,2-diazetine **4** (2 mmol) was cooled to –20 °C and a soln of the corresponding isothiocyanate or isoselenocyanate (2 mmol) in 5 mL of THF was added dropwise. After the addition, the reaction mixture was warmed to r.t. and stirred for 6 h. The solvent was then removed in vacuo and the residue was purified by recrystallization (MeOH–H_2O).

2-(4-Methoxyphenylimino)-3-methyl-*N*-*p*-tolyl-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-5-amine (5)

Yield: 89%; orange-yellow crystals; mp 150.4–157.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1 H, NH), 7.51 (d, *J* = 8.4 Hz, 2 H, CH), 7.20–7.10 (m, 4 H, CH), 6.85–6.72 (m, 6 H, CH), 3.77, 3.74 (2 s, 6 H, CH_3N, CH_3O), 2.37, 2.34 (2 s, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 144.6, 144.2, 141.8, 140.4, 137.4, 135.6, 134.6, 131.2, 130.1, 129.4, 122.8, 119.8, 118.5, 114.6 (CH, C_{quat}), 55.4 (CH_3O), 43.4 (CH_3N), 21.0, 20.8 (CH_3).

MS (DEI): *m*/*z* = 443 [M$^+$], 326, 311, 235, 165, 161, 118, 91, 65.

Anal. Calcd for $C_{25}H_{25}N_5OS$: C, 67.69; H, 5.68; N, 15.79; S, 7.23. Found: C, 67.68; H, 5.79; N, 15.78; S, 7.15.

2-(4-Methoxyphenylimino)-3-methyl-*N*-*p*-tolyl-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-5-amine (6a)
Yield: 80%; orange-yellow crystals; mp 167.2 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.71 (s, 1 H, NH), 7.49 (d, *J* = 8.6 Hz, 2 H, CH), 7.20–7.10 (m, 4 H, CH), 6.85–6.82 (m, 6 H, CH), 3.76 (s, 6 H, CH_3N, CH_3O), 2.34 (s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 156.4, 146.0, 145.9, 141.4, 141.2, 137.6, 135.8, 134.0, 131.0, 130.2, 129.4, 122.7, 119.0, 118.5, 114.7 (CH, C_{quat}), 55.4 (CH_3O), 44.5 (CH_3N), 21.0, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 499.72 (s).

MS (DEI): *m*/*z* = 491 [M^+(^{80}Se)], 374, 359, 248, 235, 197, 161, 118, 65, 43.

Anal. Calcd for $C_{25}H_{25}N_5OSe$: C, 61.22; H, 5.14; N, 14.28. Found: C, 61.14; H, 5.16; N, 14.31.

2-(4-Bromophenylimino)-3-methyl-*N*-*p*-tolyl-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-5-amine (6b)
Yield: 63%; yellow crystals; mp 179.8–182.3 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.71 (s, 1 H, NH), 7.49 (d, *J* = 8.5 Hz, 2 H, CH), 7.35 (d, *J* = 8.8 Hz, 2 H, CH), 7.22–7.10 (m, 4 H, CH), 6.77 (d, *J* = 8.5 Hz, 2 H, CH), 6.71 (d, *J* = 8.8 Hz, 2 H, CH), 3.75 (s, 3 H, CH_3N), 2.36, 2.35 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 147.2, 145.8, 145.4, 141.0, 137.4, 136.1, 134.2, 132.5, 131.3, 130.4, 129.4, 123.6, 118.9, 118.6, 116.9 (CH, C_{quat}), 44.4 (CH_3N), 21.1, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 497.52 (t, *J* = 2.6 Hz).

MS (DEI): *m*/*z* = 539 [M^+(^{80}Se^{79}Br)], 422, 260, 198, 161, 118, 91, 65.

Anal. Calcd for $C_{24}H_{22}BrN_5Se$: C, 53.45; H, 4.11; Br, 14.82; N, 12.99. Found: C, 53.28; H, 4.16; Br, n.d.; N, 12.87.

2-(4-*tert*-Butylphenylimino)-3-methyl-*N*-*p*-tolyl-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-5-amine (6c)
Yield: 84%; yellow crystals; mp 208.7–212.3 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.26 (s, 1 H, NH), 7.50 (d, *J* = 8.4 Hz, 2 H, CH), 7.36 (d, *J* = 8.8 Hz, 2 H, CH), 7.22–7.10 (m, 4 H, CH), 6.81–6.66 (m, 4 H, CH), 3.77 (s, 3 H, CH_3N), 2.35, 2.34 (2 s, 6 H, CH_3), 1.30 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 146.8, 145.8, 145.7, 145.2, 140.0, 137.6, 135.8, 134.0, 131.0, 130.2, 129.4, 126.3, 121.1, 119.1, 118.5 (CH, C_{quat}), 44.4 (CH_3N), 34.3 [*C*(CH_3)$_3$], 31.4 [C(*C*H_3)$_3$], 21.0, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 596.28 (t, *J* = 2.5 Hz).

MS (DEI): *m*/*z* = 517 [M^+(^{80}Se)], 502, 400, 385, 248, 197, 173, 161, 118, 91, 65.

Anal. Calcd for $C_{28}H_{31}N_5Se$: C, 65.11; H, 6.05; N, 13.56. Found: C, 64.90; H, 6.18; N, 13.64.

Acylheterodiazines 7a–k and 8b–l; General Procedure
To an acetone soln (30 mL) of NaSCN or KSeCN (2 mmol) the appropriate carboxylic chloride (2 mmol) was added at 0 °C and the mixture was stirred for 15 min. Then the Δ^2-1,2-diazetine **4** (2 mmol) was added and the soln was stirred for 1 h. The reaction mixture was diluted with $CHCl_3$ (25 mL) and filtered. The solvent was removed in vacuo and the residue was purified by column chromatography (alumina, $CHCl_3$–heptane, 2:1). Recrystallization ($CHCl_3$–heptane) yielded the acylheterodiazines **7** and **8**.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-2-ylidene]acetamide (7a)**
Yield: 92%; pale-yellow crystals; mp 201.4–203.9 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.55 (d, *J* = 8.4 Hz, 2 H, CH), 7.26–7.13 (m, 4 H, CH), 6.88 (d, *J* = 8.2 Hz, 2 H, CH), 3.83 (s, 3 H, CH_3N), 2.37, 2.35 (2 s, 6 H, CH_3), 2.18 (s, 3 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 180.9 (C=O), 157.4, 152.9, 144.9, 143.9, 138.4, 136.1, 136.0, 132.6, 130.3, 129.5, 119.6, 119.3 (CH, C_{quat}), 45.7 (CH_3N), 27.4, 21.0, 20.8 (CH_3).

MS (DEI): *m*/*z* = 379 [M^+], 336, 262, 247, 202, 200, 198, 177, 161, 118, 91, 65, 43, 28.

Anal. Calcd for $C_{20}H_{21}N_5OS$: C, 63.30; H, 5.58; N, 18.46; S, 8.45. Found: C, 63.30; H, 5.51; N, 18.29; S, 8.11.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-2-ylidene]propionamide (7b)**
Yield: 96%; pale-yellow crystals; mp 175.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.51 (d, *J* = 8.4 Hz, 2 H, CH), 7.25–7.11 (m, 4 H, CH), 6.88 (d, *J* = 8.4 Hz, 2 H, CH), 3.83 (s, 3 H, CH_3N), 2.47 (q, *J* = 7.5 Hz, 2 H, CH_2), 2.37, 2.34 (2 s, 6 H, CH_3), 1.12 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 184.4 (C=O), 152.9, 145.0, 144.0, 138.3, 136.2, 136.0, 132.5, 130.3, 129.5, 119.6, 119.2 (CH, C_{quat}), 45.7 (CH_3N), 33.5 (CH_2), 21.0, 20.8, 9.6 (CH_3).

MS (DEI): *m*/*z* = 393 [M^+], 364, 336, 276, 247, 235, 161, 118, 91, 57, 29.

Anal. Calcd for $C_{21}H_{23}N_5OS$: C, 64.10; H, 5.89; N, 17.80; S, 8.15. Found: C, 64.03; H, 5.66; N, 17.72; S, 7.94.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-2-ylidene]isobutyramide (7c)**
Yield: 49%; pale-yellow crystals; mp 173.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.51 (d, *J* = 8.5 Hz, 2 H, CH), 7.26–7.10 (m, 4 H, CH), 6.88 (d, *J* = 8.3 Hz, 2 H, CH), 3.84 (s, 3 H, CH_3N), 2.63 (quin, *J* = 6.9 Hz, 1 H, CH), 2.37, 2.35 (2 s, 6 H, CH_3), 1.16 (d, *J* = 6.9 Hz, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 187.4 (CO), 153.3, 145.1, 144.0, 138.2, 136.2, 135.9, 132.5, 130.3, 129.5, 119.6, 119.2 (CH, C_{quat}), 45.7 (CH_3N), 38.7 (CH), 21.0, 20.8, 19.5 (CH_3).

MS (DEI): *m*/*z* = 407 [M^+], 364, 336, 280, 247, 219, 177, 161, 132, 131, 91, 65, 43.

Anal. Calcd for $C_{22}H_{25}N_5OS$: C, 64.84; H, 6.18; N, 17.18; S, 7.87. Found: C, 64.68; H, 6.36; N, 17.08; S, 7.79.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-2-ylidene]pivalamide (7d)**
Yield: 95%; yellow crystals; mp 174.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.51 (d, *J* = 8.4 Hz, 2 H, CH), 7.25–7.11 (m, 4 H, CH), 6.88 (d, *J* = 8.2 Hz, 2 H, CH), 3.85 (s, 3 H, CH_3N), 2.37, 2.35 (2 s, 6 H, CH_3), 1.20 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 189.2 (CO), 153.4, 145.1, 144.0, 138.1, 136.2, 135.9, 132.4, 130.4, 129.5, 119.6, 119.2 (CH, C_{quat}), 45.8 (CH_3N), 41.4 [*C*(CH_3)$_3$], 27.7 [C(*C*H_3)$_3$], 21.0, 20.8 (CH_3).

MS (DEI): *m*/*z* = 421 [M^+], 364, 247, 177, 132, 118, 91, 57, 41.

Anal. Calcd for $C_{23}H_{27}N_5OS$: C, 65.53; H, 6.46; N, 16.61; S, 7.61. Found: C, 65.40; H, 6.13; N, 16.73; S, 7.63.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-thiadiazin-2-ylidene]cyclopropanecarboxamide (7e)**
Yield: 89%; pale-yellow crystals; mp 186.0–188.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.51 (d, *J* = 8.5 Hz, 2 H, CH), 7.26–7.10 (m, 4 H, CH), 6.87 (d, *J* = 8.3 Hz, 2 H,

CH), 3.83 (s, 3 H, CH_3N), 2.36, 2.34 (2 s, 6 H, CH_3), 1.85–1.74 (m, 1 H, CH), 1.04–0.97 (m, 2 H, CH_2), 0.93–0.86 (m, 2 H, CH_2).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 183.9 (CO), 152.6, 145.0, 143.9, 138.2, 136.2, 135.9, 132.5, 130.3, 129.5, 119.6, 119.2 (CH, C_{quat}), 45.7 (CH_3N), 21.0, 20.8 (CH_3), 18.9 (CH), 9.5 (CH_2).

MS (DEI): *m*/*z* = 405 [M$^+$], 364, 336, 288, 247, 220, 161, 118, 91, 69, 41, 39.

Anal. Calcd for $C_{22}H_{23}N_5OS$: C, 65.16; H, 5.72; N, 17.27; S, 7.91. Found: C, 65.16; H, 5.72; N, 17.17; S, 7.74.

_N_-[3-Methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]cyclobutanecarboxamide (7f)
Yield: 51%; pale-yellow crystals; mp 163.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.51 (d, *J* = 8.4 Hz, 2 H, CH), 7.26–7.10 (m, 4 H, CH), 6.88 (d, *J* = 8.3 Hz, 2 H, CH), 3.83 (s, 3 H, CH_3N), 3.25 (m, 1 H, CH), 2.40–2.10 (m, 10 H, CH_3, CH_2), 2.10–1.80 (m, 2 H, CH_2).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 185.4 (CO), 153.3, 145.0, 144.0, 138.3, 136.2, 136.0, 132.5, 130.3, 129.5, 119.6, 119.2 (CH, C_{quat}), 45.7 (CH_3N), 43.6 (CH), 25.8, 18.1 (CH_2), 21.0, 20.8 (CH_3).

MS (DEI): *m*/*z* = 419 [M$^+$], 364, 336, 280, 269, 247, 235, 161, 131, 118, 91, 55, 29.

Anal. Calcd for $C_{23}H_{25}N_5OS$: C, 65.84; H, 6.01; N, 16.69; S, 7.64. Found: C, 65.74; H, 5.83; N, 16.58; S, 7.52.

_N_-[3-Methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]-2,2-diphenylacetamide (7g)
Yield: 80%; yellow crystals; mp 166.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.12 (s, 1 H, NH), 7.50 (d, *J* = 8.4 Hz, 2 H, CH), 7.38–7.12 (m, 14 H, CH), 6.88 (d, *J* = 8.2 Hz, 2 H, CH), 5.19 (s, 1 H, CH), 3.75 (s, 3 H, CH_3N), 2.38, 2.35 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 181.6 (CO), 153.9, 144.6, 143.9, 140.6, 138.5, 136.1, 136.0, 132.7, 130.4, 129.5, 129.0, 128.3, 126.6, 119.6, 119.4 (CH, C_{quat}), 62.4 (CH), 46.0 (CH_3N), 21.1, 20.9 (CH_3).

MS (DEI): *m*/*z* = 531 [M$^+$], 501, 364, 337, 321, 247, 177, 165, 131, 91, 65.

Anal. Calcd for $C_{32}H_{29}N_5OS$: C, 72.29; H, 5.50; N, 13.17; S, 6.03. Found: C, 72.21; H, 5.54; N, 13.20; S, 6.15.

X-ray crystallography data for **7g**:[24] $C_{32}H_{29}N_5OS$, *M* = 531.6 g·mol^{-1}, yellow prism, size 0.06 × 0.06 × 0.05 mm^3, orthorhombic, space group $P2_12_12_1$, *a* = 8.8334(4), *b* = 14.2969(3), *c* = 21.4786(7) Å, α = 90.00, β = 90.00, γ = 90.00°, *V* = 2712.54(16) Å^3, *T* = –90 °C, *Z* = 4, ρ_{calcd} = 1.302 gcm^{-3}, μ (Mo-K$_\alpha$) = 1.55 cm^{-1}, *F*(000) = 1120, 19570 reflections in *h*(–11/9), *k*(–18/17), *l*(–27/27), measured in the range 2.71° ≤ Θ ≤ 27.50°, completeness Θ_{max} = 99.8%, 6230 independent reflections, R_{int} = 0.0676, 4493 reflections with $F_o > 4\sigma(F_o)$, 359 parameters, 0 restraints, $R1_{obs}$ = 0.0494, $wR2_{obs}$ = 0.1058, $R1_{all}$ = 0.0871, $wR2_{all}$ = 0.1246, GOOF = 0.923, Flack parameter –0.05(8), largest difference peak and hole: 0.175/–0.248 e·Å^{-3}.

_N_-[3-Methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]benzamide (7h)
Yield: 83%; pale-yellow crystals; mp 229.1 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.1 Hz, 2 H, CH), 8.12 (s, 1 H, NH), 7.54–7.42 (m, 5 H, CH), 7.25–7.15 (m, 4 H, CH), 6.90 (d, *J* = 8.3 Hz, 2 H, CH), 3.99 (s, 3 H, CH_3N), 2.37, 2.34 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 174.1 (C=O), 154.2, 144.8, 143.9, 138.6, 136.6, 136.1, 136.0, 132.6, 132.0, 130.3, 129.5, 129.5, 128.0, 119.6, 119.3 (CH, C_{quat}), 46.1 (CH_3N), 21.1, 20.8 (CH_3).

MS (DEI): *m*/*z* = 441 [M$^+$], 336, 324, 247, 161, 105, 77, 65.

Anal. Calcd for $C_{25}H_{23}N_5OS$: C, 68.00; H, 5.25; N, 15.86; S, 7.26. Found: C, 67.82; H, 5.26; N, 15.89; S, 7.13.

4-Methyl-_N_-[3-methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]benzamide (7i)
Yield: 62%; pale-yellow crystals; mp 238.0 °C (dec).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.15–8.05 (m, 3 H, NH, CH), 7.54 (d, *J* = 8.5 Hz, 2 H, CH), 7.27–7.10 (m, 6 H, CH), 6.91 (d, *J* = 8.3 Hz, 2 H, CH), 3.98 (s, 3 H, CH_3N); 2.39, 2.36 (2 s, 9 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 174.2 (CO), 154.0, 145.0, 144.0, 142.5, 138.5, 136.1, 136.0, 133.9, 132.6, 130.4, 129.6, 129.5, 128.8, 119.6, 119.3 (CH, C_{quat}), 46.1 (CH_3N), 21.6, 21.1, 20.8 (CH_3).

MS (DEI): *m*/*z* = 455 [M$^+$], 364, 348, 338, 280, 247, 235, 161, 119, 91, 65.

Anal. Calcd for $C_{26}H_{25}N_5OS$: C, 68.55; H, 5.53; N, 15.37; S, 7.04. Found: C, 68.40; H, 5.39; N, 15.23; S, 6.90.

4-Methoxy-_N_-[3-methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]benzamide (7j)
Yield: 90%; pale-yellow crystals; mp 230.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 9.0 Hz, 2 H, CH), 8.11 (s, 1 H, NH), 7.54 (d, *J* = 8.4 Hz, 2 H, CH), 7.28–7.13 (m, 4 H, CH), 6.95–6.85 (m, 4 H, CH), 3.97 (s, 3 H, CH_3N), 3.84 (s, 3 H, CH_3O), 2.38, 2.35 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 173.7 (C=O), 162.8, 153.7, 145.1, 144.0, 138.4, 136.2, 135.9, 132.5, 131.6, 130.4, 129.5, 129.3, 119.6, 119.3, 113.3 (CH, C_{quat}), 55.3 (CH_3O), 46.0 (CH_3N), 21.1, 20.8 (CH_3).

MS (DEI): *m*/*z* = 471 [M$^+$], 354, 235, 161, 135, 118, 91, 77, 65.

Anal. Calcd for $C_{26}H_{25}N_5O_2S$: C, 66.22; H, 5.34; N, 14.85; S, 6.80. Found: C, 65.98; H, 5.42; N, 14.90; S, 6.63.

_N_-[3-Methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-thiadiazin-2-ylidene]biphenyl-4-carboxamide (7k)
Yield: 86%; yellow crystals; mp 238.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.5 Hz, 2 H, CH), 8.14 (s, 1 H, NH), 7.68–7.13 (m, 13 H, CH), 6.93 (d, *J* = 8.3 Hz, 2 H, CH), 4.02 (s, 3 H, CH_3N), 2.39, 2.36 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 173.9 (CO), 154.1, 144.8, 144.6, 143.9, 140.4, 138.6, 136.1, 135.4, 132.7, 130.4, 130.0, 129.5, 128.8, 127.8, 127.2, 126.8, 119.6, 119.4 (CH, C_{quat}), 46.1 (CH_3N), 21.1, 20.9 (CH_3).

MS (DEI): *m*/*z* = 517 [M$^+$], 400, 333, 318, 280, 247, 181, 152, 118, 91, 65.

Anal. Calcd for $C_{31}H_{27}N_5OS·0.33CHCl_3$: C, 67.51; H, 4.94; N, 12.56; S, 5.75. Found: C, 67.53; H, 4.71; N, 12.82; S, 5.61.

_N_-[3-Methyl-5-(_p_-tolylamino)-6-(_p_-tolylimino)-3,6-dihydro-2_H_-1,3,4-selenadiazin-2-ylidene]propionamide (8b)
Yield: 79%; pale-yellow crystals; mp 153.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, NH), 7.52 (d, *J* = 8.6 Hz, 2 H, CH), 7.26–7.10 (m, 4 H, CH), 6.84 (d, *J* = 8.2 Hz, 2 H, CH), 3.91 (s, 3 H, CH_3N), 2.51 (q, *J* = 7.5 Hz, 2 H, CH_2), 2.38, 2.34 (2 s, 6 H, CH_3), 1.13 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 185.3 (CO), 155.3, 149.7, 145.8, 138.6, 136.6, 136.0, 132.4, 130.5, 129.5, 119.3, 118.8 (CH, C_{quat}), 47.1 (CH_3N), 33.3 (CH_2), 21.0, 20.8, 9.5 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 594.09 (t, *J* = 2.6 Hz).

MS (DEI): *m*/*z* = 441 [M$^+$(^{80}Se)], 412, 384, 324, 295, 243, 199, 155, 118, 91, 57, 29.

Anal. Calcd for $C_{21}H_{23}N_5OSe$: C, 57.27; H, 5.26; N, 15.90. Found: C, 57.08; H, 5.28; N, 15.78.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]isobutyramide (8c)**
Yield: 81%; pale-yellow crystals; mp 164.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, NH), 7.52 (d, *J* = 8.5 Hz, 2 H, CH), 7.25–7.10 (m, 4 H, CH), 6.84 (d, *J* = 8.3 Hz, 2 H, CH), 3.93 (s, 3 H, CH_3N), 2.67 (quin, *J* = 6.9 Hz, 1 H, CH), 2.38, 2.35 (2 s, 6 H, CH_3), 1.17 (d, *J* = 6.9 Hz, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 188.3 (CO), 155.7, 149.7, 145.8, 138.5, 136.4, 135.9, 132.3, 130.5, 129.5, 119.3, 118.8 (CH, C_{quat}), 47.2 (CH_3N), 38.5 (CH), 21.0, 20.8, 19.5 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 501.26 (s).

MS (DEI): *m*/*z* = 455 [M^+(^{80}Se)], 412, 338, 294, 248, 235, 161, 118, 91, 65, 43.

Anal. Calcd for $C_{22}H_{25}N_5OSe$: C, 58.15; H, 5.55; N, 15.41. Found: C, 58.10; H, 5.62; N, 15.41.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]cyclobutanecarboxamide (8d)**
Yield: 57%; pale-yellow crystals; mp 151.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, NH), 7.52 (d, *J* = 8.5 Hz, 2 H, CH), 7.26–7.10 (m, 4 H, CH), 6.85 (d, *J* = 8.3 Hz, 2 H, CH), 3.92 (s, 3 H, CH_3N), 3.29 (m, 1 H, CH), 2.40–2.10 (m, 10 H, CH_3, CH_2), 2.10–1.83 (m, 2 H, CH_2).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 186.2 (CO), 155.7, 149.7, 145.8, 138.6, 136.4, 136.0, 132.4, 130.5, 130.0, 129.5, 119.3, 118.8 (CH, C_{quat}), 47.1 (CH_3N), 43.4 (CH), 29.7, 18.2 (CH_2), 21.0, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 594.41 (s).

MS (DEI): *m*/*z* = 467 [M^+(^{80}Se)], 412, 350, 294, 269, 235, 161, 132, 118, 91, 55.

Anal. Calcd for $C_{23}H_{25}N_5OSe$: C, 59.22; H, 5.40; N, 15.01. Found: C, 59.20; H, 5.40; N, 15.12.

***N*-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]pivalamide (8e)**
Yield: 97%; yellow crystals; mp 167.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, NH), 7.52 (d, *J* = 8.6 Hz, 2 H, CH), 7.25–7.11 (m, 4 H, CH), 6.84 (d, *J* = 8.2 Hz, 2 H, CH), 3.93 (s, 3 H, CH_3N), 2.38, 2.35 (2 s, 6 H, CH_3), 1.22 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 190.2 (CO), 155.9, 149.8, 145.9, 138.4, 136.4, 135.9, 132.8, 130.5, 129.5, 128.2, 119.3, 118.8 (CH, C_{quat}), 47.2 (CH_3N), 41.2 [*C*(CH_3)$_3$], 27.6 [C(*C*H_3)$_3$], 21.0, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 596.05 (t, *J* = 2.7 Hz).

MS (DEI): *m*/*z* = 469 [M^+(^{80}Se)], 412, 384, 352, 295, 235, 225, 199, 161, 132, 118, 91, 57.

Anal. Calcd for $C_{23}H_{27}N_5OSe$: C, 58.97; H, 5.81; N, 14.95. Found: C, 59.02; H, 5.68; N, 14.87.

***N*-[5-(4-Bromophenylamino)-6-(4-bromophenylimino)-3-methyl-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]pivalamide (8f)**
Yield: 92%; pale-yellow crystals; mp 204.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, NH), 7.55–7.43 (m, 6 H, CH), 6.81 (d, *J* = 6.8 Hz, 2 H, CH), 3.93 (s, 3 H, CH_3N), 1.21 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 190.5 (C=O), 155.5, 151.0, 147.1, 137.9, 137.7, 133.1, 131.9, 120.7, 120.7, 120.7, 119.4, 115.2 (CH, C_{quat}), 47.3 (CH_3N), 41.3 [*C*(CH_3)$_3$], 27.5 [C(*C*H_3)$_3$].

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 598.20 (t, *J* = 2.5 Hz).

MS (DEI): *m*/*z* = 599 [M^+(^{80}Se^{79}Br^{81}Br)], 542, 517, 491, 397, 359, 276, 229, 199, 171, 155, 91.

Anal. Calcd for $C_{21}H_{21}Br_2N_5OSe$: C, 42.16; H, 3.54; Br, 26.72; N, 11.71. Found: C, 42.27; H, 3.55; Br, 26.95; N, 11.62.

***N*-[5-(4-Butylphenylamino)-6-(4-butylphenylimino)-3-methyl-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]pivalamide (8g)**
Yield: 88%; yellow crystals; mp 104.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, NH), 7.54 (d, *J* = 8.4 Hz, 2 H, CH), 7.24–7.09 (m, 4 H, CH), 6.86 (d, *J* = 8.0 Hz, 2 H, CH), 3.93 (s, 3 H, CH_3N), 2.68–2.54 (m, 4 H, CH_2), 1.70–1.53 (m, 4 H, CH_2), 1.48–1.28 (m, 4 H, CH_2), 1.22 [s, 9 H, $C(CH_3)_3$], 1.01–0.89 (m, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 190.2 (CO), 155.8, 149.3, 145.8, 141.0, 138.4, 137.4, 136.6, 129.8, 128.8, 119.2, 118.9 (CH, C_{quat}), 47.2 (CH_3N), 41.2 [*C*(CH_3)$_3$], 35.2, 35.0, 33.7, 33.5, 22.4, 22.3 (CH_2), 27.6 [C(*C*H_3)$_3$], 14.0 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 497.52 (s).

MS (DEI): *m*/*z* = 553 [M^+(^{80}Se)], 496, 394, 337, 267, 203, 160, 131, 91, 57.

Anal. Calcd for $C_{29}H_{39}N_5OSe$: C, 63.03; H, 7.11; N, 12.67. Found: C, 63.08; H, 7.11; N, 12.62.

***N*-[5-(4-*tert*-Butylphenylamino)-6-(4-*tert*-butylphenylimino)-3-methyl-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]pivalamide (8h)**
Yield: 83%; yellow crystals; mp 156.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.10 (s, 1 H, NH), 7.57 (d, *J* = 8.8 Hz, 2 H, CH), 7.47–7.33 (m, 4 H, CH), 6.90 (d, *J* = 8.0 Hz, 2 H, CH), 3.94 (s, 3 H, CH_3N), 1.47, 1.36, 1.22 [3 s, 27 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 190.2 (CO), 155.8, 150.3, 149.3, 149.1, 145.6, 145.5, 138.4, 136.4, 126.8, 125.8, 118.9, 118.6 (CH, C_{quat}), 47.2 (CH_3N), 41.2, 34.6, 34.0 [*C*(CH_3)$_3$], 31.4, 31.4, 27.7 [C(*C*H_3)$_3$].

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 597.19 (t, *J* = 2.5 Hz).

MS (DEI): *m*/*z* = 553 [M^+(^{80}Se)], 496, 394, 337, 203, 159, 131, 83, 57, 41.

Anal. Calcd for $C_{29}H_{39}N_5OSe$: C, 63.03; H, 7.11; N, 12.67. Found: C, 62.73; H, 7.21; N, 12.42.

***N*-{5-[4-(ethoxycarbonyl)phenylamino]-6-[4-(ethoxycarbonyl)phenylimino]-3-methyl-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene}pivalamide (8i)**
Yield: 90%; yellow crystals; mp 169.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.28 (s, 1 H, NH), 8.11 (d, *J* = 8.8 Hz, 2 H, CH), 8.04 (d, *J* = 8.8 Hz, 2 H, CH), 7.67 (d, *J* = 9.0 Hz, 2 H, CH), 6.96 (d, *J* = 8.8 Hz, 2 H, CH), 4.46–4.31 (m, 4 H, CH_2), 3.96 (s, 3 H, CH_3N), 1.46–1.35 (m, 6 H, CH_3), 1.19 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (63 MHz, $CDCl_3$): δ = 190.6, 166.2, 165.8, (CO), 155.7, 152.2, 151.1, 142.8, 137.2, 131.7, 130.8, 128.2, 124.3, 118.6, 118.1 (CH, C_{quat}), 61.0, 60.7 (CH_2), 47.4 (CH_3N), 41.3 [*C*(CH_3)$_3$], 27.5 [C(*C*H_3)$_3$], 14.4, 14.4 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 609.10 (t, *J* = 2.0 Hz).

MS (DEI): *m*/*z* = 585 [M^+(^{80}Se)], 528, 410, 353, 325, 219, 176, 145, 83, 57.

Anal. Calcd for $C_{27}H_{31}N_5O_5Se$: C, 55.48; H, 5.35; N, 11.98. Found: C, 55.53; H, 5.35; N, 11.89.

N-[3-Methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]-2,2-diphenylacetamide (8j)
Yield: 86%; yellow crystals; mp 180.0 °C (dec).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.10 (s, 1 H, NH), 7.52 (d, *J* = 8.4 Hz, 2 H, CH), 7.39–7.10 (m, 14 H, CH), 6.85 (d, *J* = 8.2 Hz, 2 H, CH), 5.24 (s, 1 H, CH), 3.85 (s, 3 H, CH_3N), 2.39, 2.36 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 182.6 (CO), 156.3, 149.2, 145.8, 140.5, 138.7, 136.2, 136.1, 132.5, 130.6, 129.5, 129.1, 128.3, 126.7, 119.4, 118.8 (CH, C_{quat}), 62.1 (CH), 47.4 (CH_3N), 21.1, 20.9 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 597.73 (t, *J* = 2.6 Hz).

MS (DEI): *m*/*z* = 579 [M^+(^{80}Se)], 501, 441, 411, 332, 295, 198, 167, 155, 91

Anal. Calcd for $C_{32}H_{29}N_5OSe$: C, 66.43; H, 5.05; N, 12.10. Found: C, 66.49; H, 5.02; N, 12.04.

X-ray crystallography data for **8j**:[24] $C_{32}H_{29}N_5OSe$, *M* = 578.5 g·mol^{-1}, yellow prism, size 0.05 × 0.04 × 0.04 mm^3, triclinic, space group *P*-1, *a* = 10.4484(4), *b* = 12.0024(5), *c* = 12.2689(5) Å, α = 109.661(2), β = 105.576(2), γ = 91.844(3)°, *V* = 1382.89(10) Å^3, *T* = –90 °C, *Z* = 2, ρ_{calcd} = 1.389 g·cm^{-3}, μ (Mo-K_α) = 13.92 cm^{-1}, *F*(000) = 596, 9958 reflections in *h*(–13/13), *k*(–15/15), *l*(–15/15), measured in the range 2.54° ≤ Θ ≤ 27.46°, completeness Θ_{max} = 98.9%, 6261 independent reflections, R_{int} = 0.0292, 5008 reflections with $F_o > 4\sigma(F_o)$, 357 parameters, 0 restraints, $R1_{obs}$ = 0.0397, $wR2_{obs}$ = 0.0853, $R1_{all}$ = 0.0589, $wR2_{all}$ = 0.0927, GOOF = 1.023, largest difference peak and hole: 0.446/–0.429 e·Å^{-3}.

4-Methyl-N-[3-methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]benzamide (8k)
Yield: 54%; pale-yellow crystals; mp 235.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.16–8.05 (m, 3 H, NH, CH), 7.54 (d, *J* = 8.4 Hz, 2 H, CH), 7.28–7.13 (m, 6 H, CH), 6.88 (d, *J* = 8.4 Hz, 2 H, CH), 4.06 (s, 3 H, CH_3N), 2.39, 2.35 (2 s, 9 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 175.1 (CO), 156.1, 149.6, 145.8, 142.7, 138.7, 136.4, 136.0, 133.6, 132.4, 130.5, 129.6, 129.5, 128.9, 119.4, 118.9 (CH, C_{quat}), 47.4 (CH_3N), 21.7, 21.0, 20.9 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 594.30 (t, *J* = 2.8 Hz).

MS (DEI): *m*/*z* = 503 [M^+(^{80}Se)], 386, 235, 198, 161, 132, 119, 91, 65.

Anal. Calcd for $C_{26}H_{25}N_5OSe$: C, 62.15; H, 5.01; N, 13.94. Found: C, 61.91; H, 4.89; N, 13.90.

4-Methoxy-N-[3-methyl-5-(*p*-tolylamino)-6-(*p*-tolylimino)-3,6-dihydro-2*H*-1,3,4-selenadiazin-2-ylidene]benzamide (8l)
Yield: 81%; pale-yellow crystals; mp 220.0 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 9.0 Hz, 2 H, CH), 8.09 (s, 1 H, NH), 7.54 (d, *J* = 8.4 Hz, 2 H, CH), 7.28–7.12 (m, 4 H, CH), 6.96–6.83 (m, 4 H, CH), 4.05 (s, 3 H, CH_3N), 3.85 (s, 3 H, CH_3O), 2.39, 2.35 (2 s, 6 H, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 174.6 (CO), 162.9, 155.8, 149.7, 145.8, 138.6, 136.4, 135.9, 132.4, 131.6, 130.5, 129.5, 129.0, 119.4, 118.8, 113.4 (CH, C_{quat}), 55.4 (CH_3O), 47.4 (CH_3N), 21.0, 20.8 (CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$): δ = 595.32 (t, *J* = 2.4 Hz).

MS (DEI): *m*/*z* = 519 [M^+(^{80}Se)], 402, 296, 235, 191, 161, 135, 119, 91, 77, 65.

Anal. Calcd for $C_{26}H_{25}N_5O_2Se$: C, 60.23; H, 4.86; N, 13.51. Found: C, 60.09; H, 4.99; N, 13.41.

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