Chemistry of Heterocyclic Compounds, Vol. 49, No. 2, May, 2013 (Russian Original Vol. 49, No. 2, February, 2013)

SYNTHESIS OF FUNCTIONALLY SUBSTITUTED 1,2,4-SELENADIAZOLES

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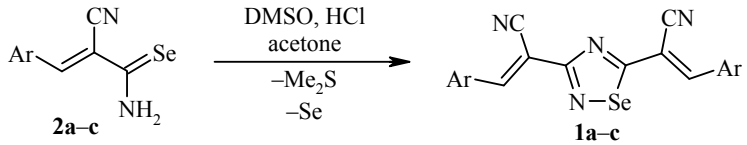
Keywords: 3-aryl-2-cyanoprop-2-eneselenoamides, cyanoselenoacetamide, DMSO-HCl, 1,2,4-selenadiazoles, oxidative dimerization.

Unlike the isomeric 1,2,3-, 1,2,5-, and 1,3,4-selenadiazoles, there are few examples of 1,2,4-selenadiazoles in the literature (for reviews of selenadiazole chemistry, see [1-4]). The main method for preparing derivatives of this heterocyclic system is the oxidative dimerization of primary selenoamides. Only the simplest 3,5-dialkyl(aryl)-1,2,4-selenadiazoles have been synthesized by this method. Iodine [5, 6], *N*-bromosuccinimide [7], phenyliodosodiacetate, poly[styrene(iodosodiacetate)] [8], and the O_2–Na_2PdCl_4 system [9] have been used as the oxidants. Formation of 1,2,4-selenadiazoles by treatment of selenoamides with α-arylsulfonyl-α-bromoacetophenones [10] and tosyl chloride [11] have also been reported. The need for chromatographic purification and overall contamination of the selenadiazoles by side products have been noted as drawbacks of these methods [4].

In our work, we have proposed for the first time a method of preparing functionally substituted 1,2,4-selenadiazoles, namely, (2*E*,2'*E*)-2,2'-(1,2,4-selenadiazole-3,5-diyl)bis(3-arylacrylonitriles) **1a-c** by mild oxidation of the available [12, 13] cyanoselenoacetamides **2a-c** using the system DMSO–HCl–acetone.



2a–c **1a–c**

1, **2 a** Ar = 4-HOC_6H_4, **b** Ar = 3,4-$(MeO)_2C_6H_3$, **c** Ar = 2-furyl

The advantages of this oxidative method include the simplicity of the procedure, fast reaction, and purity of the obtained selenadiazoles **1a-c**. The side products are Me_2S and elemental selenium, which are readily removed by filtration. It should also be noted that the use of the available and cheap oxidant DMSO–HX (X = Cl, Br) is currently limited to a few examples, e.g., the oxidation of acetophenones to arylglyoxals [14], halogenation of aromatic compounds [15], and oxidative dimerization of primary thioamides and thioureas to 1,2,4-thiadiazoles [16, 17]. The structures of compounds **1a-c** were confirmed from IR and ^{1}H NMR spectral data, HPLC-MS, and elemental analysis.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 377-380, February, 2013. Original article submitted December 7, 2012.

In conclusion, we would note that, with the presence of acrylonitrile fragments, the obtained (2*E*,2'*E*)-2,2'-(1,2,4-selenadiazole-3,5-diyl)bis(3-arylacrylonitriles) can undergo further functionalization in order to prepare novel derivatives of the rare 1,2,4-selenadiazole heterocyclic system.

IR spectra were recorded in nujol on an IKS-29 spectrophotometer. ^{1}H NMR spectra were acquired on Bruker DPX-400 (400 MHz) and DRX-500 (500 MHz) instruments using DMSO-d_6 with TMS as internal standard. HPLC-MS analysis was carried out on an Agilent 1100 chromatograph with UV diode array (215, 254, and 265 nm) and Agilent LS/MSD SL detectors with ES-API ionization. Elemental analysis was performed on a Carlo-Erba 1106 Elemental Analyzer apparatus. Melting points were measured on a Kofler hot stage apparatus and were not corrected. Purity of the prepared compounds was monitored by TLC on Silufol UV-254 plates using 1:1 acetone–hexane as eluent and iodine vapor or UV visualization. The selenoamide **2c** [12, 13] was obtained by a known method. Selenoamides **2a**,**b** were prepared by a similar method, but contained up to 20% of arylidenemalononitrile and dimer impurities. This prevented the determination of melting point or performing an elemental analysis (purification was unsuccessful due to the instability of these compounds). Since the indicated impurities did not hinder the synthesis of selenadiazoles **1a-c**, the compounds **2a-c** were oxidized without additional purification.

(*E*)-2-Cyano-3-(4-hydroxyphenyl)prop-2-eneselenoamide (2a). Freshly prepared cyanoselenoacetamide [18] (300 mg, 2.03 mmol) and 4-hydroxybenzaldehyde (250 mg, 2.05 mmol) were added to distilled water (15 ml), that had been prepared by boiling under an argon stream and cooling to 20°C. The suspension obtained was heated under an argon stream at about 50°C until homogenisation, and Et_3N (1 drop) was added. The product was stirred at this temperature for 1 min, and the precipitated selenium was removed by filtration under argon. The filtrate was left in a closed flask for 24 h at 20°C. The red-brown precipitate was filtered off and washed with water and diethyl ether. Yield 460 mg (90%). ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 6.92 (2H, d, ^3J = 8.4, H Ar); 7.90 (2H, d, ^3J = 8.4, H Ar); 8.06 (1H, s, Ar–CH=); 10.10 (1H, br. s) and 10.79 (1H, br. s, NH_2); 10.67 (1H, br. s, OH).

(*E*)-2-Cyano-3-(3,4-Dimethoxyphenyl)prop-2-eneselenoamide (2b) was prepared from the cyanoselenoacetamide and veratral by the general method [12, 13]. Yield 91%. Brown powder. ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 3.79 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 7.15 (1H, d, ^3J = 8.1, H Ar); 7.59 (1H, d, ^3J = 8.1, H Ar); 7.70 (1H, s, H Ar); 8.08 (1H, s, Ar–CH=); 10.16 (1H, br. s) and 10.86 (1H, br. s, NH_2).

(2*E*,2'*E*)-2,2'-(1,2,4-Selenadiazole-3,5-diyl)bis(3-arylacrylonitriles) (1a-c) (General Method). The unsaturated selenoamide **2a-c** (0.7 mmol) and DMSO (0.2 ml, 3.0 mmol) were introduced into a 25-ml beaker, followed by acetone (7-10 ml), and the mixture was heated to full dissolution. A 30% solution of HCl (0.2 ml, 1.9 mmol) was added dropwise with stirring, the solution cleared instantly and elemental selenium precipitated, along with evolution of Me_2S. The mixture was brought to reflux, rapidly filtered through a filter paper to remove the elemental selenium, and the precipitate was washed with boiling acetone (2 ml). Cooling the combined filtrates resulted in crystallization of the product. The suspension was maintained in an open beaker for 48 h at 25°C. The precipitate was then filtered off, then washed with EtOH and Et_2O. In the case of the selenoamide **2a**, evaporation of the acetone left an oily residue, which was recrystallized from EtOH. Analytically pure selenadiazoles **1a-c** were thus obtained.

(2*E*,2'*E*)-2,2'-(1,2,4-Selenadiazole-3,5-diyl)bis[3-(4-hydroxyphenyl)acrylonitrile] (1a). Yield 40 mg (27%). Yellow-green crystals; mp >250°C (EtOH). R_f 0.41. IR spectrum, ν, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 6.96 (2H, d, ^3J = 8.5, H Ar); 6.99 (2H, d, ^3J = 8.1, H Ar); 7.96 (2H, d, ^3J = 8.5, H Ar); 8.06 (2H, d, ^3J = 8.1, H Ar); 8.45 (1H, s, Ar-CH=); 8.48 (1H, s, Ar-CH=); 10.57 (1H, br. s, OH); 10.88 (1H, br. s, OH). Mass spectrum, *m*/*z*: 421.0 $[M+H]^+$, 419.0 $[M-H]^-$. Found %: C 57.36; H 2.98; N 13.49. $C_{20}H_{12}N_4O_4Se$. Calculated, %: C 57.29; H 2.88; N 13.36.

(2*E*,2'*E*)-2,2'-(1,2,4-Selenadiazole-3,5-diyl)bis[3-(3,4-dimethoxyphenyl)acrylonitrile] (1b). Yield 117 mg (66%). Bright-yellow crystals; mp >250°C. R_f 0.54. IR spectrum, ν, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum (500 MHz), δ, ppm (*J*, Hz): 3.84 (6H, br. s, $2OCH_3$); 3.88 (6H, br. s, $2OCH_3$); 7.18 (1H, d, ^3J = 8.3, H Ar); 7.22 (1H, d, ^3J = 8.2, H Ar); 7.60-7.64 (2H, m, H Ar); 7.79-7.81 (2H, m, H Ar); 8.49 (1H, s, Ar–CH=);

8.53 (1H, s, Ar–CH=). Mass spectrum, *m*/*z* : 509.2 $[M+H]^+$, 507.0 $[M-H]^-$. Found, %: C 57.11; H 4.09; N 11.29. $C_{24}H_{20}N_4O_4Se$. Calculated, %: C 56.81; H 3.97; N 11.04.

(2*E*,2'*E*)-2,2'-(1,2,4-Selenadiazole-3,5-diyl)bis[3-(2-furyl)acrylonitrile] (1c). Yield 84 mg (65%). Bright-yellow crystals; mp 253-255°C. R_f 0.58. IR spectrum, ν, cm^{-1}: 2229 (C≡N). ^1H NMR spectrum (500 MHz), δ, ppm (*J*, Hz): 6.84-6.85 (1H, m, H-4 Fur); 6.90-6.91 (1H, m, H-4 Fur); 7.45 (1H, d, ^3J = 3.2, H-3 Fur); 7.50 (1H, d, ^3J = 3.2, H-3 Fur); 8.15-8.16 (1H, m, H-5 Fur); 8.28-8.29 (1H, m, H-5 Fur); 8.30 (1H, s, Fur–CH=); 8.48 (1H, s, Fur–CH=). Mass spectrum, *m*/*z*: 369.0 $[M+H]^+$, 366.0 $[M-H]^-$. Found, %: C 52.41; H 2.32; N 15.37. $C_{16}H_8N_4O_2Se$. Calculated, %: C 52.33; H 2.20; N 15.26.

This work was carried out with the financial support by the President of the Ukraine (grant F47/032).

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