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4-Functionally Substituted 3-Heterylpyrazoles: IV.* 1-Phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines

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Abstract—3-Aryl(heteryl)-4-formylpyrazoles in condensation with methyl aryl(heteryl) ketones afforded 1-aryl(heteryl)-3-[3-aryl(heteryl)-4-pyrazolyl]propenones. The latter reacted with phenylhydrazine yielding 1-phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines.

The aldehyde group of 4-formylpyrazoles is frequently used for modification in desired way at this position with various structural fragments. Data were published on the synthesis from 1,3-diphenyl-4-formylpyrazole of 4-alkylidene- [2] and 4-iminopyrazoles [3]. By condensation of the aldehyde with hippuric acid was prepared 4-(1,3-diphenyl-4-pyrazolylmethylene)-2-phenyloxazolin-5-one [4], and with ethyl acetoacetate amd ammonia was obtained 4-(4-pyrazolyl)-1,4-dihydropyridine [5]. The attention attracted by some 4-substituted pyrazoles is mostly due to their biological activity [5, 6]. However no less interesting seems preparation from the 4-formylpyrazoles of previously unknown biheterocyclic structures with the other useful properties, e.g., luminescence.

It is known in particular that 1,3,5-triaryl-2-pyrazolines are activators for organic scintillators that do not require spectral mixers; these compounds find application in luminescent composite dyes as donors of electron excitation energy [7]. The target of the present study was the synthesis of new analogs of 1,3,5-triarylpyrazolines containing in *5* position a heterocyclic pyrazole substituent instead of an aryl one. Taking into account that the most convenient preparation procedure for 1,3,5-triarylpyrazolines consists in the reaction of α,β-unsaturated diaryl ketones with arylhydrazines [8, 9] we aimed at the

Table 1. Yields, melting points, IR spectra, and elemental analyses of 1-aryl(heteryl)-3-[1-phenyl-3-aryl(heteryl)-4-pyrazolyl]-3-propenones **IIIa**–**k**

Compd. no.	Yield, %	mp, °C (2-propanol)	IR spectrum, ν(C=O), cm^{-1}	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
IIIa	84	132–134[a]	1670	82.29	5.14	8.00	$C_{24}H_{18}N_2O$	82.34	5.01	8.12
IIIb	89	177–178	1665	78.01	4.69	7.82	$C_{24}H_{17}FN_2O$	78.26	4.61	7.60
IIIc	90	170–172	1660	74.47	4.58	7.58	$C_{24}H_{17}ClN_2O$	74.80	4.42	7.28
IIId	92	158–160	1665	66.89	4.21	6.40	$C_{24}H_{17}BrN_2O$	67.13	3.96	6.52
IIIe	80	114–115	1670	82.81	5.93	7.25	$C_{26}H_{22}N_2O$	82.53	5.82	7.40
IIIf	78	120–121	1660	78.71	5.03	7.24	$C_{25}H_{20}N_2O_2$	78.94	5.26	7.36
IIIg	83	173–175	1660	77.42	4.93	8.31	$C_{22}H_{16}N_2O_2$	77.64	4.70	8.23
IIIh	84	175–176	1665	74.30	4.67	7.80	$C_{22}H_{16}N_2OS$	74.15	4.49	7.86
IIIi	86	145–147	1670	74.26	4.19	7.98	$C_{22}H_{16}N_2OS$	74.15	4.49	7.86
IIIj	79	113–115	1665	78.03	5.30	7.47	$C_{23}H_{18}N_2O_2$	77.79	5.08	7.50
IIIk	86	155–156	1670	77.99	4.61	11.65	$C_{23}H_{17}N_3O$	77.86	4.84	11.96

[a] mp 135–136°C [3].

* For communication III, see [1].

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Table 2. Yields, melting points, ^{1}H NMR spectra, and elemental analyses of 1-phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines **IVa**–**k**

Compd. no.	Yield, %	mp, °C	^{1}H NMR spectrum, $(CD_3)_2SO$, δ, ppm
IVa	48	194–195	3.20 d.d (1H, CH), 4.04 d.d (1H, CH), 5.54 d.d (1H, CH), 6.74–7.86 m (20H, C_6H_5), 8.25 s (1H, CH)
IVb	52	203–204	3.31 d.d (1H, CH), 4.12 d.d (1H, CH), 5.62 d.d (1H, CH), 6.93–7.98 m (19H, H arom), 8.31 s (1H, CH)
Vc	58	198–200	3.24 d.d (1H, CH), 4.03 d.d (1H, CH), 5.48 d.d (1H, CH), 6.85–7.79 m (19H, H arom), 8.27 s (1H, CH)
IVd	53	203–205	3.23 d.d (1H, CH), 3.96 d.d (1H, CH), 5.64 d.d (1H, CH), 6.79–8.03 m (19H, H arom), 8.31 s (1H, CH)
IVe	44	191–192	1.31 t (3H, CH_3), 2.54 q (2H, CH_2), 3.30 d.d (1H, CH), 4.12 d.d (1H, CH), 5.55 d.d (1H, CH), 6.84–7.88 m (19H, H arom), 8.19 s (1H, CH)
IVf	41	190–191	3.31 d.d (1H, CH), 3.82 s (3H, CH_3O), 4.03 d.d (1H, CH), 5.53 d.d (1H, CH), 6.73–7.90 m (19H, H arom), 8.18 s (1H, CH)
IVg	49	162–164	3.24 d.d (1H, CH), 4.07 d.d (1H, CH), 5.26 d.d (1H, CH), 6.15 d (1H, CH), 6.79–7.87 m (17H, C_6H_5, CH), 8.25 s (1H, CH)
IVh	54	169–170	3.29 d.d (1H, CH), 3.97 d.d (1H, CH), 5.42 d.d (1H, CH), 6.66–7.95 m (18H, C_6H_5, CH), 8.30 s (1H, CH)
IVi	51	195–197	3.30 d.d (1H, CH), 4.05 d.d (1H, CH), 5.66 d.d (1H, CH), 6.72–7.89 m (18H, C_6H_5, CH), 8.27 s (1H, CH)
IVj	47	193–194	2.33 s (3H, CH_3), 3.27 d.d (1H, CH), 4.13 d.d (1H, CH), 5.49 d.d (1H, CH), 6.18 d (1H, CH), 6.63–7.90 m (16H, C_6H_5, CH), 8.20 s (1H, CH)
IVk	43	209–210	3.27 d.d (1H, CH), 4.03 d.d (1H, CH), 5.58 d.d (1H, CH), 6.74–7.98 m (16H, C_6H_5, CH), 8.10 s (1H, CH), 8.22 s (1H, CH), 8.64 d (1H, CH), 8.96 s (1H, CH)

Compd. no.	Found, %			Formula	Calculated, %		
	C	H	N		C	H	N
IVa	82.02	5.36	12.60	$C_{30}H_{24}N_4$	81.81	5.45	12.72
IVb	78.64	4.81	12.37	$C_{30}H_{23}FN_3$	78.60	5.02	12.22
IVc	75.49	4.59	11.57	$C_{30}H_{23}ClN_3$	75.86	4.84	11.80
IVd	69.13	4.27	10.93	$C_{30}H_{23}BrN_3$	69.36	4.43	10.78
IVe	81.74	6.12	11.95	$C_{32}H_{28}N_4$	82.05	5.98	11.96
IVf	79.46	5.32	11.71	$C_{31}H_{26}N_4O$	79.14	5.53	11.91
IVg	77.64	5.40	13.11	$C_{28}H_{22}N_4O$	78.13	5.11	13.02
IVh	75.04	5.19	12.25	$C_{28}H_{22}N_4OS$	75.33	4.93	12.55
IVi	75.08	5.23	12.76	$C_{28}H_{22}N_4OS$	75.33	4.93	12.55
IVj	78.62	5.23	12.89	$C_{29}H_{24}N_4O$	78.38	5.40	12.61
IVk	78.94	5.36	15.94	$C_{29}H_{23}N_5$	78.91	5.21	15.87

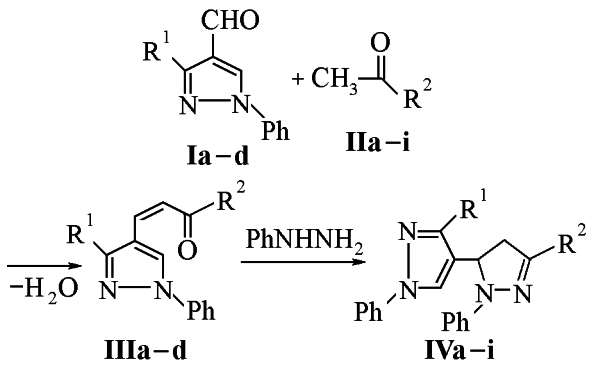
study of similar reactions with α-aryl(heteryl)-β-pyrazolyl vinyl ketones.

The preparation of only three 1-R-3-pyrazolylpropenones (R = Et, Ph, 4-MeC_6H_4) was described in the literature [2] along the reaction of 1,3-diphenyl-4-formylpyrazole with alkyl(aryl) methyl ketones [2].

In this connection we extended the series of 3-pyrazolylpropenones by carrying out the condensation not only of 1,3-diphenyl-4-formylpyrazole (**Ia**) but also of its heteroanalogs **Ib**–**d** with methyl aryl(heteryl)ketones **IIa**–**h**. We showed that the reaction between these compounds in 2-propanol at 50°C

afforded in high yield 1-aryl(heteryl)-3-[1-phenyl-3-aryl(heteryl)-4-pyrazolyl]-3-propenones (**IIIa–k**) (Table 1).

The composition and structure of the reaction products were proved by elemental and spectral analysis. For instance, in the IR spectra the absorption band of the carbonyl group conjugated with a double bond and aromatic (heteroaromatic) substituents is located in the range 1660–1670 cm^{-1} [10].



I, R^1 = Ph (**a**), 2-thienyl (**b**), 5-methyl-2-furyl (**c**), 3-pyridyl (**d**); **II**, R^2 = Ph (**a**), 4-FC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-BrC_6H_4 (d), 4-EtC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**), 2-furyl (**g**), 2-thienyl (**h**); **III, IV**, R^1 = Ph: R^2 = Ph (**a**), 4-FC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-BrC_6H_4 (**d**), 4-EtC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**), 2-furyl (**g**), 2-thienyl (**h**); R^2 = **Ph:** R^1 = **2-thienyl (i)**, 5-methyl-2-furyl (**j**), 3-pyridyl (**k**).

Pyrazolyl vinyl ketones **IIIa–k** react with phenylhydrazine at boiling for 3 h in acetic acid to afford 1-phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines **IVa–k** in 41–58% yield. The compounds obtained (Table 2) are colorless of light-yellow high-melting crystalline substances. Their composition is proved by elemental analyses, and the structure by ^{1}H NMR spectra.

In the ^{1}H NMR spectra of compounds **IVa–k** the protons of aromatic and heteroaromatic substituents in pyrazoline and pyrazole fragments appear as a set of multiplets in the typical for such protons region 6.6–8.6 ppm. The singlet signal of the proton in the *5* position of the pyrazolines ring is shifted to the region 8.1–8.3 ppm (cf. [11]) apparently due to its shielding with the pyrazoline ring. The protons of methylene and methine groups of the pyrazoline ring form an asymmetric three-spin *ABC*-system that appears in the ^{1}H NMR spectrum as 12 principal lines grouped into three doublets of doublets with an integral intensity of each one corresponding to one proton, and with *J* 2.4–3.0 Hz. Therewith the signal in the 5.4–5.7 ppm region should be apparently assigned to the methine proton, and the signals in the range 3.9–4.2 and 3.2–3.4 ppm to the methylene protons.

The results of studies on the luminescence properties of 1-phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines will be published elsewhere.

EXPERIMENTAL

IR spectra were recorded on spectrometer UR-20 from KBr pellets. ^{1}H NMR spectra were registered in DMSO-d_6 solutions on spectrometer Varian-Gemini (300 MHz), internal reference TMS.

1-Aryl(heteryl)-3-[1-phenyl-3-aryl(heteryl)-4-pyrazolyl]-3-propenones IIIa–k. To a solution of 0.005 mol of aldehyde Ia–d in 15 ml of 2-propanol was added at 18–20°C while stirring 0.005 mol of ketone IIa–h, the reaction mixture was heated to 50°C, and 1 ml of 20% aqueous sodium hydroxide was added. The mixture was stirred at 50°C for 0.5 h, then cooled to 18–20°C, and stirred for 3 h more. The separated precipitate was filtered off and crystallized from 2-propanol.

1-phenyl-3-aryl(heteryl)-5-(4-pyrazolyl)-2-pyrazolines IVa–k. To a solution of 0.02 mol of propenone **IIIa–k** in 5 ml of acetic acid was added 0.002 mol of phenylhydrazine, and the mixture was heated to boiling for 4 h. The reaction mixture was cooled, the formed precipitate was filtered off, washed with ethanol, and crystallized from acetic acid.

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