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LETTERS TO THE EDITOR

Synthesis of Aminofuropyridines via the Reaction of Aminosilanes with Pyridoxal

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Synthesis of functionalized derivatives of pyridoxal (vitamin B_6) and their biological activity are currently an active area of investigation [1–3].

We studied a possibility of modifying pyridoxal using aminosilanes and silazanes. The reactions of aliphatic and aromatic aldehydes with aminosilanes and silylamides of carboxylic acids occurred via attachment of the carbonyl reagent at the Si–N bond to form the corresponding trimethylsiloxy derivatives. In these reactions zinc chloride, lithium perchlorate, *p*-toluenesulfonic acid, and trimethylsilyl triflate were used as catalysts [4–9]. Depending on the reaction conditions, the interaction of aminosilanes with α,β-unsaturated aldehydes resulted in 1,3-bis(dialkylamino)alkenes or the corresponding aminals [10, 11].

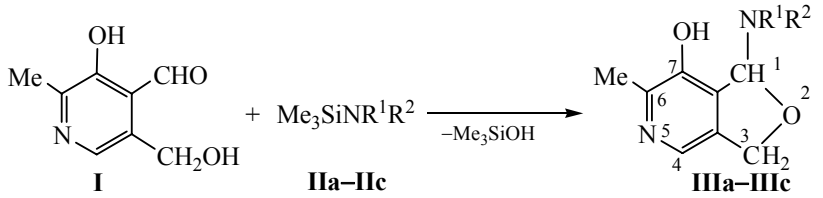
We found that pyridoxal **I** reacted with silylated linear and cyclic secondary amines to afford bicyclic furopyridinones **IIIa**–**IIIc**. The reaction proceeded at room temperature or under short heating in the absence of a catalyst. It can be assumed that the process involves initial addition of the aminosilane at the aldehyde group followed by cyclization of the intermediate with trimethylsilanol releasing. An alternative route involves the reaction of acetal form of pyridoxal [12]. Some furopyridines have been synthesized by reacting pyridoxal in this way with secondary amines under rigid conditions with the use of calcium hydride [13, 14] (Scheme 1).

The structure and composition of the products obtained were confirmed by elemental analysis, mass spectrometry, IR, ^{1}H and ^{31}P NMR spectroscopy. The ^{1}H NMR spectra of **IIIa–IIIc** contained the signals of nonequivalent endocyclic protons of the methylene group of the furan moiety.

The same reactions with silylated primary amines afforded pyridoxal azomethines **Va**–**Vc** (Scheme 2).

1-Diethylamino-6-methyl-1,3-dihydrofuro[3,4-*c*]-pyridin-7-ol (IIIa). A mixture of 1.0 g of pyridoxal **I**

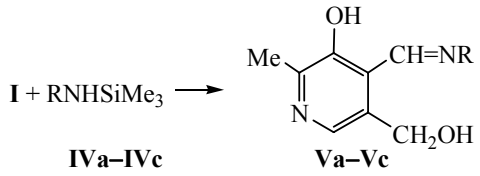
Scheme 1.



I **IIa–IIc** **IIIa–IIIc**

$R^1 = R^2 =$ Et (**a**), $R^1 =$ Me, $R^2 = CH_2Ph$ (**b**), R^1,R^2-morpholine (**c**).

Scheme 2.



R = Ph (**a**), CH(Me)Ph (**b**), CH_2Ph (**c**).

and 0.87 g of trimethylsilyldiethylamine **IIa** in 10 mL of benzene was heated at 40°C for 2 h. The precipitate was recrystallized from diethyl ether. Yield 1.0 g (78%), mp 91–92°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 1.07 t (6H, CH_3, $^3J_{HH}$ 8.22), 2.37 s (3H, CH_3), 2.66–2.77 q (4H, CH_2, $^3J_{HH}$ 8.22), 4.91 d (1H^a, CH_2O, $^2J_{HH}$ 12.47), 5.01 d (1H^б, CH_2O, $^2J_{HH}$ 12.47), 6.14 s (1H, CHO), 7.94 s (1H, CH_{Ar}). Found, %: C 64.75; H 8.36; N 12.19. $C_{12}H_{18}N_2O_2$. Calculated, %: C 64.84; H 8.16; N 12.60.

1-(*N*-Methyl-*N*-benzyl)amino-6-methyl-1,3-dihydrofuro[3,4-*c*]pyridin-7-ol (IIIb) was prepared similarly from 0.70 g of pyridoxal **I** and 0.80 g of silylamine **IIb**. Yield 0.61 g (55%), mp 113–114°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 2.19 s (3H, CH_3C), 2.43 s (3H, CH_3N), 3.71 s (2H, CH_2N), 3.80 d (1H^a, CH_2O, $^2J_{HH}$ 13.30), 4.68 d (1H^b, CH_2O, $^2J_{HH}$ 13.30), 6.20 s (1H, CHO), 7.28 m (5H, C_6H_5), 8.37 s (1H, NCH_{Ar}). Mass spectrum, *m*/*z*: 271 $[M + H]^+$. Found, %: C 71.30; H 6.61; N 10.38. $C_{16}H_{18}N_2O_2$. Calculated, %: C 71.11; H 6.67; N 10.37.

1-Morpholino-6-methyl-1,3-dihydrofuro[3,4-*c*]-pyridin-7-ol (IIIb) was prepared similarly from 0.63 g of pyridoxal **I** and 0.69 g of silylmorpholine **IIc**. Yield 0.58 g (56%), mp 171–173°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 2.40 s (3H, CH_3C), 3.63 m (4H, CH_2N), 5.04 m (6H, CH_2O), 6.26 s (1H, CHO), 7.98 s (1H, NCH_{Ar}). Found N, %: 11.64. $C_{12}H_{16}N_2O_3$. Calculated N, %: 11.86.

5-Hydroxymethyl-2-methyl-4-[(phenylimino)methyl]pyridin-3-ol (Va). A mixture of 0.68 g of pyridoxal **I**, 0.67 g of aminosilane **IVa** and 10 mL of benzene was stirred at 40°C for 3 h. The resulting product was filtered off and washed with diethyl ether. Yield 0.89 g (91%), mp 178°C. IR spectrum, ν, cm^{-1}: 1618 (C=N). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 2.47 s (3H, CH_3C), 4.57 s (2H, CH_2O), 7.06–7.45 m (5H, C_6H_5), 8.54 s (1H, NCH_{Ar}), 9.13 s (1H, CH=N), 13.78 s (1H, OH). Found N, %: 11.64. $C_{14}H_{14}N_2O_2$. Calculated N, %: 11.57.

5-Hydroxymethyl-2-methyl-4-[(phenylethylimino)-methyl]pyridin-3-ol (Vb) was obtained similarly from 0.7 g of pyridoxal **I** and 0.81 g of aminosilane **IVb**. Yield 0.61 g (55%), mp 118°C. IR spectrum, ν, cm^{-1}: 1624 (C=N). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 1.67 d (3H, C<u>H</u>$_3$CH, $^3J_{HH}$ 7.41), 2.42 s (3H, CH_3C), 2.82 q (1H, C<u>H</u>CH$_3$, $^3J_{HH}$ 7.41), 4.85 s (2H, CH_2O), 7.35 m (5H, C_6H_5), 7.94 s (1H, NCH_{Ar}), 9.17 s (1H, CH=N), 14.12 s (1H, OH). Found N, %: 10.64. $C_{16}H_{18}N_2O_2$. Calculated N, %: 10.41.

5-Hydroxymethyl-2-methyl-4-[(benzylimino)methyl]pyridin-3-ol (Vc) was obtained similarly from 0.7 g of pyridoxal **I** and 0.75 g of aminosilane **IVb**. Yield 0.64 g (59%), mp 108–111°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 2.41 s (3H, CH_3C), 2.84 s (2H, C<u>H</u>$_2$Ph), 4.85 s (2H CH_2O), 7.57 m (5H, C_6H_5), 7.95 s (1H, NCH_{Ar}), 9.19 s (1H, CH=N), 14.04 s (1H, OH). Found N, %: 10.64. $C_{15}H_{16}N_2O_2$. Calculated N, %: 10.94.

The IR spectra were recorded on a Bruker Vector-22 spectrometer in the range of 400–3600 cm^{-1} from KBr pellets. The ^{1}H NMR spectra were recorded on a Bruker Avance 600 instrument operating at 600.13 MHz relative to the signals of residual protons of the deuterated solvent. Mass spectrum (MALDI-TOF) was obtained on an Ultraflex III TOF/TOF Bruker instru-ment (*p*-nitroaniline matrix).

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