Pyrylium salts in the synthesis of 2-pyrazoline derivatives and earlier unknown substituted 3,3a,4,7-tetrahydropyrazolo[1,5-*a*]pyridin-7-ones

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New 1,3,5-substituted 2-pyrazoline derivatives were synthesized from 2,6-diphenylpyrylium perchlorate and acylhydrazines. Method for the synthesis of earlier unknown 3,3a,4,7-tetrahydropyrazolo[1,5-*a*]pyridin-7-one derivatives from pyrylium salts and cyanoacetic acid hydrazide was proposed.

Key words: pyrylium salts, acylhydrazines, 2-pyrazoline derivatives, 3,3a,4,7-tetrahydropyrazolo[1,5-*a*]pyridin-7-one derivatives.

Pyrylium salts, known already for nearly 100 years, are of permanent interest to chemists, which can be explained by high reactivity and great diversity of transformations of their carboxonium cations.[1]

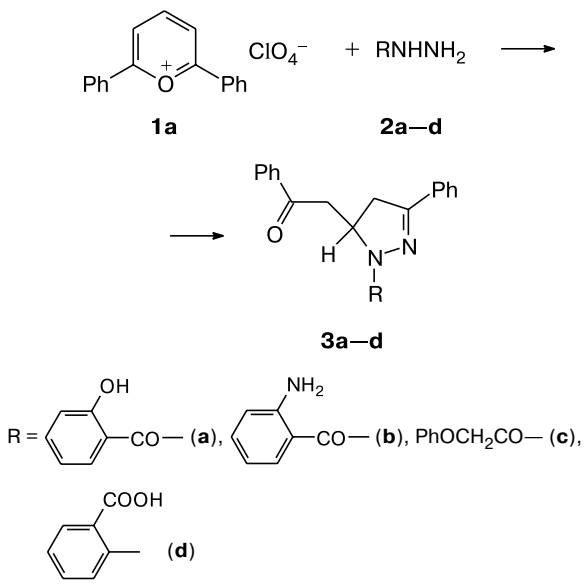
The study of the reactions of pyrylium salts with phenylhydrazine[2—5] showed that one of the main products of the interaction of 2,4,6-triphenylpyrylium cation with phenylhydrazine has cyclic 2-pyrazoline structure.[6] 2-Pyrazoline derivatives were also obtained by the reaction of 2,4,6-triphenylpyrylium salt with ethoxycarbonylhydrazine.[7] It is also known[8] that such pyrazolones can undergo further cyclization to pyrazolo[2,3-*a*]quinoline derivatives. The simplicity of the synthesis and virtually unlimited possibilities in variation of acid hydrazides make them attractive starting compounds in the synthesis of new potentially biologically active heterocycles from pyrylium salts.

We carried out the reaction of 2,6-diphenylpyrylium perchlorate **1a** with acid hydrazides **2a—c** and *o*-carboxyphenylhydrazine **2d** to isolate 2-pyrazoline derivatives **3a—d** in all the cases (Scheme 1).

It should be noted that pyrazoline **3c** is also formed with phenoxyacetic acid hydrazide **2c**, which has the methylene group, activated by the carbonyl function.

Quite different results were obtained in the reaction of pyrylium salts with cyanoacetic acid hydrazide **2e**, the methylene group of which is activated by the two electron-withdrawing groups. In this case, the process did not stop on the stage of the formation of pyrazolines, rather it led to the earlier unknown tetrahydropyrazolo[1,5-*a*]pyridin-7-one derivatives **4a—c**. A proposed mechanism of the reaction, which includes intramolecular condensation of the methylene and carbonyl groups in the intermediate pyrazolines **3e—f**, is given in Scheme 2.

Scheme 1



^{1}H NMR spectra of compounds **4a—c** (as well as of pyrazolines **3a—d**) have signals of the methylene and methyne protons, characteristic of the AB-systems. Mass spectrometry data confirm their stoichiometry. The com-

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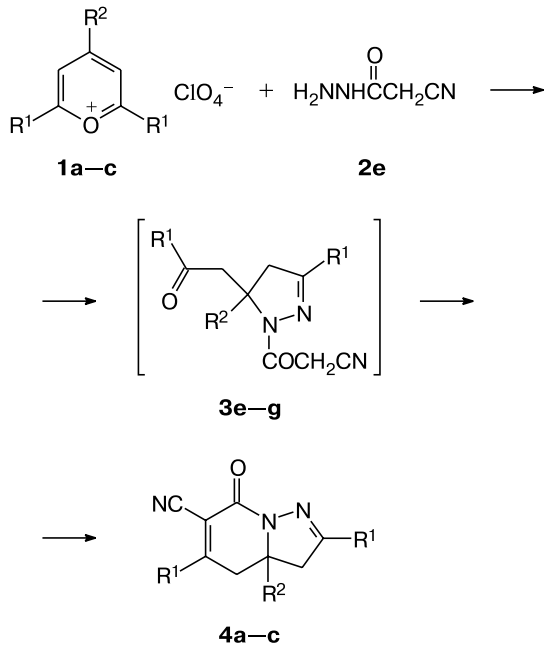
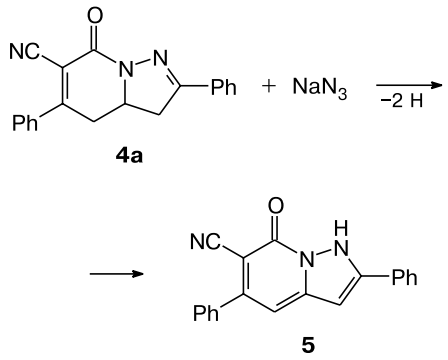
Scheme 2



R^1 = Ph, R^2 = H (**a**, **e**); R^1 = Bu^t, R^2 = H (**b**, **f**); R^1 = R^2 = Ph (**c**, **g**)

pounds are notable for the high stability. Thus, a prolonged reflux of **4a** in HOAc or DMF does not cause noticeable changes. Compound **4a** dissolves in boiling Ac_2O and can crystallize from it upon cooling. At the same time, it undergoes oxidation to 1*H*-2,5-diphenyl-6-cyanopyrazolo[1,5-*a*]pyridin-7(1*H*)-one **5** with such atypical oxidant as NaN_3 in boiling DMF (Scheme 3).

Scheme 3



Conditions: DMF, Δ, 5 h.

Experimental

IR spectra were recorded on a Specord IR-75 spectrometer in Nujol. ^{1}H NMR spectra were recorded on a Varian UNITY-300 spectrometer. Mass spectra were recorded on a Finnigan MAT INCOS 50 chromato-mass spectrometer with direct inlet of a sample into the source of ions. The starting pyrylium salts were synthesized according to the procedures described earlier.[9] Hydrazides **2a—e** were obtained according to the standard procedure[10] from the corresponding acid esters and hydrazine hydrate. Spectral characteristics of compounds obtained are given in Table 1.

1-(2-Hydroxybenzoyl)-5-phenacyl-3-phenyl-2-pyrazoline (3a). A hot solution of salicylic hydrazide (**2a**) (0.46 g, 3 mmol) was added to a boiling suspension of 2,6-diphenylpyrylium perchlorate (**1a**) (1 g, 3 mmol) in MeOH (15 mL) and the reaction mixture was refluxed for 5 min. The hot solution was placed into a glass and cooled in an ice bath. The precipitate formed was filtered off and recrystallized from EtOH (35 mL) to obtain colorless crystalline substance with m.p. 166—167 °C. The yield was 0.35 g (30%). Found (%): N, 7.37. $C_{24}H_{20}N_2O_3$. Calculated (%): N, 7.28.

1-(2-Aminobenzoyl)-5-phenacyl-3-phenyl-2-pyrazoline (3b). A hot solution of anthranilic acid hydrazide (**2b**) (0.3 g, 2 mmol) was added to a boiling suspension of salt **1a** (0.66 g, 2 mmol) in MeOH (10 mL). If the precipitate was not dissolved completely, additional amount of hydrazide was used until complete dissolution of the pyrylium salt, then, the solution was refluxed for 20 min. The mixture was cooled, pyridine (1 mL) was added, and the mixture was poured in ice-cold water, triturating with a glass stick. The mixture was kept in an ice bath until complete solidification, the precipitate was filtered off, washed with 50% aqueous MeOH, and recrystallized from Pr^iOH (80 mL). The light yellow crystalline substance with m.p. 199—200 °C was obtained. The yield was 0.26 g (33%). Found (%): N, 10.82. $C_{24}H_{21}N_3O_2$. Calculated (%): N, 10.96.

5-Phenacyl-1-phenoxyacetyl-3-phenyl-2-pyrazoline (3c). Salt **1a** (0.5 g, 1.5 mmol) was added to a solution of phenoxyacetic acid hydrazide (**2c**) (0.35 g, 2 mmol) in DMF (5 mL), this was kept for 10 min and heated to the boiling. After cooling, concentrated NH_4OH (3 mL) and H_2O (10 mL) were added. The precipitate with oil formed was cooled in an ice bath and triturated until complete solidification, filtered off, washed with H_2O, dried, and extracted with boiling isooctane (4×50 mL). The precipitates, formed after cooling, were filtered off, combined (the total yield was 0.4 g), and recrystallized from Pr^iOH (10 mL), cooling gradually (fast cooling leads to the formation of a tar), to obtain colorless crystalline substance with m.p. 130 °C. The yield was 0.2 g (33%). Found (%): N, 7.27. $C_{25}H_{22}N_2O_3$. Calculated (%): N, 7.03.

1-(2-Carboxyphenyl)-5-phenacyl-3-phenyl-2-pyrazoline (3d). A mixture of salt **1a** (1.1 g, 3.3 mmol) and *o*-hydrazinobenzoic acid (**2d**) (0.55 g, 3.6 mmol) was refluxed in MeOH (20 mL) for 5—6 min, during which dissolution of the precipitate, formation of new precipitate, and its dissolution took place. If the new precipitate was not completely dissolved, additional amount of acid was used. The reaction mixture was cooled, triturating with a glass stick, kept in an ice bath for 1.5 h, the precipitate formed was filtered off, washed with cold MeOH, and recrystallized from CH_3CN (10 mL). Colorless crystalline substance with m.p. 168—169 °C was obtained. The yield was 0.28 g (22%). Found (%): N, 7.52. $C_{24}H_{20}N_2O_3$. Calculated (%): N, 7.29.

6-Cyano-2,5-diphenyl-3,3a,4,7-tetrahydropyrazolo[1,5-*a*]-pyridin-7-one (4a). A hot solution of cyanoacetic acid hydrazide

Table 1. Spectral characteristics of compounds obtained

Compound	$[M]^+$	IR, ν/cm^{-1} (Nujol)	^{1}H NMR	
			Solvent	δ (*J*/Hz)
3a	384	1680 (CO), 1627, 1595, 1580, 1567, 1554, 1487 (arom.)	DMSO-d_6	3.10 (m, 1 H, CH_2); 3.41 (m, 1 H, CH_2); 3.64 (m, 1 H, CH_2); 3.96 (m, 1 H, CH_2); 5.18 (m, 1 H, CH); 6.86 (m, 2 H, CH_{arom}); 7.20—7.80 (m, 9 H, CH_{arom}); 8.00 (d, 2 H, CH_{arom}, *J* = 7.5); 8.10 (d, 1 H, CH_{arom}, *J* = 7.3); 11.4 (s, 1 H, OH)
3b	383	3473, 3353 (NH_2); 1667 (CO); 1627, 1607, 1574, 1554, 1487 (arom.)	DMSO-d_6	3.05 (m, 1 H, CH_2); 3.40 (m, 1 H, CH_2); 3.61 (m, 1 H, CH_2); 3.95 (m, 1 H, CH_2); 5.12 (m, 1 H, CH); 5.63 (br.s, 2 H, NH_2); 6.54 (br.t, 1 H, CH_{arom}); 6.71 (d, 1 H, CH_{arom}, *J* = 8.0); 7.10 (m, 1 H, CH_{arom}); 7.37 (m, 3 H, CH_{arom}); 7.45—7.70 (m, 6 H, CH_{arom}); 8.00 (br.d, 2 H, CH_{arom})
3c	398	1667, 1660, 1647 (CO); 1594, 1487 (arom.); 1214 (C—O—C)	$CDCl_3$	3.11 (m, 2 H, CH_2); 3.66 (m, 1 H, CH_2); 4.22 (m, 1 H, CH_2); 5.14 (m, 3 H, CH, CH_2); 7.00 (m, 3 H, CH_{arom}); 7.30 (m, 3 H, CH_{arom}); 7.35—7.65 (m, 6 H, CH_{arom}); 7.74 (m, 2 H, CH_{arom}); 8.00 (m, 2 H, CH_{arom})
3d	384	1727, 1672 (CO); 1600, 1580, 1487, 1474 (arom.)	DMSO-d_6	3.05 (m, 1 H, CH_2); 3.23 (m, 1 H, CH_2); 3.40 (m, 1 H, CH_2); 3.58 (m, 1 H, CH_2); 5.02 (m, 1 H, CH); 6.92 (t, 1 H, CH_{arom}, *J* = 7.3); 7.00—7.65 (m, 11 H, CH_{arom}); 7.88 (d, 2 H, CH_{arom}, *J* = 7.3); 12.44 (s, 1 H, OH)
4a	313	2220 (CN); 1660 (CO); 1594, 1580, 1554, 1500, 1447, 1434 (arom.)	$CDCl_3$	3.10 (m, 2 H, CH_2); 3.38 (m, 1 H, CH_2); 3.62 (m, 1 H, CH_2); 4.44 (m, 1 H, CH); 7.35—7.60 (m, 6 H, CH_{arom}); 7.64 (br.d, 2 H, CH_{arom}); 7.86 (br.d, 2 H, CH_{arom})
4b	273	2220 (CN); 1674 (CO); 1594, 1580, 1480 (arom.)	$CDCl_3$	1.24 (s, 9 H, Bu^t); 1.40 (s, 9 H, Bu^t); 2.45 (m, 1 H, CH_2); 2.63 (m, 1 H, CH_2); 3.11 (m, 1 H, CH_2); 3.95 (m, 1 H, CH)
4c		2227 (CN); 1655 (CO); 1600, 1587, 1567, 1494, 1447, 1414 (arom.)	$CDCl_3$	3.50 (d, 1 H, CH_2, *J* = 17.5); 3.65 (m, 2 H, CH_2); 3.89 (d, 1 H, CH_2, *J* = 17.5); 7.20—7.50 (m, 13 H, CH_{arom}); 7.80 (br.d, 2 H, CH_{arom})
5	311	2206 (CN); 1630 (CO); 1607, 1594, 1567, 1554 (arom.)	DMSO-d_6	6.55 (s, 1 H, CH_{arom}); 7.03 (s, 1 H, CH_{arom}); 7.30—7.60 (m, 8 H, CH_{arom}); 8.04 (m, 2 H, CH_{arom})

(**2e**) (0.5 g, 5 mmol) in MeOH (10 mL) was added to a boiling suspension of salt **1a** (1 g, 3 mmol) in MeOH (10 mL), this was refluxed for 1 min, cooled, and conc. NH_4OH (20 mL) was added. The precipitate formed was filtered off, washed few times with H_2O, EtOH, and recrystallized from CH_3CN (50 mL). Colorless crystalline substance with m.p. 291—292 °C was obtained. The yield was 0.31 g (33%). Found (%): N, 13.48. $C_{20}H_{15}N_3O$. Calculated (%): N, 13.41.

6-Cyano-2,5-di(*tert*-butyl)-3,3a,4,7-tetrahydropyrazolo[1,5-*a*]pyridin-7-one (4b). 2,6-Di(*tert*-butyl)pyrylium perchlorate (0.585 g, 2 mmol) (**1b**) was dissolved in MeOH (10 mL) under heating, a hot solution of hydrazide **2e** (0.25 g, 2.5 mmol) in MeOH (10 mL) was added, and this was refluxed for 5 min. The solution was cooled, H_2O (40 mL) and conc. NH_4OH (10 mL) were added, and this was kept for 6 h. The precipitate formed was filtered off, washed with H_2O, and dried to obtain colorless needles with m.p. 255—256 °C (from Pr^iOH). The yield was 0.35 g (64%). Found (%): N, 15.69. $C_{16}H_{23}N_3O$. Calculated (%): N, 15.37.

6-Cyano-2,3a,5-triphenyl-3,3a,4,7-tetrahydropyrazolo[1,5-*a*]pyridin-7-one (4c). A mixture of 2,4,6-triphenylpyrylium perchlorate (**1c**) (1.4 g, 3.4 mmol) and hydrazide **2e** (0.4 g, 4 mmol) was refluxed in MeOH (50 mL) until the precipitate was completely dissolved (~3.5 h), after cooling, the precipitate formed was filtered off. Concentrated NH_4OH (10 mL) and water were added to the filtrate to obtain a precipitate, which was filtered off and recrystallized from MeOH (100 mL). Colorless crystalline substance with m.p. 283—284 °C was obtained. The yield was 0.2 g (15%). Found (%): C, 79.93; H, 5.17; N, 11.05. $C_{26}H_{19}N_3O$. Calculated (%): C, 80.18; H, 4.92; N, 10.79.

6-Cyano-2,5-diphenylpyrazolo[1,5-*a*]pyridin-7(1*H*)-one (5). A mixture of **4a** (0.313 g, 1 mmol) and NaN_3 (0.13 g, 2 mmol), powdered in a mortar, was refluxed in DMF (10 mL) for 5 h and cooled, HOAc (1 mL) and water were added to obtain a precipitate, which was filtered off, washed with H_2O, boiling CH_3CN, MeOH, and recrystallized from DMF. Colorless crystalline substance with m.p. 323—325 °C was obtained. In contrast to the starting compound, it was insoluble in boiling CH_3CN. Found (%): N, 13.50. $C_{20}H_{13}N_3O$. Calculated (%): N, 13.50.

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