

Cyclocondensation of 1*H*-Indol-2-amine with Pentane-2,3,4-trione 3-Arylhydrazones

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Abstract—3-(Aryldiazenyl)-2,4-dimethyl-9*H*-pyrido[2,3-*b*]indoles were synthesized for the first time by cyclocondensation of 1*H*-indol-2-amine with pentane-2,3,4-trione 3-arylhydrazones.

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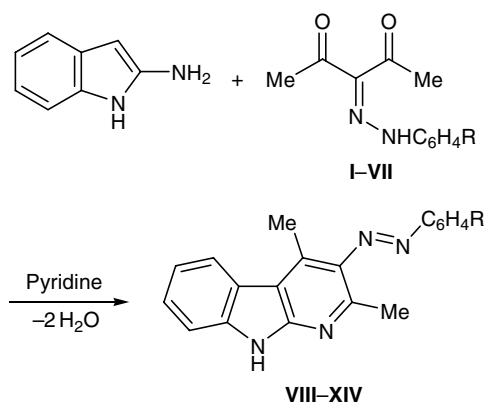
Insofar as both nitrogen atoms and carbon atom in position 3 are reactive centers in the 1*H*-indol-2-amine molecule, it reacts with β -diketones to give pyrido[2,3-*b*]indoles or pyrimido[1,2-*a*]indoles. The condensation direction strongly depends on the reaction conditions and initial reactants [1, 2]. Reactions of 1*H*-indol-2-amine with pentane-2,3,4-trione 3-arylhydrazones **I–VII** were not studied previously.

We have found that cyclocondensation of arylhydrazones **I–VII** with 1*H*-indol-2-amine occurs under mild conditions (room temperature) in pyridine. These reactions in 72 h lead to the formation of orange products that are poorly soluble in common organic solvents. The products were identified as 3-(aryldiazenyl)-2,4-dimethyl-9*H*-pyrido[2,3-*b*]indoles **VIII–XIV** whose yields ranged from 19 to 67% (Scheme 1). The product structure was confirmed by their elemental analyses and IR, ¹H NMR, and mass spectra. The elemental composition of **VIII–XIV** suggests that the condensation of hydrazones **I–VIII** with 1*H*-indol-2-amine is accompanied by elimination of two water molecules.

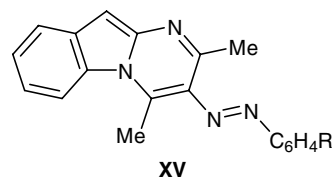
The IR spectra of **VIII–XIII** lack absorption in the region 1640–1720 cm⁻¹, indicating that both carbonyl groups in initial arylhydrazones **I–VII** are involved in the condensation. The band at 1723 cm⁻¹ in the IR spectrum of **XIV** was assigned to stretching vibrations of the ester carbonyl group. Compounds **VIII–XIV** displayed an absorption band in the region 3100–3380 cm⁻¹ due to stretching vibrations of the NH group; the presence of this band confirms that compounds **VIII–XIV** have the structure of pyrido[2,3-*b*]indoles rather than pyrimido[1,2-*a*]indoles like **XV**.

In the ¹H NMR spectra of **VIII–XIV** in trifluoroacetic acid we observed two singlets at δ 2.40–2.83 ppm from protons of the methyl groups and a multiplet in the region δ 6.80–8.36 ppm from the aromatic protons. No signal assignable to the 10-H

Scheme 1.



I, VIII, R = 2-Cl; **II, IX**, R = 2-Br; **III, X**, R = 2-I; **IV, XI**, R = 2-Me; **V, XII**, R = 3-NO₂; **VI, XIII**, R = 4-Br; **VII, XIV**, R = 4-COOEt.



proton of pyrimido[1,2-*a*]indole structure was present; according to published data, such signal is usually located in a stronger field, e.g., at δ 6.48 ppm for 8-chloro-2,3-dimethylpyrimido[1,2-*a*]indole [1].

The mass spectra of VIII and X–XIV contained the molecular ion peaks (m/z 334, 426, 314, 345, 378, and 373, respectively). The subsequent fragmentation of the molecular ions of VIII and X–XIV includes elimination of substituent from the aryl group and loss of the aryl group and nitrogen molecule to give a stable fragment ion with m/z 195. This ion was previously assigned the structure of 3,5-dimethylpyrido[2,3-*b*]indolium [2]. Decomposition of the latter leads to ions with m/z 168 and 155 as a result of elimination of HCN and CH₂CN, respectively; and expulsion of methyl group leads to fragment ion with m/z 140.

EXPERIMENTAL

The ¹H NMR spectra were recorded from solutions in trifluoroacetic acid on a Bruker Avance DRX-200 spectrometer (200 Hz). The mass spectra were run on a Finnigan MAT-8200 instrument. The IR spectra were obtained on a Vector 22 spectrometer from samples prepared as KBr pellets.

Initial pentane-2,3,4-trione 3-arylhydrazones I–VII were synthesized according to the procedure described in [3].

3-Aryldiazenyl-2,4-dimethyl-9H-pyrido[2,3-*b*]indoles VIII–XIV (general procedure). A mixture of 0.2 g (1.5 mmol) of 1H-indol-2-amine, 1.5 mmol of arylhydrazone I–VII, and 3 ml of anhydrous pyridine was stirred for 72 h at 20°C. The orange precipitate was filtered off and washed with water (until the pyridine odor disappeared), 5 ml of alcohol, and 5 ml of diethyl ether.

3-(2-Chlorophenyldiazenyl)-2,4-dimethyl-9H-pyrido[2,3-*b*]indole (VIII). Yield 0.34 g (68%), mp 282–285°C. IR spectrum, ν , cm⁻¹: 3320–3180 (NH). ¹H NMR spectrum, δ , ppm: 2.52 s (3H, CH₃), 2.78 s (3H, CH₃), 6.87–7.81 m (8H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 334 (35) [M]⁺, 299 (24), 223 (4), 195 (100), 179 (6), 168 (10), 155 (6), 140 (8), 127 (16), 111 (8), 75 (6). Found, %: C 67.74; H 4.73; Cl 10.60; N 16.31. C₁₉H₁₅ClN₄. Calculated, %: C 68.16; H 4.52; Cl 10.59; N 16.73.

3-(2-Bromophenyldiazenyl)-2,4-dimethyl-9H-pyrido[2,3-*b*]indole (IX). Yield 0.28 g (49%), mp 281–283°C. ¹H NMR spectrum, δ , ppm: 2.56 s

(3H, CH₃), 2.81 s (3H, CH₃), 6.91–7.83 m (8H, H_{arom}). Found, %: C 60.50; H 4.47; Br 21.00; N 14.82. C₁₉H₁₅BrN₄. Calculated, %: C 60.17; H 3.99; Br 21.07; N 14.77.

3-(2-Iodophenyldiazenyl)-2,4-dimethyl-9H-pyrido[2,3-*b*]indole (X). Yield 0.29 g (45%), mp 282–284°C. IR spectrum, ν , cm⁻¹: 3300–3100 (NH). ¹H NMR spectrum, δ , ppm: 2.59 s (3H, CH₃), 2.83 s (3H, CH₃), 7.17–7.61 m (8H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 426 (30) [M]⁺, 299 (26), 223 (7), 195 (100), 179 (6), 168 (8), 155 (6), 140 (8), 127 (11), 76 (11). Found, %: C 53.49; H 3.76; I 29.80; N 12.86. C₁₉H₁₅IN₄. Calculated, %: C 53.54; H 3.55; I 29.77; N 13.14.

2,4-Dimethyl-3-(2-methylphenyldiazenyl)-9H-pyrido[2,3-*b*]indole (XI). Yield 0.09 g (19%), mp 250°C. IR spectrum, ν , cm⁻¹: 3100–3293 (NH). ¹H NMR spectrum, δ , ppm: 2.23 s (3H, CH₃), 2.45 s (3H, CH₃), 2.71 s (3H, CH₃), 6.79–7.81 m (8H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 314 (52) [M]⁺, 313 (12), 299 (8), 271 (4), 223 (4), 195 (100), 179 (5), 168 (8), 155 (6), 140 (5), 127 (10), 91(22), 65 (8). Found, %: C 75.94; H 6.05; N 17.35. C₂₀H₁₈N₄. Calculated, %: C 76.41; H 5.77; N 17.82.

2,4-Dimethyl-3-(3-nitrophenyldiazenyl)-9H-pyrido[2,3-*b*]indole (XII). Yield 0.26 g (50%), mp 291–294°C. IR spectrum, ν , cm⁻¹: 3312–3220 (NH). ¹H NMR spectrum, δ , ppm: 2.52 s (3H, CH₃), 2.78 s (3H, CH₃), 7.19–8.36 m (8H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 345 (17) [M]⁺, 299 (8), 223 (6), 195 (100), 179 (6), 168 (9), 155 (7), 140 (5), 127 (10). Found, %: C 65.93; H 4.94; N 19.84. C₁₉H₁₅N₅O₂. Calculated, %: C 66.08; H 4.38; N 20.28.

3-(4-Bromophenyldiazenyl)-2,4-dimethyl-9H-pyrido[2,3-*b*]indole (XIII). Yield 0.29 g (51%), mp 294–297°C. IR spectrum, ν , cm⁻¹: 3380–3110 (NH). ¹H, δ , ppm: 2.40 s (3H, CH₃), 2.66 s (3H, CH₃), 7.19–7.90 m (8H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 378 (24) [M]⁺, 377 (8), 299 (15), 223 (4), 195 (100), 179 (7), 168 (9), 155 (16), 140 (7), 127 (12), 76 (7). Found, %: C 59.70; H 4.15; Br 21.4; N 14.42. C₁₉H₁₅BrN₄. Calculated, %: C 60.17; H 3.99; Br 21.07; N 14.77.

Ethyl 4-(2,4-dimethyl-9H-pyrido[2,3-*b*]indol-3-yl)diazenyl)benzoate (XIV). Yield 0.27 g (48%), mp 258–262°C. IR spectrum, ν , cm⁻¹: 1723 (C=O), 3100–3300 (NH). ¹H NMR spectrum, δ , ppm: 0.99 t (3H, CH₃), 2.48 s (3H, CH₃), 2.74 s (3H, CH₃), 4.02–4.06 q (2H, CH₂), 7.13–7.82 m (8H, H_{arom}). Mass spec-

trum, m/z (I_{rel} , %): 372 (35) $[M]^+$, 343 (8), 327 (3), 299 (15), 223 (3), 195 (100), 179 (4), 168 (7), 155 (6), 140 (4), 127 (4), 76 (3). Found, %: C 71.23; H 6.04; N 15.38. $\text{C}_{22}\text{H}_{20}\text{N}_4\text{O}_2$. Calculated, %: C 70.95; H 5.41; N 15.04.

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