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# REACTION OF CHLORO-DIALKOXYPHOSPHORYL-ACETALDEHYDES WITH 2-AMINOPYRIDINES

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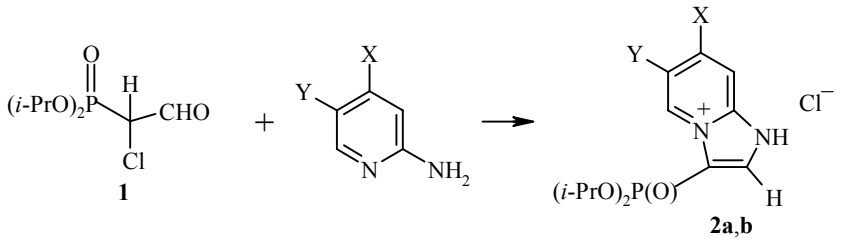
**Keywords:** 2-aminopyridine, 3-phosphorylimidazo[1,2-*a*]pyridine, chlorophosphorylacetaldehydes, hemiaminals.

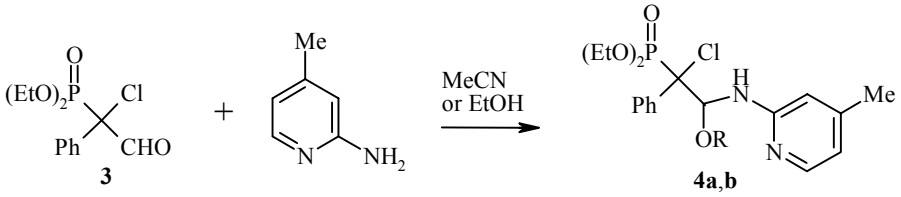
We have discovered that the reactions of chlorophosphorylacetaldehydes **1** and **3** with substituted 2-aminopyridines lead to various products, depending on the structure of the aldehyde.

The reactions of chloro aldehyde **1** with 2-aminopyridine lead to heterocyclization and formation of the 3-phosphorylimidazo[1,2-*a*]pyridines hydrochlorides **2a** and **2b** in 80-85% yield.




**2 a** X = Me, Y = H; **b** X = H, Y = Cl

We have previously shown that phenylphosphoryl aldehydes **3** react with nitrogen- and sulfur-containing bi- and polyfunctional nucleophilic reagents and undergo heterocyclization [1]. However, the expected heterocyclization in the reaction of chlorophenylphosphorylacetaldehyde **3** with 2-amino-4-methylpyridine in acetonitrile or ethanol does not occur. The reaction proceeds only at the aldehyde group and leads to hemiaminals **4a** and **4b**.




**4 a** R = H; **b** R = Et

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The structures of **4a** and **4b** were demonstrated by $^{1}H$ and $^{31}P$ NMR spectroscopy and confirmed by X-ray diffraction structural analysis. The results of the X-ray diffraction study will be published separately.

**3-Diisopropoxyphosphoryl-6-methylimidazo[1,2-*a*]pyridine Hydrochloride (2a).** A mixture of aldehyde **1** (0.49 g, 2 mmol) and 2-amino-4-methylpyridine (0.22 g, 2 mmol) in ethanol (30 ml) was heated at reflux for 10 h. The solvent was evaporated and 10 ml 1:1 acetonitrile–ether was added. The crystalline precipitate was filtered off and recrystallized from acetonitrile to give 0.54 g (80%) **2a**; mp 144-145°C. IR spectrum, ν, $cm^{-1}$: 1280, 1635, 3300. $^{31}P$ NMR spectrum, δ, ppm: 10.5. $^{1}H$ NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.10 (12H, t, $4CH_3$); 2.30 (3H, s, $CH_3$); 4.70 (2H, m, 2OCH); 6.80 (1H, d, 5-H); 6.90 (1H, br. s, NH); 7.00 (1H, d, 7-H); 8.10 (1H, d, 4-H); 8.60 (1H, d, =CH–). Found, %: Cl 10.43; N 8.77; P 9.32. $C_{14}H_{22}ClN_2O_3P$. Calculated, %: Cl 10.67; N 8.42; P 9.32.

**5-Chloro-3-diisopropoxyphosphorylimidazo[1,2-*a*]pyridine Hydrochloride (2b)** was obtained analogously in 85% yield; mp 177-179°C (acetonitrile). IR spectrum, ν, $cm^{-1}$: 1280, 1640, 3300. $^{31}P$ NMR spectrum, δ, ppm: 10.53. $^{1}H$ NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.20 (12H, t, $4CH_3$); 2.30 (3H, s, $CH_3$); 4.70 (2H, m, 2OCH); 6.80 (1H, d, 7-H); 7.00 (1H, br. s, NH); 7.60 (1H, dd, 6-H); 8.20 (1H, d, 4-H); 8.30 (1H, d, =CH–). Found, %: Cl 19.45; N 9.25; P 8.78. $C_{13}H_{19}Cl_2N_3O_3P$. Calculated, %: C 20.11; N 7.93; P 8.78.

**Diethyl Ester of 1-Chloro-2-hydroxy-2-(4-methyl-2-pyridyl)amino-1-phenylethylphosphonic Acid (4a).** A mixture of aldehyde **3** (0.58 g, 2 mmol) and 2-amino-4-methylpyridine (0.22 g, 2 mmol) in acetonitrile (20 ml) was heated at reflux for 10 h. The solvent was evaporated. The precipitate was recrystallized from ethanol to give 0.66 g (82%) **4a**; mp 136-137°C. IR spectrum, ν, $cm^{-1}$: 1285, 3200, 3340. $^{31}P$ NMR, δ, ppm: 18.35, 18.47. $^{1}H$ NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.15 (6H, m, $2CH_3$); 2.10 (3H, d, $CH_3$); 4.00 (4H, m, $2OCH_2$); 5.20 (1H, d, OCH); 6.50 (1H, d, 5-H); 6.90 (1H, br. s, NH); 7.30 (1H, d, 3-H); 7.75 (5H, m, Ph); 7.90 (1H, d, 6-H); 9.80 (1H, br. s, OH). Found, %: Cl 8.86; N 7.08; P 7.75. $C_{18}H_{24}ClN_2O_4P$. Calculated, %: Cl 8.91; N 7.03; P 7.78.

**Diethyl Ester of 1-Chloro-2-ethoxy-2-(4-methyl-2-pyridyl)amino-1-phenylethylphosphonic Acid (4b).** A mixture of aldehyde **3** (0.58 g, 2 mmol) and 2-amino-4-methylpyridine (0.22 g, 2 mmol) in ethanol (30 ml) was heated at reflux for 12 h. The solvent was evaporated and 10 ml 1:1 ether–hexane was added to the reaction mixture. The precipitate formed was filtered off and recrystallized from acetonitrile to give 0.74 g (87%) **4b**; mp 140-142°C. IR spectrum, ν, $cm^{-1}$: 1150, 1280, 3200. $^{31}P$ NMR spectrum, δ, ppm: 17.2, 18.1. $^{1}H$ NMR spectrum ($(CD_3)_2CO$), δ, ppm: 1.10 (9H, m, $3CH_3$); 2.20 (3H, d, $CH_3$); 4.00 (6H, m, $3OCH_2$); 5.30 (1H, d, OCH); 6.50 (1H, d, 5-H); 6.80 (1H, br. s, NH); 7.30 (1H, d, 3-H); 7.70 (5H, m, Ph); 7.90 (1H, d, 6-H). Found, %: Cl 8.34; N 6.61; P 7.32. $C_{20}H_{28}ClN_2O_4P$. Calculated, %: Cl 8.32; N 6.56; P 7.27.

## REFERENCES

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