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SYNTHESIS OF DERIVATIVES OF 3,5,7,11-TETRAAZA-TRICYCLO[7.3.1.0^{2,7}]TRIDEC-2-ENE-8-SELENONE

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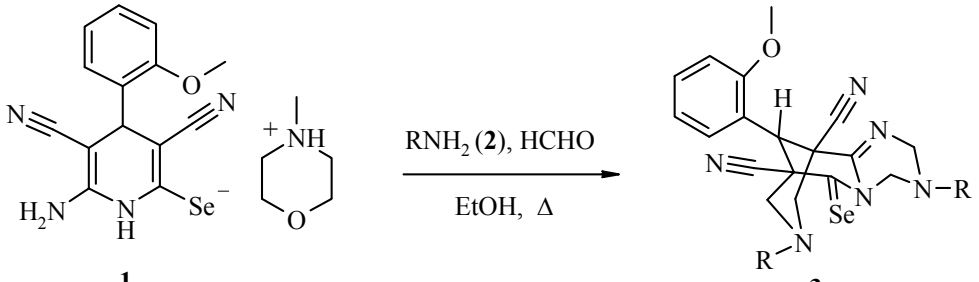
Selenium heterocycles display a broad spectrum of biological activity [1, 2], which accounts for the interest in this area of chemistry. We have developed a method for the synthesis of a new selenium heterocyclic system, namely, 3,5,7,11-tetraazatricyclo[7.3.1.0^{2,7}]tridec-2-ene-8-selenone. Thus, we have found that 1,4-dihydropyridine-2-selenolate **1** undergoes the Mannich reaction with primary amines **2** in the presence of excess formaldehyde to give selenones **3** in 45-53% yield.



1 **3**

2, **3 a** R = 4-MeC$_6$H$_4$, **b** R = Me

The structure of selenones **3** was supported by ^{1}H NMR and IR spectrometry. The ^{1}H NMR spectra of selenones **3** are in good accord with the data for related 8-trioxo-3,5,7,11-tetraazatricyclo[7.3.1.0^{2,7}]tridec-2-enes [3-7], whose structure was demonstrated unequivocally by X-ray diffraction crystallographic analysis [5-7].

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 spectrophotometer for vaseline mulls. The elemental analysis was carried out on a Perkin-Elmer C,H,N-analyzer. The purity of the products was

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monitored by thin-layer chromatography on Silufol UV-254 plates with 1:1 acetone–hexane as the eluent using iodine vapor and a UV detector for development. The melting points were determined on a Koefler block and were uncorrected.

N-Methylmorpholinium 6-Amino-3,5-dicyano-4-(2-methoxyphenyl)-1,4-dihydropyridine-2-selenolate (1) was obtained in 88% yield according to our general procedure [8]; mp 170-172°C. IR spectrum, ν, cm^{-1}: 1650 (C=C), 2190, 2180 (2 C≡N), 3420, 3315, 3255 (NH_2, NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.27 (1H, s, NH); 7.23-6.85 (4H, m, Ar); 5.74 (2H, br. s, NH_2); 4.75 (1H, s, H-4); 3.85 (3H, s, OCH_3); 3.70 (4H, br. pseudosinglet, CH_2–N–CH_2); 2.64 (4H, br. pseudosinglet, CH_2–O–CH_2); 2.40 (3H, s, NCH_3). Found, %: C 52.03; H 5.36; N 15.97%. $C_{19}H_{23}N_5O_2Se$. Calculated, %: C 52.78; H 5.31; N 16.20.

Preparation of tetraazatricyclo[7.3.1.0^{2,7}]tridec-2-ene-8-selenones 3 (General Method). A mixture of selenolate **1** (0.6 g, 1.4 mmol), primary amine **2** (3 mmol), and excess 37% formaldehyde (27 mmol, 2 ml) in ethanol (20 ml) was heated at reflux under argon until the starting reagents dissolve completely (about 2-3 min), then rapidly filtered through a paper filter, and left for 24 h at room temperature in an argon atmosphere. The precipitate formed was filtered off and washed with ethanol and hexane.

13-(2-Methoxyphenyl)-5,11-di(4-methylphenyl)- 8-selenoxy-3,5,7,11-tetraazatricyclo[7.3.1.0^{2,7}]tridec-2-ene-1,9-dicarbonitrile (3a) was obtained in 45% yield (0.37 g); mp 194-196°C (ethanol). IR spectrum, ν, cm^{-1}: 1646 (C=N), 2250 (2 C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.30-6.59 (12H, m, 3Ar); 5.75 (2H, dd, AB system, ^2J = 13.3, two H-4); 4.94 (2H, dd, AB system, ^2J = 17.3, two H-6); 4.67 (1H, s, H-13); 3.92 (2H, dd, AB system, ^2J = 11.8, two H-12 or two H-10); 3.85 (3H, s, OCH_3); 3.74 (2H, dd, AB system, ^2J = 11.4, two H-10 or two H-12); 2.24, 2.14 (each 3H, both s, $2CH_3$). Found, %: C 63.98; H 5.16; N 14.92. $C_{32}H_{30}N_6OSe$. Calculated, %: C 64.75; H 5.09; N 14.16.

13-(2-Methoxyphenyl)-5,11-dimethyl-8-selenoxo-3,5,7,11-tetraazatricyclo[7.3.1.0^{2,7}]tridec-2-ene-1,9-dicarbonitrile (3b) was obtained in 53% yield (0.32 g); mp 207-209°C (ethanol). IR spectrum, ν, cm^{-1}: 1648 (C=N), 2190 (2 C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.38-6.95 (4H, m, Ar); 5.32 (2H, dd, AB system, ^2J = 12.6, two H-4); 4.48 (1H, s, H-13); 4.35 (2H, dd, AB system, ^2J = 17.1, two H-6); 3.90 (3H, s, OCH_3); 3.37 (2H, dd, AB system, ^2J = 10.2, two H-12 or two H-10); 3.07 (2H, dd, AB system, ^2J = 10.8, two H-10 or two H-12); 2.99 and 2.43 (each 3H, both s, $2NCH_3$). Found, %: C 53.67; H 5.08; N 18.77. $C_{20}H_{22}N_6OSe$. Calculated, %: C 54.42; H 5.02; N 19.04.

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