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ORIGINAL PAPER

Facile synthesis of 3-aryl-1-((4-aryl-1,2,3-selenadiazol-5-yl)sulfanyl)isoquinolines

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A new series of 1,2,3-selenadiazoles containing an aryl or a 3-arylisoquinoline sulfanyl moiety at carbons 4 and 5, respectively, was prepared by cyclization of the respective semicarbazones in the presence of selenium(II) oxide and tetrahydrofuran at 70–75 °C. Semicarbazones required for the reaction were obtained from 2-((3-arylisoquinolin-1-yl)sulfanyl)-1-phenylethanones, *I*, by a reaction with semicarbazide hydrochloride in ethanol/water mixture and potassium acetate base.
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Introduction

Selenadiazoles are organoselenium compounds that possess a broad-spectrum of potent antitumor and other related biological activities (Niculescu-Duvaz, 2001; Murray et al., 1963; Burger & Abraham, 2003). The use of the selenium containing compounds synthesis has steadily increased and it has been utilized in organic synthesis (Takimiya et al., 2004). Though a large scale of thiadiazoles is known, only few selenadiazoles have been reported (Al-Smadi & Ratrout, 2004a, 2004b; Cillo & Lash, 2004; Vernon et al., 1983). The synthesis of an 1,2,3-selenadiazole was first reported by Lalezari et al. (1969, 1973) and Yalpani et al. (1971) and it was done by analogy with the 1,2,3-thiadiazole system (Hurd & Mori, 1955; Saravanan et al., 2006, 2008). Selenium compounds have many applications; they are electroluminescent (Yang et al., 2005), and potential candidates for two-photon absorption, nonlinear optics, and sensor applications (Ostrowski et al., 2003; Velusamy et al., 2005). Isoquinoline derivatives represent a group of the most active compounds with a wide spectrum of biological activities. They are widely used as pharmaceuticals and agrochemicals. A number of papers mention the use of isoquinolines and their thio analogues' derivatives in medicinal chemistry. Thus, their synthesis has been of great interest in the preparation of biologically active selenium and sulfur containing heterocyclic compounds.

Heterocyclic compounds containing selenium are of interest due to their biological and synthetic applications. Synthesis of 1,2,3-selenadiazoles is of recent interest as they are not only versatile intermediates for the preparation of alkynes and other selenium compounds (Al-Smadi & Ratrout, 2004a, 2004b), but they also have attracted much attention for their biological characteristics like their antifungal, antibacterial, antimicrobial, and insecticidal activities (Kandeel et al., 1994; Schatz, 1960). The chemistry of 1,2,3-selenathiadiazoles has been recently reviewed by different researchers (Arsenyan et al., 2002; Morzherin et al., 2003; Saravanan et al., 2006; Dehaen et al., 2004; Meier & Voigt, 1972). In continuation of our study on 1,2,3-selenadiazoles, the synthesis of yet an-

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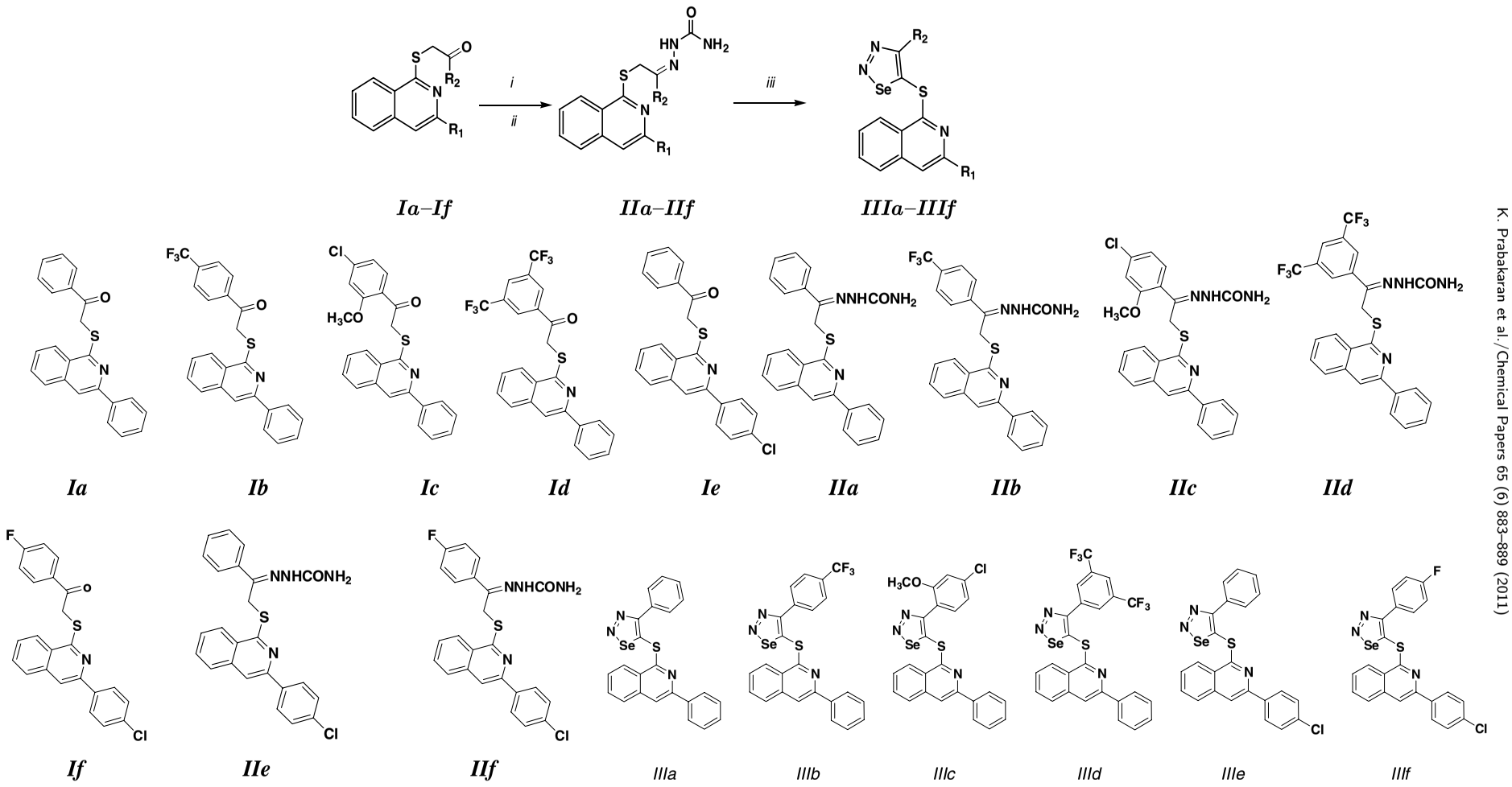

Fig. 1. Synthesis of 1-(3,4-disubstituted-1,2,3-selenadiazol-5-ylthio)isoquinolines semicarbazide hydrochloride, *i*) KOAc, ethanol, reflux; *ii*) water, stirring; *iii*) SeO_2, THF, reflux.

other 1,2,3-selenadiazole system with a potential functionality in its skeleton is reported and the target molecules are expected to have enhanced their biological activity. As a part of our ongoing research on organosulfur and organoselenium compounds, 3-substituted isoquinolines and their thionate derivatives were reported earlier (Prabakaran & Nawaz Khan, 2010; Manivel & Nawaz Khan, 2009; Manivel et al., 2009a, 2009b, 2010). Based on the aforementioned importance of selenium containing compounds and their further utilization in organic synthesis, a new series of 3-aryl-1-((4-aryl-1,2,3-selenadiazol-5-yl)sulfanyl) isoquinolines, *III*, from their corresponding semicarbazones is reported herein (Fig. 1).

Experimental

All reagents purchased from Sigma–Aldrich (India), Lancaster (India), and Qualigens (India) were used without further purification. Infrared (IR) spectra were recorded at room temperature from 4000 cm^{-1} to 400 cm^{-1} using Avatar 330 (ALPHA-T, Bruker, India) equipped with a deuterated triglycine sulfate detector. Most of the obtained vibrational bands of the IR spectrum were identified. ^{1}H NMR and ^{13}C NMR spectra (400 MHz for ^{1}H and 100 MHz for ^{13}C) of the compounds were obtained using a Bruker Spectrospin Avance DPX400 Ultrashield 400 MHz spectrometer (Bruker, India) and chemical shifts were reported in δ relative to tetramethylsilane (TMS) as an internal standard. Mass spectra were obtained using an Agilent mass spectrometer 6200 series accurate (Agilent, India). Melting points were determined using open capillaries and are uncorrected (a model BUCHI M-565, Büchi, Switzerland). Elemental analysis was carried using an Elementar–Vario Micro cube CHNSO analyser (Elementar, Germany). The 2-((3-arylisoquinolin-1-yl)sulfanyl)-1-phenylethanones, *I*, required for the present study were obtained according to a procedures reported earlier (Manivel et al., 2010; Hathwar et al., 2007a, 2007b; Tajudeen & Nawaz Khan, 2007; Mohana Roopan et al., 2008).

General procedure for the preparation of semicarbazones, IIa–IIf, and 1,2,3-selenadiazole derivatives, IIIa–IIIf

To *I*, (0.3 mmol), the filtrate obtained from a mixture of semicarbazide hydrochloride (2.1 mmol) and potassium acetate (2.1 mmol) in absolute ethanol (8 mL) heated under reflux condition for 30 min and filtered to remove precipitated NaCl was added and mixed, the resulting solution was heated and refluxed in a pressure tube for 16 h. The reaction was monitored by the LC-MS technique. Then, the reaction mixture was diluted with cold water (8 mL) and stirred for 30 min. Yellow semicarbazone, *II*, was separated in high purity and yield (76–93 %). Semicarbazones, *II*, (0.24 mmol) were dissolved in tetrahydrofuran (THF) (4 mL) under vigorous stirring. The above solution was treated with selenium(II) oxide (SeO_2) powder (2.4 mmol) and heated at 70–75 °C. The reactions were monitored by thin layer chromathography (TLC) (eluent: hexane/ethyl acetate, φ_r = 7 : 3) until the completion of the reaction (4 h). In TLC, the products appeared to be significantly less polar compared to the polar semicarbazones. The reaction mixtures were filtered to remove excess SeO_2, and the filtrates were concentrated to dryness under vacuum to afford crude selenadiazoles, *III*, which were further purified by column chromatography using petrol ether/ethyl acetate gradient elution (from $\varphi_r = 9 : 1$ to $\varphi_r = 17 : 2$) and afforded pure compound in good yields (78–91 %).

Results and discussion

The experiments were started with an attempted synthesis of semicarbazones, *II*, from *I*, through a reaction with semicarbazide hydrochloride in the presence of absolute ethanol and potassium acetate under reflux conditions and stirring in the presence of water. Semicarbazones, *II*, when treated afterwards with SeO_2 in the presence of THF at 70–75 °C afforded the desired products, *III*, in good yields and high purity (Fig. 1).

Optimization of the semicarbazone formation was carried out by reacting 2-((3-phenyl-isoquinolin-1-yl)sulfanyl)-1-phenylethanone, *Ia*, with semicarbazide hydrochloride in the presence of ethanol/water mixture ($\varphi_r = 15 : 1$), potassium acetate in a round bottom flask, under reflux at 90 °C. When the reaction was analyzed by LC-MS, only 40 % conversion to the desired product and 59 % of the starting material was present after 16 h of the reaction. Then, the reaction continued for different time periods and the corresponding conversions are shown in Table 1. However, when the reaction was carried out in a pressure tube at 90 °C, it was successfully completed within 16 h providing the products in excellent yields. A comparison of results obtained from both methods is presented in Table 1.

Considering these optimized results, various semicarbazones were synthesized, isolated, purified by recrystallization in ethanol, and characterized by spectral techniques such as LC-MS, ^{1}H NMR and ^{13}C NMR. Purified semicarbazones were then allowed to react with SeO_2, in THF, in pressure tubes at 70–75 °C for 4 h to afford the desired products, *III*, (Fig. 1). Optimization of the reaction was studied by varying the amount of SeO_2 and that of the solvents. From Table 2 it is clear that an increase in the amount of SeO_2 increased the yield steadily. Similarly, the reaction of *IIa* and SeO_2 in various solvents was found to be proceeding well when THF was used (Table 3, en-

Table 1. Comparison of conventional (C) and pressure tube (P) methods in the reaction of *Ia* and semicarbazide hydrochloride

Method	Time	Product *II*[a] conversion
	h	%
C	16	40
P	16	92
C	24	55
P	24	–
C	36	65
P	36	–
C	48	80
P	48	–
C	60	85
P	60	–

a) LC-MS purity.

Table 2. SeO_2 optimization in the reaction of *IIa* (0.24 mmol)

Entry	SeO_2	Yield[a]
	mmol	%
1	1.00	36
2	1.20	43
3	1.44	58
4	1.68	69
5	1.92	73
6	2.16	87
7	2.40	91
8	2.64	91
9	2.88	91

a) LC-MS purity.

Table 3. Effect of solvent in the reaction of *IIa* and SeO_2

Entry	Solvent	Yield[a]/%
1	Acetic acid	55
2	Toluene	63
3	*o*-Xylene	58
4	THF	89
5	1,4-Dioxane	64
6	Acetonitrile	67

a) Isolated yields.

try 4) unlike the other solvents tested, i.e. acetic acid, toluene, *o*-xylene, 1,4-dioxane, and acetonitrile, which provided lower yields (Table 3).

Results of the selenadiazoles, *III*, synthesis are summarized in Table 4. Products of the reaction were isolated, purified by column chromatography and characterized by spectral techniques such as IR, LC-MS, ^{1}H NMR, ^{13}C NMR, and elemental analysis (Tables 4 and 5).

The characteristic IR spectra showed bands for

Table 4. Characterization data of newly prepared compounds semicarbazones *IIa–IIf* and selenadiazoles *IIIa–IIIf*

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.
			C	H	N	S	%	°C
IIa	$C_{24}H_{20}N_4OS$	412.14	69.88	4.89	13.58	7.77	88	234–235
			69.81	4.83	13.55	7.69		
IIb	$C_{25}H_{19}F_3N_4OS$	480.12	62.49	3.99	11.66	6.67	86	253–254
			62.51	3.94	11.62	6.59		
IIc	$C_{25}H_{21}ClN_4O_2S$	476.11	62.95	4.44	11.75	6.72	76	249–250
			62.88	4.38	11.71	6.65		
IId	$C_{26}H_{18}F_6N_4OS$	548.11	56.93	3.31	10.21	5.85	83	242–243
			56.87	3.26	10.16	5.79		
IIe	$C_{24}H_{19}ClN_4OS$	446.10	64.49	4.28	12.54	7.17	93	245–246
			64.41	4.22	12.48	7.11		
IIf	$C_{24}H_{18}ClFN_4OS$	464.09	62.00	3.90	12.05	6.90	90	246–247
			62.03	3.84	12.01	6.87		
IIIa	$C_{23}H_{15}N_3SSe$	445.02	62.16	3.40	9.46	7.22	91	195–196
			62.12	3.36	9.41	7.17		
IIIb	$C_{24}H_{14}F_3N_3SSe$	513.00	56.26	2.75	8.20	6.26	83	252–255
			56.22	2.69	8.17	6.21		
IIIc	$C_{24}H_{16}ClN_3OSSe$	508.99	56.65	3.17	8.26	6.30	78	168–169
			56.58	3.11	8.21	6.26		
IIId	$C_{25}H_{13}F_6N_3SSe$	580.99	51.73	2.26	7.24	5.52	88	278–281
			51.67	2.21	7.17	5.46		
IIIe	$C_{23}H_{14}ClN_3SSe$	478.98	57.69	2.95	8.78	6.70	90	203–204
			57.61	2.90	8.72	6.65		
IIIf	$C_{23}H_{13}ClFN_3SSe$	496.97	55.60	2.64	8.46	6.45	89	217–218
			55.56	2.57	8.39	6.39		

Table 5. Spectral data of newly prepared compounds semicarbazones *IIa–IIf* and selenadiazoles *IIIa–IIIf*

Compound	Spectral data
IIa	IR, $\tilde{\nu}$/cm^{-1}: 3472, 3394, 3281, 3196, 3138, 1713, 1586, 1491, 1437, 1308, 1159, 984, 846, 761, 686, 576, 470 ^{1}H NMR (DMSO-d_6) δ: 9.80 (s, 1H), 8.32–8.31 (d, 2H, J = 7.2 Hz), 8.24 (s, 1H), 8.10–8.03 (dd, 2H, J = 19.6 Hz, J = 8.4 Hz), 7.93–7.91 (m, 2H), 7.83–7.79 (t, 1H, J = 7.2 Hz), 7.66–7.62 (t, 1H, J = 7.2 Hz), 7.57–7.53 (t, 2H, J = 7.2 Hz), 7.47–7.44 (t, 1H, J = 7.2 Hz), 7.30–7.29 (m, 3H), 6.62 (bs, 2H), 4.92 (s, 2H) ^{13}C NMR (DMSO-d_6), δ: 157.1, 156.8, 148.6, 141.4, 138.3, 136.6, 136.2, 131.3, 128.9, 128.6, 128.2, 128.0, 127.8, 126.6, 125.1, 123.8, 113.4 MS, m/z: 413 (M^+ + 1)
IIb	IR, $\tilde{\nu}$/cm^{-1}: 3476, 3396, 3283, 3198, 3139, 1716, 1589, 1490, 1438, 1308, 1159, 986, 846, 762, 686, 576 ^{1}H NMR (DMSO-d_6) δ: 10.02 (s, 1H), 8.29–8.26 (d, 2H, J = 9.7 Hz), 8.21 (s, 1H), 8.12–8.01 (m, 4H), 7.81–7.77 (t, 1H, J = 7.2 Hz), 7.62–7.44 (m, 6H), 6.69 (bs, 2H), 4.93 (s, 2H) ^{13}C NMR (DMSO-d_6) δ: 157.3, 157.0, 149.1, 141.0, 140.4, 138.7, 136.6, 131.7, 129.2, 128.4, 128.3, 127.4, 127.0, 125.5, 125.4, 125.3, 124.2, 113.9, 24.2 MS, m/z: 481 (M^+ + 1)
IIc	IR, $\tilde{\nu}$/cm^{-1}: 3282, 3199, 3158, 2925, 2854, 1717, 1645, 1593, 1492, 1465, 1407, 1325, 1284, 1251, 1228, 1153, 1045, 958, 889, 848, 773, 692, 657, 524 ^{1}H NMR (DMSO-d_6) δ: 9.84 (bs, 1H), 8.15–8.13 (d, 2H, J = 8.3 Hz), 7.99–7.95 (m, 2H), 7.95–7.75 (t, 1H, J = 7.2 Hz), 7.65–7.40 (m, 5H), 7.12–7.10 (d, 1H, J = 10.8 Hz), 7.04 (s, 1H), 6.75 (m, 1H), 6.43 (bs, 2H), 4.59 (bs, 2H), 3.85 (s, 3H) ^{13}C NMR ($CDCl_3$) δ: 158.3, 153.7, 151.5, 143.3, 138.5, 136.8, 136.3, 132.7, 131.6, 129.1, 128.9, 128.2, 127.9, 127.8, 124.9, 123.8, 121.0, 120.7, 117.8, 112.4, 55.9, 31.9 MS, m/z: 477 (M^+ +1)
IId	IR, $\tilde{\nu}$/cm^{-1}: 3283, 3198, 3155, 2925, 1727, 1668, 1627, 1589, 1544, 1471, 1436, 1406, 1326, 1282, 1251, 1215, 1153, 1076, 1045, 999, 958, 887, 850, 767, 690, 617, 567, 518, 399 ^{1}H NMR (DMSO-d_6) δ: 10.18 (bs, 1H), 8.43 (s, 2H), 8.27–8.24 (m, 3H), 8.04–8.01 (t, 2H, J = 10.8 Hz), 7.90 (bs, 1H), 7.82–7.79 (t, 1H, J = 7.2 Hz), 7.63–7.60 (t, 1H, J = 7.2 Hz), 7.51–7.40 (m, 3H), 6.95–6.80 (bs, 2H), 5.05 (s, 2H) ^{13}C NMR (DMSO-d_6) δ: 157.1, 156.7, 149.1, 139.9, 139.7, 138.5, 136.7, 131.8, 129.2, 128.4, 128.3, 127.3, 126.9, 125.6, 124.2, 114.0, 23.6 MS, m/z: 549 (M^+ + 1)
IIe	IR, $\tilde{\nu}$/cm^{-1}: 3274, 3180, 3120, 2927, 1707, 1645, 1591, 1467, 1409, 1325, 1284, 1253, 1157, 1128, 1101, 1045, 960, 873, 773, 692, 661, 522 ^{1}H NMR (DMSO-d_6) δ: 9.80 (s, 1H), 8.34–8.32 (d, 2H, J = 8.4 Hz), 8.25 (s, 1H), 8.09–8.07 (d, 1H, J = 8.4 Hz), 8.03–8.01 (d, 1H, J = 8.0 Hz), 7.91 (bs, 2H), 7.83–7.79 (t, 1H, J = 7.2 Hz), 7.66–7.58 (m, 3H), 7.31 (bs, 3H), 6.60 (bs, 2H), 4.89 (s, 2H) ^{13}C NMR (DMSO-d_6) δ: 157.8, 157.2, 147.8, 142.0, 137.6, 137.1, 136.5, 134.0, 131.8, 129.3, 129.0, 128.8, 128.7, 128.5, 126.7, 125.6, 124.3, 114.1, 24.2 MS, m/z: 447 (M^+ + 1)
IIf	IR, $\tilde{\nu}$/cm^{-1}: 3321, 3200, 3125, 1712, 1645, 1581, 1525, 1498, 1459, 1406, 1326, 1299, 1276, 1172, 1137, 1043, 958, 856, 770, 696, 523 ^{1}H NMR (DMSO-d_6) δ: 9.83 (s, 1H), 8.34–8.32 (d, 2H, J = 8.8 Hz), 8.28 (s, 1H), 8.10–8.08 (d, 1H, J = 8.0 Hz), 8.05–8.03 (d, 1H, J = 8.0 Hz), 7.97–7.93 (m, 2H), 7.85–7.81 (t, 1H, J = 8.0 Hz), 7.68–7.64 (t, 1H, J = 8.4 Hz), 7.61–7.57 (m, 2H), 7.14–7.10 (t, 2H, J = 8.8 Hz), 6.62 (bs, 2H), 4.88 (s, 2H) ^{13}C NMR (DMSO-d_6) δ: 157.2, 147.8, 141.1, 137.6, 136.5, 134.0, 131.8, 129.2, 129.0, 128.8, 128.5, 125.6, 124.3, 115.5, 115.3, 114.1 MS, m/z: 465 (M^+ + 1)
IIIa	IR, $\tilde{\nu}$/cm^{-1}: 3058, 2962, 2919, 2852, 1491, 1444, 1262, 1095, 1023, 802, 749, 687, 512 ^{1}H NMR ($CDCl_3$) δ: 8.30–8.28 (d, 1H, J = 8.4 Hz), 8.08–8.05 (m, 4H), 7.98–7.96 (d, 1H, J = 8.4 Hz), 7.89 (s, 1H), 7.84–7.80 (t, 1H, J = 6.8 Hz), 7.71–7.54 (m, 7H) ^{13}C NMR ($CDCl_3$) δ: 138.4, 131.7, 129.4, 129.2, 128.9, 128.8, 128.8, 128.2, 128.0, 127.8, 125.0, 123.8, 118.0 MS, m/z: 446 (M^+ + 1)
IIIb	IR, $\tilde{\nu}$/cm^{-1}: 3059, 2926, 2856, 1729, 1584, 1494, 1446, 1396, 1316, 1259, 1212, 1094, 1024, 881, 804, 743, 688 ^{1}H NMR ($CDCl_3$) δ: 8.27–8.25 (d, 1H, J = 8.4 Hz), 8.05–8.03 (d, 2H, J = 7.2 Hz), 7.95–7.91 (t, 3H, J = 9.2 Hz), 7.86 (s, 1H), 7.81–7.77 (t, 1H, J = 7.2 Hz), 7.66–7.56 (m, 4H), 7.44–7.42 (d, 2H, J = 8.0 Hz) ^{13}C NMR (DMSO-d_6) δ: 157.8, 157.4, 149.5, 141.7, 140.3, 138.3, 136.4, 131.9, 129.9, 128.2, 128.0, 127.8, 127.3, 125.7, 125.6, 125.2, 124.5, 113.7 MS, m/z: 514 (M^+ + 1)
IIIc	IR, $\tilde{\nu}$/cm^{-1}: 2919, 2852, 1557, 1489, 1447, 1309, 1270, 1218, 988, 879, 824, 778, 742, 517 ^{1}H NMR ($CDCl_3$) δ: 8.18–8.16 (d, 1H, J = 8.4 Hz), 8.05–8.03 (d, 2H, J = 8.0 Hz), 7.93–7.91 (t, 1H, J = 8.4 Hz), 7.84 (s, 1H), 7.79–7.75 (t, 1H, J = 7.6 Hz), 7.65–7.60 (m, 3H), 7.57–7.51 (m, 2H), 7.18–7.14 (m, 2H), 3.88 (s, 3H) ^{13}C NMR ($CDCl_3$) δ: 158.0, 153.7, 151.5, 143.3, 138.6, 136.8, 136.4, 132.7, 131.6, 129.2, 129.0, 128.2, 128.0, 127.9, 125.0, 123.9, 121.1, 120.7, 117.8, 112.4, 56.0 MS, m/z: 510 (M^+ + 1)

Table 5. (continued)

Compound	Spectral data
IIId	IR, $\tilde{\nu}$/cm^{-1}: 3057, 2923, 2853, 1728, 1584, 1494, 1446, 1390, 1316, 1256, 1212, 1094, 1024, 881, 804, 743, 689, 595, 512 ^{1}H NMR ($CDCl_3$) δ: 8.27–8.25 (d, 1H, J = 8.4 Hz), 8.19–8.17 (d, 2H, J = 8.0 Hz), 8.04–8.02 (d, 2H, J = 8.4 Hz), 7.97–7.95 (d, 2H, J = 8.0 Hz), 7.89–7.87 (m, 3H), 7.83–7.79 (t, 1H, J = 8.0 Hz), 7.71–7.67 (t, 1H, J = 8.4 Hz), 7.65–7.61 (t, 2H, J = 6.8 Hz), 7.59–7.55 (t, 1H, J = 7.2 Hz) ^{13}C NMR ($CDCl_3$) δ: 158.3, 153.8, 151.5, 143.3, 138.5, 136.8, 136.5, 132.7, 131.6, 129.1, 128.9, 128.3, 127.9, 127.4, 124.9, 123.8, 117.8, 114.3, 22.6 MS, m/z: 582 (M^+ + 1)
IIIe	IR, $\tilde{\nu}$/cm^{-1}: 3058, 2962, 2919, 2852, 1491, 1444, 1262, 1095, 1023, 802, 749, 687, 512 ^{1}H NMR ($CDCl_3$) δ: 8.28–8.25 (d, 1H, J = 8.4 Hz), 8.03–7.97 (m, 4H), 7.95–7.93 (d, 1H, J = 8.0 Hz), 7.84 (s, 1H), 7.82–7.78 (t, 1H, J = 6.8 Hz), 7.69–7.65 (t, 1H, J = 7.2 Hz) 7.64–7.59 (m, 4H) 7.55–7.51 (t, 1H, J = 7.6 Hz) ^{13}C NMR ($CDCl_3$) δ: 157.9, 151.1, 150.2, 140.8, 136.9, 136.7, 135.4, 133.3, 131.9, 129.4, 129.4, 129.2, 128.9, 128.2, 127.8, 125.1, 123.9, 117.9 MS, m/z: 479 (M^+ + 1)
IIIf	IR, $\tilde{\nu}$/cm^{-1}: 3059, 2966, 2918, 2858, 1490, 1444, 1264, 1095, 1023, 802, 749, 687, 516 ^{1}H NMR ($CDCl_3$) δ: 8.27–8.24 (d, 1H, J = 8.4 Hz), 8.01–7.93 (m, 5H), 7.84–7.79 (m, 2H), 7.71–7.67 (t, 1H, J = 7.6 Hz), 7.61–7.58 (d, 2H, J = 8.4 Hz), 7.33–7.29 (t, 2H, J = 8.4 Hz) ^{13}C NMR ($CDCl_3$) δ: 150.8, 150.2, 136.8, 136.7, 135.4, 131.9, 131.3, 131.3, 129.4, 129.2, 128.3, 127.9, 125.0, 123.8, 118.0, 116.0, 115.8 MS, m/z: 497 (M^+ + 1)

the formation of semicarbazone derivatives, *II*, where the two characteristic bands at 3200–3400 cm^{-1} and 1645–1720 cm^{-1} were assigned to the N—H and C═O stretching, and the band at 1580–1630 cm^{-1} due to C═N suggested the condensation of different ketones, *I*, and semicarbazide. Symmetric and asymmetric C—H stretching modes of the methylene group appeared as a shoulder just below 3000 cm^{-1} in all semicarbazone derivatives. The appearance of bands corresponding to C═C and N═N also showed the formation of 1,2,3-selenadiazole rings; also bands corresponding to C—S at 760 cm^{-1}, C—Se—N at 802 cm^{-1} were observed.

Structures of semicarbazones, *II*, and selenadiazoles, *III*, were further confirmed by ^{1}H NMR and ^{13}C NMR. In semicarbazone, *II*, the N—H and NH_2 protons appeared as a singlet at δ 9.8–10.1 and a broad singlet at δ 6.43–6.89, respectively. Structures of hydrazones, *II*, were further supported by ^{13}C NMR spectra. Disappearance of the ketonic carbon (C═O) signal from the starting ketones, *I*, confirmed the formation of semicarbazone derivatives. The formation of 1,2,3-selenadiazole rings, *III*, was also supported by the absence of signals of ═N—NH—NH_2 in all compounds. The disappearance of methylene singlets which occurred in hydrazones, *II*, at δ 3.85–5.05, arising due to the cyclization forming 1,2,3-selenadiazole rings (Fig. 2), confirmed the cyclization of semicarbazones, *II*, and SeO_2. In addition, signals corresponding to the aromatic region appeared in the expected range for all compounds studied. Structures of the selenadiazoles were further supported by the ^{13}C NMR spectra. The appearance of characteristic signals for C-4 and C-5 carbon atoms also clearly favored the formation of 1,2,3-selenadiazole rings in all compounds. Signals due to the aromatic carbons resonate at their usual positions.

It is worth mentioning that in the present study, effective cyclization of hydrazones in the presence of SeO_2 can be attributed to the increasing acidity of the active methylene, which prevents the decomposition of 1,2,3-selenadiazoles into acetylenes and thus ensures their thermal stability.

Conclusions

A facile method for the synthesis of new selenadiazoles containing the isoquinoline ring moiety has been established. The presented methodology was found to be efficient in terms of yield and purity.

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