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DIRECT INTRODUCTION OF THE PYRAZOLIDINE SUBSTITUENT INTO THE PYRAZOLONE NUCLEUS

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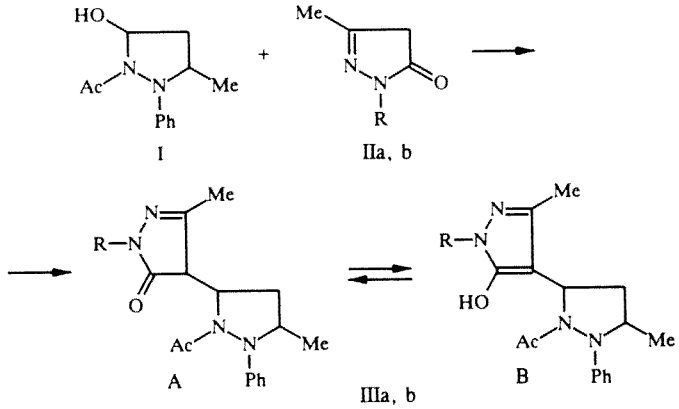
Until recently, the reaction of hydroxypyrazolidine with indole was the only example of the direct introduction of the pyrazolidine substituent into π-donor heterocyclic molecules [1].

We found that 1-acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine (I) reacts with the 3-methylpyrazol-5-ones (IIa,b) without preliminary activation on the surface of an adsorbent (DEAE-cellulose, polyamide) in the absence of a solvent to form the previously inaccessible 4-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)-3-methylpyrazol-5-ones (IIIa,b).



Similarly to other pyrazol-5-ones [2], compound (IIIa) exists in solutions as the mixture of two tautomeric forms, A and B. The adduct (IIIb) has the preferred structure of the hydroxypyrazole B, using PMR and IR.

It should be noted that, notwithstanding the low yields, the solid-phase method is at present the only method for the synthesis of the pyrazolidinylpyrazolones (IIIa) and (IIIb), which present interest for the investigation of their biological activity.

3-Methyl-4-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)pyrazol-5-one (IIIa). ($C_{16}H_{20}N_4O_2$). Onto the twentyfold amount, by weight, of polyamide (of the firm Woelm) are applied sequentially the solutions of 3-methylpyrazol-5-one (IIa) in the minimal amount of abs. methanol and 1-acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine (I) in benzene. The solvents are removed *in vacuo*. The mixture is heated in a constant-temperature cabinet for 4 days at 60°C. The reaction products are extracted with ethanol. Purification is performed by the method of flash-chromatography on SiO_2. The yield is 28%. The mp is 143°C. The IR spectrum is as follows: 1640 cm^{-1} (C=N, CH_3CO), 1735 cm^{-1} (C=O ring), and 3000-3400 cm^{-1} (OH, NH). The PMR spectrum ($CDCl_3$) is as follows: 1.24 ppm (3H, d, 3'-CH_3), 2.05 ppm (3H, s, 3-CH_3), 2.13 ppm (3H, s, CH_3CO), 2.43 ppm (2H, m, 4'-H), 3.40 ppm (0.7H, m, 4-H), 4.22 ppm (1H, m, 3'-H), 5.21 ppm (1H, m, 5'-H), and 6.8-7.5 ppm (5H, m, C_6H_5). The ^{13}C NMR spectrum ($CDCl_3$) is as follows: 12.29 ppm (3'-CH_3), 21.05 ppm ($\underline{CH_3}CO$), 33.52 ppm ($C_{(4')}$), 50.69 ppm ($C_{(3')}$), 62.25 ppm ($C_{(5')}$), 177.98 ppm ($CH_3\underline{C}O$), 19.07 ppm (3-CH_3), 99.69 ppm ($C_{(4)}$), 148.85 ppm ($C_{(3)}$), 156.88 ppm ($C_{(5)}$), 115.35 ppm, 122.90 ppm, 129.53 ppm, and 142.35 ppm (C_6H_5). The mass spectrum, given as m/z (I, %), is as follows: M^+ 300 (2), 257 (3), 185 (3), 177 (10), 176 (11), 161 (18), 160 (17), 150 (29), 149 (13), 108 (13), 107 (65), 93 (22), 91 (42), 77 (100), and 65 (18).

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1-Phenyl-3-methyl-4-(1-acetyl-2-phenyl-3-methyl-5-pyrazolidinyl)pyrazol-5-one (IIIb). ($C_{22}H_{24}N_4O_2$). This compound is obtained by analogy with compound (IIIa) on the surface of DEAE-cellulose (of the firm Reanal), and is isolated chromatographically on SiO_2. The yield is 12%. The IR spectrum is as follows: 1620 cm^{-1}, 1640 cm^{-1} (C=N, CH_3CO), and 2500-3000 cm^{-1} (OH). The PMR spectrum ($CDCl_3$) is as follows: 1.30 ppm (3H, d, 3'-CH_3), 1.86 ppm (3H, s, 3-CH_3), 2.15 ppm (3H, s, CH_3CO), 2.47 ppm (2H, m, 4'-H), 4.28 ppm (1H, m, 3'-H), 5.25 ppm (1H, m, 5'-H), 6.7-7.9 ppm (10H, m, $2C_6H_5$), and 11.40 ppm (1H, s, OH). The ^{13}C NMR spectrum ($CDCl_3$) is as follows: 15.62 ppm (3'-CH_3), 21.12 ppm ($\underline{C}H_3CO$), 33.13 ppm ($C_{(4')}$), 52.12 ppm ($C_{(3')}$), 62.70 ppm ($C_{(5')}$), 176.45 ppm ($CH_3\underline{C}O$), 18.84 ppm (3-CH_3), 96.76 ppm ($C_{(4)}$), 149.20 ppm ($C_{(3)}$), 152.90 ppm ($C_{(5)}$), 116.00 ppm, 121.15 ppm , 125.57 ppm, 128.25 ppm, 128.70 ppm, 129.35 ppm, 138.63 ppm, and 145.24 ppm ($2C_6H_5$). The mass spectrum, given as the m/z (I, %), is as follows: M^+ 376 (7), 358 (7), 333 (12), 232 (8), 226 (59), 211 (65), 200 (76), 185 (80), 161 (85), 107 (64), 105 (40), 93 (74), 91 (57), and 77 (100).

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