SIMPLE METHOD FOR THE SYNTHESIS OF BICYCLIC PYRIDINE BASES FROM 1-ETHYNYLCYCLOALKANOLS AND CARBOXYLIC ACID CHLORIDES

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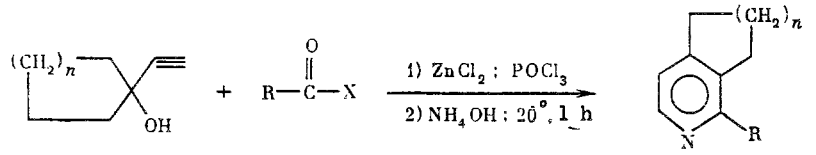
Recently we proposed an original method for the synthesis of trisubstituted pyridines by the condensation of the acyclic ethynylcarbinols or vinylacetylenes with carboxylic acid chlorides in the presence of zinc chloride and ammonia [1]. We found that if the acylic acetylenes in this reaction are replaced by cyclic ethynylcarbinols it is possible to obtain 2-alkyl-3,4-cycloalkenopyridines, the synthesis of which by other methods is fairly complicated. The highest yields of the 2-alkyl(aryl)-3,4-cycloalkenopyridines from ethynylcarbinols and carboxylic acid chlorides were obtained with the two-component $ZnCl_2 - POCl_3$ catalyst. When promoting additions of titanium tetrachloride and aluminum chloride were used, the yields of the respective pyridines were not greater than 10-15%.

Thus, for example, in the reaction of 1-ethynylcyclopentanol with acetyl chloride in the presence of the $ZnCl_2 - POCl_3$ (1:1) catalyst under mild conditions (20°C, 1 h) with subsequent treatment of the mixture with ammonium hydroxide at 0°C the 2-methyl-3,4-cyclopentenopyridine (I) is formed with high selectivity and with an overall yield of ~55%. The replacement of acetyl chloride by acetyl bromide and acetyl iodide increases the yield of (I) to ~85 and 93%, respectively. Butyryl and valeryl acid chlorides react similarly, giving the pyridines (II) and (III) with yields of 47 and 50%.

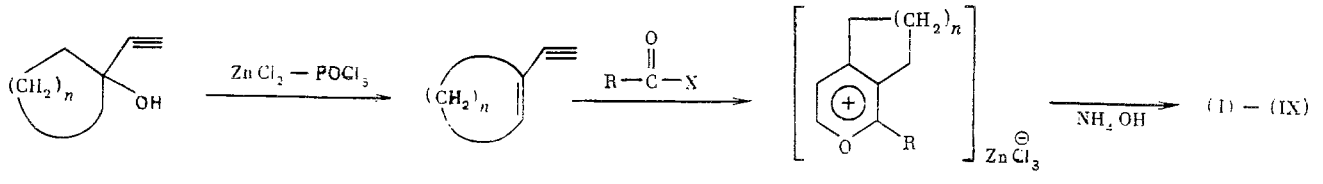


(I) — (IX)

X = Cl, Br, I; $n = 1$, R = Me (I); $n = 1$, R = Pr (II); $n = 1$, R = Br (III); $n = 2$, R = Me (IV); $n = 2$, R = *i*-Bu (V); $n = 2$, R = Bu (VI); $n = 3$, R = Me (VII); $n = 3$, R = *i*-Bu (VIII); $n = 3$, R = Bu (IX).

Fairly high yields of the 2-alkyl-3,4-cycloalkenopyridines (IV)-(IX) (40-50%) were obtained in the reaction of 1-ethynylcyclohexanol or 1-ethynylcycloheptanol with the acid chlorides of C_2-C_5 aliphatic carboxylic acids. In the transition to the bromides and iodides of the respective carboxylic acids the pyridines (IV)-(IX) can be obtained with yields of not less than 75%.

Analysis of published data [2-6] and of our own results made it possible to conclude that the formation of the molecules of the bicyclic pyridines (I)-(IX) from ethynylcarbinols and carboxylic acid halides takes place through the formation of pyrylium salts, which are converted into compounds (I)-(IX) when treated with ammonium hydroxide, according to the following scheme:



The developed method for the synthesis of bicyclic pyridines by the condensation of cyclic ethynylcarbinols with carboxylic acid halides in the presence of equimolar amounts

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of $ZnCl_2-POCl_3$ have opened up a new, simple and effective method for the synthesis of difficultly obtainable pyridine bases.

EXPERIMENTAL

The substituted cyclic ethynylcarbinols with ~99% purity were obtained according to [7]. The products were analyzed on a Chrom 41 chromatograph with a flame-ionization detector (column length 1.2 m, 15% of Apiezon on Zeolite 545, nitrogen — carrier gas). The PMR spectra were recorded on a Tesla BS-467 instrument at 60 MHz in deuterochloroform. The mass spectra were obtained on a MX-1306 instrument of 70 eV with the ionization chamber at 200°C.

General Procedure for the Synthesis of Cycloalkenopyridines in the Presence of $ZnCl_2-POCl_3$. In a round-bottomed flash provided with a reflux condenser and a thermometer we placed 0.8 mole of the respective aliphatic carboxylic acid chloride, 0.1 mole of zinc chloride, and 0.1 mole of phosphorus oxychloride. While continuously stirring and cooling (to 0°C), we slowly added dropwise 0.1 mole of the cyclic ethynylcarbinol. The temperature of the reaction mass was raised to 35-40°C, and it was then cooled to 20°C. The warmed dark-brown reaction mass was stirred at about 20°C for 1 h. The obtained catalyzate was added slowly to ammonium hydroxide (a 23% solution) which had been cooled to 0°C. The product was extracted with ether (3 × 100 ml), and the extract was dried with anhydrous magnesium sulfate. After removal of the solvent the residue was placed in a column of aluminum oxide and eluted with a 5:1 mixture of ether and hexane.

2-Methyl-3,4-cyclopentenopyridine (I). Bp 143°C (14 mm Hg); n_D^{20} 1.5720. PMR spectrum (δ, ppm): 2.08 m (2H, CH_2), 2.30 s (3H, CH_3), 2.78 m (4H, CH_2), 6.78 d (1H, CH), 8.03 d (1H, CH). M^+ 133. Found %: C 81.10; H 8.3; N 10.6. $C_9H_{11}N$. Calculated %: C 81.20; H 8.27; N 10.53.

2-Propyl-3,4-cyclopentenopyridine (II). Bp 174°C (15 mm Hg); n_D^{20} 1.6320. PMR spectrum (δ, ppm): 0.83 t (3H, CH_3), 1.67-2.08 m (6H, CH_2), 2.75 m (4H, CH_2), 6.75 d (1H, CH), 8.08 d (1H, CH). M^+ 161. Found %: C 81.98; H 9.30; N 8.72. $C_{11}H_{15}N$. Calculated %: C 81.99; H 9.32; N 8.70.

2-Butyl-3,4-cyclopentenopyridine (III). Bp 120°C (12 mm Hg); n_D^{20} 1.6015. PMR spectrum (δ, ppm): 0.98 t (3H, CH_3), 1.55-2.08 m (6H, CH_2), 2.75-2.78 m (6H, CH_2), 6.75 d (1H, CH), 8.08 d (1H, CH). M^+ 175. Found %: C 82.30; H 9.69; N 8.01. $C_{12}H_{17}N$. Calculated %: C 82.29; H 9.71; N 8.00.

2-Methyl-3,4-cyclohexenopyridine (IV). Bp 158°C (14 mm Hg); n_D^{20} 1.6000. PMR spectrum (δ, ppm): 1.67 m (4H, CH_2), 2.27 s (3H, CH_3), 2.52 m (4H, CH_2), 6.7 d (1H, CH), 8.2 d (1H, CH). M^+ 147. Found %: C 81.60; H 8.79; N 9.62. $C_{10}H_{13}N$. Calculated %: C 81.63; H 8.84; N 9.52.

2-Isobutyl-3,4-cyclohexenopyridine (V). Bp 165°C (14 mm Hg); n_D^{20} 1.5900. PMR spectrum (δ, ppm): 0.90 d (6H, CH_3), 1.63-1.67 m (5H, CH, CH_2), 2.52-2.75 m (6H, CH_2), 6.70 d (1H, CH), 8.02 d (1H, CH). M^+ 189. Found %: C 82.54; H 10.05; N 7.41. $C_{13}H_{19}N$. Calculated %: C 82.53; H 10.03; N 7.44.

2-Butyl-3,4-cyclohexenopyridine (VI). Bp 190°C (15 mm Hg); n_D^{20} 1.5590. PMR spectrum (δ, ppm): 0.93 t (3H, CH_3), 1.58-1.67 m (8H, CH_2), 2.52-2.75 m (6H, CH_2), 6.70 d (1H, CH), 8.02 d (1H, CH). M^+ 189. Found %: C 82.50; H 10.00; N 7.50. $C_{13}H_{19}N$. Calculated %: C 82.54; H 10.05; N 7.41.

2-Methyl-3,4-cycloheptenopyridine (VII). Bp 174°C (14 mm Hg); n_D^{20} 1.5730. PMR spectrum (δ, ppm): 1.67 m (6H, CH_2), 2.20 s (3H, CH_3), 2.60 m (4H, CH_2), 6.80 d (1H, CH), 8.00 d (1H, CH). M^+ 161. Found %: C 81.98; H 9.30; N 8.72. $C_{11}H_{15}N$. Calculated %: C 81.99; H 9.32; N 8.70.

2-Isobutyl-3,4-cycloheptenopyridine (VIII). Bp 120°C (13 mm Hg); n_D^{20} 1.5710. PMR spectrum (δ, ppm): 0.83 d (6H, CH_3), 1.63-1.65 m (9H, CH, CH_2), 2.67 m (4H, CH_2), 6.78 d (1H, CH), 8.02 d (1H, CH). M^+ 203. Found %: C 82.74; H 10.31; N 6.95. $C_{14}H_{21}N$. Calculated %: C 82.76; H 10.34; N 6.90.

2-Butyl-3,4-cycloheptenopyridine (IX). Bp 220°C; n_D^{20} 1.5715. PMR spectrum (δ, ppm): 0.98 t 0.98 t (3H, CH_3), 1.57-1.65 m (10H, CH_2), 2.67-2.78 m (6H, CH_2), 6.78 d (1H, CH), 8.08 d (1H, CH). M^+ 203. Found %: C 82.72; H 10.3; N 6.98. $C_{14}H_{21}N$. Calculated %: C 82.76; H 10.34; N 6.90.

CONCLUSIONS

A new, simple and effective method was developed for the synthesis of difficultly obtainable bicyclic pyridine bases by the condensation of cyclic ethynylcarbinols with carboxylic acid anhydrides in the presence of an equimolar $ZnCl_2-POCl_3$ mixture followed by treatment with ammonium hydroxide.

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SYNTHESIS OF PHOSPHONIUM 1,3,2,5-DIOXABORATAPHOSPHORINANES

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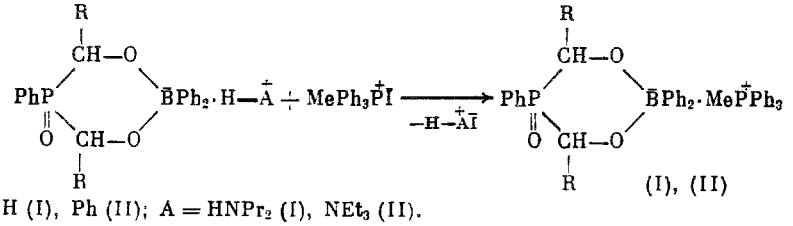
Reactions of bis(α-hydroxyalkyl)phosphines or their oxides, sulfides, and selenides with esters of diphenylboric acid in the presence of tertiary, secondary, primary, and aromatic amines or ammonia yield 1,3,2,5-dioxaborataphosphorinanes [1-3], which display complex-salt tautomerism [1-5]. The presence of the ammonium cation in the structures of the compounds is responsible for the ease and unambiguity of the proceeding of reactions with electrophiles [6]. It seemed of interest to substitute the ammonium for a phosphonium cation. However, reaction of bis(hydroxymethyl)phenylphosphine with the isobutyl ester of diphenylboric acid in the presence of triphenylphosphine did not give phosphonium 1,3,2,5-dioxaborataphosphorinane.

One of the tautomeric forms of ammonium 1,3,2,5-dioxaborataphosphorinanes consists of a salt structure for which an ion-exchange reaction is possible. Indeed, when ammonium 1,3,2,5-dioxaborataphosphorinanes were reacted with phosphonium salts in the two-phase system organic solvent–water the ion-exchange reaction took place and for the first time phosphonium 1,3,2,5-dioxaborataphosphorinanes (I) and (II) were isolated.



R = H (I), Ph (II); A = $HNPr_2$ (I), NEt_3 (II).

Derivatives (I) and (II) are crystalline compounds. In their IR spectra absorptions of hydroxyl and ammonium groups are not present. In the ^{31}P NMR spectra of these compounds there are two signals of equal intensity. In the PMR spectra of compound (I) the ratio of

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