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CHEMISTRY

New Spiro Derivatives of Isoselenourea in 1,3-Selenazine Series

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In recent time, the chemistry of selenium derivatives is a burgeoning field of modern chemistry [1]. Selenium derivatives attract interest not only as compounds with unique properties but also as biologically active substances. Thus, recent studies showed that selenium is an important component for functioning of many biological systems [2].

We have developed a method of synthesis of previously unknown 2-aminospiroselenazines **5a**–**5d**, cyclic derivatives of isoselenourea without substituents at the bicyclic fragment of molecule. The method is based on the intramolecular cyclization of selenoureas **3a**–**3d** containing γ,σ-unsaturated fragment (Scheme 1). Isoselenocyanates **1a**–**1d** were used as starting compounds. They were obtained by refluxing a mixture of the corresponding arylformamides, phosgene, and selenium powder in toluene in the presence of triethylamine [3, 4]. Resulting isoselenocyanates **1a**–**1d** were converted to substituted selenoureas **3a**–**3d** by the reaction with γ,σ-unsaturated amine, 2-(cyclohexen-1-yl)amine (**2**).

The selenoureas were refluxed in 48% aqueous hydrobromic acid. An addition of hydrogen bromide at the double bond of the cyclohexene fragment takes place. Resulting 1''-[2'-(1-bromocyclohexyl)ethyl]-3''-arylselenoureas **4a**–**4d** immediately undergo intramolecular cyclization to give the corresponding N-substituted 1-selena-3-azaspiro[5.5]undec-2-en-2-ylamines **5a**–**5d** in total yield of 60–80%.

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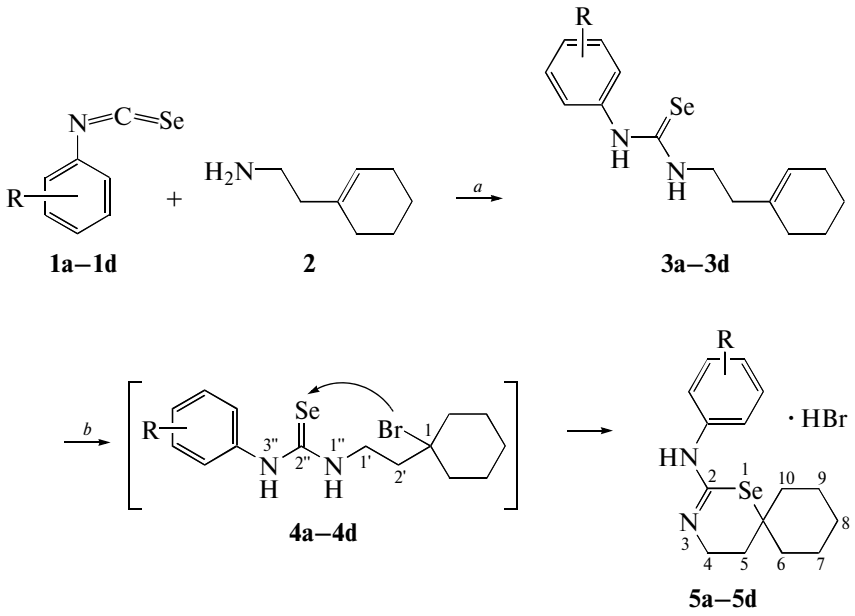
EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker CXP-200 spectrometer (Germany) using deuteriochloroform as a solvent, chemical shifts are represented on the δ scale relative to Me_4Si. Melting points were determined on a Boetius hot stage apparatus and were uncorrected. Solutions were evaporated on a rotary evaporator in a vacuum of a water-jet pump.

Procedure for the synthesis of N-substituted 1-selena-3-azaspiro[5.5]undec-2-en-2-ylamines 5a–5d. A solution of 0.01 mol of substituted arylisoselenocyanate in 20 mL of ether was added dropwise with stirring to a solution of 2'-(cyclohexen-1-yl)amine **2** (1.25 g, 0.01 mol) in 20 mL of ether. The reaction mixture was stirred at ambient temperature for 2–5 h until precipitate formed. The resulting precipitate of selenourea **3** was separated by filtration, dried, suspended in 10 mL of 48% hydrobromic acid, and refluxed for 5 h. After completion of the reaction, the mixture was cooled, diluted with 20 mL of water, and 50 mL of methylene chloride was added. The organic layer was separated and dried with sodium sulfate. The drying agent was separated by filtration, and the filtrate was concentrated. The residue was recrystallized from isopropanol to give N-substituted 1-selena-3-azaspiro[5.5]undec-2-en-2-ylamine **5** as hydrobromide.

Phenyl(1-selena-3-azaspiro[5.5]undec-2-en-2-yl)amine hydrobromide 5a. Light brown crystals, mp 147–149°C, yield 79%.

^{1}H NMR (δ, ppm): 1.37 (m, 3H, C(8)H_2, C(7)H<u>H</u>H), 1.69 (m, 5H, C(6)H<u>H</u>, C(7)H<u>H</u>, C(9)H_2, C(10)H<u>H</u>), 2.14 (m, 4H, C(6)<u>H</u>H, C(10)<u>H</u>H, C(5)H_2), 3.71 (m, 2H, C(4)H_2), 7.28 (m, 2H, H_{arom}), 7.40 (m, 3H, H_{arom}), 10.92 (s, 1H, NH), 11.26 (s, 1H, NH).



R = H (**a**), 4-*i*-Pr (**b**), 4-F (**c**), 3-Cl-4-Me (**d**).
(*a*) acetone, reflux, 2 h; (*b*) HBr (48%), 100°C, 5 h.

Scheme 1.

4-Isopropylphenyl(1-selena-3-azaspiro[5.5]undec-2- en-2-yl)amine hydrobromide 5b. Cream-white crystals, mp 118–120°C, yield 75%.

^{1}H NMR (δ, ppm, *J*, Hz): 1.25 (d, 6H, *J* 6.8, $CH(C\underline{H}_3)_2$), 1.43 (m, 3H, $C(8)H_2$, $C(7)\underline{H}H$), 1.68 (5H, m, $C(6)H\underline{H}$, $C(7)H\underline{H}$, $C(9)H_2$, $C(10)H\underline{H}$), 2.08 (4H, $C(6)\underline{H}H$, $C(10)\underline{H}H$, $C(5)H_2$), 2.93 (m, 1H, $C\underline{H}(CH_3)_2$), 3.69 (m, 2H, $C(4)H_2$), 7.17 (d, 1H, *J* 8.6, H_{arom}), 7.26 (d, 1H, *J* 8.6, H_{arom}), 10.83 (s, 1H, NH), 11.09 (s, 1H, NH).

4-Fluorophenyl(1-selena-3-azaspiro[5.5]undec-2-en-2-yl)amine hydrobromide 5c. Cream-white crystals, mp 197–199°C, yield 80%.

^{1}H NMR (δ, ppm): 1.32 (m, 3H, $C(8)H_2$, $C(7)\underline{H}H$), 1.62 (m, 5H, $C(6)H\underline{H}$, $C(7)H\underline{H}$, $C(9)H_2$, $C(10)H\underline{H}$), 2.06 (m, 4H, $C(6)\underline{H}H$, $C(10)\underline{H}H$, $C(5)H_2$), 3.63 (m, 2H, $C(4)H_2$), 7.04 (m, 2H, H_{arom}), 7.20 (m, 2H, H_{arom}), 10.88 (s, 1H, NH), 11.17 (s, 1H, NH).

3-Chloro-4-methylphenyl(1-selena-3-azaspiro[5.5]undec-2-en-2-yl)amine hydrobromide 5d. Light brown crystals, mp 198–200°C, yield 79%.

^{1}H NMR (δ, ppm, *J*, Hz): 1.30 (m, 3H, $C(8)H_2$, $C(7)\underline{H}H$), 1.62 (m, 5H, $C(6)H\underline{H}$, $C(7)H\underline{H}$, $C(9)H_2$, $C(10)H\underline{H}$), 2.04 (m, 4H, $C(6)\underline{H}H$, $C(10)\underline{H}H$, $C(5)H_2$), 2.31 (s, 3H, CH_3), 3.65 (m, 2H, $C(4)H_2$), 7.03 (dd, 1H, *J* 2.2, 8.6, H_{arom}), 7.19 (d, 1H, *J* 8.6, H_{arom}), 7.20 (d, 1H, *J* 2.2, H_{arom}), 9.29 (br s, 2H, NH_2).

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