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LETTERS TO THE EDITOR

SYNTHESIS OF 1-ARYL-4-FORMYLPYRAZOLES FROM ACETALDEHYDE N-ARYLHYDRAZONES BY THE VILSMEIER–HAACK METHOD

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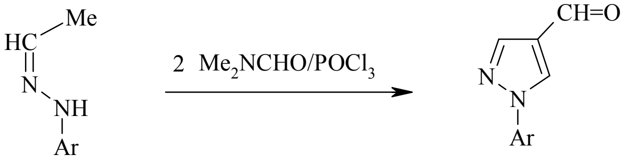
Two methods are usually employed for the synthesis of 1-aryl-4-formylpyrazoles. The first is based on formylation at position 4 of 1-arylpyrazoles under the conditions of the Vilsmeier–Haack reaction [1, 2] or transformation of 1-aryl-4-chloropyrazoles according to Sommelet [3]. A second approach, supposing the formation of the pyrazole ring in the presence of an aldehyde group, was tried in the case of the condensation of triformylmethane with phenylhydrazine [4, 5].

Earlier [6-8] it was established that the formylation of the N-arylhydrazones of aryl methyl ketones by the DMF–$POCl_3$ system leads to the formation of 3-substituted 1-aryl-4-formylpyrazoles, whereas the analogous reaction of the N,N-dialkylhydrazones of aromatic aldehydes leads to the 2-dialkylhydrazones of 1-arylglyoxals [9]. The N-monosubstituted hydrazones of aldehydes have not been investigated in the Vilsmeier–Haack reaction.

We found that acetaldehyde N-arylhydrazones **1a-c** undergo formylation when treated with the Vilsmeier–Haack reagent with subsequent intramolecular cyclocondensation to the 1-aryl-4-formylpyrazoles **2a-c**.



1a–c **2a–c**

1, 2 a Ar = Ph, **b** Ar = 4-ClC_6H_4, **c** Ar = 4-MeC_6H_4

The ^1H and ^{13}C NMR spectra were recorded on a Varian-Gemini spectrometer (300 and 75 MHz respectively) in DMSO-d_6 with TMS as internal standard.

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1-Aryl-4-formylpyrazoles 2a-c. To DMF (40 ml), cooled to 0-5°C, we added with stirring $POCl_3$ (27 g, 0.175 mol) over 0.5 h and then at the same temperature a solution of the hydrazone **1a-c** (0.05 mol) in DMF (10 ml). The temperature of the reaction mixture was raised to 90°C, and the mixture was stirred for 3 h, cooled to room temperature, poured into iced water (200 ml), and neutralized with crystalline sodium carbonate to pH 8. The precipitate was filtered off, purified by chromatography on Al_2O_3 (3:1 hexane–chloroform), and crystallized from 50% ethanol.

Compound 2a. Yield 38%; mp 84-85°C (mp 85°C [3]). IR spectrum, ν, cm^{-1}: 1700 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.37 (1H, t, *J* = 7.8, H-4'); 7.52 (2H, t, *J* = 7.8, H-3',5'); 7.89 (2H, d, *J* = 7.9, H-2',6'); 8.19 (1H, s, H-5); 9.12 (1H, s, H-3); 9.91 (1H, s, CH=O). ^{13}C NMR spectrum, δ, ppm: 119.82 (C-2',6'); 125.69 (C-4); 128.03 (C-4'); 129.79 (C-3',5'); 130.04 (C-5); 139.14 (C-1'); 141.69 (C-3); 184.07 (CH=O). Found, %: C 69.61; H 4.74; N 16.07. $C_{10}H_8N_2O$. Calculated, %: C 69.76; H 4.68; N 16.27.

Compound 2b. Yield 47%; mp 120-121°C. IR spectrum, ν, cm^{-1}: 1705 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.42 (2H, d, *J* = 8.0, H-2',6'); 7.64 (2H, d, *J* = 8.0, H-3',5'); 8.12 (1H, s, H-5); 8.40 (1H, s, H-3); 9.93 (1H, s, CH=O). ^{13}C NMR spectrum, δ, ppm: 120.92 (C-2',6'); 125.84 (C-4); 129.82 (C-3',5'); 129.96 (C-5); 133.64 (C-4'); 137.63 (C-1'); 141.82 (C-3); 183.85 (CH=O). Found, %: C 58.00; H 3.45; N 13.66. $C_{10}H_7ClN_2O$. Calculated, %: C 58.13; H 3.41; N 13.56.

Compound 2c. Yield 42%; mp 89-90°C. IR spectrum, ν, cm^{-1}: 1700 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.34 (3H, s, CH_3); 7.33 (2H, d, *J* = 7.6, H-2',6'); 7.77 (2H, d, *J* = 7.6, H-3',5'); 8.23 (1H, s, H-5); 9.16 (1H, s, H-3); 9.89 (1H, s, CH=O). ^{13}C NMR spectrum, δ, ppm: 20.97 (CH_3); 119.64 (C-2',6'); 125.80 (C-4); 130.53 (C-3',5'); 132.50 (C-5); 137.09 (C-1'); 137.62 (C-4'); 141.49 (C-3); 185.28 (CH=O). Found, %: C 70.80; H 5.45; N 15.14. $C_{11}H_{10}N_2O$. Calculated, %: C 70.95; H 5.41; N 15.04.

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