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LETTERS TO THE EDITOR

Synthesis and Intramolecular Heterocyclization of *N*-Anabasinylacetic Acid *N*-Phenylthiosemicarbazide

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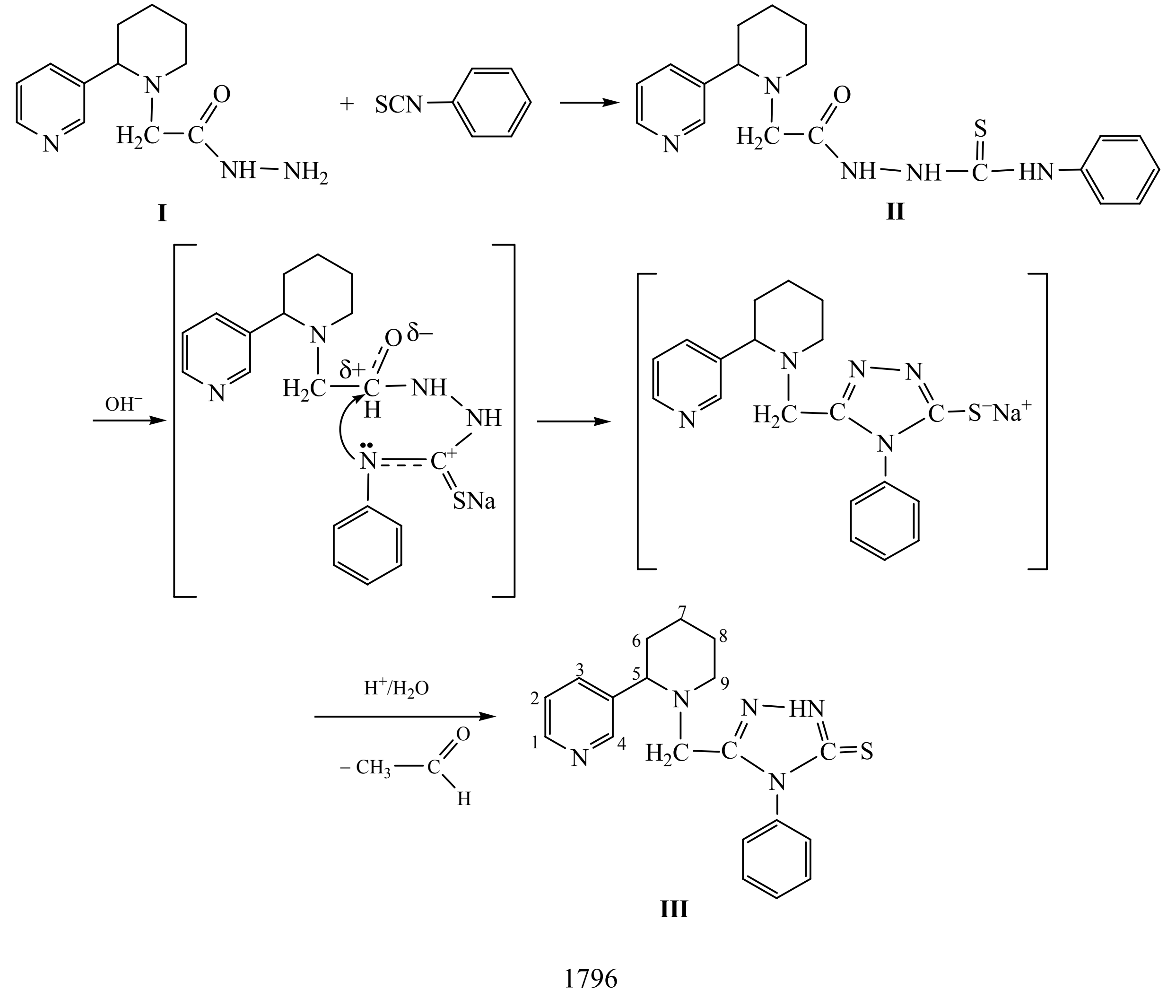
One of the promising directions in screening of the new potentially antibacterial derivatives of alkaloid anabasine is preparation of its thiosemicarbazide derivatives, since they are known for a wide range of biological activity [1].

Extending the study on modification of anabasine [2], we synthesized *N*-anabasinylacetic acid *N*-phenylthiosemicarbazide **II** by interaction of *N*-anabasinylacetic acid hydrazide **I** with phenylisothiocyanate in ethanol, having achieved the yield of 74%.



Acidification of aqueous alkaline solution of the prepared phenylthiocarbazide derivative **II** led to its intramolecular heterocyclization to form 4-phenyl-5-anabasinomethyl-1,2,4-triazole-3-thione **III**.

Compounds **II** and **III** were white crystalline solids, soluble in many polar and nonpolar organic solvents. Composition and structure of **II** and **III** were confirmed by elemental analysis, IR and ^{1}H NMR spectroscopy.

The initial *N*-anabasinylacetic acid hydrazide **I** was obtained as described in [3].

***N*-Anabasinylacetic acid *N*-phenylthiosemicarbazide (II).** 1.35 g (0.011 mol) of phenylisothiocyanate was added to a solution of 2.34 g (0.01 mol) of the *N*-anabasinylacetic acid hydrazide in 10 ml of 2-propanol. The mixture was refluxed at 50–60°C for 10 h. The reaction progress was monitored by TLC. After cooling down, the appeared white crystalline precipitate was filtered off, washed with small amount of cold 2-propanol, and recrystallized from 2-propanol. Yield 2.73 g (74%), mp 100–102°C. IR spectrum, ν, cm^{-1}: 3279, 3272, 3106 (NH), 1660 (C=O), 1510–1590 (NH-Ar), 1270 (C=S). ^{1}H NMR, δ, ppm (*J*, Hz): 1.25–1.70 m (6H, H^6, H^7, H^8), 2.96 t (1H, H^5, *J* 14.04), 8.36 d.d (1H, H^2, *J* 1.68), 8.60 s (1H, H^4), 7.46 d (1H, H^3, *J* 7.8), 8.51 d.d (1H, H^1, *J* 1.65), 7.33 s (2H, CH$_2$), 10.40 s [1H, NH(C=O)], 9.80 s (1H, NH), 13.72 s [1H, N$\underline{H}$(C=S)], 7.00–7.80 m (5H, Ar). Found, %: C 61.76; H 6.27; N 18.95. $C_{19}H_{23}N_5OS$. Calculated, %: C 61.89; H 6.31; N 18.99.

4-Phenyl-5-anabasinomethyl-1,2,4-triazole-3-thione (III). 3.69 g (0.01 mol) of *N*-anabasinylacetic acid *N*-phenylthiosemicarbazide **II** was added to the aqueous alkaline solution of 0.40 g (0.01 mol) of NaOH in 30 ml of distilled water. The reaction mixture was heated at 85°C for 2 h. After cooling, the mixture was neutralized with hydrochloric acid to pH 6–7. The formed precipitate was filtered off and recrystallized from 2-propanol. Yield 1.40 g (40%), milky powder, mp 135–136°C. IR spectrum, ν, cm^{-1}: 1619 (C=N), 1270 (C=S). ^{1}H NMR spectrum (500 MHz), δ, ppm (*J*, Hz): 1.20–1.65 m (6H, H^6, H^7, H^8), 2.96 t (1H, H^5, *J* 14.04), 7.07 d.d (1H, H^2, *J* 4.78), 8.14 d.d (1H, H^4, *J* 1.86), 7.22 d (1H, H^3, *J* 7.28), 8.36 d.d (1H, H^1, *J* 4.73), 7.36 s (2H, CH$_2$), 13.73 s (1H, NH), 7.54–7.62 m (5H, Ar). Found, %: C 64.93; H 6.02; N 19.93. $C_{19}H_{21}N_5S$. Calculated, %: C 65.09; H 6.29; N 20.11.

IR spectra were recorded with Nicolet AVATAR-320 Fourier-spectrometer in KBr pellets. The ^{1}H NMR spectra were recorded with Bruker DRX500 spectrometer (500 MHz) in DMSO-d_6; TMS was used as internal standard. TLC analysis was performed on Sorbfil plates using isopropyl alcohol–benzene–ammonia mixture (10:5:2) as eluent and detection with iodine vapors. Melting points were determined with Boetius apparatus.

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