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SYNTHESIS OF FURYLPYRAZOLES AND PYRAZOLYLINDOLES FROM 1-ACYL-2-HETERYL-1-NITROETHENES

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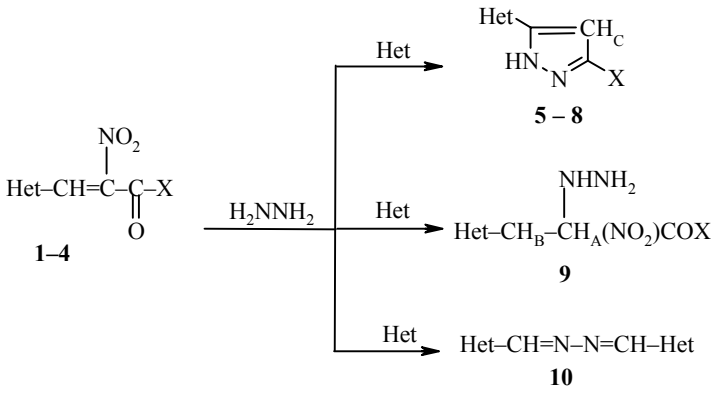
Many substituted furans and indoles have high pharmacological activity such as furacilin, furazolidon, furazonal, indopan, mexamin, diazolin, and indomethacin [1].

The high reactivity of 1-acyl-2-heteryl-1-nitroethenes [2], which contain strongly electron-withdrawing nitro and carbonyl functions at the double bond provides for the construction of new diheterocyclic structures.

We have shown that the reaction of 1-acetyl- and 1-benzoyl-2-heteryl-1-nitroethenes **1-4** with hydrazine proceeds in ethanol at room temperature without catalyst with a nitroene ketone–hydrazine hydrate ratio 1:2 to give heterocyclization products, namely, furyl- and indolylpyrazoles **5-8**.



1, 5, 9 Het = furyl-2, **2, 3, 6, 7, 10** Het = 1-Me-Ind-3, **4, 8** Het = 1-Ac–Ind-3;
1, 3–5, **7–9** X = Ph, **2, 6** X = Me

Addition product **9** was isolated in the case of *gem*-acylnitroethenes of furan series **1**. This finding indicates that the initial attack of hydrazine on the 1-acyl-2-heteryl-1-nitroethenes studied is at the C=C double bond. The feasibility of heterocyclization of the linear adducts formed in the first step is convincingly demonstrated in the conversion of **9** into pyrazole **5** in ethanol in the presence of hydrazine.

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An additional product, namely, the azine of 3-formyl-1-methylindole **10**, is formed along with pyrazoles **6** and **7** in the case of *gem*-acetyl- and *gem*-benzoylnitroethenes **2** and **3**, which contain an N-methylindole substituent. In these cases, the bisadducts formed in the initial step from the monoadducts decompose with the loss of acetyl- or benzoylnitromethine anions to give the azine.

The melting point of pyrazole **5** is close to the value reported by Musante [3]. The other substituted pyrazoles **6-8** are obtained for the first time.

The structures of **5-10** were supported by elemental analysis, spectroscopy, and mass spectrometry. A mixed probe of **10** with the product independently synthesized from 3-formyl-1-methylindole did not give a depressed melting point.

The substituted pyrazoles synthesized contain two different heterocyclic pharmacophores, namely, furyl or indole and pyrazole substituents, and hold potential biological activity.

5-(2-Furyl)-3-phenylpyrazole (5); mp 164-165°C (hexane) (173°C (ethanol) [3]). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 13.40 (1H, s, NH); 6.60-7.90 (9H, m, H_C, Ph, furyl). Found, %: N 13.53. $C_{13}H_{10}N_2O$. Calculated, %: N 13.33.

1-Methyl-3-(3-methyl-5-pyrazolyl)indole (6); mp 188-189°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.65 (3H, s, CH_3); 3.85 (3H, s, NCH_3); 7.00-8.00 (6H, m, H_C, Ind). Found, %: N 19.89. $C_{13}H_{13}N_3$. Calculated, %: N 19.90.

1-Methyl-3-(3-phenyl-5-pyrazolyl)indole (7); mp 201-202°C (ethanol). Mass spectrum, *m/z*: 273 ($M^{+\cdot}$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.85 (3H, s, NCH_3); 6.90-8.00 (11H, m, H_C, Ph, Ind). Found, %: N 15.23. $C_{18}H_{15}N_3$. Calculated, %: N 15.38.

1-Acetyl-3-(3-phenyl-5-pyrazolyl)indole (8); mp 208-209°C (ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.70 (3H, s, $COCH_3$); 8.45 (1H, s, NH); 6.90-8.05 (11H, m, H_C, Ph, Ind). Found, %: N 13.74. $C_{19}H_{15}N_3O$. Calculated, %: N 13.95.

3-(2-Furyl)-3-hydrazino-2-nitro-1-phenyl-1-propanone (9); mp 111-112°C (ethanol). Mass spectrum, *m/z*: 275 ($M^{+\cdot}$). ^{1}H NMR spectrum (DMSO-d_6): 5.14 (1H, s, CH_B); 10.25 (1H, s, NH); 6.61 (2H, s, NH_2); 7.30-7.90 (9H, m, CH_A, Ph, furyl). Found, %: C 56.55; H 4.81; N 15.33. $C_{13}H_{13}N_3O_4$. Calculated, %: C 56.72; H 4.72; N 15.27.

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