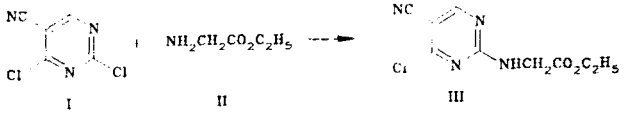
SYNTHESIS OF ETHYL ESTER OF N-(4-CHLORO-5-CYANO-2-PYRIMIDINYL)-AMINOACETIC ACID

S. P. Tumkyavichyus and Yu. P. Karmalavichyute

UDC 547.853

It is known that in the reactions of 2,4-dichloropyrimidines having electron-acceptor groups at the 5-position with amines, the substitution of the chlorine atom at the 4-position predominates and 4-amino derivatives of pyrimidine are formed [1-3]. We have found that in the reaction of 2,4-dichloropyrimidine-5-carbonitrile (I) with ethyl aminoacetate (II) in a mixture of an aqueous solution of sodium bicarbonate and chloroform, the chlorine atom is substituted at the 2-position of the pyrimidine ring and the ethyl ester of N-(4-chloro-5-cyano-2-pyrimidinyl)acetic acid (III) is formed. The formation of the isomeric ethyl ester of N-(2-chloro-5-cyano-4-pyrimidinyl)aminoacetic acid was not detected.



I II III

The hydrochloride of compound II (1.15 g, 8.3 mmoles) is added in portions, with stirring, to a mixture of 1.0 g (5.8 mmoles) of compound I [4], 8 ml of chloroform and 14 ml of a saturated solution of $NaHCO_3$. The mixture is stirred for 30 min at 20°C, the chloroform layer is separated, and 0.98 g (71%) of compound III are obtained, mp 128-129°C (from ethanol). PMR spectrum (DMSO-D_6): 1.4 (3H, t, (CH_3), 4.17-4.55 (4H, m, NCH_2 + OCH_2), 8.9 (1H, s, 6-H), 9.25 ppm (1H, t, NH). IR spectrum (in mineral oil): 1745 (C=O), 2240 (C≡N), 3280 cm^{-1} (NH). To confirm the structure of compound III, the methyl esters of N-(4-methylthio-5-cyano-2-pyrimidinyl)- and N-(2-methylthio-5-cyano-4-pyrimidinyl)aminoacetic acids (IV, V) were synthesized by independent methods. Compound IV was obtained from ethyl ester III and CH_3SNa in a methanol solution, The isomeric ester V was synthesized by reacting methyl aminoacetate with 2-methylthio 4-chloropyrimidines-5-carbonitrile, obtained by the method in [5] from 3,4-dihydro-2-methylthio-4-oxopyrimidine-5-carbonitrile and $POCl_3$.

Compound IV. Yield 57%, mp 167-169°C (from methanol). PMR spectrum (CF_3COOH): 2.25 (3H, s, SCH_3), 3.47 (3H, s, OCH_3), 4.10 (2H, d, CH_2), 7.97 (1H, s, CH), 8.35 ppm (1H, br.s, NH). IR spectrum (KBr): 890, 907, 973, 1021, 1099, 1113, 1133, 1227, 1279, 1320, 1370, 1383, 1723 (C=O), 2217 (C=N), 3427 cm^{-1} (NH).

Compound V. Yield 63%, mp 168-169°C (from methanol). PMR spectrum (CF_3COOH): 2.27 (3H, s, SCH_3), 3.45 (3H, s, OCH_3), 4.17 (2H, d, CH_2), 7.90 (1H, br.s, NH, 8.07 ppm (1H, s, CH). IR spectrum (KBR): 930, 970, 1093, 1143, 1187, 1233, 1247, 1273, 1300, 1313, 1360, 1380, 1400, 1720 (C=O), 2217 (C N), 3367 cm^{-1} (NH). The IR and PMR spectra of compounds IV and V are not identical, which confirms the structure of compound III.

The data of the elemental analysis of compounds III-V correspond to the calculated ones.

LITERATURE CITED

1. I. V. Bol'dyrev, O. M. Polubrik, L. N. Markovskii, and V. M. Cherkasov, Khim. Geterotsokl. Soedin., No. 11, 1545 (1980).
2. A. Albert and J. Clark, J. Chem. Soc., No. 5, 1666 (1964).
3. M. Pesson, M. Antoine, S. Chabassier, S. Geiger, P. Girard, D. Richer, P. Lajudie, E. Horvath, B. Leriche, and S.Pathe, Eur. J. Med. Chem., 9, 591 (1974).
4. E. F. Godefroi, J. Org. Chem., 27, 2264 (1962).
5. A. A. Santilli, D. H. Kim, and S. Wanser, J. Heterocycl. Chem., 8, 445 (1971).

V. Kapsukas Vil'nyus State University, Vil'nyus 232734. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, p. 560, April, 1988. Original article submitted April 2, 1986; revision submitted September 29, 1987.

0009-3122/88/2404-0465$12.50