One-pot synthesis of 5-arylamino-1,3,4-selenadiazol-2(3*H*)-ones from arylisoselenocyanates

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A one-pot reaction of arylisoselenocyanates, hydrazine and bis(trichloromethyl) carbonate, in the presence of a base provides an efficient route for the synthesis of 5-arylamino-1,3,4-selenadiazol-2(3*H*)-ones in good to excellent yields. A plausible mechanism is proposed for the reaction.

Keywords: arylisoselenocyanates, selenadiazole, bis(trichloromethyl) carbonate, cyclisation, tandem reaction

Selenium, a recognised dietary antioxidant, is now known to be an essential component of the active sites of several enzymes, including glutathione peroxidase (GSH-Px)[1–2] and thioredoxin reductase.[3] The interest in the chemistry of organoselenium compounds has increased in a few decades due to their synthetic applications[4–5] and biological activities.[6–7] It has been reported that selenium-containing heterocycles show anti-cancer,[8–11] anti-inflammatory,[12–13] antibacterial,[14–15] antileishmanial[16] and antioxidant properties.[17–19]

Useful key starting materials for preparation of selenium-containing heterocycles include selenoamides, selenoureas, selenazadienes, and isoselenocyanates. Among all these reagents, aryl and alkyl isoselenocyanates have emerged as powerful tools for the synthesis of selenium-containing heterocycles because of their convenient preparation, low toxicity, relative stability, and excellent reactivity.[20–27]

Bis(trichloromethyl) carbonate (**BTC**), as a bis-electrophilic reagent, has proved to be safe and advantageous due to its low vapour pressure and high stability. It has been successfully employed as an efficient carbonyl activator for the one-step cycloaddition with two types of nucleophiles. We have studied **BTC** for several years and have explored some of its applications.[28–30]

Addition of a base as an acid scavenger enhances the reaction rate[31–33] and the presence of a base could increase the nucleophilicity of the reactants.

To the best of our knowledge, the preparation of 1,3,4-selenadiazole derivatives is only described in two papers,[34–35] and the preparation of 1,3,4-selenadiazol-ones has not been reported. We now report a one-pot synthesis of novel 5-phenylamino-1,3,4-selenadiazol-2(3*H*)-ones for the first time from isoselenocyanates.

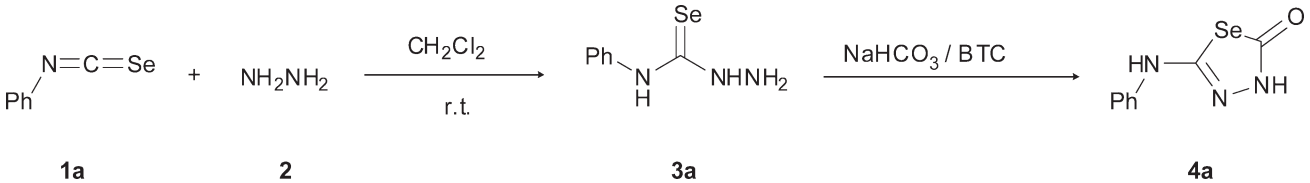
Results and discussion

When isoselenocyanatobenzene, hydrazine hydrate and **BTC** were mixed in dichloromethane at room temperature for several hours, TLC showed the formation of a new product in low yield which was confirmed to be 5-(phenylamino)-5-arylamino-1,3,4-selenadiazol-2(3*H*)-one (**4a**) (Scheme 1). This result encouraged us to modify the reaction conditions to improve the yield.

Isoselenocyanatobenzene **1a** was selected as the substrate to optimise the reaction conditions. When isoselenocyanatobenzene and hydrazine hydrate were stirred in CH_2Cl_2 at room temperature selenosemicarbazide **3a** was afforded in high yield.[36] However, when **3a** was treated with **BTC** in the presence of NaOH for 12 h, only 35% of the desired product **4a** was obtained (Table 1, entry 1). Other bases were evaluated and $NaHCO_3$ proved to be superior to NaOH, Na_2CO_3, Et_3N and Bu_3N (entries 1–4). Other solvents such as toluene, EtOH, ethyl acetate, H_2O, 1,4-dioxane, THF and nitromethane were also tried but lower yields resulted. Several ratios of base to **BTC** were also studied and the best ratio of $NaHCO_3$/**BTC** for the reaction was 7.5:1. Furthermore, reaction temperature and time were also examined. Although an increase of reaction temperature would increase the reaction rate, it did not improve the yield.

On the basis of these results, the optimal reaction conditions for achieving the highest yield was carrying out the reaction in CH_2Cl_2 at room temperature stirred at 7.5:1 ratio of $NaHCO_3$ to **BTC** for 2 h. Under these optimised conditions, 5-phenylamino-1,3,4-selenadiazol-2(3*H*)-one **4a** was obtained in 83% yield (Table 1, entry 7). The structure of the product was confirmed by NMR, MS, HRMS and IR data.

Under the optimised reaction conditions, the scope of substrates **1** and **2** (Scheme 2) was probed. Firstly, various alkyl-isoselenocyanates were tested and the results are summarised in Table 2. Generally, a higher yield was achieved when an arylisoselenocyanate was used compared to its alkyl analogue (Table 2, entries 1–6), and even better with an electron donating group on the aromatic ring (entries 2–3). In addition, phenylhydrazine instead of hydrazine hydrate was also investigated (Table 2, entries 7–9). The reaction proceeded smoothly at room temperature in good yields except for isoselenocyanatobenzene, which afforded the corresponding product **4g** in relatively low yield. Furthermore, introduction of an electron-withdrawing group on the arylhydrazine decreased the reaction yields (Table 2, compare entries 12–14 to entries 7, 9 and 11), and electron donating groups on the aromatic isoselenocyanate increased the reaction yield in reaction with either 4-chlorophenylhydrazine or 4-methoxyphenylhydrazine (Table 2, entries 12–17).



1a **2** **3a** **4a**

Scheme 1 One-pot synthesis of 5-(phenylamino)-5-arylamino-1,3,4-selenadiazol-2(3*H*)-one.

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Table 1 The optimisation of the reaction conditions for the formation of 5-phenylamino-5-arylamino-1,3,4-selenadiazol-2(3*H*)-one **4a**[a]

Entry	Base	Solvents	Base/BTC	Yields/%[b]
1	NaOH	CH_2Cl_2	6.0:1	35
2	Et_3N	CH_2Cl_2	6.0:1	52
3	Na_2CO_3	CH_2Cl_2	3.0:1	50
4	Bu_3N	CH_2Cl_2	6.0:1	57
5	$NaHCO_3$	CH_2Cl_2	6.0:1	65
6	$NaHCO_3$	CH_2Cl_2	7.0:1	75
7	$NaHCO_3$	CH_2Cl_2	7.5:1	83
8	$NaHCO_3$	CH_2Cl_2	8.0:1	81
9	$NaHCO_3$	toluene	7.5:1	53
10	$NaHCO_3$	CH_3CH_2OH	7.5:1	Trace
11	$NaHCO_3$	AcOEt	7.5:1	68
12	$NaHCO_3$	H_2O	7.5:1	0
13	$NaHCO_3$	1,4-dioxane	7.5:1	26
14	$NaHCO_3$	THF	7.5:1	Trace
15	$NaHCO_3$	CH_3NO_2	7.5:1	35

[a] The reaction was monitored by TLC.
[b] Isolated yields based on isoselenocyanatobenzene.

Based on the results described, we propose a plausible mechanism (Scheme 3). Nucleophilic addition of the amino group of the hydrazines **2** to isoselenocyanates **1** leads to the adduct intermediate **3**, which then reacts with the bis-electrophilic reagent **BTC** to form intermediate **5**. In the presence of sodium bicarbonate, the intermediate **5** undergoes a cyclisation to afford the final heterocycle **4**.

In conclusion, we used the tandem reaction of arylisoselenocyanates, hydrazine and **BTC** to synthesise selenium-containing heterocycles. A variety of 5-arylamino-1,3,4-selenadiazol-2-ones could be prepared in good yields in the presence of sodium bicarbonate by this simple, convenient and efficient procedure. The use of $NaHCO_3$, the short reaction time, mild reaction conditions, green-chemistry features and commercially available starting materials offer specific advantages of the method.

Table 2 Preparation of 5-arylamino-3-aryl-5-arylamino-1,3,4-selenadiazol-2(3*H*)-ones **4a–q** from aryl isoselenocyanates **1**[a]

Entry	R^1	R^2	Compound	Products	Yield/%[b]
1	Ph	H	**3a**	**4a**	83
2	*p*-Me-Ph	H	**3b**	**4b**	88
3	*p*-OMe-Ph	H	**3c**	**4c**	94
4	*p*-Cl-Ph	H	**3d**	**4d**	85
5	Cyclohexyl	H	**3e**	**4e**	70
6	*n*-Bu	H	**3f**	**4f**	62
7	Ph	Ph	**3g**	**4g**	57
8	*p*-Me-Ph	Ph	**3h**	**4h**	85
9	*p*-OMe-Ph	Ph	**3i**	**4i**	88
10	*p*-Cl-Ph	Ph	**3j**	**4j**	80
11	*o*-Me-Ph	Ph	**3k**	**4k**	75
12	Ph	***p***-Cl-Ph	**3l**	**4l**	57
13	*p*-OMe-Ph	***p***-Cl-Ph	**3m**	**4m**	62
14	*o*-Me-Ph	***p***-Cl-Ph	**3n**	**4n**	58
15	*p*-OMe-Ph	***p***-OMe-Ph	**3o**	**4o**	78
16	*o*-Me-Ph	***p***-OMe-Ph	**3p**	**4p**	75
17	*p*-Cl-Ph	***p***-OMe-Ph	**3q**	**4q**	69

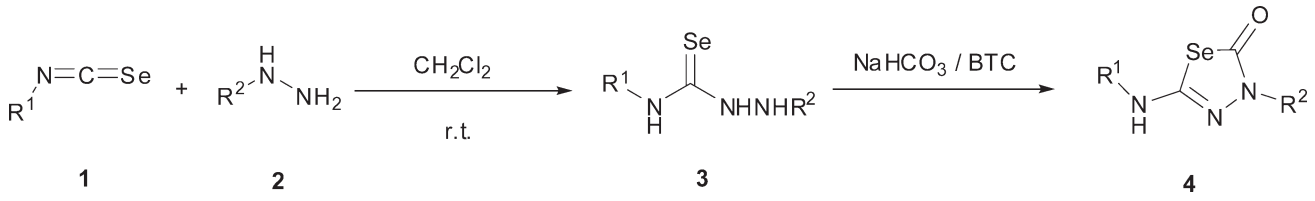
[a] The reactions were carried out in the presence of isoselenocyanates (R≡N=C=Se, 1 mmol), hydrazines (R_2NHNH_2, 1 mmol), **BTC** (0.33 mmol) and $NaHCO_3$ (2.5 mmol) in CH_2Cl_2 at r.t. for 2 h.
[b] Isolated yields based on isoselenocyanates.

Experimental

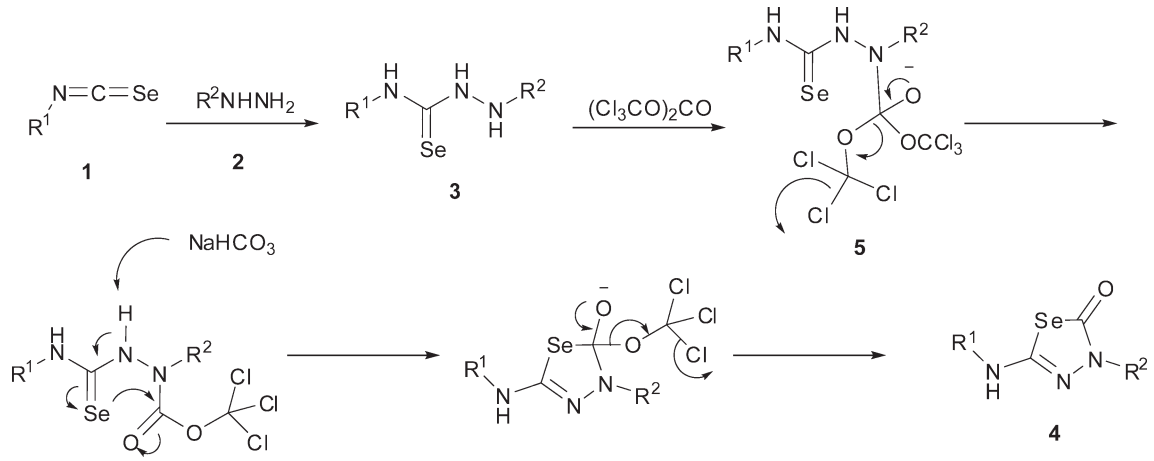
Melting points were determined using a Büchi B-540 apparatus and are uncorrected. IR Spectra: Nicolet Avatar-370 spectrometer, in KBr; υ in cm^{-1}. ^1H and ^{13}C NMR Spectra: Varian Mercury Plus-400 instrument, in (d_6) DMSO or $CDCl_3$ at 400 and 100 MHz, resp.; δ in ppm, *J* in Hz. ESI-MS: Thermo Finnigan LCQ Advantage (ESI) or Trace DSQ (EI) instrument; in *m/z*. HRMS: Agilent 6210 TOF instrument.

Synthesis of 5-arylamino-1,3,4-selenadiazol-2(3H)-ones; typical procedure

To a dichloromethane solution of isoselenocyanatobenzene **1a** (0.182 g, 1 mmol) was added 85% hydrazine hydrate (0.059 g, 1 mmol) at room temperature. After the reaction was complete (monitored by TLC, 30 min), $NaHCO_3$ (0.210 g, 2.5 mmol) and



Scheme 2 Preparation of 5-arylamino-5-arylamino-1,3,4-selenadiazol-2(3*H*)-ones **4a-q** from aryl isoselenocyanates.



Scheme 3 A plausible mechanism proposed for the formation of **4**.

bis (trichloromethyl) carbonate (0.1g, 0.33 mmol) were added. The reaction mixture was stirred for 1.5 h. The mixture was washed with water and the organic layer was separated, dried over $MgSO_4$, and evapourated. The residue was subjected to column chromatography on silica gel using petroleum ether:AcOEt = 8:1 to 4:1 as eluent system, affording **4a** (0.199 g, 83%) as colourless crystals.

5-(Phenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4a**): Colourless crystals; yield, 83%; m.p. 168.1–168.8 °C; IR: ν_{max} = 3139, 1669, 1599, 1577, 1548, 1401, 1319, 1253, 751 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.63 (s, 1H, NH), 9.67 (s, 1H, NH), 7.40 (dd, J_1 = 0.8 Hz, J_2 = 8.4 Hz, 2H, ArH), 7.28 (t, J = 8.4 Hz, 2H, ArH), 6.94 (t, J = 7.2 Hz, 1H, ArH); ^{13}C NMR (DMSO-d_6): δ 171.4 (C=O), 149.5 (C=N), 140.7, 128.9 (CH×2), 121.3, 117.0 (CH×2); EI-MS: 243 (18), 241 (92, M^+), 239 (46), 237 (23), 77 (100); HRMS-ESI: Calcd for $C_8H_8N_3OSe$ $(M+H)^+$ 241.9833; found: 241.9826.

5-(4-Methylphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4b**): Yellow solid; yield, 88%; m.p. 150.2–150.7 °C; IR: ν_{max} = 3161, 1665, 1595, 1568, 1515, 1401, 1309, 1229, 1102, 814 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.56 (s, 1H, NH), 9.55 (s, 1H, NH), 7.28 (d, J = 8.4 Hz, 2H, ArH), 7.08 (d, J = 8.4 Hz, 2H, ArH), 2.23 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 171.4 (C=O), 149.6 (C=N), 138.3, 130.2, 129.3 (CH×2), 117.2 (CH×2), 20.3 (CH_3); ESI-MS: *m/z* (%) = 258 (10), 256 (100, M^+ +1), 254 (5); HRMS-ESI: Calcd for $C_9H_8N_3OSe$ $(M-H)^-$ 253.9833; found: 253.9841.

5-(4-Methoxyphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4c**): Pink solid; yield, 94%; m.p. 133.8–134.4 °C; IR: ν_{max} = 3156, 1668, 1606, 1578, 1510, 1401, 1248, 1033, 824 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.52 (s, 1H, NH), 9.46 (s, 1H, NH), 7.32 (d, J = 8.8 Hz, 2H, ArH), 6.87 (d, J = 8.8 Hz, 2H, ArH), 3.71 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6): δ 171.3 (C=O), 154.1 (C=N), 150.0, 134.2, 118.9 (CH×2), 114.2 (CH×2), 55.2 (OCH_3); ESI-MS: *m/z* (%) = 272 (17), 270 (100, M^- -1), 268 (37), 267 (26), 266 (20); HRMS-ESI: Calcd for $C_9H_9N_3O_2SeNa$ $(M+Na)^+$ 293.9758; found: 293.9752.

5-(4-Chlorophenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4d**): Yellow crystals; yield, 85%; m.p. 183.0–183.8 °C; IR: ν_{max} = 3301, 3199, 3130, 1664, 1639, 1578, 1545, 1491, 1403, 1319, 1258, 1102, 816 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.70 (s, 1H, NH), 9.82 (s, 1H, NH), 7.43 (d, J = 8.8 Hz, 2H, ArH), 7.33 (d, J = 8.8 Hz, 2H, ArH); ^{13}C NMR (DMSO-*d6*): δ 171.4 (C=O), 149.2 (C=N), 139.6, 128.8 (CH×2), 124.7, 118.5 (CH×2); EI-MS: *m/z* (%) = 277 (40), 275 (92, M^+), 273 (50), 271 (20), 218 (100); HRMS-ESI: Calcd for $C_8H_7ClN_3OSe$ $(M+H)^+$ 275.9443; found: 275.9435.

5-(Cyclohexylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4e**): Colourless solid; yield, 70%; m.p. 142.2–142.8 °C; IR: ν_{max} = 3441, 3184, 2929, 2849, 1661, 1595, 1400, 1322, 1086 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.08 (s, 1H, NH), 6.94 (d, J = 7.2 Hz, 1H, NH), 3.39–3.34 (m, 1H, CH), 1.92–1.87 (m, 2H, CH_2), 1.69–1.65 (m, 2H, CH_2), 1.55–1.51 (m, 1H, CH_2), 1.31–1.12 (m, 5H, CH_2); ^{13}C NMR (DMSO-d_6): δ 171.6 (C=O), 152.8 (C=N), 51.7, 32.4 (CH_2×2), 25.3, 24.2 (CH_2×2); ESI-MS: *m/z* (%) = 248 (17), 246 (100, M^- -1), 244 (43), 242(12); HRMS-ESI: Calcd for $C_8H_{13}N_3OSeNa$ $(M+Na)^+$ 270.0122; found: 270.0117.

5-(Butylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4f**): Oil; yield, 62%; IR: ν_{max} = 3420, 1651, 1552, 1384, 1048, 1025, 1001 cm^{-1}; ^1H NMR (DMSO-d_6): δ 11.13 (s, 1H, NH), 6.99 (s, 1H, NH), 3.11–3.07 (m, 2H, CH_2N), 1.50–1.44 (m, 2H, CH_2), 1.34–1.29 (m, 2H, CH_2), 0.88 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 171.5 (C=O), 153.7 (C=N), 42.5, 30.6, 19.6, 13.6; EI-MS: *m/z* (%) = 223 (10), 221 (50, M^+), 219 (25), 217(13), 66 (100); HRMS-ESI: Calcd for $C_6H_{12}N_3OSe$ $(M+H)^+$ 222.0146; found: 222.0140.

3-Phenyl-5-(phenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4g**): Purple solid; yield, 57%; m.p. 174.5–175.3 °C; IR: ν_{max} = 3425, 3154, 1661, 1601, 1571, 1400, 1343, 1294, 706 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.95 (s, 1H, NH), 7.78–7.75 (m, 2H, ArH), 7.51–7.47 (m, 4H, ArH), 7.36–7.29 (m, 3H, ArH), 7.00 (t, J = 7.2 Hz, 1H, ArH); ^{13}C NMR (DMSO-d_6): δ 168.1 (C=O), 147.2 (C=N), 140.2, 138.2, 129.1 (CH×2), 128.9 (CH×2), 126.1, 122.0 (CH×3), 117.4 (CH×2); ESI-MS: *m/z* (%) = 318 (19), 316 (100, M^- -1), 314 (45), 312 (17); HRMS-ESI: Calcd for $C_{14}H_{12}N_3OSe$ $(M+H)^+$ 318.0146; found: 318.0140.

5-(4-Methylphenylamino)-3-phenyl-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4h**): Yellow solid; yield, 85%; m.p. 176.8–177.4 °C; IR: ν_{max} = 3330, 3130, 1665, 1598, 1543, 1512, 1401, 1301, 1253, 1094, 813, 751, 689 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.85 (s, 1H, NH), 7.75 (d, J = 7.6 Hz, 2H, ArH), 7.48 (t, J = 8.0 Hz, 2H, ArH), 7.37 (d, J = 8.4 Hz, 2H, ArH), 7.30 (t, J = 7.2 Hz, 1H, ArH), 7.14 (d, J = 8.4 Hz, 2H, ArH), 2.25 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 168.1 (C=O), 147.4 (C=N), 138.3, 137.8, 131.0, 129.5 (CH×2), 129.0 (CH×2), 126.1, 121.9 (CH×2), 117.6 (CH×2), 20.3 (CH_3); ESI-MS: *m/z* (%) = 332 (20), 330 (100, M^- -1), 328 (50), 326 (22); HRMS-ESI: Calcd for $C_{15}H_{14}N_3OSe$ $(M+H)^+$ 332.0302; found: 332.0295.

5-(4-Methoxyphenylamino)-3-phenyl-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4i**): Pink solid; yield, 88%; m.p. 155.0–155.7 °C; IR: ν_{max} = 3422, 3131, 1660, 1599, 1570, 1509, 1400, 1250, 1033, 840 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.76 (s, 1H, NH), 7.76 (d, J = 8.0 Hz, 2H, ArH), 7.47 (t, J = 8.4 Hz, 2H, ArH), 7.42 (d, J = 8.8 Hz, 2H, ArH), 7.29 (t, J = 7.2 Hz, 1H, ArH), 6.93 (d, J = 8.8 Hz, 2H, ArH), 3.73 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6): δ 168.0 (C=O), 154.5 (C=N), 147.6, 138.3, 133.6, 128.9 (CH×2), 126.0, 121.9 (CH×2), 119.2 (CH×2), 114.3 (CH×2), 55.2 (OCH_3); EI-MS: *m/z* (%) = 349 (20), 347 (100, M^+), 345 (50); HRMS-ESI: Calcd for $C_{15}H_{14}N_3O_2Se$ $(M+H)^+$ 348.0251; found: 348.0247.

5-(4-Chlorophenylamino)-3-phenyl-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4j**): Yellow crystals; yield, 80%; m.p. 246.0–246.6 °C; IR: ν_{max} = 3320, 3196, 3125, 1665, 1651, 1574, 1541, 1490, 1403, 1313, 1251, 1094, 817, 686 cm^{-1}; ^1H NMR (DMSO-d_6): δ 10.10 (s, 1H, NH), 7.75 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 2H, ArH), 7.52–7.47 (m, 4H, ArH), 7.39 (d, J = 9.2 Hz, 2H, ArH), 7.32 (t, J = 7.2 Hz, 1H, ArH); ^{13}C NMR (DMSO-d_6): δ 168.1 (C=O), 147.1 (C=N), 139.1, 138.1, 129.0 (CH×4), 126.3, 125.4, 122.1 (CH×2), 118.9 (CH×2); EI-MS: *m/z* (%) = 353 (40), 351 (100, M^+), 349 (50), 347 (22); HRMS-ESI: Calcd for $C_{14}H_9ClN_3OSe$ $(M-H)^-$ 349.9599; found: 349.9585.

5-(2-Methylphenylamino)-3-phenyl-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4k**): Yellow solid; yield,75%; m.p. 132.2–133.1 °C; IR: ν_{max} = 3358, 1658, 1578, 1535, 1455, 1255, 1093, 747, 693 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.08 (s, 1H, NH), 7.84 (d, J = 7.6 Hz, 1H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.45 (t, J = 7.6 Hz, 2H, ArH), 7.33–7.25 (m, 2H, ArH), 7.23–7.18 (m, 2H, ArH), 7.00 (t, J = 7.2 Hz, 1H, ArH), 2.30 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 168.8 (C=O), 148.9 (C=N), 138.4, 138.3, 130.8, 129.0 (CH×2), 128.5, 126.7, 126.2, 123.7, 122.1 (CH×2), 120.9, 18.2 (CH_3); ESI-MS: *m/z* (%) = 332 (19), 330 (100, M^- -1), 328 (44); HRMS-ESI: Calcd for $C_{15}H_{13}N_3OSeNa$ $(M+Na)^+$ 354.0122; found: 354.0125.

3-(4-ChloroPhenyl)-5-(phenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4l**): Yellow solid; yield, 57%; m.p. 194.5–194.9 °C; IR: ν_{max} = 3415, 3149, 1659, 1614, 1483, 1401, 1363, 1298, 1086, 838 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.98 (s, 1H, NH), 7.82 (d, J = 9.2 Hz, 2H, ArH), 7.55 (d, J = 9.2 Hz, 2H, ArH), 7.48 (d, J = 8.8 Hz, 2H, ArH), 7.35 (t, J = 7.6 Hz, 2H, ArH), 7.02 (t, J = 7.6 Hz, 1H, ArH); ^{13}C NMR (DMSO-d_6): δ 168.3 (C=O), 147.5 (C=N), 140.1, 137.0, 129.8, 129.1 (CH×2), 128.9 (CH×2), 123.3 (CH×2), 122.1, 117.5 (CH×2); ESI-MS: *m/z* (%) = 352 (42), 350 (100, M^- -1), 348 (48), 346(16); HRMS-ESI: Calcd for $C_{14}H_{10}ClN_3OSeNa$ $(M+Na)^+$ 373.9575; found: 373.9564.

3-(4-Chlorophenyl)-5-(4-methoxyphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4m**): Yellow solid; yield, 62%; m.p. 194.2–194.6 °C; IR: ν_{max} = 3342, 1665, 1599, 1550, 1509, 1401, 1253, 1086, 1033, 822 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.79 (s, 1H, NH), 7.81 (d, J = 8.8 Hz, 2H, ArH), 7.53 (d, J = 8.8 Hz, 2H, ArH), 7.41 (d, J = 9.2 Hz, 2H, ArH), 6.93 (d, J = 9.2 Hz, 2H, ArH), 3.73 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6): δ 168.1 (C=O), 154.6 (C=N), 147.8, 137.1, 133.5, 129.7, 128.8 (CH×2), 123.2 (CH×2), 119.3 (CH×2), 114.3 (CH×2), 55.2 (OCH_3); ESI-MS: *m/z* (%) = 382 (44), 381 (15), 380 (100, M^- -1), 378 (46); HRMS-ESI: Calcd for $C_{15}H_{13}ClN_3O_2Se$ $(M+H)^+$ 381.9862; found: 381.9850.

3-(4-Chlorophenyl)-5-(2-methylphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4n**): Pink solid; yield,58%; m.p. 168.3–169.2 °C; IR: ν_{max} = 3382, 1662, 1588, 1538, 1489, 1455, 1304, 1256, 825, 740 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.11 (s, 1H, NH), 7.83 (d, J = 8.0 Hz, 1H, ArH), 7.76 (d, J = 8.8 Hz, 2H, ArH), 7.51 (d, J = 8.8 Hz, 2H, ArH), 7.24–7.19 (m, 2H, ArH), 7.02 (t, J = 7.6 Hz, 1H, ArH), 2.29 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 168.7 (C=O), 149.0 (C=N), 138.1, 137.1, 130.6, 129.7, 128.8 (CH×2), 128.5, 126.5, 123.7, 123.2 (CH×2), 121.0, 18.0 (CH_3); ESI-MS: *m/z* (%) = 402 (62); 400 (100, M^- + Cl), 398 (45), 366 (30), 364 (75, M^- -1), 362 (33); HRMS-ESI: Calcd for $C_{15}H_{12}ClN_3OSeNa$ $(M+Na)^+$ 387.9732; found: 387.9723.

3-(4-Methoxyphenyl)-5-(4-methoxyphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4o**): Pink solid; yield:78%; m.p. 151.7–153.2 °C; IR: ν_{max} = 3419, 3242, 1656, 1597, 1571, 1509, 1298, 1254, 1033, 833 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.09 (s, 1H, NH), 7.86

(d, *J* = 9.2 Hz, 2H, ArH), 7.51 (d, *J* = 9.2 Hz, 2H, ArH), 7.06 (d, *J* = 9.2 Hz, 2H, ArH), 7.02 (d, *J* = 9.2 Hz, 2H, ArH), 3.88 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 162.2 (C=O), 160.5 (C=N), 159.7, 141.4, 131.5, 127.9 (CH×2), 127.7, 126.7 (CH×2), 114.7 (CH×2), 114.0 (CH×2), 55.6 (OCH_3), 55.5 (OCH_3); ESI-MS: *m/z* (%) = 378 (20), 376 (100, M^- -1), 374 (46); HRMS-ESI: Calcd for $C_{16}H_{15}N_3O_3SeNa$ $(M+Na)^+$ 400.0176; found: 400.0165.

3-(4-Methoxyphenyl)-5-(2-methylphenylamino)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4p**): Pink solid; yield,75%; m.p. 140.6–142.1 °C; IR: ν_{max} = 3378, 1660, 1582, 1540, 1509, 1251, 1094, 830, 741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.63 (d, *J* = 9.2 Hz, 2H, ArH), 7.45 (d, *J* = 7.2 Hz, 1H, ArH), 7.23 (t, *J* = 7.2 Hz, 2H, ArH), 7.11 (t, *J* = 7.2 Hz, 1H, ArH), 6.93 (d, *J* = 9.2 Hz, 2H, ArH), 6.40 (s, 1H, NH), 3.83 (s, 3H, OCH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 167.7 (C=O), 157.7 (C=N), 150.4, 137.6, 131.1, 130.8, 129.5, 126.9, 124.9, 124.0 (CH×2), 121.1, 113.7 (CH×2), 55.1 (OCH_3), 17.4 (CH_3); ESI-MS: *m/z* (%) = 362 (21), 360 (100, M^- -1), 358 (51); HRMS-ESI: Calcd for $C_{16}H_{15}N_3O_2SeNa$ $(M+Na)^+$ 384.0227; found: 384.0224.

5-(4-Chlorophenylamino)-3-(4-methoxyphenyl)-5-arylamino-1,3,4-selenadiazol-2(3H)-one (**4q**): Red solid; yield,69%; m.p. 133.4–134.8 °C; IR: ν_{max} = 3341, 1667, 1580, 1533, 1509, 1244, 1096, 826 740 cm^{-1}; ^1H NMR (DMSO-d_6): δ 10.03 (s, 1H, NH), 7.57 (d, *J* = 8.8 Hz, 2H, ArH), 7.46 (d, *J* = 8.8 Hz, 2H, ArH), 7.34 (d, *J* = 8.8 Hz, 2H, ArH), 7.00 (d, *J* = 8,8 Hz, 2H, ArH), 3.78 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6): δ 167.5 (C=O), 157.2 (C=N), 146.7, 138.9, 131.0, 128.7 (CH×2), 125.1, 124.1 (CH×2), 118.6 (CH×2), 113.9 (CH×2), 55.3 (OCH_3); ESI-MS: *m/z* (%) = 382 (43), 380 (100, M^- -1), 378 (52); HRMS-ESI: Calcd for $C_{15}H_{12}ClN_3O_2SeNa$ $(M+Na)^+$ 403.9681; found: 403.9675.

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