α,β-Unsaturated Ketones Derived from Acetylpyridines. V.* Preparation and Structure of Some Heterocyclic Analogs of 1,3,5-Triphenyl-2-pyrazoline

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By the reaction of some diazachalcones and (furfurylidenemethyl)pyridylketones with phenylhydrazine or some of its *para* substituted derivatives under the catalytic effect of 10% tetramethylammonium hydroxide, nineteen hitherto not described heterocyclic analogs of 1,3,5-triphenyl-2-pyrazoline were prepared. Their structure was elucidated by interpretation of their infrared, ultraviolet, fluorescence, and nuclear magnetic resonance spectra, respectively. On the basis of the results of fluorescence spectra, the possible application of these compounds as optical brightening agents was shown.

In our previous work [1], we described the preparation of pyridine analogs of 1,3,5-triphenyl-2-pyrazoline (TPP) and showed the importance of these compounds in practice mainly as optical brightening agents.

Because TPP and its derivatives are of great interest at present, we devoted attention to this group of compounds henceforth. Using the previously described method [1], we prepared heterocyclic analogs with the supposed brightening properties.

While in [1] we studied closer mainly the substitution of phenyls of TPP for pyridyl either in the 3 or the 5 position, in the present work we focused our attention on the substitution of phenyls for pyridyl and furyl, respectively, in both positions at the same time.

Synthesis of these compounds was carried out by the reaction of isomeric diazachalcones [3] and (furfurylidenemethyl)pyridylketones [2] with phenylhydrazine and some of its derivatives (Scheme 1).

There are several methods advised in the literature for the distinction of pyrazolines from isomeric phenylhydrazones which arise during the reaction, for instance, the *Knorr*'s colour test [9], the characteristic fluorescence of pyrazolines [10], and others [11—13]. Because the mentioned methods do not always give unambiguous results [14], spectral methods [8, 14—22, 25] are used for structural determinations at present.

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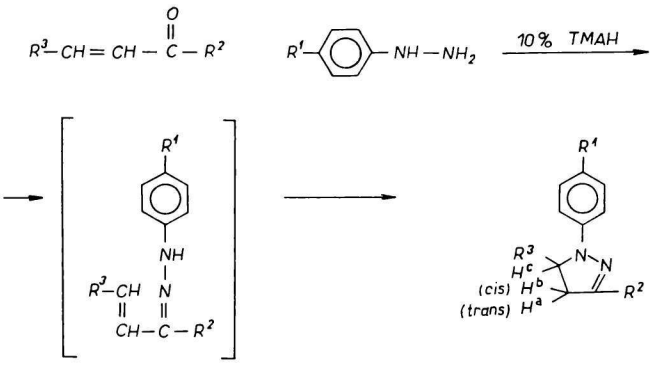
Abbreviations:

TPP 1,3,5-triphenyl-2-pyrazoline.
TMAH tetramethylammonium hydroxide.



Scheme 1

Compounds *II*—*XIII*: R^1 = H, CH_3, Cl, $CO_2C_2H_5$,
R^2 = 2-, 3-, 4-pyridyl,
R^3 = 2-furyl.

Compound *IV*: R^1 = H,
$R^2 = R^3$ = 3-pyridyl.

Compounds *XV*—*XX*: $R^1 = CO_2C_2H_5$,
$R^2 = R^3$ = 2-, 3-, 4-pyridyl.

Experimental

The starting diazachalcones and (furfurylidenemethyl)pyridylketones were prepared by Claisen—Schmidt condensation of pyridinecarbaldehydes and 2-furaldehyde with methylpyridylketones (acetylpyridines) in the presence of diethylamine as catalyst [3, 2]. The starting chalcone was prepared according to the procedure of *Kohler* and *Chadwell* [4].

p-Tolylhydrazine, *p*-chlorophenylhydrazine, and ethyl-*p*-hydrazinobenzoate were obtained according to [5—7]. Phenylhydrazine and tetramethylammonium hydroxide (TMAH) were commercial products (Lachema, Brno and The British Drug Houses Ltd.).

The heterocyclic analogs of TPP obtained from diazachalcones and (furfurylidenemethyl)pyridylketones by the reaction with phenylhydrazine and its *p*-substituted derivatives using the method described in [1] are presented in Table 1. TPP, used as a standard substance for determining the structure of the synthesized compounds, was prepared by the same method [1] from chalcone and phenylhydrazine.

The purity of the prepared compounds was checked by thin-layer chromatography (Silufol) in the system benzene—ethanol 9 : 1 (compounds *II*—*XIII*) and 7 3 (compounds *XIV*—*XX*). The detection was done in ultraviolet light.

Ultraviolet absorption spectra were taken on the CF 4 (Optica, Milano) spectrophotometer using 1 cm quartz cells. Spectroscopic grade ethanol was used to prepare the pyrazoline solutions ($1.3—1.5 \times 10^{-5}$ M).

Infrared spectra were measured with a double-beam UR-10 (Zeiss, Jena) instrument in the 1800—670 cm^{-1} range. The spectra were measured in KBr discs (1 mg/800 mg

Table 1

Survey of the prepared pyrazolines

No.	R^1	R^2	R^3	Formula	M	Calculated/found % C	% H	% N	Yield [%]	M.p. [°C] (Kofler) Solvent	R_F values
I	H	phenyl	phenyl	$C_{21}H_{18}N_2$	298.51	84.53 84.46	6.08 6.38	9.39 9.50	80	133—134[a] ethanol—water	
II	H	2-pyridyl	2-furyl	$C_{18}H_{15}N_3O$	289.34	74.72 74.43	5.23 5.26	14.52 14.61	59	104—105 ethanol—water	0.84
III	H	3-pyridyl	2-furyl	$C_{18}H_{15}N_3O$	289.34	74.72 74.53	5.23 5.46	14.52 14.79	54	109—110 ethanol—water	0.45
IV	H	4-pyridyl	2-furyl	$C_{18}H_{15}N_3O$	289.34	74.72 74.68	5.23 5.50	14.52 14.66	58	129—131 ethanol—water	0.36
V	CH_3	2-pyridyl	2-furyl	$C_{19}H_{17}N_3O$	303.37	75.24 74.98	5.64 5.51	13.85 13.72	38	108—110 ethanol—water	0.73
VI	CH_3	3-pyridyl	2-furyl	$C_{19}H_{17}N_3O$	303.37	75.24 75.31	5.64 5.78	13.85 13.93	50	132—133 ethanol—water	0.42
VII	CH_3	4-pyridyl	2-furyl	$C_{19}H_{17}N_3O$	303.37	75.24 75.04	5.64 5.78	13.85 13.64	79	147—149 ethanol—water	0.34
VIII	Cl	2-pyridyl	2-furyl	$C_{18}H_{14}ClN_3O$	323.79	66.77 66.92	4.36 4.52	12.97 13.16	39	115—117 ethanol—water	0.68
IX	Cl	3-pyridyl	2-furyl	$C_{18}H_{14}ClN_3O$	323.79	66.77 66.52	4.36 4.44	12.97 12.08	30	120—123 ethanol—water	0.45
X	Cl	4-pyridyl	2-furyl	$C_{18}H_{14}ClN_3O$	323.79	66.77 66.67	4.36 4.37	12.97 13.26	44	166—167 ethanol—water	0.28
XI	$CO_2C_2H_5$	2-pyridyl	2-furyl	$C_{21}H_{19}N_3O_3$	361.40	69.79 69.64	5.29 5.47	11.62 11.45	31	154—156 ethanol	0.42
XII	$CO_2C_2H_5$	3-pyridyl	2-furyl	$C_{21}H_{19}N_3O_3$	361.40	69.79 70.07	5.29 5.47	11.62 11.80	24	129—131 ethanol	0.26
XIII	$CO_2C_2H_5$	4-pyridyl	2-furyl	$C_{21}H_{19}N_3O_3$	361.40	69.79 69.47	5.29 5.24	11.62 11.86	55	168—169 ethanol	0.18

Table 1 (Continued)

No.	R^1	R^2	R^3	Formula	M	Calculated/found			Yield [%]	M.p. [°C] (Kofler) Solvent	R_F values
						% C	% H	% N			
XIV	H	3-pyridyl	3-pyridyl	$C_{19}H_{16}N_4$	300.35	75.97 76.18	5.36 5.47	18.65 18.92	40	142—143 ethanol	0.71
XV	$CO_2C_2H_5$	2-pyridyl	2-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 70.70	5.41 5.63	15.04 15.00	62	122—124 ethanol	0.80
XVI	$CO_2C_2H_5$	3-pyridyl	2-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 71.20	5.41 5.63	15.04 14.99	62	158—160 ethanol	0.74
XVII	$CO_2C_2H_5$	2-pyridyl	3-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 71.12	5.41 5.64	15.04 14.78	59	148—149 ethanol	0.78
XVIII	$CO_2C_2H_5$	3-pyridyl	3-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 70.65	5.41 5.68	15.04 15.16	27	160—161.5 ethanol	0.67
XIX	$CO_2C_2H_5$	4-pyridyl	3-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 71.19	5.41 5.62	15.04 15.12	30	178—179.5 ethanol	0.60
XX	$CO_2C_2H_5$	2-pyridyl	4-pyridyl	$C_{22}H_{20}N_4O_2$	372.43	70.95 71.20	5.41 5.39	15.04 14.96	46	159—160 ethanol	0.78

a) Reference [23] gives m.p. 134—135°C (from ethanol).

KBr). The calibration was checked against the spectrum of polystyrene foil (25 μm thickness). The accuracy of the frequency reading was ± 1 cm^{-1}. The region 3500—3200 cm^{-1} was examined regarding the absorption by stretching vibration of N—H in chloroform solutions (0.03—0.15 M with regard to the solubility) in NaCl cells of 0.97 mm thickness. Traces of moisture were removed from the dried chloroform on the column of blue silica gel before the measurement.

NMR spectra of pyrazolines *I*, *II*, *XII*, *XIV*, and *XVIII* in deuteriochloroform were taken on Tesla BS 487 A spectrometer of the operating frequency 80 MHz. Hexamethyldisiloxane was used as a standard and the results were calculated with regard to tetramethylsilane.

Fluorescence spectra were obtained in ethanol solutions ($1.3—1.5 \times 10^{-4}$ M) using 1 cm quartz cells on the CF 4 (Optica, Milano) spectrophotometer adapted for the measurement of fluorescence.

Results and Discussion

The synthesis of heterocyclic analogs of TPP (Table 1) was accomplished by the reaction of the appropriate (furfurylidenemethyl)pyridylketones and diazachalcones, respectively, with phenylhydrazines (Scheme 1) under the catalytic action of 10% TMAH [1]. Also in this case the employed method was advantageous. All the supposed 2-pyrazolines from (furfurylidenemethyl)pyridylketones (compounds *II*—*XIII*) could be prepared in sufficient yields. On the other hand, the reaction of diazachalcones with ethyl-*p*-hydrazinobenzoate gave positive results in six cases only (compounds *XV*—*XX*) out of the total eight available [3] diazachalcones. We failed to explain the reason of the observed anomaly satisfactorily. It is interesting that these complications connected with the preparation of heterocyclic analogs of TPP by the mentioned method are the only ones observed so far.

From diazachalcones, only the derivatives substituted by *p*-ethoxycarbonylphenyl in position 1 were prepared because only these derivatives of TPP were significant from the point of view of their supposed application. In this connection, our findings are in agreement with the results of works [8, 24].

The obtained well crystallizing compounds were of light yellow and yellow colour stable in the air and light (excluding compounds *VI*, *X*, and *XII*). In solutions of organic solvents and in the solid state they showed blue (compounds *XI*, *XII*, *XV*—*XVIII*, *XX*) or bluish-green and green (compounds *II*—*X*, *XIII*, *XIV*, *XIX*) fluorescence.

In a series of the substituted pyrazolines prepared from (furfurylidenemethyl)pyridylketones (compounds *II*—*XIII*), the R_F values of isomeric compounds (*e.g. II*—*IV*, *V*—*VII*) decrease with regard to the position of the nitrogen atom in the pyridyl residues in the series 2 > 3 > 4 (Table 1) similarly as we found it with other pyridine analogs of TPP with one pyridyl in the molecule [1]. In the group of pyrazolines with two pyridyl residues (compounds *XIV*—*XX*), the situation is complicated as we failed to synthesize some of these compounds.

At studying the ultraviolet absorption spectra of TPP and some of its derivatives [8, 14—20, 25], it was found that these compounds showed two significant maxima (at 240 and 360 nm). There are several opinions about their origin in the literature [20]. Besides, some derivatives and heterocyclic analogs of TPP show the third maximum at 300 nm which is obviously attributed to the specific effect of the substituent [15].

In this work, we studied the ultraviolet absorption spectra of TPP (compound *I*)

Table 2

Spectral characteristics of the synthesized compounds

No.	Ultraviolet spectra						Infrared spectra [cm^{-1}]				Fluorescence spectra	
	λ_{max} [nm]	10^{-4}	λ'_{max} [nm]	10^{-}	λ''_{max} [nm]	10^{-}	ν(C=N) (--C=C--)	ν(Ar—N)	ν(CH—N)	δ(C—H)	λ_{max} [nm]	relative intensity [%]
I	242	1.46			355	1.88	1599	1326 1336	1126	695 705	450	100
II	247	1.35	301	0.50	371	2.10	1599	1333	1121	691 696	486	61
III	246	1.35	308	0.62	370	1.73	1600	1336	1123	695 706	485	68
IV	251	1.67	298	0.35	384	1.99	1597	1337	1127	694	487	58
V	246	1.39	312	0.50	375	1.96	1616	1325	1129	705	490	25
VI	245	1.60	313	0.76	372	1.71	1616	1318 1336	1133	707	490	21
VII	253	1.82	303	0.37	390	1.99	1599 1618	1317 1332	1133	688	505	26
VIII	257	1.32	322	0.75	371	2.15	1601	1326	1129	706	485	64
IX	260	1.43	319	0.90	369	1.92	1601	1318 1336	1127	708	467	77
X	256	1.65	316	0.43	381	2.08	1598	1311 1335	1130	688	488	62
XI	240	1.03	292	1.25	375	3.34	1608	1335	1110	699	448	153
XII	239	1.23	302	1.05	373	3.11	1607	1312	1109	708	446	150
XIII	244	1.18	290	1.23	384	2.02	1602	1312	1111	687	461	145
XIV	246	1.59	308	0.69	368	1.83	1600	1334	1119	709	463	159
XV	240	1.07	295	1.06	376	3.42	1609	1337	1110	700	451	158
XVI	242	1.25	303	1.23	373	2.36	1607	1340	1113	707	448	206
XVII	239	1.04	293	1.01	375	3.26	1609	1337	1104	712	450	174
XVIII	240	1.29	304	1.16	372	3.13	1607	1310	1115	706	448	162
XIX	244	1.24	290	1.25	383	3.06	1600	1337	1110	714	461	155
XX	238	1.09	291	1.04	374	3.32	1609	1333	1108	695	449	167

and its dipyridyl analog (compound *XIV*), both used as standards, as well as those of other synthesized compounds. The region of absorption maxima is in agreement with the hitherto published values for the compounds of the pyrazoline type (Table 2).

Infrared spectra of the prepared compounds show absorption bands belonging to the vibrations of C=N, Ar—N, CH—N, and C—H groups (Table 2) which are taken for the proof of the pyrazoline structure [8, 15—18, 21]. In the region 3200—3500 cm^{-1}, none of the prepared compounds in chloroform solutions showed the band belonging to the stretching vibration of the N—H bonds, which is characteristic for the isomeric phenylhydrazones [14].

Table 3

NMR spectra of some synthesized compounds

No.	Coupling constants [cps]			Chemical shift [p.p.m.]		
	*J*ac	*J*bc	*J*ab	δH^a	δH^b	δH^c
I	7.75	12.12	17.12	3.07	3.81	5.21
II	7.0	12.0	17.67	3.49	3.84	5.36
XIV	7.25	12.0	17.25	3.11	3.88	5.34
XII	7.0	11.25	17.50	3.35	3.74	5.47
XVIII	6.25	12.25	17.50	3.16	3.94	5.45
a	6.0	12.0	17.0	3.06	3.76	5.35

a) Data for this compound ($R^1 = CO_2CH_3$, R^2 = 3-pyridyl, R^3 = phenyl) are taken from the literature [18].

In the infrared spectra of all prepared compounds in the region 1390 cm^{-1}, we have also identified bands of medium or low intensity which are attributed to the deformational vibration of CH_2 group of the pyrazoline ring [14—18]. We do not present, however, the found values in Table 2 because NMR spectroscopy will give the most convincing proof of the presence of this group.

We have taken the NMR spectra of some synthesized compounds (*I*, *II*, *XII*, *XIV*, *XVIII*). It is evident from the results given in Table 3 that these compounds contain three protons in their molecule belonging to the CH_2 and CH groups of the pyrazoline ring. Two protons in position 4 we labelled as H^a and H^b and the proton in position 5 as H^c. In Table 3 there are presented the chemical shifts of protons H^a, H^b, and H^c and the coupling constants *J*ab, *J*ac, and *J*bc of these compounds together with the analogous values for the model compounds. From Table 3 it is apparent that the results are in agreement with the hitherto published values for the compounds of this group [18, 22] and they can, together with the results of the infrared spectra, prove that the synthesized compounds have the supposed pyrazoline structure.

The structure of the prepared compounds was confirmed also by the results of their fluorescence spectra. It follows from the so far published works [8, 15, 17, 18, 25] that the fluorescent properties have pyrazolines only, while the isomeric phenylhydrazones have none. We observed fluorescence in all cases of the prepared pyrazolines with the maximum at 446—505 nm (Table 2). It is also clear from the table that the intensity of fluorescence of some pyrazolines (compounds *XI*—*XX*) exceeds that of the used standard (TPP) by about 40—100%. The majority of these compounds has the fluorescence maximum at 450 nm and therefore shows blue fluorescence; others show bluish-

-green or green fluorescence. Therefore, compounds *XI*, *XII*, *XV—XVIII*, and *XX* seem to be the most advantageous from the point of view of their supposed application. Our conclusions are indirectly corroborated by findings [8, 24] that pyrazolines with the esterified carboxyl group are practically applicable as optical brightening agents.

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References

1. Szücs L., *Chem. Zvesti* **23**, 677 (1969).
2. Krasnec Ľ., Ďurinda J., Szücs L., *Chem. Zvesti* **15**, 558 (1961).
3. Ďurinda J., Kolena J., Szücs L., Krasnec Ľ., Heger J., *Československ. Farm.* **16**, 14 (1967).
4. Kohler E. P., Chadwell H. M., *Organic Syntheses, Coll. Vol.* **I**, 78 (1946).
5. McPherson A., Stratton C., *J. Amer. Chem. Soc.* **37**, 908 (1915).
6. Wieland H., Popper C., Seefried H., *Ber.* **55**, 1827 (1922).
7. Thoms H., Ritsert K., *Ber. Deut. Pharm. Ges.* **31**, 71 (1921).
8. Maruyama T., Kawai M., Kuroki N., Konishi K., *Kogyo Kagaku Zasshi* **69**, 86 (1966).
9. Knorr L., *Justus Liebigs Ann. Chem.* **238**, 200 (1887).
10. Strauss F., *Ber.* **51**, 1457 (1918).
11. Neunhoeffer O., Rosahl D., *Chem. Ber.* **86**, 226 (1953).
12. Ried W., Dankert G., *Chem. Ber.* **90**, 2707 (1957).
13. Ralford L., Peterson W., *J. Org. Chem.* **1**, 544 (1937).
14. Lavrušin V. F., Cukerman S. V., Burjakovskaja E. G., *Chim. Geterocykl. Sojedin.* **1965**, 323.
15. Willey R. H., Jarboe C. H., Hayes F. N., Hansbury F., Nielsen J. T., Callahan P. X., Sellars M. C., *J. Org. Chem.* **23**, 732 (1958).
16. Sandler S. R., Loshaek S., Broderick E., Tsou K. C., *J. Phys. Chem.* **66**, 404 (1962).
17. Toi Y., Kawai M., Isagawa K., Maruyama T., Fushizaki Y., *Nippon Kagaku Zasshi* **86**, 1322 (1965).
18. Toi Y., Kawai M., Isagawa K., Fushizaki Y., *Nippon Kagaku Zasshi* **88**, 1095 (1967).
19. Nurmuchametov R. N., Tisčenko V. G., *Spektrosk.* **23**, 83 (1967).
20. Cukerman S. V., Burjakovskaja E. G., Lavrušin V. F., *Opt. Spektrosk.* **26**, 541 (1969).
21. Cukerman S. V., Burjakovskaja E. G., Rozum J. S., *Ž. Prikl. Spektrosk.* **8**, 453 (1968).
22. Hassner A., Michelson M. J., *J. Org. Chem.* **27**, 3974 (1962).
23. Knorr L., Laubmann H., *Ber.* **21**, 1209 (1888).
24. Wagner A., Schellhammer C. W., Petersen S., *Angew. Chem.* **78**, 69 (1966).
25. Raciszewski Z., Stephen J. F., *J. Amer. Chem. Soc.* **91**, 4338 (1969).

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