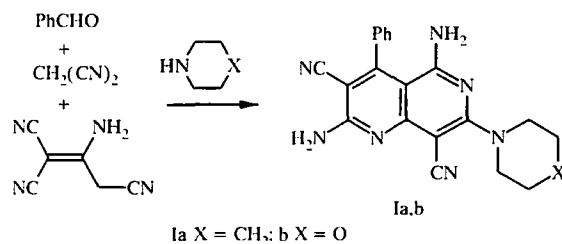


SYNTHESIS OF 1,6-NAPHTHYRIDINES CONTAINING A CYCLIC AMINE RESIDUE USING THE CASCADE HETEROCYCLIZATION METHOD

S. V. Roman, V. D. Dyachenko, and V. P. Litvinov

The only known method for introduction of cyclic amine residues into naphthyridine molecules is substitution of the chlorine or, less commonly, bromine atoms by reaction with cyclic amines. Many of the derivatives obtained by this method show significant pharmacological activity [1].

We have shown for the first time that multi-component condensation (refluxing in ethanol for 6 h) of benzaldehyde with malononitrile and its dimer in the presence of a twofold excess of piperidine or morpholine gives the previously unknown 1,6-naphthyridines Ia,b. Hence, in a single stage process, there occurs not only the construction of the naphthyridine system but also the introduction into it of a saturated nitrogen heterocyclic residue. Refinement of the process scheme, including the formation of likely intermediates, is the subject of further investigations.



2,5-Diamino-3,8-dicyano-4-phenyl-7-piperidino-1,6-naphthyridine (Ia). Yield 63%; mp 225-227°C (decomp.). IR spectrum (vaseline oil): 3250, 3360, 3375, 3420 (NH₂), 2215 (CN), 1625, 1658 cm⁻¹ (δ_{NH₂}). PMR spectrum (DMSO-d₆): 8.21 (2H, br. s, NH₂); 7.46 (5H, m, H_{Ph}); 6.85 (2H, br. s, NH₂); 3.00 (4H, t, J = 6.7 Hz, CH₂NCH₂); 1.57 ppm (6H, m, CH₂CH₂CH₂). Found, %: C 68.15; H 5.24; N 26.61. C₂₁H₁₉N₇. Calculated, %: C 68.27; H 5.18; N 26.55.

2,5-Diamino-3,8-dicyano-7-morpholino-4-phenyl-1,6-naphthyridine (Ib). Yield 76%; mp 251-253°C (decomp.). IR spectrum (vaseline oil): 3210-3400 (NH₂), 2205 (CN), 1610, 1645 (δ_{NH₂}). PMR spectrum (DMSO-d₆): 8.65 (2H, br. s, NH₂); 7.45 (5H, m, H_{Ph}); 6.84 (2H, br. s, NH₂); 3.75 (4H, t, J = 6.7 Hz, CH₂OCH₂); 3.09 ppm (4H, t, J = 6.7 Hz, CH₂NCH₂). Found, %: C 64.78; H 4.50; N 26.53. C₂₀H₁₇N₇O. Calculated, %: C 64.47; H 4.62; N 26.40.

REFERENCES

1. A. S. Noravyan, E. G. Paronikyan, and S. A. Vartanyan, *Khim.-Farm. Zh.*, **19**, 790 (1985).

Taras Shevchenko Pedagogical State University, Lugansk 348011, Ukraine; e-mail: kgb@lpgi.lugansk.ua.
N. D. Zelinsky Institute for Organic Chemistry, Moscow 117913, Russia; e-mail: vpl@cacr.ioc.ac.ru. Translated from *Khimiya Geterotsiklicheskih Soedinenii*, No. 10, pp. 1435-1436, October, 1999. Original article submitted July 27, 1999.