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POLYFUNCTIONAL PYRAZOLES.
2*. 1-ARYL-3-BENZOYL-4-FORMYL- AND 4-CARBOXYPYRAZOLES

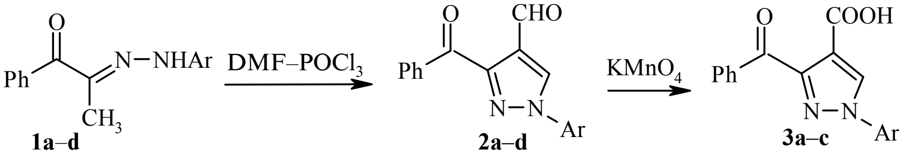
M. K. Bratenko[1], **V. A. Chornous**[1], **and M. V. Vovk**[2]

Cyclization of 1-phenylpropane-1,2-dione monoarylhydrazones under Vilsmeier-Haack conditions gave 1-aryl-3-benzoyl-4-formylpyrazoles which were converted to 1-aryl-3-benzoyl-4-carboxypyrazoles using potassium permanganate in aqueous pyridine medium.

Keywords: propiophenone hydrazones, carboxypyrazoles, formylpyrazoles, Vilsmeier-Haack reaction.

The method for preparing 3-aryl-4-formylpyrazoles [2, 3] by cyclizing aryl methyl ketone hydrazones under Vilsmeier-Haack conditions can be successfully used in the synthesis of 4-formylpyrazoles which are functionalized in the 3 position by heteroaromatic [4] and in the 1 position by a 2-cyanoethyl [1] substituent. In this work we present the results of using the indicated reaction to prepare previously unknown 1-aryl-3-benzoyl-4-formylpyrazoles and also the conversion of the latter to 4-carboxypyrazoles.

The reaction of propiophenone monoarylhydrazones **1a-d** with a mixture of DMF and $POCl_3$ leads to the formation of the 1-aryl-3-benzoyl-4-formylpyrazoles **2a-d** in 58-73% yield. Their structure was in agreement with the results of analytical and spectroscopic measurements (Tables 1 and 2). The IR spectra of the aldehydes **2** in the region 1710-1715 cm^{-1} show some overlap of the C=O stretching absorptions for the formyl and benzoyl groups. Their ^1H NMR spectra show both signals for the aromatic substituent protons and also characteristic formyl group (10.07-9.32 ppm) and pyrazole ring (9.11-9.32 ppm) proton singlets.



1, 2 a Ar = C_6H_5; **b** Ar = 4-FC_6H_4; **c** Ar = 4-$CH_3C_6H_4$; **d** Ar = 4-$CH_3OC_6H_4$;
3 a Ar = C_6H_5; **b** Ar = 4-FC_6H_4; **c** Ar = 4-$CH_3OC_6H_4$

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* For Communication 1, see [1].

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[1] Bukovinian State Medicinal Academy, Chernovtsy 274000, Ukraine. [2] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev 263660; e-mail: vovk@fuib.com, igoriv@users.univers.cv.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 515-517, April, 2001. Original article submitted May 6, 1999.

TABLE 1. Characteristics of Compounds Sythesized

Com-pound	Empirical formula	Found, % Calculated, % C	 H	 N	mp, °C (ethanol)	Yield, %
2a	$C_{17}H_{12}N_2O_2$	74.28 73.91	4.07 4.38	10.20 10.14	133-135	68
2b	$C_{17}H_{11}FN_2O_2$	69.03 69.38	3.67 3.77	9.28 9.52	126-128	73
2c	$C_{18}H_{14}N_2O_2$	75.04 74.77	4.51 4.86	9.73 9.65	141-143	64
2d	$C_{18}H_{14}N_2O_3$	70.69 70.58	4.76 4.57	9.01 9.15	123-124	58
3a	$C_{17}H_{12}N_2O_3$	70.21 69.86	4.33 4.10	9.18 9.58	189-190	54
3b	$C_{17}H_{11}FN_2O_3$	66.13 65.80	3.31 3.54	9.17 9.03	195-196	48
3c	$C_{18}H_{14}N_2O_4$	67.31 67.08	4.59 4.34	8.45 8.69	155-156	34

TABLE 2. Spectroscopic Characteristics of Compounds **2a-d**, **3a-c**

Com-pound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm		
	C=O (O–H)	CHO/COOH (1H)	5-H (1H)	Ar
2a	1710	10.16	9.27	7.18-7.73 (10H, m)
2b	1715	10.22	9.32	7.47-8.18 (9H, m)
2c	1710	10.19	9.22	7.12-7.63 (9H, m) 2.29 (3H, s, CH_3)
2d	1710	10.07	9.11	7.04.73 (9H, m) 3.79 (3H, s, CH_3)
3a	1730 (2630)	12.69	9.03	7.12-7.90 (10H, m)
3b	1725 (2620)	12.53	8.96	7.21-8.17 (9H, m)
3c	1725 (2625)	12.79	9.08	7.10-7.89 (9H, m) 3.82 (3H, s, CH_3)

In order to obtain pyrazole carboxylic acids we have studied the oxidation of the pyrazole carboxaldehydes **2** using potassium permanganate. It was found that the action of the latter in aqueous pyridine medium on the aldehydes **2a,b,d** gave satisfactory yields (34-54%) of the acids **3a-c** (Tables 1 and 2). In the case of aldehyde **2c** the separation of pure reaction product could not be achieved since oxidation of the aldehyde group occurred along with oxidation of the methyl group of the tolyl substituent.

The ^1H NMR spectra of the 3-benzoylpyrazole-4-carboxylic acids, recorded in DMSO-d_6 solvent, identified protons in the aromatic substituents (7.04-8.18 ppm), the pyrazole ring (8.96-9.08 ppm), and the OH group (12.53-17.79 ppm). In the IR spectra the OH group appeared as a broad band shifted to the region 2620-2630 cm^{-1}, pointing to the presence of associated dimers which are formed through hydrogen bonding.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument using KBr tablets. ^1H NMR spectra were taken on a Varian Gemini spectrometer (300 MHz) using DMSO-d_6 solvent.

1-Phenylpropane-1,2-dione 2-Arylhydrazones (1a,c) were prepared by a known method [5] while compounds **1b,d** were obtained for the first time.

1-Phenylpropane-1,2-dione 2-(4-Fluorophenyl)hydrazone (1b). Yield 81%; mp 173-175°C. IR spectrum, cm^{-1}: 1660 (C=O), 3330 (N–H). Found, %: C 70.73; H 4.95; N 11.32. $C_{15}H_{13}FN_2O$. Calculated, %: C 70.30; H 5.11; N 10.93.

1-Phenylpropane-1,2-dione 2-(4-methoxyphenyl)hydrazone (1d). Yield 61%; mp 141-143°C. IR spectrum, cm^{-1}: 1665 (C=O), 3340 (N–H). Found, %: C 71.99; H 6.40; N 10.08. $C_{16}H_{16}N_2O_2$. Calculated, %: C 71.62; H 6.01; N 10.44.

1-Aryl-3-benzoyl-4-formylpyrazoles (2a-d). $POCl_3$ (20 g, 0.13 mol) was added with stirring to dry DMF (20 ml) which had been cooled to 0°C. After 5 min, the hydrazone **1a-d** (0.005 mol) in DMF (20 ml) was added at such a rate that the temperature of the reaction mixture did not exceed 10°C. The product was then stirred for a further 0.5 h at the same temperature, 1 h at room temperature, and finally 2.5 h at 60°C. After cooling, the reaction mixture was poured into ice (200 g) and 10% NaOH was added to pH 7-8. The precipitated product was filtered off, washed with water, dried, and recrystallized from ethanol.

1-Aryl-3-benzoyl-4-carboxypyrazoles (3a-c). A solution of $KMnO_4$ (1.58 g, 0.01 mol) in water (10 ml) was added with stirring to a suspension of aldehyde **2a,b,d** (0.01 mol) in pyridine (10 ml) at room temperature. The reaction mixture was stirred for 3 h, a solution of NaOH (1%, 50 ml) added, and stirring continued for 2 h at 50°C. After cooling, the inorganic precipitate was filtered off and washed with water. The combined filtrate and the water from the precipitate washing were acidified with HCl (6 N) to pH 4. The precipitated **3** formed was filtered off, washed with water, dried, and crystallized from glacial acetic acid.

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