3-AMINO-2-CARBAMOYL-4,6-DIPHENYL-4,5- AND -4,7-DIHYDROTHIENO-[2,3-b]PYRIDINES

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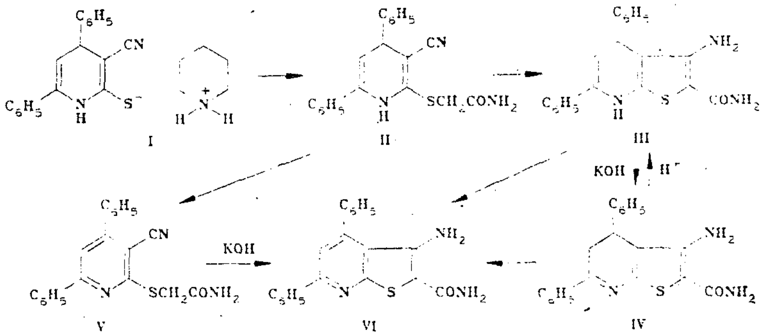
UDC 547.735'825'828.07:542.422.25

The treatment of piperidinium salts of 3-cyano-1,4-dihydropyridine-2-thiols with alkyl halides leads to 2-alkylthio-3-cyano-1,4-dihydropyridines [1]. We have shown that alkylation of the piperidinium salt (I) of 4,6-diphenyl-3-cyano-1,4-dihydropyridine-2-thiol with iodoacetamide gives carbamoylmethylthio derivative II, which, by the action of an equimolar amount of a base with heating to 50-60°C, gives a mixture of 3-amino-2-carbamoyl-4,6-diphenyl-4,7-dihydrothieno[2,3-b]pyridine (III) and 3-amino-2-carbamoyl-4,6-diphenyl-4,5-dihydrothieno[2,3-b]-pyridine (IV) in a ratio of 1:1. In the presence of excess base the principal product is IV. It was established by PMR spectroscopy that dihydropyridine II initially undergoes cyclization to 4,7-dihydrothienopyridine III, which then undergoes isomerization to 4,5-dihydrothienopyridine IV. Acidification of a solution of IV in d_6-DMSO gives rise to reverse isomerization. Thus facile interconversions of 1,4- and 3,4-dihydropyridines have been demonstrated for the first time in the case of condensed derivatives of pyridine.



As compared with 4,5-dihydrothienopyridine IV, 4,7-dihydrothienopyridine III is easily oxidized to the known 3-amino-2-carbamoyl-4,6-diphenylthieno[2,3-b]pyridine (VI) [2], which was also obtained by cyclization of 2-carbamoylmethylthio-4,6-diphenyl-3-cyanopyridine (V) by sodium hydroxide. Compound V is readily formed by oxidation of dihydropyridine II with sodium nitrite.

Compound II. This compound, with mp 187-189°C (from ethanol) was obtained in 79% yield. IR spectrum: 1668 (C=C), 1695 (C=O), 2198 (C≡N), 3190, 3360 cm^{-1} (NH and NH$_2$). PMR spectrum (d_6-DMSO): 10.23 (1H, broad s, NH), 8.00 and 7.69 (2H, broad s, CONH$_2$), 7.2-7.6 (10H, m, 2C$_6$H$_5$), 3.80 and 3.64 (1H each, d, J = 15.0 Hz, SCH$_2$), 5.16 (1H, d, J = 5.0 Hz, 5-H), 4.38 ppm (1H, d, J = 5.0 Hz, 4-H).

Compound III. PMR spectrum (d_6-DMSO): 9.06 (1H, broad s, NH), 6.38 (2H, broad s, CONH$_2$), 5.98 (2H, broad s, 3-NH$_2$), 7.1-8.0 (10H, m, 2C$_6$H$_5$), 5.03 (1H, d, J = 5.0 Hz, 5-H), 4.38 ppm (1H, d, J = 5.0 Hz, 4-H).

Compound IV. This compound, with mp 194-196°C (from ethanol), was obtained in 83% yield. IR spectrum: 1645 (C=O), 3180-3440 cm^{-1} (NH$_2$). PMR spectrum (d_6-DMSO): 7.1-8.0 (10H, m, 2C$_6$H$_5$), 6.90 (2H, broad s, CONH$_2$), 6.42 (2H, broad s, 3-NH$_2$), 4.36 (1H, dd, J = 1.6 and 9.2 Hz, 4-H), 3.54 and 3.12 ppm (1H each, J = 17.6 Hz and 1.6 Hz, J = 17.6 Hz and 9.2 Hz, 5-CH$_2$). The results of elementary analysis of the substances were in agreement with the calculated values.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 563-564, April, 1987. Original article submitted October 10, 1986.

0009-3122/87/2304-0472$12.50

LITERATURE CITED

1. A. A. Krauze, Yu. É. Pelcher, Z. A. Kalme, and G. Ya. Dubur, Khim. Geterotsikl. Soedin., No. 8, 1140 (1984).
2. A. M. Shestopalov and Yu. A. Sharanin, Zh. Org. Khim., 20, 1991 (1984).