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REGIOSELECTIVE HETEROCYCLIZATION OF PHOSPHORYL-α-CHLOROACETALDEHYDES WITH 2,3-DIAMINOPYRIDINE

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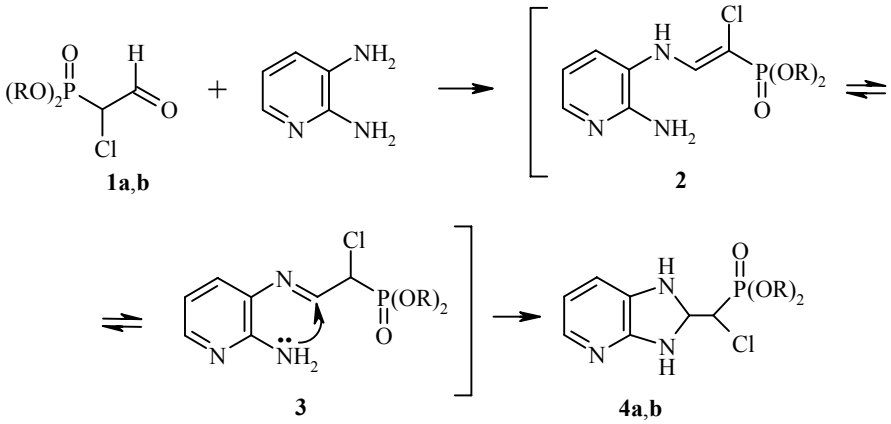
The heterocyclization of phosphoryl-α-chloroacetaldehydes **1a** and **1b** with 2,3-diaminopyridine, in contrast to the reaction of other α-halocarbonyl compounds [1-4], proceeds regioselectively with involvement of the aldehyde fragment and both amino groups to give 2-(dialkoxyphosphorylchloro)methylimidazolidino[4,5-*b*]-pyridines **4a** and **4b** in 69-73% yield.



1, **4 a** R = Et, **b** R = *i*-Pr

Enamine **2** is probably formed in the first step as the result of attack of the more nucleophilic amino group at the aldehyde fragment and exists in the imine tautomeric form **3**. Stabilization of imine **3** may proceed through three pathways: a) attack of the exocyclic nitrogen atom at the chloromethine group but this is excluded due to the large separation between the reaction sites; b) attack of the amino group at the chloromethine group but this pathway is also unlikely due to the low nucleophilicity of the NH_2 group, and c) addition of the amino group at the imine fragment. The strong electrophilicity of the imine carbon atom facilitates addition of the amino group and leads to formation of the imidazolidino ring.

The structure of phosphonates **4a** and **4b** was indicated by ^{1}H NMR spectroscopy on a Tesla BW-567 spectrometer and ^{31}P NMR spectroscopy on a Bruker WP-80 spectrometer at 32 MHz.

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2-(Diethoxyphosphorylchloro)methylimidazolidino[4,5-*b*]pyridine (4a). A solution of aldehyde **1a** (1.07 g, 5 mmol) in ether (10 ml) was added with rapid stirring to a suspension of 2,3-diaminopyridine (0.545 g, 5 mmol) in ether (20 ml) cooled to from -5° to -10°C. The reaction mixture was stirred with cooling for 3 h. Then, the solvent was removed and heterocycle **4a** was separated as a brown oil. Yield of **4a** 1.05 g (69%). IR spectrum, ν, cm^{-1}: 1260 (P=O), 3300 (NH). ^{31}P NMR spectrum: 11.2 ppm. ^{1}H NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.25 (6H, t, $2CH_3$); 3.70 (1H, q, $2COCH_2$); 4.25 (1H, q, CH); 6.00 (2H, br. s, 2NH); 6.50 (1H, dd, 6-H); 7.00 (1H, dd, 7.45 (1H, d, 5-H). Found, %: Cl 11.58; N 13.77; P 10.09. $C_{11}H_{17}ClN_3O_3P$. Calculated, %: Cl 11.62; N 13.75; P 10.15.

2-(Diisopropoxyphosphorylchloro)methylimidazolidino[4,5-*b*]pyridine (4b) was obtained analogously as an oil from aldehyde **1b** (1.22 g, 5 mmol) and 2,3-diaminopyridine (0.548 g, 5 mmol). Yield of **4b** 1.23 g (73%). ^{31}P NMR spectrum: 11.8 ppm. ^{1}H NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.30 (12H, d, $4CH_3$); 3.80 (1H, q, CHCl); 4.25 (1H, q, CH); 4.75 (1H, m, 2COCH); 5.90 (2H, br. s, 2NH); 6.50 (1H, dd, 7-H); 7.40 (1H, d, 5-H). Found, %: Cl 10.61; N 12.65; P 9.25. $C_{13}H_{21}ClN_3O_3P$. Calculated, %: Cl 10.64; N 12.59; P 9.29.

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