1,2-Diaza-1,3-Butadienes: A New Approach to the Synthesis of Selenoheterocycles

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1,2-Diaza-1,3-butadienes react easily with selenoureas to produce 2-selenazolin-4-one derivatives and with selenobenzamide to afford 2-selenazoline derivatives, the stereochemistries of which were determined. Whereas 2-selenazoline derivatives of $4R^*,5R^*$ configuration undergo aromatization under basic conditions, 2-selenazolin-4-ones, under different reaction conditions, appear to be attractive entry compounds to conjugated azoalkenes, 5,5-disubstituted selenazolin-4-ones, and spiro-condensed heterocyclic systems including selenazolinone rings.

Introduction

In recent decades, considerable attention has been devoted to the synthesis of selenium-containing heterocyclic compounds, because of their interesting reactivities[1] and potential pharmaceutical significance.[2]

Recent reports demonstrate that many syntheses of five- or six-membered heterocycles containing both selenium and nitrogen[3] are based on cycloaddition reactions of selenaazadiene systems,[3a] reactions of isoselenocyanates,[3b,3c] or reactions between primary selenoamide and α,β-unsaturated ketones,[3d] bisacyl chlorides,[3e] or α-haloacyl halides.[3f]

In continuation of our investigations designed to develop the usefulness of conjugated azo-ene systems[4] as building blocks in heterocyclic compounds,[5] we wish to report here a new synthetic approach to selenoheterocycles, starting from 1,2-diaza-1,3-butadienes.

Results and Discussion

Since selenoamides are known to display selenoamide−selenoimidate tautomerism and to possess two nucleophilic sites, we considered their reactivity to be of interest in view of the ability of conjugated azoalkenes to undergo nucleophilic attack.[5a]

We have preliminarily reported the results of reactions between 1,2-diaza-1,3-butadienes and selenoureas or primary selenoamide.[6]

1,2-Diaza-1,3-butadienes **1a**−**d** reacted with selenourea (**2a**) or *N*,*N*-dimethylselenourea (**2b**) in MeOH at 0 °C to yield 2-selenazolin-4-one derivatives, mainly in the hydrazono forms **4a**−**h** (Scheme 1 and Table 1).

The reaction probably proceeds by nucleophilic addition of the selenium atom of the selenourea derivatives at the terminal carbon of the heterodiene moiety. Subsequent intramolecular nucleophilic attack by the imidic NH at the carboxylate group at C-4 of Michael adduct intermediate **3** with the loss of an alcohol molecule should result in the selenazolinone ring closure, according to our previous findings with analogous materials.[7]

In ^{1}H NMR spectra of **4a**−**h**, each proton geminal to the selenium atom appeared as a strong singlet and a weak doublet centered around the singlet. This doublet, with a coupling constant of 14−16 Hz, was attributed to the splitting caused by the presence of selenium isotope ^{77}Se, with a natural abundance of 7.5%. $J(^{13}C\text{-}^{77}Se)$ values of 60−61 Hz observed for C-5 in compounds **4a**−**h** were typical of sp^3 carbon coupling with selenium.

Pure tautomeric forms **4** or **4′** were frequently isolable through fractional crystallization.

We next investigated reactions between conjugated azoalkenes and selenobenzamide, and it was found that the behavior in the regioselectivity of the closing step was different from that observed for thiobenzamide with the same reagents.[7]

In fact, **1a**−**d** reacted with selenobenzamide (**2c**) in MeOH or in CH_2Cl_2 at 0 °C to afford 2-selenazoline derivatives **5** and **5′** in different ratios (Scheme 1, Table 1). These compounds had originated from nucleophilic addition of the selenium atom at the terminal carbon of the heterodiene system and subsequent ring closure on the hydrazone function of **3**. The structures of **5** and **5′** were established by ^{1}H and ^{13}C NMR spectroscopy. In the ^{13}C NMR, the J ($^{13}C\text{-}^{77}Se$) values observed for the C-5 resonances (δ =

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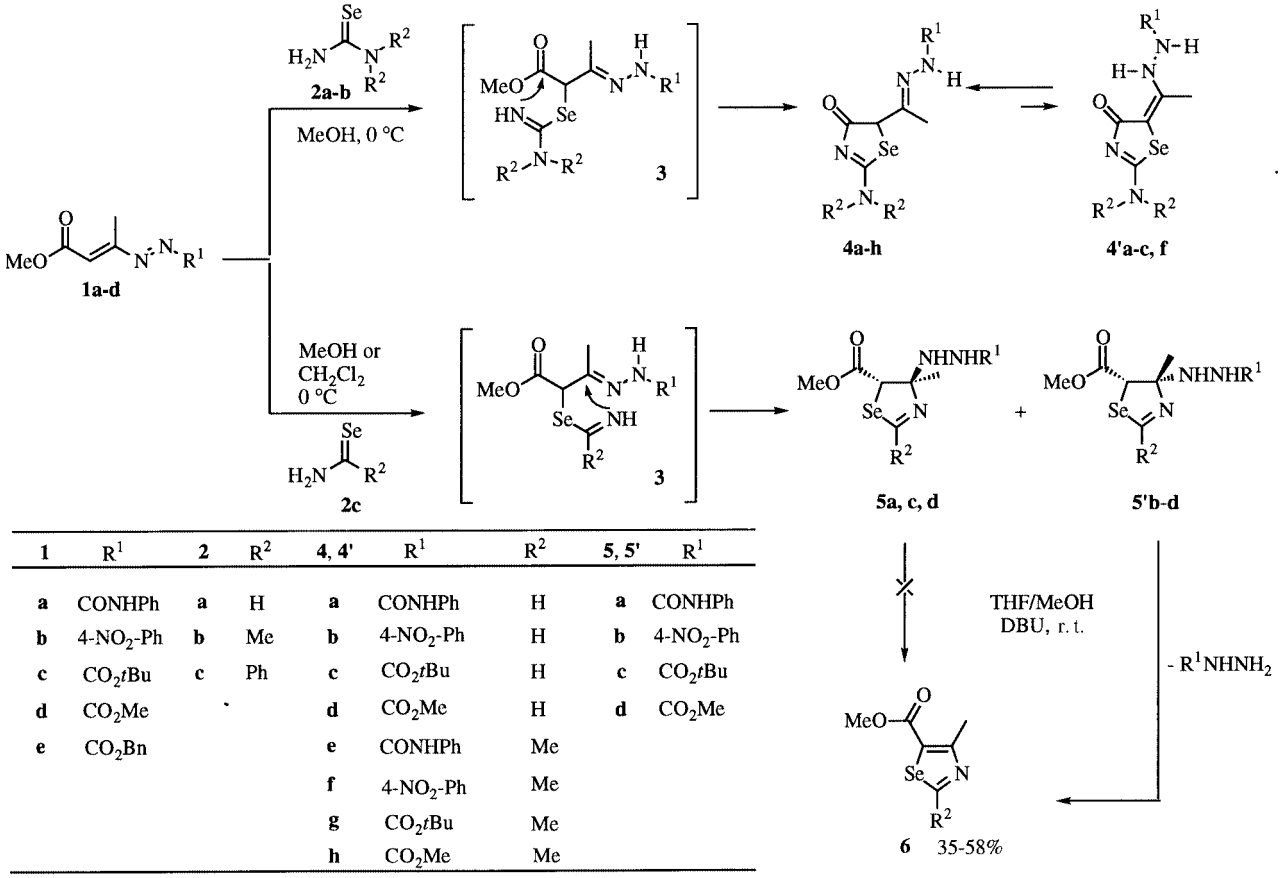


1	R^1	2	R^2	4, 4'	R^1	R^2	5, 5'	R^1
a	CONHPh	a	H	a	CONHPh	H	a	CONHPh
b	4-NO_2-Ph	b	Me	b	4-NO_2-Ph	H	b	4-NO_2-Ph
c	CO_2tBu	c	Ph	c	CO_2tBu	H	c	CO_2tBu
d	CO_2Me			d	CO_2Me	H	d	CO_2Me
e	CO_2Bn			e	CONHPh	Me		
				f	4-NO_2-Ph	Me		
				g	CO_2tBu	Me		
				h	CO_2Me	Me		

Scheme 1

Table 1. Yields and reaction times required for 2-selenazolin-4-ones **4**, **4′** and 2-selenazolines **5**, **5′**

Reagents	Products	Yield (%)	Reaction time (h)
1a+2a	**4a**	85[a]	0.25
	4′a	5[a]	
1b+2a	**4b+4′b**	84[b]	1
1c+2a	**4c**	62[a]	0.25
	4′c	18[a]	
1d+2a	**4d**	71[a]	0.25
1a+2b	**4e**	82[a]	1.5
1b+2b	**4f**	63[a]	0.5
	4′f	21[a]	
1c+2b	**4g**	73[a]	0.25
1d+2b	**4h**	77[a]	0.25
1a+2c	**5a**	68[c]	2
1b+2c	**5′b**	62[c]	2
1c+2c	**5c**	58[c]	1
	5′c	36[c]	
1d+2c	**5d**	46[c]	0.25
	5′d	36[c]	

[a] Yield of pure isolated product. [b] Referenced to a crystallized mixture of **4b** and **4′b**. [c] Referenced to pure isolated isomer.

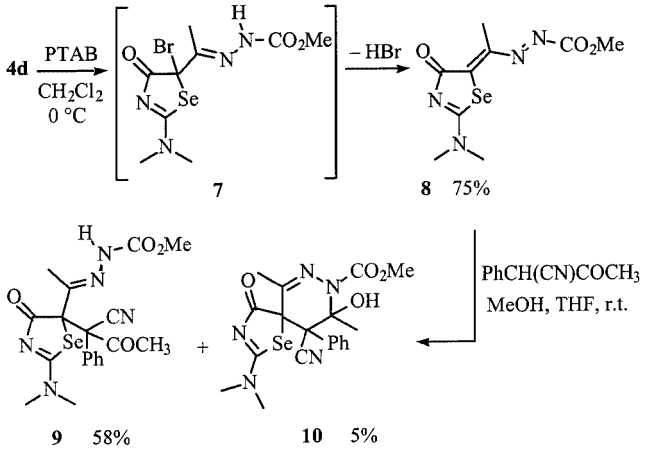
54.3−55.9 ppm), the presence of singlets ascribable to C-4 at δ = 99.0−100.5 ppm together with $J(^1H\text{-}^{77}Se)$ values of 14−16 Hz, and NH−NH coupling constants of 4.8−5.0 Hz in the ^1H NMR spectra of **5c**, **5′c**, and **5′d** were consistent with 2-selenazoline structures. These compounds, containing two asymmetric centers at C-4 and C-5, consisted of diastereomers that could often be successfully separated by chromatography (Scheme 1, Table 1). The stereochemistries of the cyclized products **5** and **5′** were determined by NOE experiments in [D_6]DMSO solutions.

In compound **5d**, upon irradiation of the NH signal at δ = 5.49 ppm, NOE effects were observed for the proton at δ = 4.91 ppm (8%), for the NH at δ = 8.38 ppm (5%), and for the CH_3 group at δ = 1.47 ppm (4%).

In compound **5′d**, irradiation of the CH_3 group at C-4 caused an 8.3% enhancement of the proton at C-5. From comparison of NOE experiments, **5′b-d** each featured a *cis* relationship between the methyl at C-4 and the proton at C-5. Upon treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in a THF/MeOH mixture (1:1) at room temperature, compounds **5′b−d** afforded methyl 4-methyl-2-phenyl-1,3-selenazole-5-carboxylate (**6**, yields from 35 to 58%) whereas the same treatment of **5a**, **5b**, and **5d** did not reveal any formation of **6**, suggesting that the aromatization process involved an *anti* elimination of the hydrazine moiety.

In order to verify its synthetic usefulness, different reactions were carried out with 2-selenazolin-4-one derivative **4**. Thus, the introduction of a bromine atom at C-5 in compound **4d** by use of phenyltrimethylammonium tribromide (PTAB) in CH_2Cl_2 at 0 °C and subsequent treatment with

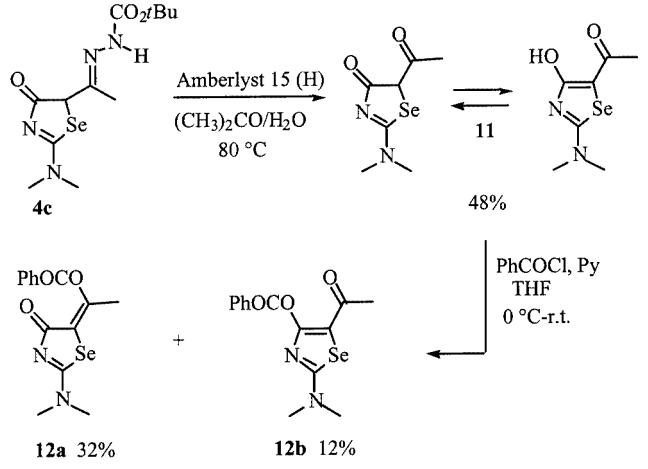
aqueous Na_2CO_3 provided methyl 2-{1-[2-dimethylamino-4-oxo-1,3-selenazol-5(4*H*)-ylidene]ethyl}diazene-1-carboxylate (**8**) in good yield (75%). Owing to the electronic nature of such a compound, we examined its reactivity towards a nucleophilic reagent. Base-catalyzed addition of α-(acetylphenyl)acetonitrile to **8** in THF afforded the 1,4-conjugate adduct **9** (58%) in the *E* configuration[8] and 1-selena-3,7,8-triazaspiro[4.5]deca-2,6-dien-4-one derivative **10** (5%) (Scheme 2).



Scheme 2

From spectroscopic evidence, derivative **10** consisted of a diastereomeric mixture (70:30 ratio by ^1H NMR) and originated from intramolecular NH nucleophilic attack on the acetyl group of the Michael adduct **9** in the *Z* configuration.

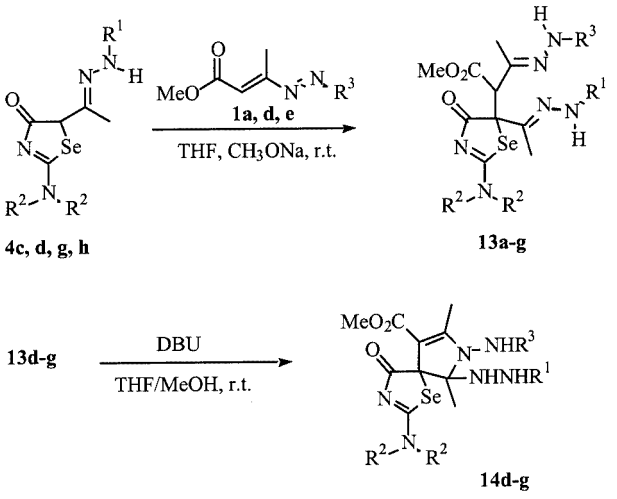
With the goal of obtaining the 5-acetyl-4-hydroxyselenazole derivative, *tert*-butyl 2-[1-(2-amino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]hydrazine-1-carboxylate (**4c**) was subjected to deprotection with Amberlyst 15 (H) as catalyst in a refluxing $(CH_3)_2CO/H_2O$ mixture (Scheme 3).[9] This reaction involved the hydrolytic removal of the NH-BOC-hydrazo protecting group[10] of the carbonyl function at C-5 of the selenazolinone ring, to afford



Scheme 3

derivative **11** as a tautomeric mixture (48.2%). By classic derivatization of **11** with PhCOCl, esters **12a** (32.0%) and **12b** (12.0%) were obtained (Scheme 3).

Because of the acidity of the protons at C-5, 2-selenazolin-4-one derivatives **4** should behave as nucleophiles. In fact, the base-promoted addition of **4c**, **4d**, **4g**, and **4h** to 1,2-diaza-1,3-butadienes **1a**, **1d**, and **1e** in THF at room temperature afforded 5,5-disubstituted 2-selenazolin-4-one derivatives **13a–g** as diastereomeric mixtures (Scheme 4, Table 2).



4	R^1	R^2	1	R^3	13, 14	R^1	R^2	R^3
c	CO_2tBu	H	**a**	CONHPh	**a**	CO_2tBu	H	CO_2Me
d	CO_2Me	H	**d**	CO_2Me	**b**	CO_2tBu	H	CONHPh
g	CO_2tBu	Me	**e**	CO_2Bn	**c**	CO_2Me	H	CO_2Me
h	CO_2Me	Me			**d**	CO_2tBu	Me	CO_2Me
					e	CO_2tBu	Me	CONHPh
					f	CO_2Me	Me	CO_2Me
					g	CO_2Me	Me	CO_2Bn

Scheme 4

Table 2. Yields and reaction times required for 5,5-disubstituted 2-selenazolin-4-one derivatives **13a–g** and 1-selena-3,7-diazaspiro[4.4]nona-2,8-dien-4-one derivatives **14d–g**

Reagents	Products	Yield (%)	*dr*	Reaction time (h)
4c+1d	**13a**	75[a]	86:14	24
4c+1a	**13b**	69[a]	83:17	24
4d+1d	**13c**	83[a]	80:20	24
4g+1d	**13d**	63[a]	88:12	24
4g+1a	**13e**	74[a]	76:24	24
4h+1d	**13f**	58[a]	87:13	12
4h+1e	**13g**	60[a]	85:15	30
13d	**14d**	44		24
13e	**14e**	46		24
13f	**14f**	48		24
13g	**14g**	32		24

[a] Referenced to diastereomeric mixtures.

Compounds **13a−g** were then treated with DBU in THF/MeOH mixtures at room temperature. Although **13a−c** afforded intractable crude products under these conditions, compounds **13d−g** gave rise to 1-selena-3,7-diazaspiro[4.4]nona-2,8-dien-4-one derivatives **14d−g** (Scheme 4, Table 2) in which both hydrazone side chains had participated in pyrroline ring closure.[11] Intramolecular nucleophilic attack by the hydrazone nitrogen of the first side chain on the hydrazone carbon at C-5 of the second side chain produced the new spiro-condensed heterocyclic system.

Conclusions

We report here a new route to selenoheterocycles starting from conjugated azoalkenes. An interesting difference in behavior between selenobenzamide and selenoureas in the regioselectivity of the intramolecular closure step of the Michael adducts was observed. Selenobenzamide preferentially produced 2-selenazolines, in contrast with the results previously obtained with thiobenzamide and the same substrates,[7] whereas selenoureas afforded 2-selenazolin-4-one derivatives mainly in their hydrazono forms. These latter compounds were demonstrated to be susceptible to further synthetic transformations and so in turn represent useful starting compounds for spiro-condensed heterocyclic systems incorporating the 2-selenazolin-4-one nucleus.

Experimental Section

General: Selenoureas **2a−b** were commercial materials and were used without further purification. Selenobenzamide (**2c**) was obtained according to a literature procedure.[12] Solvents were purchased and were used without further purification, with the exception of THF, which was distilled from sodium hydroxide. "Light petroleum ether" refers to the fraction of b.p. 40−60 °C. 1,2-Diaza-1,3-butadienes **1a−e** were synthesized as standard *E*/*Z* isomeric mixtures according to previously reported procedures.[4a,13] Melting points were determined in open capillary tubes and are uncorrected. IR-FT spectra were obtained as Nujol mulls. Mass spectra were measured at an ionizing voltage of 70 eV. All ^{1}H NMR and ^{13}C NMR spectra were recorded at 200 or 400 MHz and at 50.32 or 100.56 MHz, respectively, in [D$_6$]DMSO solutions unless specified otherwise. Chemical shifts (δ_H) are reported relative to TMS as internal standard. All coupling constant values (*J*) are given in Hz. Chemical shifts (δ_C) are reported relative to [D$_6$]DMSO as internal standard, unless otherwise stated, in a broad band decoupled mode; the multiplicities were obtained by means of 135 and 90° DEPT experiments to aid in assignment (q = methyl, t = methylene, d = methyne, s = quaternary). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; br, broad; all the NH, NH$_2$, and OH moieties exchanged with D$_2$O. Diastereomeric ratios (*dr* values) of compounds **10** and **13a−g** (unassigned configurations) were obtained from ^{1}H NMR spectra; the NMR spectroscopic data of the major diastereomer are marked*. Precoated silica gel plates (0.25 mm) were employed for analytical thin layer chromatography and silica gel 60 Å (35−70 μ) for column chromatography. All new compounds showed satisfactory elemental analysis (C ±0.35; H ±0.30, N ±0.30). The chemical names were generated with ADC/IUPAC Name (Version 3.50, April 5, 1998), Advanced Chemistry Development Inc., Toronto, ON (Canada).

General Procedure for the Synthesis of 2-Selenazolin-4-one Derivatives 4a−h, 4′a-c, and 4′f: The conjugated azoalkene **1a−d** (1 mmol) was rapidly added at 0 °C to a magnetically stirred solution of the selenoureas **2a−b** (1 mmol) in MeOH (20 mL). Stirring was maintained until the disappearance of the reagents (0.25−1.5 h, monitored by TLC), and the major products **4a** and **4c−h** were directly filtered off in vacuo or obtained by crystallization from an appropriate solvent after complete removal of MeOH. Derivatives **4′a**, **4′c**, and **4′f** were obtained after complete evaporation of the mother liquor and subsequent crystallization from MeOH/Et$_2$O. The reaction between **2a** and **1b** produced an inseparable mixture of **4b** and **4′b** (hydrazono form/hydrazino form 46:54%, respectively, established by ^{1}H NMR).

2-Amino-[1-(4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]-*N*-phenylhydrazine-1-carboxamide (4a): Yield: 287 mg (85%), white powder from MeOH, m.p. 143−144 °C (dec.). ^{1}H NMR: δ = 1.78 (s, 3 H, CH$_3$), 5.48 (s, $J^1_{H\text{-}^{77}Se}$ = 13.9 Hz, 1 H, CH, D$_2$O exch.), 6.99 (t, *J* = 7.6 Hz, 1 H, ArH), 7.28 (t, *J* = 7.8 Hz, 2 H, ArH), 7.59 (d, *J* = 7.7 Hz, 2 H, ArH), 8.88 (s, 1 H, NH), 9.04 and 9.42 (2 s, 2 H, NH$_2$), 9.80 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.6 (q), 61.9 (d, $J^{13}_{C\text{-}^{77}Se}$ = 60.4 Hz), 119.3 (d), 122.4 (d), 128.6 (d), 139.1 (s), 145.0 (s), 153.3 (s), 176.6 (s, $J^{13}_{C\text{-}^{77}Se}$ = 122.7 Hz), 187.5 (s) ppm. IR: ṽ = 3480, 3374, 3207, 1712, 1662, 1636, 1597, 1542 cm^{-1}. C$_{12}$H$_{13}$N$_5$O$_2$Se (338.2): calcd. C 42.47, H 3.86, N 20.65; found C 42.22, H 3.59, N 20.85.

1-{1-[2-Amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene]ethyl}-4-phenylsemicarbazide (4′a): Yield: 17 mg (5%), white powder from MeOH/Et$_2$O, m.p. 151−152 °C (dec.). ^{1}H NMR: δ = 1.98 (s, 3 H, CH$_3$), 7.01 (t, *J* = 7.4 Hz, 1 H, ArH), 7.31 (t, *J* = 7.6 Hz, 2 H, ArH), 7.50 (d, *J* = 8.2 Hz, 2 H, ArH), 8.84 (br. s, 4 H, 2 NH and NH$_2$), 12.35 (s, 1 H, NH) ppm. IR: ṽ = 3455, 3331, 3204, 1715, 1683, 1664, 1644, 1591, 1562 cm^{-1}. C$_{12}$H$_{13}$N$_5$O$_2$Se (338.2): calcd. C 42.47, H 3.86, N 20.65; found C 42.82, H 3.59, N 20.90.

2-Amino-5-{1-[2-(4-nitrophenyl)hydrazono]ethyl}-1,3-selenazol-4(5*H*)-one (4b) and 2-Amino-5-{1-[2-(4-nitrophenyl)-hydrazino]ethylidene}-1,3-selenazol-4-one (4′b): Yield: 286 mg (84%), yellow powder from MeOH. ^{1}H NMR: δ = 1.88 and 2.01 (2 s, 6 H, 2 CH$_3$), 5.43 (s, $J^1_{H\text{-}^{77}Se}$ = 13.8 Hz, 1 H, CH, D$_2$O exch.), 7.21 (d, *J* = 9.1 Hz, 2 H, ArH), 8.11 (d, *J* = 9.1 Hz, 2 H, ArH), 8.18 (d, *J* = 9.4 Hz, 2 H, ArH), 8.38 (d, *J* = 9.4 Hz, 2 H, ArH), 8.57 and 8.80 (2 br s, 4 H, 2 NH and NH$_2$), 9.04 and 9.40 (2 br s, 2 H, NH$_2$), 10.07 (s, 1 H, NH) ppm. IR: ṽ = 3568, 3388, 3328, 3265, 3118, 1735, 1719, 1685, 1647, 1601, 1560, 1490, 1336 cm^{-1}. C$_{11}$H$_{11}$N$_5$O$_3$Se (340.2): calcd. C 38.84, H 3.26, N 20.59; found C 39.17, H 3.01, N 20.81.

***tert*-Butyl 2-[1-(2-Amino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]hydrazine-1-carboxylate (4c):** Yield: 198 mg (62%), white powder from MeOH, m.p. 133−134 °C (dec.). ^{1}H NMR: δ = 1.43 (s, 9 H, *t*Bu), 1.71 (s, 3 H, CH$_3$), 5.26 (s, $J^1_{H\text{-}^{77}Se}$ = 13.8 Hz, 1 H, CH, D$_2$O exch.), 8.99 and 9.35 (2 br s, 2 H, NH$_2$), 9.70 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.8 (q), 28.1 (q), 62.0 (d, $J^{13}_{C\text{-}^{77}Se}$ = 61.1 Hz), 79.5 (s), 147.7 (s), 152.9 (s), 176.4 (s, $J^{13}_{C\text{-}^{77}Se}$ = 122.5 Hz), 187.4 (s) ppm. IR: ṽ = 3217, 3150, 3038, 1728, 1708, 1669, 1538 cm^{-1}. C$_{10}$H$_{16}$N$_4$O$_3$Se (319.2): calcd. C 37.63, H 5.05, N 17.55; found C 37.91, H 4.78, N 17.75.

***tert*-Butyl 2-{1-[2-Amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene]-ethyl}hydrazine-1-carboxylate (4′c):** Yield: 57 mg (18%), light grey

powder from MeOH/Et_2O, m.p. 149−150 °C (dec.). ^1H NMR: δ = 1.45 (s, 9 H, *t*Bu), 1.88 (s, 3 H, CH_3), 8.71 (br. s, 4 H, 2 NH and NH_2) ppm. IR: ṽ = 3339, 3210, 3185, 1724, 1644, 1574 cm^{-1}. $C_{10}H_{16}N_4O_3Se$ (319.2): calcd. C 37.63, H 5.05, N 17.55; found C 37.39, H 4.77, N 17.82.

Methyl 2-[1-(2-Amino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]hydrazine-1-carboxylate (4d): Yield: 197 mg (71%), light orange powder from MeOH, m.p. 125−126 °C (dec.). ^1H NMR: δ = 1.74 (s, 3 H, CH_3), 3.66 (s, 3 H, OCH_3), 5.30 (s, $J^1_{H\text{-}^{77}Se}$ = 14.0 Hz, 1 H, CH, D_2O exch.), 9.00 and 9.38 (2 br s, 1 H, NH_2), 10.05 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.7 (q), 51.8 (q), 61.8 (d, $J^{13}_{C\text{-}^{77}Se}$ = 60.8 Hz), 148.5 (s), 154.4 (s), 176.3 (s, $J^{13}_{C\text{-}^{77}Se}$ = 121.6 Hz), 187.2 (s) ppm. IR: ṽ = 3273, 3251, 3029, 1727, 1695, 1637 cm^{-1}. $C_7H_{10}N_4O_3Se$ (277.1): calcd. C 30.34, H 3.64, N 20.22; found C 30.62, H 3.37, N 20.47.

1-[(2-Dimethylamino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]-4-phenylsemicarbazide (4e): Yield: 300 mg (82%), white powder from MeOH, m.p. 170−175 °C (dec).^1H NMR: δ = 1.79 (s, 3 H, CH_3), 3.16 and 3.27 [2 s, 6 H, $N(CH_3)_2$], 5.60 (s, $J^1_{H\text{-}^{77}Se}$ = 14.8 Hz, 1 H, CH, D_2O exch.), 7.00 (t, *J* = 7.8 Hz, 1 H, ArH), 7.28 (t, *J* = 7.8 Hz, 2 H, ArH), 7.60 (d, *J* = 7.8 Hz, 2 H, ArH), 8.90 (s, 1 H, NH), 9.83 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.6 (q), 40.4 (q), 41.1 (q), 63.3 (d, $J^{13}_{C\text{-}^{77}Se}$ = 60.1 Hz), 119.2 (d), 122.3 (d), 128.5 (d), 139.0 (s), 144.2 (s), 153.2 (s), 175.9 (s, $J^{13}_{C\text{-}^{77}Se}$ = 122.2 Hz), 185.6 (s) ppm. IR: ṽ = 3346, 3187, 1675, 1596, 1578 cm^{-1}. $C_{14}H_{17}N_5O_2Se$ (366.3): calcd. C 45.91, H 4.68, N 19.12; found C 46.13, H 4.93, N 18.90.

2-(Dimethylamino)-5-{1-[2-(4-nitrophenyl)hydrazono]ethyl}-1,3-selenazol-4(5*H*)-one (4f): Yield: 232 mg (63%), yellow powder from MeOH, m.p. 139−142 °C (dec.). ^1H NMR: δ = 1.89 (s, 3 H, CH_3), 3.14 and 3.26 [2 s, 6 H, $N(CH_3)_2$], 5.54 (s, $J^1_{H\text{-}^{77}Se}$ = 15.2 Hz, 1 H, CH, D_2O exch.), 7.21 (d, *J* = 9.1 Hz, 2 H, ArH), 8.10 (d, *J* = 9.1 Hz, 2 H, ArH), 10.06 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.2 (q), 40.4 (q), 41.0 (q), 63.7 (d, $J^{13}_{C\text{-}^{77}Se}$ = 61.0 Hz), 111.8 (d), 125.8 (d), 138.6 (s), 145.5 (s), 151.0 (s), 175.9 (s, $J^{13}_{C\text{-}^{77}Se}$ = 121.5 Hz), 185.6 (s) ppm. IR: ṽ = 3266, 1682, 1593, 1573, 1489, 1324 cm^{-1}. $C_{13}H_{15}N_5O_3Se$ (368.3): calcd. C 42.40, H 4.11, N 19.02; found C 42.64, H 3.89, N 19.27.

2-(Dimethylamino)-5-{1-[2-(4-nitrophenyl)hydrazino]ethylidene}-1,3-selenazol-4-one (4′f): Yield: 77 mg (21%), red orange powder from MeOH, m.p. 130−132 °C (dec.). ^1H NMR: δ = 2.02 (s, 3 H, CH_3), 3.21 and 3.29 [2 s, 6 H, $N(CH_3)_2$], 7.61 (br. s, 1 H, NH), 8.19 (d, *J* = 9.2 Hz, 2 H, ArH), 8.37 (d, *J* = 9.2 Hz, 2 H, ArH), 9.10 (br. s, 1 H, NH) ppm. IR: ṽ = 3575, 3297, 1646, 1615, 1593, 1582, 1489, 1333 cm^{-1}. $C_{13}H_{15}N_5O_3Se$ (368.3): calcd. C 42.40, H 4.11, N 19.02; found C 42.63, H 4.32, N 18.77.

***tert*-Butyl 2-[1-(2-Dimethylamino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]hydrazine-1-carboxylate (4g):** Yield: 253 mg (73%), white powder from MeOH, m.p. 112−115 °C (dec.). ^1H NMR: δ = 1.45 (s, 9 H, *t*Bu), 1.73 (s, 3 H, CH_3), 3.14 and 3.25 [2 s, 6 H, $N(CH_3)_2$], 5.38 (s, $J^1_{H\text{-}^{77}Se}$ = 14.0 Hz, 1 H, CH, D_2O exch.), 9.75 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.8 (q), 28.0 (q), 40.3 (q), 41.0 (q), 63.4 (d, $J^{13}_{C\text{-}^{77}Se}$ = 54.8 Hz), 79.5 (s), 147.1 (s), 152.8 (s), 175.9 (s, $J^{13}_{C\text{-}^{77}Se}$ = 121.7 Hz), 185.6 (s) ppm. IR: ṽ = 3206, 1715, 1699, 1680, 1570 cm^{-1}. $C_{12}H_{20}N_4O_3Se$ (347.3): calcd. C 41.50, H 5.80, N 16.13; found C 41.72, H 6.05, N 15.85.

Methyl 2-[1-(2-Dimethylamino-4-oxo-4,5-dihydro-1,3-selenazol-5-yl)ethylidene]hydrazine-1-carboxylate (4h): Yield: 235 mg (77%), white powder from EtOAc, m.p. 142−143 °C. ^1H NMR: δ = 1.74 (s, 3 H, CH_3), 3.14 and 3.25 [2 s, 6 H, $N(CH_3)_2$], 3.67 (s, 3 H, OCH_3), 5.42 (s, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, 1 H, CH, D_2O exch.), 10.09 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 12.9 (q), 40.4 (q), 41.1 (q), 51.9 (q), 62.3 (d, $J^{13}_{C\text{-}^{77}Se}$ = 61.4 Hz), 148.1 (s), 154.5 (s), 175.9 (s, $J^{13}_{C\text{-}^{77}Se}$ = 122.4 Hz), 185.6 (s) ppm. IR: ṽ = 3212, 3052, 1734, 1717, 1687, 1581 cm^{-1}. $C_9H_{14}N_4O_3Se$ (305.2): calcd. C 35.42, H 4.62, N 18.36; found C 35.77, H 4.84, N 18.15.

Procedure for the Synthesis of 2-Selenazoline Derivatives 5a, 5c, 5′c, 5d, and 5′d: Conjugated azoalkene **1** was added portionwise at 0 °C to a magnetically stirred solution of selenobenzamide (**2c**, 184 mg, 1 mmol) in CH_2Cl_2 (5 mL, **1a**−**b**) or in MeOH (5 mL, **1c**−**d**). The reaction was complete in 0.25−2 h (monitored by TLC). The solvent was then removed under reduced pressure and the crude product was purified by flash chromatography on silica gel, eluting with cyclohexane/EtOAc mixtures, or by crystallization with an appropriate solvent.

Methyl (4*S,5*R**)-{4-[2-(Anilinocarbonyl)hydrazino]-4-methyl-2-phenyl-4,5-dihydro-1,3-selenazol-5-yl}acetate (5a):** Yield: 293 mg (68%), white powder from CH_2Cl_2/Et_2O, m.p. 115−117 °C (dec.). ^1H NMR: δ = 1.38 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 5.04 (s, $J^1_{H\text{-}^{77}Se}$ = 14.0 Hz, 1 H, CH), 6.29 (br. s, 1 H, NH), 6.95 (t, *J* = 7.2 Hz, 1 H), 7.26 (t, *J* = 7.2 Hz, 2 H, ArH), 7.41−7.61 (m, 5 H, ArH and NH), 7.72 (d, *J* = 8.1 Hz, 2 H, ArH), 8.71 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 19.0 (q), 52.9 (q), 54.3 (d, $J^{13}_{C\text{-}^{77}Se}$ = 58.4 Hz), 99.3 (s), 118.1 (d), 121.7 (d), 128.3 (d), 128.6 (d), 128.7 (d), 131.8 (d), 134.3 (s), 139.4 (s), 156.5 (s), 161.1 (s) 169.8 (s) ppm. IR: ṽ = 3340, 3275, 3249, 1722, 1678, 1662, 1620, 1592 cm^{-1}. $C_{19}H_{20}N_4O_3Se$ (431.4): calcd. C 52.77, H 4.67, N 12.96; found C 52.60, H 4.67, N 13.09.

Methyl (4*R,5*R**)-{4-Methyl-4-[2-(4-nitrophenyl)hydrazino]-2-phenyl-4,5-dihydro-1,3-selenazol-5-yl}acetate (5′b):** Yield: 269 mg (62%), light yellow powder from Et_2O-light petroleum ether, m.p. 95−98 °C (dec.). ^1H NMR: δ = 1.55 (s, 3 H, CH_3), 3.65 (s, 3 H, OCH_3), 4.98 (s, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, 1 H, CH), 5.72 (br. s, 1 H, NH), 6.93 (d, *J* = 9.2 Hz, 2 H, ArH), 7.44−7.60 (m, 3 H, ArH), 7.74 (d, *J* = 8.0 Hz, 2 H, ArH), 8.00 (d, *J* = 9.2 Hz, 2 H, ArH), 8.33 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 22.8 (q), 52.6 (q), 55.9 (d, $J^{13}_{C\text{-}^{77}Se}$ = 59.8 Hz), 99.1 (s), 110.2 (d), 125.6 (d), 128.3 (d), 128.6 (d), 131.7 (d), 134.0 (s), 136.2 (s), 156.5 (s), 160.4 (s) 169.8 (s) ppm. IR: ṽ = 3329, 3265, 3214, 1714, 1621, 1603, 1505, 1345 cm^{-1}. $C_{18}H_{18}N_4O_4Se$ (433.3): calcd. C 49.89, H 4.19, N 12.93; found C 50.20, H 4.08, N 13.21.

***tert*-Butyl (4*S**,5*R**)-2-[5-(Methoxycarbonyl)-4-methyl-2-phenyl-4,5-dihydro-1,3-selenazol-4-yl]hydrazine-1-carboxylate (5c):** Yield: 239 mg (58%), yellow crystals from Et_2O-light petroleum ether, m.p. 121−122 °C (dec.). ^1H NMR: δ = 1.31 (s, 9 H, *t*Bu), 1.47 (s, 3 H, CH_3), 3.66 (s, 3 H, OCH_3), 4.90 (s, 1 H, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, CH), 5.32 (d, J_{NHNH} = 4.8 Hz, 1 H, NH), 7.40−7.57 (m, 3 H, ArH), 7.69 (d, *J* = 6.5 Hz, 2 H, ArH), 8.19 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 20.6 (q), 28.1 (q), 52.3 (q), 54.4 (d, $J^{13}_{C\text{-}^{77}Se}$ = 59.9 Hz), 78.4 (s), 100.6 (s), 128.6 (2d), 131.7 (d), 134.3 (s), 156.2 (s), 161.1 (s) 170.9 (s) ppm. IR: ṽ = 3280, 3173, 1733, 1619, 1608, 1581 cm^{-1}. $C_{17}H_{23}N_3O_4Se$ (412.3): calcd. C 49.52, H 5.62, N 10.19; found C 49.60, H 5.44, N 10.29.

***tert*-Butyl (4*R**,5*R**)-2-[5-(Methoxycarbonyl)-4-methyl-2-phenyl-4,5-dihydro-1,3-selenazol-4-yl]hydrazine-1-carboxylate (5′c):** Yield: 148 mg (36%), colorless glass. ^1H NMR: δ = 1.34 (s, 9 H, *t*Bu), 1.53 (s, 3 H, CH_3), 3.68 (s, 3 H, OCH_3), 4.87 (s, 1 H, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, CH), 5.31 (d, J_{NHNH} = 5.0 Hz, 1 H, NH), 7.42−7.57 (m, 3 H, ArH), 7.68 (d, *J* = 6.7 Hz, 2 H, ArH), 7.98 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 23.0 (q), 28.1 (q), 52.5 (q), 55.8 (d, $J^{13}_{C\text{-}^{77}Se}$ = 60.0 Hz), 78.5 (s), 99.0 (s), 128.4 (d), 128.5 (d), 131.6 (d), 134.1 (s),

155.7 (s), 159.4 (s), 170.1 (s) ppm. IR: $\tilde{\nu}$ = 3425, 3302, 1738, 1720, 1618, 1581 cm^{-1}. $C_{17}H_{23}N_3O_4Se$ (412.3): calcd. C 49.52, H 5.62, N 10.19; found C 49.44, H 5.73, N 10.21.

Methyl (4*S,5*R**)-2-[5-(Methoxycarbonyl)-4-methyl-2-phenyl-4,5-dihydro-1,3-selenazol-4-yl]hydrazine-1-carboxylate (5d):** Yield: 170 mg (46%), yellow foam. ^1H NMR: δ = 1.47 (s, 3 H, CH_3), 3.51 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 4.91 (s, $J^1_{H\text{-}^{77}Se}$ = 14.0 Hz, 1 H, CH), 5.49 (br. s, 1 H, NH), 7.42−7.59 (m, 3 H, ArH), 7.70 (d, *J* = 7.9 Hz, 2 H, ArH), 8.38 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 20.5 (q), 51.5 (q), 52.3 (q), 54.4 (d, $J^{13}_{C\text{-}^{77}Se}$ = 58.6 Hz), 100.5 (s), 128.7 (2d), 133.7 (d), 134.2 (s), 157.5 (s), 163.3 (s), 170.8 (s) ppm. IR: $\tilde{\nu}$ = 3301, 3173, 1737, 1674, 1615, 1578 cm^{-1}. $C_{14}H_{17}N_3O_4Se$ (370.3): calcd. C 45.41, H 4.63, N 11.35; found C 45.71, H 4.61, N 11.11.

Methyl (4*R,5*R**)-2-[5-(Methoxycarbonyl)-4-methyl-2-phenyl-4,5-dihydro-1,3-selenazol-4-yl]hydrazine-1-carboxylate (5′d):** Yield: 133 mg (36%), light pink powder from Et_2O/light petroleum ether, m.p. 108−111 °C (dec.). ^1H NMR: δ = 1.51 (s, 3 H, CH_3), 3.54 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 4.87 (s, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, 1 H, CH), 5.38 (d, J_{NHNH} = 5.0 Hz, 1 H, NH), 7.42−7.58 (m, 3 H, ArH), 7.69 (d, *J* = 6.5 Hz, 2 H, ArH), 8.32 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 22.6 (q), 51.6 (q), 52.5 (q), 55.4 (d, $J^{13}_{C\text{-}^{77}Se}$ = 58.4 Hz), 99.1 (s), 128.5 (d), 128.8 (d), 131.8 (d), 134.2 (s), 157.3 (s), 159.6 (s), 170.5 (s) ppm. IR: $\tilde{\nu}$ = 3340, 3284, 1725, 1709, 1614, 1581 cm^{-1}. $C_{14}H_{17}N_3O_4Se$ (370.3): calcd. C 45.41, H 4.63, N 11.35; found C 45.24, H 4.92, N 11.34.

Methyl 4-Methyl-2-phenyl-1,3-selenazole-5-carboxylate (6): DBU (152 mg, 1 mmol) in a THF/MeOH mixture (1:1, 5 mL) was added dropwise to a magnetically stirred solution of **5′b−d** (1 mmol) in the same solvent mixture (10 mL). The light pink solution was left to stand at room temperature until the complete disappearance of the reagent (36−48 h, monitored by TLC). The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography on a silica gel column, eluting with cyclohexane/EtOAc mixtures, to obtain pure derivative **6** in 35−58% yield. White powder from light petroleum ether, m.p. 72−74 °C. ^1H NMR: δ = 2.88 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 7.45−7.57 (m, 3 H, ArH), 7.91−7.97 (m, 2 H, ArH) ppm. ^{13}C NMR: δ = 23.1 (q), 57.6 (q), 132.1 (d), 134.3 (s), 134.5 (d), 136.8 (d), 140.1 (s), 165.9 (s), 168.6 (s), 181.3 (s) ppm. IR: $\tilde{\nu}$ = 1716, 1523 cm^{-1}. MS: *m*/*z* (%) = 281 [M^+ + 1] (100). $C_{12}H_{11}NO_2Se$ (280.2): calcd. C 51.44, H 3.96, N 5.00; found C 51.22, H 4.17, N 5.18.

Procedure for the Synthesis of Methyl 2-{1-[2-Dimethylamino-4-oxo-1,3-selenazol-5(4*H*)-ylidene]ethyl}diazene-1-carboxylate (8): PTAB (mg 413.5, 1.1 mmol) was added portionwise to a stirred solution of compound **4h** (mg 305, 1 mmol) in CH_2Cl_2 (20 mL), maintained at 0° C. Stirring was continued for 5 h, and the formed yellow suspension was then transferred into a separating funnel and washed with water (1×) and with satd. Na_2CO_3 (4×). The red organic layer was dried with Na_2SO_4 and filtered, and the solvent was evaporated under reduced pressure to obtain a residue that, on treatment with Et_2O, furnished pure derivative **8**. Yield: 227 mg (75%), dark orange powder from Et_2O, m.p. 140 °C (dec.). ^1H NMR ($CDCl_3$): δ = 2.61 (s, 3 H, CH_3), 3.21 and 3.43 [2 s, 6 H, $N(CH_3)_2$], 4.06 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.2 (q), 40.4 (q), 40.9 (q), 54.9 (q), 148.2 (s), 153.4 (s), 161.8 (s), 174.4 (s), 181.2 (s) ppm. IR: $\tilde{\nu}$ = 1756, 1683, 1600, 1591 cm^{-1}. $C_9H_{12}N_4O_3Se$ (303.2): calcd. C 35.66, H 3.99, N 18.48; found C 35.80, H 3.99, N 18.57.

Procedure for the Synthesis of Michael Adduct 9 and 1-Selena-3,7,8-triazaspiro[4.5]deca-2,6-dien-4-one Derivative 10: A catalytic amount of sodium methoxide was added to a magnetically stirred solution of α-acetylphenylacetonitrile (159 mg, 1 mmol) in THF (10 mL); after 5 min the conjugated azoalkene **8** (303 mg, 1 mmol) was added portionwise. Stirring was maintained at room temperature until the disappearance of the reagents (36 h, monitored by TLC). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on a silica gel column, eluting with cyclohexane/EtOAc mixtures, to obtain pure derivatives **9** and **10**.

Compound 9: Yield: 268 mg (58%), white powder from Et_2O, m.p. 188−190 °C (dec.). ^1H NMR: δ = 1.78 (s, 3 H, CH_3), 2.59 (s, 3 H, $COCH_3$), 2.96 and 2.98 [2 s, 6 H, $N(CH_3)_2$], 3.71 (s, 3 H, OCH_3), 7.30−7.32 (m, 2 H ArH), 7.39−7.41 (m, 3 H, ArH), 10.38 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.8 (q), 27.9 (q), 40.0 (q), 40.8 (q), 52.2 (q), 61.3 (s), 80.2 (s), 119.0 (s), 128.0 (s), 128.4 (d), 129.2 (d), 129.4 (d), 146.1 (s), 154.4 (s), 177.3 (s), 183.4 (s), 198.4 (s) ppm. IR: $\tilde{\nu}$ = 3230, 3169, 2238, 1716, 1677, 1566 cm^{-1}. $C_{19}H_{21}N_5O_4Se$ (462.4): calcd. C 49.36, H 4.58, N 15.15; found C 49.37, H 4.57, N 15.24.

Compound 10: Yield: 23 mg (5%), white powder from Et_2O; *dr* 70:30. ^1H NMR: δ = 1.59* and 1.74 (2 s, 3 H, CH_3), 1.98* and 2.15 (2 s, 3 H, $COCH_3$), 3.06, 3.16*, and 3.24* [3 s, 6 H, $N(CH_3)_2$], 3.69* and 3.75 (2 s, 3 H, OCH_3). 7.05−7.74 (2 m, 5 H ArH), 8.44* and 8.47 (s and br s, 1 H, OH) ppm. ^{13}C NMR: δ = 21.1 and 21.9 (2 q), 25.9 and 30.6 (2 q), 40.8, 41.4, and 41.5 (3 q), 53.9 and 54.6 (2 q), 62.0 and 66.4 (2 s), 82.6 and 82.7 (2 s), 99.0 and 99.2 (2 s), 118.9 and 120.2 (2 s), 127.2 and 127.6 (2 d), 128.4 and 128.6 (2 d), 129.1 and 129.5 (2 d), 130.3 and 132.4 (2 s), 142.3 and 145.1 (2 s), 151.5 and 154.4 (2 s), 172.6 and 177.0 (2 s), 181.9 (s) ppm. IR: $\tilde{\nu}$ = 3060, 3034, 2774, 2241, 1733, 1660, 1619, 1571 cm^{-1}. $C_{19}H_{21}N_5O_4Se$ (462.4): calcd. C 49.36, H 4.58, N 15.15; found C 49.39, H 4.58, N 15.11.

Procedure for the Synthesis of 1-[2-(Dimethylamino)-4-hydroxy-1,3-selenazol-5-yl]ethan-1-one (11): Compound **4g** (347 mg, 1 mmol) was heated under reflux in a Me_2CO/H_2O mixture (10:1, 10 mL) in the presence of Amberlyst 15 (H) (500 mg) for 10 h. The resin was filtered off and, after evaporation of the solvent under reduced pressure, the residue was crystallized with EtOAc/Et_2O to obtain derivative **11**. Yield: 112 mg (48%), light yellow powder from EtOAc/Et_2O, m.p. 85−87 °C. ^1H NMR ($CDCl_3$): δ = 2.11 and 2.42 (2 s, 3 H, $COCH_3$), 3.09, 3.17, 3.34, and 3.37 [4 s, 6 H, $N(CH_3)_2$], 5.31 and 14.03 (s and br s, $J^1_{H\text{-}^{77}Se}$ = 16.0 Hz, 1 H, CH and OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.6 (q), 27.3 (q), 40.0 (q), 40.1 (q), 41.3 (q), 41.4 (q), 65.9 (d, $J^{13}_{C\text{-}^{77}Se}$ = 61.0 Hz), 103.1 (s), 171.4 (s), 172.8 (s), 176.6 (s), 183.4 (s), 184.6 (s) 198.8 (s) ppm. IR: $\tilde{\nu}$ = 3241, 2725, 1637, 1615 cm^{-1}. MS: *m*/*z* (%) = 234 [M^+ 1] (15), 192 (7), 71 (100). $C_7H_{10}N_2O_2Se$ (233.1): calcd. C 36.06, H 4.32, N 12.02; found C 36.10, H 4.27, N 12.21.

Procedure for the Synthesis of Benzoyl Derivatives of 11 (12a−b): Pyridine (158 mg, 2 mmol) and benzoyl chloride (281 mg, 2 mmol) in THF (5 mL) were added to a magnetically stirred suspension of **11** (233 mg, 1 mmol) in THF (5 mL), maintained at 0° C. The temperature was allowed to rise to room temperature and the stirring was maintained for 24 h. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 and washed in a separating funnel with satd. $NaHCO_3$ and with brine. The organic layer was dried with Na_2SO_4 and filtered, and the solvent was evaporated under reduced pressure to furnish a red oil that was purified by flash chromatography on a silica gel column (eluent cyclohexane/EtOAc mixtures) to afford pure compounds **12a−b**.

1-[2-(Dimethylamino)-4-oxo-1,3-selenazol-5(4*H*)-ylidene]ethyl Benzoate (12a): Yield: 103 mg (32%), white powder from light pet-

roleum ether, m.p. 155−158 °C. ^{1}H NMR ($CDCl_3$): δ = 2.70 (s, 3 H, CH_3), 3.07 and 3.35 [2 s, 6 H, $N(CH_3)_2$], 7.50 (t, *J* = 7.6 Hz, 2 H, ArH), 7.65 (t, *J* = 7.6 Hz, 1 H, ArH), 8.08 (d, *J* = 7.6 Hz, 2 H, ArH) ppm. ^{13}C NMR: δ = 18.4 (q), 40.0 (q), 40.9 (q), 123.2 (s), 128.5 (d), 128.7 (d), 130.0 (d), 134.0 (s), 156.4 (s), 162.8 (s), 170.7 (s), 179.9 (s) ppm. IR: ṽ = 2740, 1682, 1640, 1566 cm^{-1}. MS: *m*/*z* (%) = 338 [M^+ + 1] (100). $C_{14}H_{14}N_2O_2Se$ (321.2): calcd. C 49.86, H 4.18, N 8.31; found C 49.61, H 4.36, N 8.31.

5-Acetyl-2-(dimethylamino)-1,3-selenazol-4-yl Benzoate (12b): Yield: 38 mg (12%), light yellow powder from Et_2O/light petroleum ether, m.p. 129−130 °C. ^{1}H NMR ($CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 3.12 and 3.13 [2 s, 6 H, $N(CH_3)_2$], 7.52 (t, *J* = 8.0 Hz, 2 H, ArH), 7.65 (t, *J* = 8.0 Hz, 1 H, ArH), 8.20 (d, *J* = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR: δ = 27.4 (q), 40.0 (q), 40.7 (q), 118.3 (s), 128.2 (d), 128.7 (d), 130.3 (d), 134.2 (s), 154.6 (s), 163.6 (s), 170.5 (s), 189.0 (s) ppm. IR: ṽ = 2734, 1628, 1599, 1572 cm^{-1}. MS: *m*/*z* (%) = 338 [M^+ + 1] (100). $C_{14}H_{14}N_2O_2Se$ (321.2): calcd. C 49.86, H 4.18, N 8.31; found C 49.84, H 4.45, N 8.22.

General Procedure for the Synthesis of 5,5-Disubstituted 2-Selenazolin-4-one Derivatives 13a−g: A catalytic amount of sodium methoxide was added to a magnetically stirred suspension of selenazolinone **4c−d** or solution of selenazolinone **4g−h** (1 mmol) in THF (20 mL), followed by the conjugated azoalkene **1a**, **1d**, or **1e**. The reaction mixture was maintained at room temperature until the complete disappearance of the reagents (12−30 h, monitored by TLC). The solvent was removed under reduced pressure, and the oily residue was crystallized from the appropriate solvents to give compounds **13a−g** as diastereomeric mixtures.

Compound 13a: Yield: 379 mg (75%), light yellow powder from EtOAc/light petroleum ether; *dr* 86:14. ^{1}H NMR: δ = 1.38 and 1.44* (2 s, 9 H, *t*Bu), 1.68* and 1.76 (2 s, 3 H, CH_3), 1.95 and 2.15* (2 s, 3 H, CH_3), 3.54 (s, 3 H, OCH_3), 3.62 (s, 3 H, OCH_3), 4.25 and 4.34* (2 s, 1 H, CH), 8.32 and 9.03 (2 br s, 2 H, NH_2), 9.52 (br. s, 1 H, NH), 9.95 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.2 and 14.0 (2 q), 19.2 and 20.7 (2 q), 28.10 (q), 51.6 (q), 51.9 (q), 55.8 (d), 73.7 (s), 79.5 (s), 148.2 (s), 149.7 (s), 152.8 (s), 154.2 (s), 169.2 (s), 182.3 (s), 188.4 (s) ppm. IR: ṽ = 3389, 3217, 1729, 1662, 1647, 1634 cm^{-1}. $C_{17}H_{26}N_6O_7Se$ (505.4): calcd. C 40.40, H 5.19, N 16.63; found C 40.28, H 5.29, N 16.61.

Compound 13b: Yield: 398 mg (69%), light yellow powder from EtOAc/Et_2O; *dr* 83:17. ^{1}H NMR: δ = 1.38 and 1.42* (2 s, 9 H, *t*Bu), 1.73* and 1.78 (2 s, 3 H, CH_3), 2.05 and 2.17* (2 s, 3 H, CH_3), 3.56 (s, 3 H, OCH_3), 4.32 and 4.47* (2 s, 1 H, CH), 6.99 (t, *J* = 7.3 Hz, 1 H, ArH), 7.28 (t, *J* = 7.3 Hz, 2 H, ArH), 7.94 (d, *J* = 7.3 Hz, 2 H, ArH), 8.09 (br. s, 1 H, NH), 8.97 and 9.20 (2 br s, 2 H, NH_2), 9.55 (br. s, 1 H, NH), 9.59 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.4 and 14.1 (2 q), 19.4 and 20.9 (2 q), 27.9 and 28.10 (2 q), 52.2 (q), 56.3 (d), 74.0 (s), 79.6 (s), 118.3 (d), 122.4 (d), 128.9 (d), 138.9 (s), 148.1 (s), 148.4 (s), 152.4 (s), 154.9 (s), 169.3 (s), 179.6 (s), 188.0 (s) ppm. IR: ṽ = 3388, 3318, 3262, 3179, 1756, 1741, 1715, 1687, 1637, 1606, 1595 cm^{-1}. $C_{22}H_{29}N_7O_6Se$ (566.5): calcd. C 46.65, H 5.16, N 17.31; found C 46.90, H 5.02, N 17.48.

Compound 13c: Yield: 384 mg (83%), light orange powder from EtOAc; *dr* 80:20. ^{1}H NMR: δ = 1.69* and 1.87 (2 s, 3 H, CH_3), 1.98 and 2.12 (2 s, 3 H, CH_3), 3.53 (s, 3 H, OCH_3), 3.60 (s, 3 H, OCH_3), 3.64 (s, 3 H, OCH_3), 4.27 and 4.32* (2 s, 1 H, CH), 8.82 and 9.04 (2 br s, 2 H, NH_2), 9.91 (s, 2 H, 2 NH) ppm. ^{13}C NMR: δ = 13.1 and 14.0 (2 q), 18.9 and 19.1 (2 q), 51.7 (q), 51.8 (q), 51.9 (q), 56.0 (d), 73.6 (s), 148.8 (s), 149.7 (s), 154.2 (s), 154.5 (s), 169.2 (s), 182.3 (s), 188.4 (s) ppm. IR: ṽ = 3268, 3192, 1737, 1715, 1637, 1522 cm^{-1}. $C_{14}H_{20}N_6O_7Se$ (463.3): calcd. C 36.29, H 4.35, N 18.14; found C 36.59, H 4.13, N 18.00.

Compound 13d: Yield: 336 mg (63%), beige powder from EtOAc/light petroleum ether; *dr* 88:12. ^{1}H NMR: δ = 1.36 and 1.44* (2 s, 9 H, *t*Bu), 1.67* and 1.71 (2 s, 3 H, CH_3), 1.81 and 2.16* (2 s, 3 H, CH_3), 3.14*, 3.20, and 3.24* [3 s, 6 H, $N(CH_3)_2$], 3.54 (s, 3 H, OCH_3), 3.62 (s, 3 H, OCH_3), 4.28 and 4.36* (2 s, 1 H, CH), 9.52* and 9.61 (2 br s, 1 H, NH), 9.86 and 9.99* (2 br s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.1 (q), 19.1 (q), 28.1 (q), 39.7 and 40.7 (2 q), 51.7 (q), 51.8 (d), 51.9 (q), 55.7 (d), 75.3 (s), 79.5 (s), 147.6 (s), 149.7 (s), 152.8 (s), 154.2 (s), 169.0 (s), 181.3 (s), 188.7 (s) ppm. IR: ṽ = 3250, 3155, 1752, 1693, 1671, 1575 cm^{-1}. $C_{19}H_{30}N_6O_7Se$ (533.4): calcd. C 42.78, H 5.67, N 15.75; found C 42.93, H 5.80, N 15.94.

Compound 13e: Yield: 440 mg (74%), white powder from EtOAc/Et_2O; *dr* 76:24. ^{1}H NMR: δ = 1.44 *and 1.45 (2 s, 9 H, *t*Bu), 1.73* and 1.75 (2 s, 3 H, CH_3), 1.86 and 2.19* (2 s, 3 H, CH_3), 3.06, 3.07, 3.18*, and 3.26* [4 s, 6 H, $N(CH_3)_2$], 3.58* and 3.70 (2 s, 3 H, OCH_3), 4.34 and 4.49* (2 s, 1 H, CH), 6.96−7.02 (m, 1 H, ArH), 7.24−7.34 (m, 2 H, ArH), 7.46 and 7.55 (2 d, 2 H, *J* = 8.0 Hz, ArH), 8.21 and 8.31* (2 s, 1 H, NH), 9.57*, 9.59*, 9.70, and 9.86 (4 s, 2 H, 2 NH) ppm. ^{13}C NMR: δ = 13.3 and 13.5 (2 q), 16.6 and 19.1 (2 q), 28.1 (q), 39.9, 40.8, and 41.2 (3 q), 52.1 and 52.3 (2 q), 55.5 e 56.1 (2 d), 75.3 and 77.5 (2 s), 79.4 and 79.6 (2 s), 118.1 and 118.6 (2 d), 122.2 and 122.5 (2 d), 128.7 and 128.9 (2 d), 138.7 and 138.9 (2 s), 147.6 (s), 148.2 (s), 152.3 (s), 152.8 and 153.1 (2 s), 169.1 and 171.4 (2 s), 179.0 (s), 186.3 (s) ppm. IR: ṽ = 3366, 3343, 3306, 3223, 1742, 1719, 1690, 1677, 1579 cm^{-1}. $C_{24}H_{33}N_7O_6Se$ (594.5): calcd. C 48.49, H 5.59, N 16.49; found C 48.38, H 5.63, N 16.72.

Compound 13f: Yield: 285 mg (58%), white powder from Et_2O; *dr* 87:13. ^{1}H NMR: δ = 1.68* and 1.74 (2 s, 3 H, CH_3), 1.98 and 2.14* (2 s, 3 H, CH_3), 3.07, 3.11, 3.15*, and 3.24* [4 s, 6 H, $N(CH_3)_2$], 3.55 (s, 3 H, OCH_3), 3.62 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 4.27 and 4.35* (2 s, 1 H, CH), 9.95 and 10.00 (2 br s, 2 H, 2 NH) ppm. ^{13}C NMR: δ = 13.2 (q), 19.0 (q), 39.9 and 40.7 (2 q), 51.9 (q), 52.0 (q), 52.1 (q), 55.8 (d), 75.1 (s), 148.5 (s), 149.9 (s), 154.3 (s), 154.5 (s), 169.1 (s), 181.3 (s), 186.8 (s) ppm. IR: ṽ = 3242, 3152, 3089, 1741, 1716, 1669, 1574 cm^{-1}. $C_{16}H_{24}N_6O_7Se$ (491.4): calcd. C 39.11, H 4.92, N 17.10; found C 39.44, H 4.90, N 17.07.

Compound 13g: Yield: 340 mg (60%), white powder from Et_2O; *dr* 85:15. ^{1}H NMR: δ = 1.67* and 1.74 (2 s, 3 H, CH_3), 1.98 and 2.15* (2 s, 3 H, CH_3), 3.10, 3.13, 3.22*, and 3.24* [4 s, 6 H, $N(CH_3)_2$], 3.54 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 4.28 and 4.35* (2 s, 1 H, CH), 5.05−5.13 (m, 2 H, OCH_2Ph), 7.24−7.42 (m, 5 H, ArH), 9.89* and 9.95 (2 s, 1 H, NH), 10.04 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.2 (q), 19.0 (q), 39.9 and 40.7 (2 q), 52.0 (q), 52.2 (q), 55.8 (d), 66.0 (t), 75.0 (s), 128.1 (d), 128.3 (d), 128.4 (d), 136.5 (s), 147.8 (s), 148.4 (s), 154.3 (s), 154.5 (s), 169.1 (s), 181.3 (s), 186.8 (s) ppm. IR: ṽ = 3243, 1751, 1735, 1700, 1685, 1676, 1565 cm^{-1}. $C_{22}H_{28}N_6O_7Se$ (567.5): calcd. C 46.57, H 4.97, N 14.81; found C 46.81, H 5.01, N 15.08.

General Procedure for the Synthesis of 1-Selena-3,7-diazaspiro[4.4]nona-2,8-dien-4-one Derivatives 14d−g: DBU (1 mmol) in a THF/MeOH mixture (1:1, 5 mL) was added dropwise to a magnetically stirred solution of **13d−g** (1 mmol) in the same solvent mixture (10 mL). The light yellow solution, maintained at room temperature, darkened, and the reaction was complete in 24 h (monitored by TLC). The solvent was removed under reduced pressure and the dark residue was purified by flash chromatography on a silica gel column, eluting with EtOAc or EtOAc/MeOH mixtures, to give pure derivatives **14d−g**.

Compound 14d: Yield: 235 mg (44%), white powder from Et_2O, m.p. 135 °C (dec.). ^1H NMR: δ = 1.37 (s, 9 H, *t*Bu), 1.41 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 3.10 and 3.32 [2 s, 6 H, $N(CH_3)_2$], 3.55 (s, 3 H, OCH_3), 3.67 (s, 3 H, OCH_3), 5.82 (s, 1 H, NH), 7.89 (s, 1 H, NH), 8.85 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 11.8 (q), 21.7 (q), 28.0 (q), 39.5 (q), 41.2 (q), 50.5 (q), 52.4 (q), 78.7 (s), 81.5 (s), 89.5 (s), 100.4 (s), 155.6 (s), 156.3 (s), 162.7 (s), 163.1 (s), 174.3 (s), 186.7 (s) ppm. IR: $\tilde{\nu}$ = 3326, 3277, 3253, 1754, 1737, 1699, 1613, 1573 cm^{-1}. $C_{19}H_{30}N_6O_7Se$ (533.4): calcd. C 42.78, H 5.67, N 15.75; found C 42.68, H 5.76, N 15.81.

Compound 14e: Yield: 273 mg (46%), beige powder from Et_2O, m.p. 146 °C (dec.). ^1H NMR: δ = 1.15 (s, 3 H, CH_3), 1.36 (s, 9 H, *t*Bu), 2.16 (s, 3 H, CH_3), 3.19 and 3.25 [2 s, 6 H, $N(CH_3)_2$], 3.50 (s, 3 H, OCH_3), 5.83 (d, J_{NHNH} = 4.0 Hz, 1 H, NH), 6.99 (t, *J* = 7.4 Hz, 1 H, ArH), 7.28 (t, *J* = 7.4 Hz, 2 H, ArH), 7.60 (d, *J* = 7.4 Hz, 2 H, ArH), 8.12 (br. s, 1 H, NH), 8.36 (s, 1 H, NH), 8.85 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 11.6 (q), 14.8 (q), 28.0 (q), 39.6 (q), 40.8 (q), 50.0 (q), 79.0 (s), 82.0 (s), 86.6 (s), 100.3 (s), 118.3 (d), 122.5 (d), 128.7 (d), 138.9 (s), 155.5 (s), 156.2 (s), 160.4 (s), 163.8 (s), 180.2 (s), 189.3 (s) ppm. IR: $\tilde{\nu}$ = 3304, 3285, 3256, 1688, 1673, 1597, 1568 cm^{-1}. $C_{24}H_{33}N_7O_6Se$ (594.5): calcd. C 48.49, H 5.59, N 16.49; found C 48.70, H 5.42, N 16.61.

Compound 14f: Yield: 236 mg (48%), beige powder from Et_2O, m.p. 141 °C (dec.). ^1H NMR: δ = 1.41 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 3.10 and 3.25 [2 s, 6 H, $N(CH_3)_2$], 3.54 (s, 3 H, OCH_3), 3.56 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 6.01 (br. s, 1 H, NH), 8.18 (s, 1 H, NH), 8.71 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 11.8 (q), 21.8 (q), 39.7 (q), 41.3 (q), 50.7 (q), 52.4 (q), 52.5 (q), 81.3 (s), 89.5 (s), 100.4 (s), 156.3 (s), 156.8 (s), 163.0 (s), 163.2 (s), 174.4 (s), 187.0 (s) ppm. IR: $\tilde{\nu}$ = 3310, 3270, 3233, 3198, 1750, 1713, 1697, 1657, 1622, 1568 cm^{-1}. $C_{16}H_{24}N_6O_7Se$ (491.4): calcd. C 39.11, H 4.92, N 17.10; found C 39.10, H 5.10, N 16.92.

Compound 14g: Yield: 182 mg (32%), light pink powder from Et_2O, m.p. 138 °C (dec.). ^1H NMR: δ = 1.41 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 3.11 and 3.26 [2 s, 6 H, $N(CH_3)_2$], 3.55 (s, 3 H, OCH_3), 3.56 (s, 3 H, OCH_3), 5.12 (d, *J* = 12.0 Hz, 1 H, $OCH_2CH_aCH_bPh$), 5.15 (d, *J* = 12.0 Hz, 1 H, $OCH_2CH_aCH_bPh$), 5.98 (s, 1 H, NH), 7.39 (br. s, 5 H ArH), 8.18 (s, 1 H, NH), 8.78 (s, 1 H, NH) ppm. ^{13}C NMR: δ = 11.8 (q), 21.8 (q), 39.9 (q), 41.3 (q), 50.8 (q), 52.5 (q), 66.8 (t), 81.4 (s), 89.6 (s), 100.5 (s), 128.1 (d), 128.4 (d), 128.7 (d), 136.3 (s), 156.0 (s), 156.9 (s), 162.9 (s), 163.3 (s), 174.5 (s), 187.1 (s) ppm. IR: $\tilde{\nu}$ = 3318, 3251, 3211, 1752, 1723, 1686, 1606, 1568 cm^{-1}. $C_{22}H_{28}N_6O_7Se$ (567.5): calcd. C 46.57, H 4.97, N 14.81; found C 46.88, H 4.90, N 14.66.

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