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SYNTHESIS OF 5-R-BENZYL-2-IMINOSELENAZOLIDIN-4-ONES

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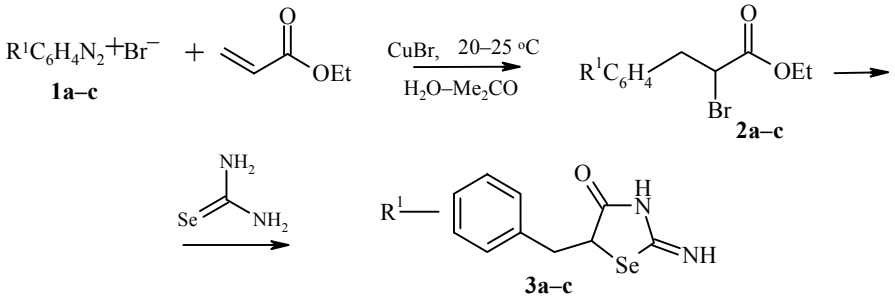
Interest in the synthesis of selenazole derivatives is related largely to the biological activity of these compounds [1-3]. A convenient method for the synthesis of substituted selenazoles involves the reaction of α-halo ketones with compounds containing the selenamide fragment, $H_2NC(Se)R$ [1]. Less attention has been given to the reaction of the latter with α-halo carboxylic acids and their derivatives to give selenazolidin-4-ones [4, 5].

We have developed a simple method for the synthesis of such compounds using acrylates **2a-c**, which are obtained from the bromoarylation of arenediazonium salts **1a-c**. Acrylates **2a-c** react with selenourea upon brief heating at reflux in ethanol in the presence of pyridine to give iminoselenazolidinones **3a-c**. Dehydrobromination of α-bromo esters **2a-c** does not occur and **3a-c** were obtained in high yield. This method yields 2-iminoselenazolidin-4-one derivatives containing benzyl substituents at $C_{(5)}$, which opens the pathway for the synthesis of selenium analogs of 5-R-benzyl-2,4-thiazolidinediones, some of which have antidiabetic activity [6].



1-3 **a** R = H; **b** R = 4-Me; **c** R = 2-Cl

The ^{1}H NMR spectra were taken in DMSO-d_6 at 500 MHz.

5-Benzyl-2-iminoselenazolidin-4-one (3a). A solution of benzenediazonium bromide **1a** obtained by the diazotization of aniline (100 mmol) was added dropwise with stirring to a mixture of ethyl acrylate (10 ml) and CuBr (1.5 g) in acetone (50 ml). The reaction was continued until nitrogen was no longer liberated. Then, water (200 ml) was added and the organic layer was separated. Distillation in vacuum gave 10.3 g (40%) ethyl ester of 2-bromo-3-phenylpropanoic acid **2a**; bp 115-117°C (2 mm Hg), n_D^{20} 1.5330. A sample of **2a** (1.0 g, 4.1 mmol) and selenourea (0.5 g, 4.1 mmol) were dissolved in ethanol (15 ml). Then, pyridine (0.4 ml) was

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added and the mixture was heated at reflux for 30 min. The precipitate formed was recrystallized from 1:1 ethanol–DMF to give 0.83 g (80%) **3a**; mp 202-203°C. ^{1}H NMR spectrum, δ, ppm,(*J*, Hz): 2.95 (1H, dd, ^2J = 14.0, ^3J = 11.0, CH_2); 3.64 (1H, dd, ^2J = 14.0, ^3J = 3.7, CH_2); 4.67 (1H, dd, ^3J = 11.0, ^3J = 3.7, CH); 7.16-7.28 (5H, m, C_6H_5); 8.53 (1H, s, NH); 8.92 (1H, s, NH). Found, %: C 47.38; H 3.82; N 10.94. $C_{10}H_{10}N_2OSe$. Calculated, %: C 47.44; H 3.98; N 11.07.

2-Iminoselenazolidin-4-ones 3b and 3c were obtained analogously.

2-Imino-5-(4-methylbenzyl)selenazolidin-4-one (3b) was obtained in 73% yield; mp 207°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.31 (3H, s, CH_3); 2.91 (1H, dd, ^2J = 14.1, ^3J = 10.8, CH_2); 3.60 (1H, dd, ^2J = 14.1, ^3J = 3.9, CH_2); 4.64 (1H, dd, ^3J = 10.8, ^3J = 3.9, CH); 7.05 (2H, d, C_6H_4); 7.10 (2H, d, C_6H_4); 8.52 (1H, s, NH); 8.90 (1H, s, NH). Found, %: C 49.33; H 4.45; N 10.36. $C_{11}H_{12}N_2OSe$. Calculated, %: C 49.45; H 4.53; N 10.48.

5-(2-Chlorobenzyl)-2-iminoselenazolidin-4-one (3c) was obtained in 83% yield; mp 193-194°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.07 (1H, dd, ^2J = 14.4, ^3J = 10.5, CH_2); 3.80 (1H, dd, ^2J = 14.4, ^3J = 3.6, CH_2); 4.78 (1H, dd, ^3J = 10.5, ^3J = 3.6, CH); 7.18-7.26 (2H, m, C_6H_4); 7.31 (1H, m, C_6H_4); 7.35 (1H, m, C_6H_4); 7.35 (1H, m, C_6H_4); 8.60 (1H, s, NH); 9.02 (1H, s, NH). Found, %: C 41.63; H 3.02; N 9.52. $C_{10}H_9ClN_2OSe$. Calculated, %: C 41.76; H 3.15; N 9.74.

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