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SHORT COMMUNICATIONS

Synthesis of 1,3-Dialkyl-5-(pyrrol-1-yl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-ones

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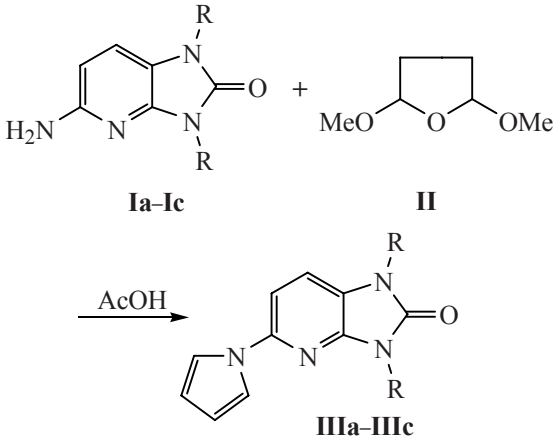
Derivatives of imidazo[4,5-*b*]pyridine, structural analogs of purine, exhibit versatile biological action: antiviral, cytostatic, antimicrobial, fungicidal, cardiovascular, secretoinhibitory, and they are also antagonists of angiotonin [1].

In extension of the research on the synthesis of tricyclic imidazopyridine derivatives containing an imidazole, triazole, and pyrrolidine fragments [2] it seemed purposeful using synthetic methods to build up in the structure of imidazo[4,5-*b*]pyridine a pyrrole ring.

The pyrrole ring is known to be present in the composition of many antibiotics [3]. This stimulates the search for new biologically active compounds including the fragments of imidazo[4,5-*b*]pyridine and pyrrole. Applying the Clauson–Kaas reaction [4] we synthesized imidazo[4,5-*b*]pyridine derivatives containing a pyrrole fragment at the C^5 atom of the pyridine ring. In the condensation of 5-amino-1,3-dialkyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-ones **Ia–Ic** with 2,5-dimethoxytetrahydrofuran (**II**) in glacial acetic acid we obtained 1,3-dialkyl-1,3-dihydro-5-(pyrrol-1-yl)-2*H*-imidazo[4,5-*b*]-pyridin-2-ones **IIIa–IIIc** in 50–80% yield.



Ia–Ic **II**

IIIa–IIIc

Obtained compounds **IIIa–IIIc** are well soluble in water and organic solvents (alcohols, benzene) and are readily purified from these solvents. The synthesized compounds are stable and are not oxidized in air. The composition and structure of compounds **IIIa–IIIc** were confirmed by elemental analysis and ^{1}H NMR spectra. In the ^{1}H NMR spectra of compounds **IIIa–IIIc** alongside the signals of alkyl groups of the imidazole ring, protons H^6 (7.52–7.55 ppm) and H^7 (7.24–7.25 ppm) of the pyridine ring singlet signals are present from protons $H^{2'}$ – $H^{5'}$ of the pyrrole fragment in the region 6.25 and 7.54–7.58 ppm. The prerequisite fact of the possible interest in compounds synthesized **IIIa–IIIc** for pharmacology consists in the presence in their structure of the N-substituted pyrroles that are important synthons in the synthesis of biologically active substances [5], and the fragments of pyrrole derivatives are included in the composition of a number of drugs [3].

General synthetic procedure. To a dispersion of 1.21 mmol of reagent **Ia–Ic** in 2 – 3 ml of glacial acetic acid was added 1.21 mmol of 2,5-dimethoxytetrahydrofuran (**II**), and the mixture was heated for 0.5 h at 130°C. Then the excess acetic acid was distilled off to dryness, and the residue was dissolved in warm hexane. The precipitate was filtered off and recrystallized.

1,3-Dimethyl-5-(pyrrol-1-yl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (IIIa). Yield 0.22 g (80%),

mp 101–103°C (heptane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.32 t (3H, N^1CH_3), 3.46 s (3H, N^3CH_3), 6.25 s (2H, $H^{3'}$, $H^{4'}$), 7.25 d (1H, H^7, *J* 8.4 Hz), 7.52d (1H, H^6, *J* 8.4 Hz), 7.54 s (2H, $H^{2'}$, $H^{5'}$). Found, %: C 62.98; H 5.24; N 24.39. $C_{12}H_{12}N_4O$. Calculated, %: C 63.14; H 5.30; N 24.55.

5-(Pyrrol-1-yl)-1,3-diethyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (IIIb). Yield 0.19 g (63%), mp 88–90°C (heptane). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.36 t (3H, $N^1CH_2CH_3$), 1.42 t (3H, $N^3CH_2CH_3$), 3.96 q (2H, $N^1CH_2CH_3$), 4.02 q (3H, $N^3CH_2CH_3$), 6.25 s (2H, $H^{3'}$, $H^{4'}$), 7.24 d (1H, H^7, *J* 8.4 Hz), 7.55 d (1H, H^6, *J* 8.4 Hz), 7.58 s (2H, $H^{2'}$, $H^{5'}$). Found, %: C 65.42; H 6.23; N 21.71. $C_{24}H_{20}N_4O$. Calculated, %: C 65.60; H 6.29; N 21.86.

1,3-Dibenzyl-5-(pyrrol-1-yl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (IIIc). Yield 0.23 g (50%), mp 133–135°C (decene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.12 s (2H, $N^1CH_2C_6H_5$), 5.17 s (2H, $N^3CH_2C_6H_5$), 6.25 s (2H, $H^{3'}$, $H^{4'}$), 7.24 d (1H, H^7, *J*8.4Hz), 7.42 br.s (5H, $N^1CH_2C_6H_5$), 7.50 br.s (5H, $N^3CH_2C_6H_5$), 7.52 d (1H, H^6, *J*8.4Hz), 7.54s (2H, $H^{2'}$, $H^{5'}$). Found, %: C 75.60; H 5.25; N 14.58. $C_{24}H_{20}N_4O$. Calculated,%: C75.76; H 5.30; N 14.73.

^{1}H NMR spectra of compounds were registered on a spectrometer Bruker Avance II 400 at operating frequency 400 MHz. The purity and homogeneity of compounds obtained was performed by TLC on Silufol UV-254 plates (eluent ethanol, development in iodine vapor and under UV irradiation). The synthesis of compounds **Ia–Ic** was published in [6].

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