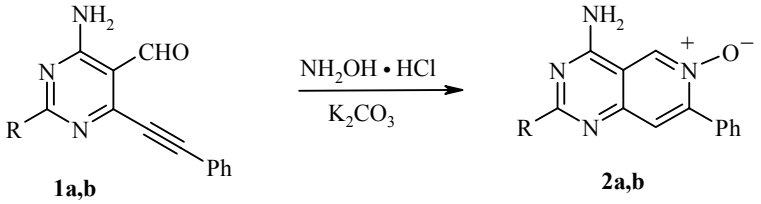
SYNTHESIS OF 4-AMINO-7-PHENYLPYRIDO[4,3-*d*]PYRIMIDINE 6-OXIDES

N. Cikotiene, R. Buksnaitiene, and A. Brukstus

Keywords: arylethynylpyrimidines, pyrido[4,3-*d*]pyrimidines, cyclization

Recently some alkylderivatives were synthesized in our laboratory and their use for obtaining pyrrole[3,2-*d*]pyrimidine 7-oxides [1,2] and pyrido[4,3-*d*]pyrimidines [3] respectively was demonstrated. In a continuation of investigations in this direction, we have discovered a previously unknown simple synthesis for 4-amino-7-phenylpyrido[4,3-*d*]pyrimidine 6-oxides. These compounds may serve as excellent synthons for polysubstituted pyrido[4,3-*d*]pyrimidines which are exciting interest because of their biological activity [4-6].

Boiling 6-(phenylethynyl)pyrimidine-5-carbaldehydes **1a,b** with hydroxylamine hydrochloride in the presence of potassium carbonate in an ethanol–water mixture led to the formation of 4-amino-7-phenylpyrido[4,3-*d*]pyrimidine 6-oxides **2a,b** in yields of 90 and 82% respectively.



1a,b **2a,b**

1, 2 **a** R = SCH_3, **b** R = NH_2

IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum BX II, while ^1H and ^{13}C NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded with a Varian Unity Inova spectrometer (300 and 75 MHz, respectively).

The 4-amino-6-(phenylethynyl)pyrimidine-5-carbaldehydes starting materials **1a,b** were synthesized as reported in [3].

4-Amino-2-methylthio-7-phenylpyrido[4,3-*d*]pyrimidine 6-oxide (2a). A solution of 4-amino-2-methylthio-6-(phenylethynyl)pyrimidine-5-carbaldehyde **1a** (0.2 g, 0.74 mmol), hydroxylamine hydrochloride (0.06 g, 0.86 mmol), and potassium carbonate (0.057 g, 0.37 mmol) in 50% ethanol (10 ml) was boiled for 10 h, cooled, and the precipitate was filtered and recrystallized from an ethanol–water mixture to give compound **2a** (0.21 g, 90%), mp 260°C. IR spectrum (nujol), ν, cm^{-1}: 3324, 3305 (NH_2), 1242 (NO). ^1H NMR spectrum, δ, ppm: 2.50 (3H, s, SCH_3); 7.46-7.48 (3H, m, ArH); 7.52 (1H, s, CH); 7.79-7.83 (2H, m, ArH); 8.05 (2H, br. s, NH_2); 9.34 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 13.2, 109.5, 122.6, 127.4, 129.1, 129.2, 132.2, 134.4, 146.0, 151.8, 157.6, 170.3. Found, %: C 58.99; H 4.15; N 19.79. $C_{14}H_{12}N_4OS$. Calculated, %: C 59.14; H 4.25; N 19.70.

Department of Organic Chemistry, Vilnius University, Vilnius LT-03225, Lithuania; e-mail: inga.cikotiene@chf.vu.lt. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, 619-620, April, 2007. Original article submitted November 3, 2006

0009-3122/07/4304-0515

2,4-Diamino-7-phenylpyrido[4,3-*d*]pyrimidine 6-oxide (2b) was synthesized analogously to compound **2a**, recrystallized from a 2-propanol–DMSO mixture; yield 82%, mp >300°C. IR spectrum (nujol), ν, cm^{-1}: 3402, 3385, 3324, 3305 (NH_2), 1243 (NO). ^1H NMR spectrum, δ, ppm: 6.89 (2H, br. s, NH_2); 7.42-7.45 (3H, m, ArH); 7.53 (1H, S, CH); 7.82-7.86 (2H, m, ArH); 8.10 (2H, br. s, NH_2); 9.18 (1H, s, CH). Found, %: C 61.58; H 4.61; N 27.70. $C_{13}H_{11}N_5O$. Calculated, %: C 61.65; H 4.38; N 27.65.

REFERENCES

1. I. Susvilo, A. Brukstus, S. Tumkevicius, *Synlett.,* 1151 (2003).
2. S. Tumkevicius and I. Susvilo, *Khim. Geterotsikl. Soedin.,* 1546 (2004). [*Chem. Heterocycl. Comp.,* **40**, 1335 (2004)].
3. I. Susvilo, R. Palskite, S. Tumkevicius, and A. Brukstus, *Khim. Geterotsikl. Soedin.,* 298 (2005). [*Chem. Heterocycl. Comp.,* **41**, 268 (2004)].
4. A. M. Thompson, D. K. Muray, W. L. Eliot, D. W. Fry, J. A. Nelson, H. D. Showalter, B. J. Roberts, P. W. Vincent, and W. A. Denny, *J. Med. Chem.,* **40,** 3915 (1997).
5. J. B. Smail, B. D. Palmer, G. W. Rewcastle, W. A. Denny, D. J. McNamara, E. M. Dobrusin, A. J. Bridges, H. Zhou, H. D. H. Showalter, R. T. Winters, W. R. Leopold, D. W. Fry, J. M. Nelson, V. Slintak, W. L. Elliot, B. J. Roberts, P. W. Vincent, S. J. Patmore, *J. Med. Chem*., **42**, 1803 (1999).
6. M. D. Meyer, R. J. Altenbach, H. Bai, F. Z. Basha, W. A. Carroll, J. F. Kerwin, S. A. Lebold, E. Lee, J. K. Pratt, K. B. Sippy, K. Tietje, M. D. Wendt, M. E. Brune, S. A. Bruckner, A. A. Hancock, and I. Drizin, *J. Med. Chem.,* **44,** 1971 (2001).