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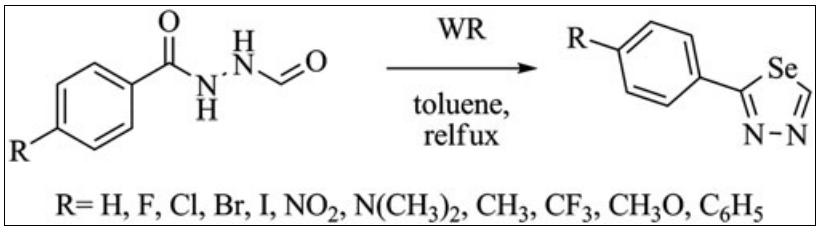

New series of 1,3,4-selenadiazoles was obtained. The method of synthesis employs the Woollins' reagent and *N*,*N*′-diacylhydrazides. Reaction in toluene leads to monosubstituted 1,3,4-selenadiazoles with a yield 26–57%.

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INTRODUCTION

Organoselenium chemistry has been developing since the discovery that selenium is an essential microelement for animals [1]. Further research demonstrated that compounds containing selenium can be used in pharmaceutical industry as ingredients of therapeutic drugs [2,3]. Besides these properties, mentioned substances can also become interesting reagents in organic synthesis [2,4,5] and can be applied as superconductors [2,6].

One of the groups of compounds in question are 1,3,4-selenadiazoles. There is still not much detailed information about this particular group; but its analogues, 1,3,4-thiadiazoles, have been tested in the context of such medical functionalities as antibacterial [7,8], antiviral [9], anti-inflammatory [10,11], analgesic [10], antitumor [12,13], anticonvulsant [8,14], antidepressant [15], and antifungal [12]. Their isomers, 1,2,3-selenadiazoles, have been mainly subjected to antibacterial [16], antiviral [17], and antifungal [18] properties tests.

1,3,4-selenadiazoles were synthesized as early as in 1904 [19]. The process consisted in heating up *N*,*N*′-diacetylhydrazine with phosphorus pentaselenide under reduced pressure. Other syntheses involved a reaction between selenobenzamides and hydrazine hydrate [20], reaction of *N*,*N*-dimethylformamide azine with hydrogen selenide [21], acidic (acid-catalysed) cyclization of 1,4-diacylselenocarbazides [22], reaction of carboxylic acid, phosphoryl chloride with selenosemicarbazides [23]. A recent method uses Woollins' reagent (WR) with *N*,*N*′-diacylhydrazines [24]. WR (2,4-diphenyl-1,3-diselenadiphosphetane 2,4-diselenide [PhP(Se)(μ-Se)]$_2$) is an analogous to Lawesson's reagent that acts as a good sulphuring agent [25,26]. It is used for selenation reactions, for example, preparation of trifluoroselenoacetic acid [27], synthesis of selenoaldehydes [28], reaction of arylnitriles and WR producing primary arylselenoamides [29] and synthesis benzo[*c*]selenophenes from benzo[*c*]furans [30].

RESULTS AND DISCUSSION

We decided to synthesise a series of monosubstituted 1,3,4-selenadiazoles, because only 2,5-disubstituted 1,3,4-selenadiazoles have been obtained so far, and we chose WR as the best reagent for the synthesis of 1,3,4-selenadiazoles. Mechanism of these reactions is still unknown; but it is likely to lead from selenation of both carbonyl groups to cyclization with hydrogen selenide emission. In this study, we report the method of synthesis and characterisation of new selenacyclic compounds (Scheme 1).

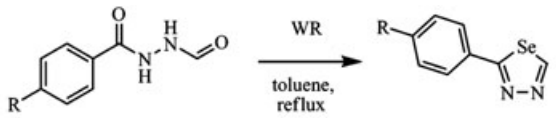
The general procedure provided compounds (**1**–**11**) in satisfactory yields (26–57%). Additionally, in several cases, the final product was contaminated by appropriate 1,3,4-oxadiazole (significant for R = H, F, Cl, CF_3, about 40%). There is no systematic reason for different level of this contamination.

EI analysis gave peaks mainly corresponding to the loss of HCN, HNCSe molecules, and $^{\bullet}C_2HN_2Se$ radical from molecular ions.

EXPERIMENTAL

N,*N*′-Diacylhydrazines were synthesized using perfluorophenyl 4-substituted benzoates and formic hydrazide as described by Zhao and Burke [31]. All reactions were carried out under argon atmosphere. Toluene was dried and distilled before use. Melting points (uncorrected) were determined on Boethius apparatus. Chromatography was performed on silica gel 60 (70–230 mesh, Merck) and silica gel 60 TLC plates (Merck). EI mass spectrometric experiments were carried out on a Varian 4000 Ion Trap

Scheme 1. Synthesis of monosubstituted 1,3,4-selenadiazoles.



R	Compound	Yield [%]	R	Compound	Yield [%]
H	**1**	34	$N(CH_3)_2$	**7**	41
F	**2**	56	CH_3	**8**	53
Cl	**3**	48	CF_3	**9**	44
Br	**4**	52	CH_3O	**10**	57
I	**5**	35	C_6H_5	**11**	40
NO_2	**6**	26			

GC/MS using a Factor Four fused silica capillary column (CP8944, 30 m × 0.25 mm, df = 0.25 μm, VF-5ms). Exact mass data were obtained on an AMD Intectra 402 two-sector mass spectrometer of B/E geometry with an accelerating voltage of 8 kV, an electron energy 70 eV, and an ion source temperature of 200°C in relation to perfluorokerosene (Fluka). The ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DRX 600 spectrometer, operating at frequencies 599.936, 150.868 MHz, respectively, while ^{19}F NMR experiments were carried out on Varian Mercury 300 apparatus (spectral frequency 282.352 MHz for ^{19}F nucleus). Concentrations of the samples used for NMR measurements were 10–20 mg per 0.7 mL of solvent. All spectra were recorded using standard acquisition parameters at 298 K. Elementary analyses (C, H, N) were obtained on a Vario EL III analyser. Selenium content was determined by XRF measurements on MiniPal2 spectrometer (Panalytical) after dissolving of the sample in HNO_3.

General procedure for the synthesis of monosubstituted 1,3,4-selenadiazoles. Commercially available WR (Aldrich) (1 mmol) was added to the suspension of appropriate *N*-aryl-*N*′-formylhydrazine (1 mmol) in 25 mL of dry toluene. The mixture was refluxed for 24 h (TLC controlled: dichloromethane/diethyl ether 5:1 as eluent—unless stated otherwise). Then, the solvent was evaporated and the residue was dissolved in dichloromethane and purified by chromatography on silica gel (CH_2Cl_2/Et_2O 5:1 as eluent—unless stated otherwise).

2-Phenyl-1,3,4-selenadiazole (1). Reaction with *N*-benzoyl-*N*′-formylhydrazine, according to the general procedure, gave product 1 as a brownish yellow semi-solid (34%, 71 mg), mp 119–122°C. ^{1}H NMR ($CDCl_3$): δ 9.96 (s, 1H, $^2J_{Se,H}$ = 56.6 Hz); 7.96 (m, 2H); 7.51 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$): δ 175.38; 157.28; 132.43; 131.30; 129.24; 128.98 ppm. MS: *m*/*z* 210 (M^+); 183; 103; 77. HRMS: *m*/*z* calcd for $C_8H_6N_2Se$: 209.96962, found: 209.96915. Anal. Calcd. for $C_8H_6N_2Se$: C, 45.95; H, 2.89; N, 13.40; Se, 37.76. Found: C, 45.88; H, 2.58; N, 13.27; Se, 37.99.

2-(4-Fluorophenyl)-1,3,4-selenadiazole (2). Reaction with *N*-(4-fluorobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 2 as a flesh-colored solid (56%, 127 mg), mp 66–67°C. ^{1}H NMR ($CDCl_3$): δ 9.96 (s, 1H, $^2J_{Se,H}$ = 57.0 Hz); 7.96 (dd, 2H, *J* = 8.9, 5.2 Hz); 7.17 (dd, 2H, *J* = 8.9, 8.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 173.97; 164.41; 157.24; 130.90; 128.83; 116.41 ppm. ^{19}F NMR ($CDCl_3$): δ –108.25 (tt, 1F, $J_{H,F}$ = 8.3, 5.2 Hz) ppm. MS: *m*/*z* 228 (M^+); 201; 121; 95. HRMS: *m*/*z* calcd for $C_8H_5FN_2Se$: 227.96019, found: 227.95907. Anal. Calcd. for $C_8H_5FN_2Se$: C, 42.31; H, 2.22; N, 12.34; Se, 34.77. Found: C, 42.11; H, 2.36; N, 12.09; Se, 35.00.

2-(4-Chlorophenyl)-1,3,4-selenadiazole (3). Reaction with *N*-(4-chlorobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 3 as a flesh-colored solid (48%, 117 mg), mp 88–89°C. ^{1}H NMR ($CDCl_3$): δ 9.98 (s, 1H, $^2J_{Se,H}$ = 57.0 Hz); 7.90 (d, 2H, *J* = 8.4 Hz); 7.45 (d, 2H, *J* = 8.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 174.11; 157.43; 137.43; 131.08; 130.13; 129.54 ppm. MS: *m*/*z* 244 (M^+); 217; 137; 102; 75. HRMS: *m*/*z* calcd for $C_8H_5ClN_2Se$: 243.93065, found: 243.92879. Anal. Calcd. for $C_8H_5ClN_2Se$: C, 39.45; H, 2.07; N, 11.50; Se, 32.42. Found: C, 39.71; H, 2.06; N, 11.34; Se, 32.60.

2-(4-Bromophenyl)-1,3,4-selenadiazole (4). Reaction with *N*-(4-bromobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 4 as a flesh-coloured solid (52%, 150 mg), mp 122–123°C. ^{1}H NMR ($CDCl_3$): δ 9.97 (s, 1H, $^2J_{Se,H}$ = 57.1 Hz); 7.82 (d, 2H, *J* = 8.5 Hz); 7.61 (d, 2H, *J* = 8.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 174.14; 157.43; 132.51; 131.52; 130.31; 125.82 ppm. MS: *m*/*z* 288 (M^+); 261; 182; 102; 75. HRMS: *m*/*z* calcd for $C_8H_5BrN_2Se$: 287.88013, found: 287.88201. Anal. Calcd. for $C_8H_5BrN_2Se$: C, 33.36; H, 1.75; N, 9.73; Se, 27.42. Found: C, 33.20; H, 1.91; N, 9.78; Se, 27.23.

2-(4-Iodophenyl)-1,3,4-selenadiazole (5). Reaction with *N*-(4-iodobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 5 as a flesh-coloured solid (35%, 117 mg), mp 152–155°C. ^{1}H NMR ($CDCl_3$): δ 9.96 (s, 1H, $^2J_{Se,H}$= 57.0 Hz); 7.82 (d, 2H, *J* = 8.5 Hz); 7.68 (d, 2H, *J* = 8.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 174.35; 157.36; 138.48; 132.07; 130.34; 97.90 ppm. MS: *m*/*z* 336 (M^+); 309; 229; 102; 73. HRMS: *m*/*z* calcd for $C_8H_5IN_2Se$: 335.86626, found: 335.86415. Anal. Calcd. for $C_8H_5IN_2Se$: C, 26.68; H, 1.50; N, 8.36; Se, 23.57. Found: C, 26.82; H, 1.58; N, 8.45; Se, 23.50.

2-(4-Nitrophenyl)-1,3,4-selenadiazole (6). Reaction with *N*-(4-nitrobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 6 as a greenish yellow solid (26%, 66 mg), mp 175–178°C. ^{1}H NMR ($CDCl_3$): δ 10.09 (s, 1H, $^2J_{Se,H}$ = 57.3 Hz); 8.36 (m, 2H); 8.17 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$): δ 172.76; 158.72; 149.14; 138.07; 129.74; 124.48 ppm. MS: *m*/*z* 255 (M^+); 228; 182; 102; 75. HRMS: *m*/*z* calcd for $C_8H_5N_3O_2Se$: 254.95470, found: 254.95391. Anal. Calcd. for $C_8H_5N_3O_2Se$: C, 37.81; H, 1.98; N, 16.54; Se, 31.07. Found: C, 37.77; H, 1.90; N, 16.46; Se, 31.26.

2-(4-Dimethylaminophenyl)-1,3,4-selenadiazole (7). Reaction with *N*-(4-dimethylaminobenzoyl)-*N*′-formylhydrazine, according to the general procedure, gave product 7 as greenish yellow solid (41%, 103 mg), mp 113–114°C. ^{1}H NMR ($CDCl_3$): δ 9.78 (s, 1H, $^2J_{Se,H}$ = 56.9 Hz); 7.82 (d, 2H, *J* = 9.1 Hz); 6.71 (d, 2H, *J* = 9.0 Hz); 3.05 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$): δ 175.60; 154.77; 152.20; 128.42; 128.04; 111.61; 40.13 ppm. MS: *m*/*z* 253 (M^+); 146; 129; 102. HRMS: *m*/*z* calcd for $C_{10}H_{11}N_3Se$: 253.01182, found: 253.01329. Anal. Calcd. for $C_{10}H_{11}N_3Se$: C, 47.63; H, 4.40; N, 16.66; Se, 31.31. Found: C, 47.72; H, 4.26; N, 16.79; Se, 31.40.

2-(4-Methylphenyl)-1,3,4-selenadiazole (8). Reaction with *N*-(4-methylbenzoyl)-*N*′-formylhydrazine, according to the general procedure (CH_2Cl_2/Et_2O 6:1 as eluent), gave product 8 as a brownish yellow semi-solid (53%, 119 mg), mp 30–31°C. ^{1}H NMR ($CDCl_3$): δ 9.91 (s, 1H, $^2J_{Se,H}$ = 56.6 Hz); 7.83 (d, 2H, *J* = 7.9 Hz); 7.26 (d, 2H, *J* = 7.8 Hz); 2.39 (s, 3H)

ppm. ^{13}C NMR ($CDCl_3$): δ 175.41; 156.79; 141.83; 129.95; 129.88; 128.95; 21.50 ppm. MS: *m/z* 224 (M^+); 197; 117; 91. HRMS: *m/z* calcd for $C_9H_8N_2Se$: 223.98527, found: 223.98703. Anal. Calcd. for $C_9H_8N_2Se$: C, 48.45; H, 3.61; N, 12.55; Se, 35.39. Found: C, 48.52; H, 3.31; N, 12.69; Se, 35.55.

2-(4-Trifluoromethylphenyl)-1,3,4-selenadiazole (9). Reaction with *N*-(4-trifluoromethylbenzoyl)-*N′*-formylhydrazine, according to the general procedure (CH_2Cl_2/Et_2O 6:1 as eluent), gave product 9 as a flesh-coloured solid (44%, 122 mg), mp 91–92°C. ^{1}H NMR ($CDCl_3$): δ 10.05 (s, 1H, $^2J_{Se,H}$ = 57.1 Hz); 8.09 (d, 2H, *J* = 8.5 Hz); 7.74 (d, 2H, *J* = 8.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 173.71; 158.11; 135.67; 132.77; 129.20; 126.21; 123.58 ppm. ^{19}F NMR ($CDCl_3$): δ −63.45 (s, 3F) ppm. MS: *m/z* 278 (M^+); 251; 172; 145; 75. HRMS: *m/z* calcd for $C_9H_5F_3N_2Se$: 277.95700, found: 277.95548. Anal. Calcd. for $C_9H_5F_3N_2Se$: C, 39.01; H, 1.82; N, 10.11; Se, 28.49. Found: C, 38.83; H, 2.02; N, 10.15; Se, 28.58.

2-(4-Methoxyphenyl)-1,3,4-selenadiazole (10). Reaction with *N*-(4-methoxybenzoyl)-*N′*-formylhydrazine, according to the general procedure (CH_2Cl_2/Et_2O 7:1 as eluent), gave product 10 as a flesh-coloured solid (57%, 136 mg), mp 71–73°C. ^{1}H NMR ($CDCl_3$): δ 9.87 (s, 1H, $^2J_{Se,H}$ = 56.9 Hz); B 7.89 (d, 2H, *J* = 8.9 Hz); 6.97 (d, 2H, *J* = 8.8 Hz); 3.86 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$): δ 174.92; 162.09; 156.29; 130.58; 125.30; 114.62; 55.49 ppm. MS: *m/z* 240 (M^+); 133; 90. HRMS: *m/z* calcd for $C_9H_8N_2OSe$: 239.98018, found: 239.98194. Anal. Calcd. for $C_9H_8N_2OSe$: C, 45.20; H, 3.37; N, 11.71; Se, 33.02. Found: C, 44.99; H, 3.41; N, 12.03; Se, 32.79.

2-[1,1′-Biphenyl]-4-yl-1,3,4-selenadiazole (11). Reaction with *N*-(4-phenylbenzoyl)-*N′*-formylhydrazine, according to the general procedure, gave product 11 as a flesh-coloured solid (40%, 114 mg), mp 123–124°C. ^{1}H NMR ($CDCl_3$): δ 9.94 (s, 1H, $^2J_{Se,H}$ = 56.7 Hz);. 8.02 (d, 2H, *J* = 8.0 Hz); 7.76 (d, 2H, *J* = 7.8 Hz); 7.63 (d, 2H, *J* = 7.8 Hz); 7.47 (t, 2H, *J* = 7.5 Hz); 7.39 (t, 1H, *J* = 7.0 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ 175.04; 157.07; 144.11; 139.71; 131.42; 129.51; 129.00; 128.14; 127.88; 127.10 ppm. MS: *m/z* 286 (M^+); 259; 179; 151; 76. HRMS: *m/z* calcd for $C_{14}H_{10}N_2Se$: 286.00092, found: 286.00023. Anal. Calcd. for $C_{14}H_{10}N_2Se$: C, 58.96; H, 3.53; N, 9.82; Se, 27.68. Found: C, 59.17; H, 3.36; N, 9.70; Se, 27.95.

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