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CASCADE SYNTHESIS OF PYRIMIDO-[4,3-*b*][1,3,5] SELENADIAZINE DERIVATIVES

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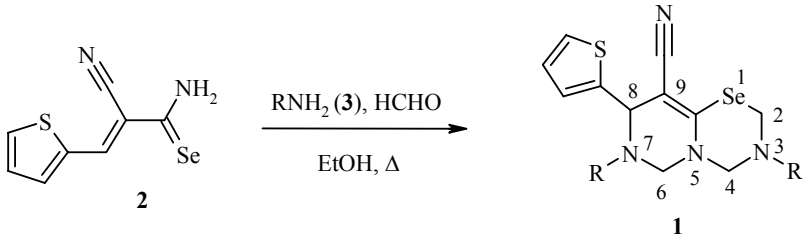
The interest in the chemistry of selenium heterocycles is largely due to the broad spectrum of their biological activity [1, 2]. Derivatives of 1,3,5-selenadiazine form a relatively little studied class of heterocyclic compounds. The methods reported for preparation of the 1,3,5-selenadiazine ring have been based on the reaction of 1,3-dichloro-1,3-bis(dimethylamino)-2-azapropenylium chlorides with selenamides or selenoureas [3, 4], the multicomponent reaction of benzylamine, sodium hydroselenide, and formaldehyde with aryl selenoisocyanates in acid media [5], the recyclization of 1,3,5-oxaselenazine [6, 7], and the reaction of dialkyl(1-aryl-1-chloro-2-aza-1-propenylidene)immonium perchlorate with N-acylselenoureas [8]. Butler and Fox [9] have described the preparation of a selenadiazine derivative as the result of recyclization of a 1,2,4-selenadiazolium salt. Condensed derivatives of 1,3,5-selenadiazines have not been described in the literature.



2 **1**

1, **3 a** R = 4-MeC_6H_4, **b** R = CH_2Ph

We have developed a one-pot cascade method for the preparation of derivatives of pyrimido[4,3-*b*][1,3,5]selenadiazine (**1**) starting from (2-thienyl)methylidenecyanoselenoacetamide (**2**) [10, 11]. Selenamide **2** readily undergoes the Mannich reaction with primary amines **3** and excess formaldehyde upon brief heating at reflux to give **1a** and **1b** in 38-50% yield.

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The ^{1}H NMR spectra were taken on a Bruker Avance II 400 spectrometer at 400 MHz in DMSO-d_6 with TMS as the internal standard. The IR spectra were taken on an IKS-29 spectrometer in vaseline mull. The elemental analyses were carried out on a Perkin-Elmer C,H,N-analyzer. The reaction course and purity of the products were monitored by thin-layer chromatography on Silufol UV-254 plates using 3:5 acetone–hexane as the eluent. The plates were developed with iodine vapor. The melting points were determined on a Koefler block.

Pyrimido[4,3-*b*][1,3,5]selenadiazines 1 (General Method). A mixture of selenoamide **2** (0.6 g, 2.5 mmol), amine **3** (5.2 mmol), and 37% formalin (1.0 ml, 12.5 mmol) in ethanol (30 ml) was heated at reflux for about 2-3 min in an argon atmosphere until the starting reagents were dissolved, rapidly filtered through filter paper, and left for 24 h at room temperature in an argon atmosphere. The precipitate formed was filtered off and washed with ethanol and hexane.

3,7-Di(4-methylphenyl)-8-(2-thienyl)-3,4,7,8-tetrahydro-2H,6H-pyrimido[4,3-b][1,3,5]selenadiazine-9-carbonitrile (1a) was obtained in 50% yield (0.61 g); mp 173-175°C (acetone). IR spectrum, ν, cm^{-1}: 1605 (C=C); 2165 (C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.31 (1H, m, H-5 thienyl); 6.86-7.01 (10H, m, 2Ar, H-3 thienyl, H-4 thienyl); 5.27 (2H, d, ^2J = 10.9, NCH_2Se); 5.13 (1H, s, H-8), 4.83 (2H, br. pseudo-s, NCH_2N); 4.46 (2H, d, ^2J = 12.8, NCH_2N); 2.30, 2.31 (3H each, both s, $2CH_3$). Found, %: C 60.12; H 4.87; N 11.53. $C_{25}H_{24}N_4SSe$. Calculated, %: C 61.09; H 4.92; N 11.40.

3,7-Dibenzyl-8-(2-thienyl)-3,4,7,8-tetrahydro-2H,6H-pyrimido[4,3-*b*][1,3,5]selenadiazine-9-carbonitrile (1b) was obtained in 38% yield (0.47 g); mp 127-130°C. IR spectrum, ν, cm^{-1}: 1605 (C=C); 2175 (C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.24-7.36 (11H, m, 2Ar, H-5 thienyl); 6.96-7.03 (2H, m, H-3 thienyl, H-4 thienyl); 4.83 (2H, d, ^2J = 10.2, NCH_2Se); 4.35 (1H, s, H-8); 3.98 (2H, br. s, $NCH_2C_6H_5$); 3.89 (2H, br. s, $NCH_2C_6H_5$); 3.82 (2H, d, ^2J = 12.6, NCH_2N). Found, %: C 60.59; H 4.83; N 11.57. $C_{25}H_{24}N_4SSe$. Calculated, %: C 61.09; H 4.92; N 11.40.

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