Microwave-assisted, facile route to 1*H*-pyrazolo[3,4-*b*]quinolines

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Abstract

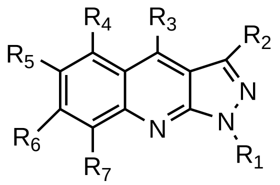
Aromatic aldehydes have been reported to react with 5-anilinopyrazoles in the presence of $ZnCl_2$ to give the corresponding benzylidenopyrazoles. In this paper evidence is given that the corresponding products are, in fact, 1H- pyrazolo[3,4-*b*]quinolines. This observation opens a novel route to these compounds. They show a blue emission in the solid state and, therefore, they are useful blue luminophores for electroluminescent devices. The synthetic procedure reported in the literature was significantly modified and improved by application of microwave heating. In our modified synthesis the reaction time was reduced from the usual 5 to 8 h to 5 to 7 min and the reaction products were formed without contamination.

Keywords: Luminophores, microwave-assisted, benzylidenopyrazoles

Introduction

Organic luminophores are used in constructing electroluminescent diodes (EL) as well as large-surface displays. Such devices have been known since the 60's. Simultaneously, the electroluminescence of organic compounds became of considerable interest after the discovery by Pope of the blue emission from a single crystal of anthracene under high voltage[1,2]. However, the possible use of organic luminophores in commercial EL devices was only taken seriously after Tang's[3] paper in which an intensive blue emission from a two-layer EL device at relatively low voltage was reported. In 1990 a breakthrough in the application of organic luminophores occurred by the discovery of emission from polymeric materials[4].

Success in the application of organic low-molecular weight and/or polymeric materials in electroluminescent devices[5,6] has stimulated considerable interest in the development of new types of organic and polymeric materials. Such materials can emit red, green, violet, blue and other light. Blue emission is particularly difficult to obtain from inorganic luminophores although recently intensively emitting gallium nitride was introduced as a promising blue luminophore[7]. But many organic compounds emit blue light in solution as well as in the solid state. Just recently we have made use of 1H-pyrazolo[3,4-*b*]quinolines (**1**) as blue emitters in the form of thin films made by vacuum evaporation[8].

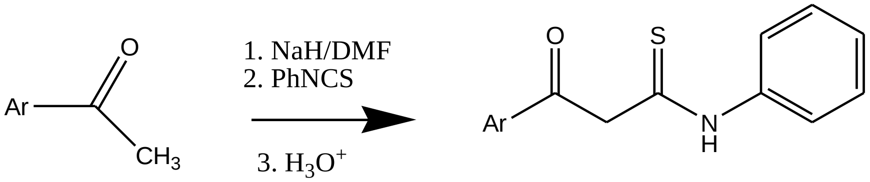


(1)

Such compounds are also useful emitters when doped into polymeric matrices as well as co-polymerized with corresponding monomers, for instance, N-vinylcarbazole[9,10]. The brightness of electroluminescent devices based on pyrazolo[3,4-*b*]quinolines reached 100-400cd/m^2. Therefore, there is considerable interest and potential in novel compounds from this heterocyclic series. Novel compounds with more intense blue emission and prolonged, stable emission are particularly in demand. In our search for new blue emitting materials we decided to prepare 1,3-disubstituted -4-benzylidene-5-N-arylpyrazoles, reported[11] to be strongly emitting blue luminophores. The synthesis of these compounds was described by Michaelis[11] in 1911. The studies presented in our paper reveal that the compounds identified by Michaelis as benzylidenopyrazoles are, in fact, pyrazolo[3,4-*b*]quinolines.

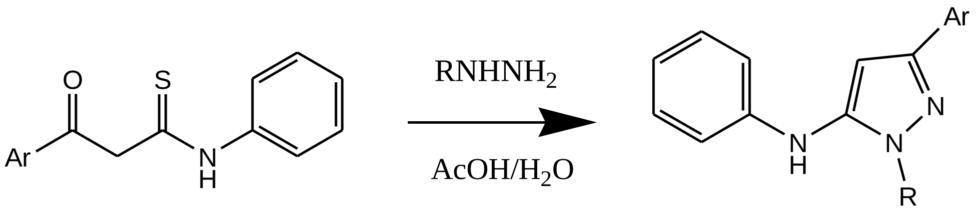
Results and Discussion

The 1,3-disubstituted-5-N- arylpyrazoles were available from the reaction of acetophenones with isothiocyanates in the presence of sodium hydride. In the first step β-ketothioanilides (**2**) were formed.



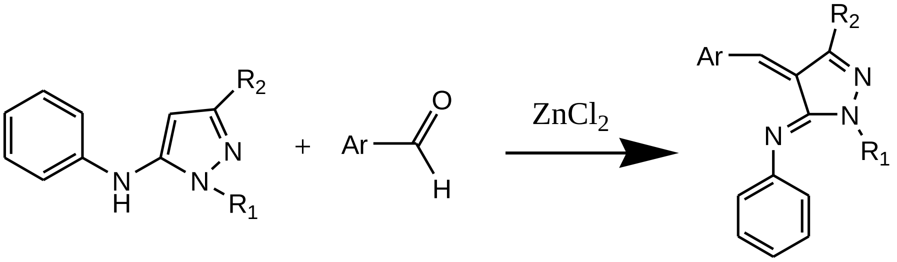
(2)

The corresponding β-ketothioanilides subsequently reacted with hydrazines producing 5-anilinopyrazoles (**3**).



(3)

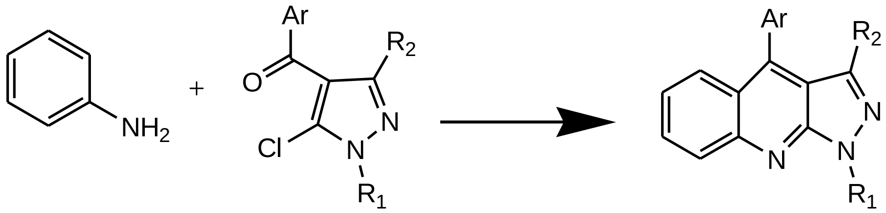
According to Michaelis the condensation of (**3**) with aromatic aldehydes in the presence of $ZnCl_2$ produced corresponding 4-benzylidenepyrazole derivatives (**4**)



(3) **(4)**

required 5-8 h heating at 140-150 °C and the reaction yield reached 50 - 75%. However, our application of microwave heating reduced the reaction time to 7-15 min with slightly lower yield but the products were obtained pure The resulting products exhibited strong blue fluorescence in solution (toluene, ethanol) as well as in the solid state. A thorough structural analysis showed that Michaelis came to the wrong conclusion by characterizing his compounds as benzylidenepyrazoles. The one-proton chemical shift belonging to a C-sp^2 -bonded hydrogen atom of the benzylidene moiety, which should be located in the region of 4-5 ppm in the ^1H NMR spectra of potential (**4**), was absent. Moreover, the pattern of chemical shifts of the protons in the benzo moiety was identified to be that of a quinoline. Thus, towards higher field there was a doublet with J=8.6 of H_8, a one proton triplet with J=7.6 of H_7, a one proton doublet with J=8.6 of H_5 and a one proton signal of H_6 that overlapped with the signals of the protons of the phenyl moieties. All the compounds obtained by Michaelis appear to be 1H-pyrazolo[3,4-*b*]quinolines (**6**).

We confirmed our structural assignment by an independent synthesis of (**6**) formerly reported by Hennig *et al*.[12]. Thus, anilines were reacted with 4-aroyl-5-chloro-1,3-disubstituted pyrazoles (**5**). The reaction proceeded over 3 h at 200-220 °C and provided 1H-pyrazolo[3,4-*b*]quinolines (**6**) with yields reaching 70% depending on the identity of the starting materials.



(5) **(6)**

The desired reaction products were mixed with tars and the isolation and purification of final products was difficult. The product (**6**) exhibited strong fluorescence typical for known (**1**). Melting points were identical with these given by Michaelis in his original report[11].

Conclusions

Reaction of 5-N-arylpyrazoles with aromatic aldehydes provides a facile route to 1H-pyrazolo[3,4-*b*]quinolines, particularly when microwaves are used as a source of energy. This method provides a convenient synthesis of 4-substituted-1H- pyrazolo[3,4-*b*]quinoline derivatives which otherwise would be available with difficulty using a classical Friedländer synthesis[13].

Experimental Section

Synthesis of 1*H*-pyrazolo[3,4-b]quinolines (General procedures) A) from pyrazoles and aromatic aldehydes

a) By conventional heating

A mixture of the corresponding pyrazole (0.01 mole), aromatic aldehyde (0.02 mole) and anhydrous $ZnCl_2$ (0.02 mole) was heated in the oil bath at 140-150 °C for 24 h. The reaction product was digested with boiling ethanol (25 mL) and then transferred to conc. ammonium hydroxide (25 mL). The precipitated solid was filtered and dried in the air. The crude product was developed with chloroform on a chromatographic column packed with neutral alumina (activity 1 of Merck, Darmstadt, Germany).

b) By microwave heating

Pyrazole (0.01 mole), aromatic aldehyde (0.02 mole) and anhydrous $ZnCl_2$ (0.02 mole) were heated in ethylene glycol in a domestic microwave oven (Whirlpool AKL 535, 800 W) operating at 2450 MHz. When using 20% of the nominal power the reaction time varied from 5 to 7 min depending on the compound. The reaction product was digested with 10% hydrochloric acid (25 mL). The precipitated solid was filtered and dried in the air. The crude product was developed with chloroform on a chromatographic column packed with neutral alumina (activity 1 of Merck, Darmstadt, Germany).

B) From 4-aroyl-5-chloro pyrazoles and anilines

4-Aroyl-5-chloro pyrazoles (0.01 mole) and aniline (0.05 mole) were heated for 3 h in sulfolane (10 mL) at 200-220 °C. After cooling to room temperature the reaction mixture was poured into 10% hydrochloric acid. The precipitated solid after drying was developed with chloroform on a chromatographic column packed with neutral alumina (activity 1., Merck, Darmstadt, Germany).

3,4-Diphenyl-1-methyl-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 8 min heating). Pale yellow crystals; 40% ; m.p. 175-8 °C (ethanol). ^{1}H NMR (500 MHz,$CDCl_3$) δ (ppm):7.00-7.11(m,4H,H_{aromat}); 7.13 (t, *J*=6.68Hz, 1H, H-4"); 7.17-7.24 (m,4H, H_{aromat}); 7.28-7.34 (m,2H,H-6,H-4'); 7.70-7.74 (t, *J*=7.66Hz, 1H, H-7); 7.87-7.90 (d, *J*=8.67Hz, 1H, H-5); 8.15-8.17 (d, *J*=8.7Hz, 1H, H-8) ; ^{13}C NMR ($CDCl_3$) δ (ppm): 33.96 (N-Me); 113.48 (C-3a); 123.02 (C-4a); 123.38 (C-4'); 127.17 (C-5);127.23 (C-4"); 127.45; 127.85; 128.25 (C-6); 128.40 (C-8);128.89; 130.26 (C-7); 130.32; 132.88 (C-1'); 134.89; 144.45; 144.84; 148.62 (C-3); 150.77 (C-9a). Anal.

Calcd for $C_{23}H_{17}N_3$: C, 82.37; H, 5.11; N, 12.52; Found: C, 82.34; H, 5.03; N, 12.48.

1,4-Diphenyl-3-methyl-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 8 min heating, procedure Aa, 3 hrs heating). Pale yellow crystals; Ab 71%, Aa 70%; m.p. 165-7 ºC (ethanol), 170-171 ºC [12]. ^{1}H NMR (500 MHz,CDCl$_3$) δ (ppm):2.11(s,3H,Me); 7.25 (t, *J*=7.4Hz,1H,H-4'); 7.32 (t, *J*=7.25Hz,1H,H-4"); 7.41-7.45 (m,4H,H-3",5"); 7.50-7.57 (m,5H,H-2",6"; H-3',5' ; H-6); 7.68 (d, *J*=8.64,1H,H-5); 7,70 (d, *J*=8.64;1H-5); 7.70 (t, *J*=7.61,1H,H-7); 8.17 (d, *J*=8.56Hz,1H,H-8); 8.50 (d, *J*=7.38Hz,2H,H-2',6'); ^{13}C NMR (CDCl$_3$) δ (ppm):14.88 (3-Me); 116.27 (C-3a); 120.28 (C-2',6'); 123.56 (C-4a); 123.87 (C-4"); 124.86 (C-4'); 126.91 (C-5); 128.22 (C-2",6"); 128.71 (C-6); 128.93 (C-8); 128.98 (C-3',5'); 129.67 (C-3",5"); 130.23 (C-7); 134.98; 139.97; 143.76; 144.35; 148.43 (C-3); 150.11 (C-9a). Anal. Calcd for $C_{23}H_{17}N_3$: C, 82.37; H, 5.10 N, 12.52; Found: C, 82.23; H, 5.08; N 12.34.

1,3,4-Triphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Aa, 8 min heating ; procedure Ab, 3 hrs heating). Yellow needles; Aa 63%, Ab 70%; m.p. 216-8 ºC (toluene). ^{1}H NMR (500 MHz,CDCl3) δ (ppm):7.05 (t, *J*=7.36Hz,2H,H-3"',5"'); 7.12-7.16 (m,3H,H-4",H-3",5"); 7.21-7.22 (m,4H,H-2",6",2"',6"'); 7.31 (2t,2H,H-6,H-4'); 7.38 (t,1H,H-4"'); 7.57 (t, *J*=8.04,2H,H-3',5'); 7.88 (d,1H,H-5); 8.22 (d,1H,H-8); 8.61(d, *J*=7,6, 2H,H-2',6').

^{13}C NMR (CDCl$_3$) δ (ppm): 114.95 (C-3a); 120.91(C-2',6'); 123.51 (C-4a); 124.12 (C-4"'); 125.38 (C-4'); 127.03 (C-5); 127.49 (C-3"',5"'); 127.56 (C-4"); 127.87 (C-2"',6"'); 128.35 (C-6); 129.03; 129.06; 129.11(C-8); 130.36 (C-2",6"); 130.41 (C-7); 132.61; 134.54; 139.94; 144.61; 146.77(C-8a); 148.56 (C-3); 150.25 (C-9a). Anal. Calcd for $C_{28}H_{19}N_3$: C, 84.63; H, 4.82; N, 10.56 ; Found: C, 84.46; H, 4.86; N, 10.78.

3,6-Dimethyl-4-(4'-methoxyphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Aa, 8 hrs; procedure Ab , 10 min heating; procedure B, 3 hrs heating). Yellow needles; Aa 50%, Ab 65%; m.p. 184 ºC (ethanol), 184 ºC[11]. ^{1}H NMR (500 MHz,CDCl$_3$) δ (ppm): 2,12(s,3H,6-Me); 2.38(s,3H,3-Me); 3.90(s,3H,OMe); 7.08(d, *J*=8.5Hz,2H,H-2",6"); 7.24(t, *J*=7.3 Hz,1H, H-4'); 7.34(d, *J*=8.45 Hz,2H, H-3",5"); 7.44(s,1H,H-5); 7.50-7.54(m,3H, H-7,H-3',5'); 8.04(d, *J*=8.72 Hz,1H,H-8); 8.49(d, *J*=8.4Hz, 2H, H-2',6'); ^{13}C NMR (CDCl$_3$) δ (ppm): 15.02(3-Me); 21.58(6-Me); 55.28(O-Me); 113.58; 116.50(C-3a); 120.07; 123.81; 128.90; 130.94; 132.69; 133.36(C-6); 140.02; 143.33; 143.68; 147.06; 149.82(C-9a); 159.82(C-4"). Anal. Calcd. for $C_{25}H_{21}N_{3O}$: C, 79.13; H, 5.58; N, 11.07 ; Found: C, 79.01; H, 5.48; N, 11.18.

1,3-Diphenyl-4-(3-pyridyl)-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 8 min). Pale yellow needles, 64%, m.p. 216-220 ºC (ethanol). ^{1}H NMR (500 MHz, CDCl$_3$) δ (ppm): 7.11(d, 5H); 7.20-7.24(m,1H); 7.32(t, *J*=7.35 Hz, 1H,); 7.40(t, *J*=7.38 Hz, 1H); 7.46(d,J=7.71 Hz, 1H); 7.57 (t, *J*=7.87 Hz, 2H, H-3',5'); 8.24(d, *J*=8.54 Hz, 1H, H-8); 8.53(s,1H, H-2$_{\text{Pyridyl}}$) ; 8.55(d, *J*=3.76 Hz, H-6$_{\text{Pyridyl}}$); 8.59(d, *J*=7.85 Hz, 2H, H-2',6'); ^{13}C NMR (CDCl$_3$) δ (ppm): 115.18(C-3a); 120.85; 122.61; 123.23(C-4a); 124.67; 125.53; 126.05; 127.78; 128.01; 129.02; 129.21; 129.28; 130.52; 130.60; 132.05; 137.42; 139.69; 140.13; 146.24; 148.47; 149.34; 149.94(C-9a); 150.27. Anal. Calcd. for $C_{27}H_{18}N_4$: C, 81.39; H, 4.55; N, 14.06; Found: C, 81.24; H, 4.48; N, 13.81.

3-(2-Naphthyl)-1-phenyl-4-(3-pyridyl)-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 9 min). Yellow crystals; 54%; m.p. 234 ºC (ethanol). ^{1}H NMR(CDCl$_3$) δ (ppm): 6.93(t, *J*=6.31Hz,$1H_{Pyridyl}$, H-5); 7.29(d, *J*=8.37Hz,$1H_{Pyridyl}$, H-4); 7.35(t, *J*=7.40Hz,1H,H-6); 7.76(d, *J*=7.9Hz,H-5); 7.79-7.82((d, *J*=7.69Hz,$1H_{Naphthyl-l}$)+ H-7); 8.28(d, *J*=8.67Hz,1H,H-8); 8.38(d, *J*=4.90Hz,$1H_{Pyridyl}$, H-6); 8.62(d, *J*=8.13Hz,2H,H-2',6'); 8.64(s,1H,$H_{Pyridyl}$, H-2); ^{13}C NMR($CDCl_3$) δ (ppm): 115.22(C-3a); 121.02(C-2',6'); 122.65; 123.35; 124.77(C-4a); 125.67; 126.15; 126.17; 126.41; 126.45; 127.41; 127.54; 128.21; 129.09(C-3',5'); 129.15; 129.36; 129.38; 130.71; 132.65; 132.73; 137.51; 139.73; 140.23; 146.11(C-8a); 148.53(C-3); 149.53; 150.11(C-9a); 150.32. Anal. Calcd. for $C_{31}H_{20}N_4$: C, 83.02; H, 4.49; 12.49; Found: C, 82.78; H, 4.09; N, 12.34.

3-Methyl-1-phenyl-4-(4'-toluoyl)-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 8 min). Yellow crystals; 42%; m.p. 205-7 ^{o}C (cyclohexane). ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 2.17(s,3H,Me); 2.53(s,3H,4-C_6H_4-CH3), 7.24-7.42(m,6H); 7.57(t,2H); 8.2(d, 1H); 8.50(d,2H). Anal. Calcd. for $C_{25}H_{20}N_2$: C, 86.18; H, 5.79; N, 8.04; Found: C, 86.34; H, 5.60; N, 8.15.

3,6-Dimethyl-1-phenyl-4-(4'-toluoyl)-1*H*-pyrazolo[3,4-*b*]quinoline (procedure Ab, 8min). Yellow crystals; 58%; m.p. 197-8 ^{o}C (cyclohexane) ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm):2.14(s,3H,Me); 2.44(s,3H,6-CH_3); 2.53(s,3H,4-C_6H_4-CH3), 7.23-7.60(m,9H); 81.12(d, 1H); 8.49(d,2H). Anal. Calcd. for $C_{26}H_{22}N_2$: C, 86.15; H, 6.12; N 7.73; Found: C, 86.08; H, 6.21; N, 7.85.

Preparation of 1,3-disubstituted-5-*N*-arylpyrazoles

The corresponding pyrazoles were prepared according to the literature: 1 and 3 [11]; 2, 4, and 5 [14]. NMR spectra lack the characteristics of known compounds reported in the literature[11,14]. Our melting points were identical with those originally reported.

3-Methyl-1-phenyl-5-*N*-phenylpyrazol (1). Colorless needles; 67%; m.p.. 120 ^{o}C (ethanol).

1,3-Diphenyl-5-*N*-phenylpyrazol (2). Colorless crystals; 78%; m.p. 153 ^{o}C (ethanol).

3-Methyl-1-phenyl-5-*N*-(4'-toluoyl)-pyrazol (3). Colorless needles; 65%; m.p. 111 ^{o}C (ethanol).

3-(2'-Naphthyl)-1-phenyl-5-*N*-phenylpyrazole (4). Light yellow crystals; 58%; 175-8 ^{o}C (ethanol). ^{1}H NMR(250 MHz, $CDCl_3$) δ (ppm): 5.51(s, 1H, N-H); 6.61(s,1H, C4-H); 6.91 -7.02 (m,3H); 7.22-7.51(m, 7H); 7.66(d,2H); 7.85(t,3H); 8.04(d,1H); 8.29(s,1H). Anal. Calcd. for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.44; Found: C, 81.34; H, 5.47; N, 12.35.

1-Phenyl-3-(3'-pyridyl)-5-*N*-phenylpyrazole (5). Pale yellow crystals; 71%; 135-7 ^{o}C (ethanol). ^{1}H NMR(250 MHz, $CDCl_3$) δ (ppm): 6.44(s,1H,N-H); 6.47(s,1H,C4-H); 6.90(t, *J*=7.3Hz,1H,H_{N5-Ph}-4); 6.97(d, *J*=8.1Hz,2H,H_{N5-Ph}-2,6); 7.21-7.27(m,4H,H_{5N-Ph}-3,5; H_{N1-Ph}-4; $H_{3Pyridyl}$-5); 7.36(t, *J*=7.7Hz,2H,H_{N1-Ph}-3,5); 7.57(d, *J*=7.7Hz,2H,H_{N1-Ph}-2,6); 8.09(d, *J*=7.9Hz,1H,$H_{3Pyridyl}$-4); 8,38(d, *J*=3,9Hz,1H,$H_{3Pyridyl}$ -6); 8,90(s,1H,$H_{3Pyridyl}$-2). ^{13}C NMR($CDCl_3$) δ (ppm): 93.45; 115.80(C_{N5-Ph}2,6); 120.76; 123.27; 124.09(C_{N1-Ph}-2,6); 127.55; 129.05;129.13/ 129,28($C_{N1Ph/N5Ph}$-3,5); 132.50; 138.18; 142.75/ 142.93($C_{N1Ph/N5Ph}$-1); 146.68; 148.19; 148.44. Anal. Calc. for $C_{20}H_{16}N_4$: C,76.91; H, 5.16; N, 17.93; Found: C, 76.57; H, 5.02; N, 17.67.

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