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A Facile Synthesis of 4-Aryl-1*H*-pyrazolo[3,4-*b*]quinolines

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A novel synthesis of 1*H*-pyrazolo[3,4-*b*]quinolines, luminophores for electroluminescent devices, was developed. Conventional heating (180–190°C in ethylene glycol) or microwave exposure of a three-component mixture of an aromatic aldehyde, 3-substituted 1-phenyl-4,5-dihydro-1*H*-pyrazol-5-one and aromatic amine produced 4-aryl-1*H*-pyrazolo[3,4-*b*]quinolines.

Key words: anilines, aromatic aldehydes, cyclizing condensation, organic luminophores, pyrazolin-5-ones

After the synthesis of the first 1*H*-pyrazolo[3,4-*b*]quinoline [1] by Friedländer condensation of anthranilic aldehyde and 1-(2-chlorophenyl)-3-methyl-4,5-dihydro-1*H*-pyrazol-5-one further syntheses of that heterocyclic system were aiming at biologically active compounds. Numerous 1*H*-pyrazolo[3,4-*b*]quinolines induce interferon and show antiviral [2–4] and antimalarial [5] activity. 1,3-Disubstituted 1*H*-pyrazolo[3,4-*b*]quinolines strongly fluoresce in solution, and some of these compounds have been proposed as optical brighteners [6,7]. Beside fluorescence in solution [8,9], 1*H*-pyrazolo[3,4-*b*]quinolines exhibit strong fluorescence also in the solid state, a desirable property for high performance electroluminescent devices.

Since the demonstration of efficient electroluminescence in two-layer molecular devices with organic luminophores by Tang and Van Slyke [10], considerable progress in the application of organic compounds for this purpose is noted. The discovery [11] that poly(*p*-phenylene vinylene) PPV can be used as an electroluminescent polymer in light-emitting diodes has spurred research efforts in the synthesis of luminescent of polymers [12].

Recently, 1*H*-pyrazolo[3,4-*b*]quinolines have been applied in light emitting devices as low molecular compounds [13,14], as dopants of polyvinylcarbazole PVK [15] and as luminescent copolymers [16]. The most important synthetic methods of 1*H*-pyrazolo[3,4-*b*]quinolines include the Friedländer (with anthranilic aldehyde) and Niementowski (with anthranilic acid) reactions, the reaction of 5-chloro-4-formylpyrazoles with substituted anilines [17], and the reaction of 4-aroyl-5-chloropyrazole [18]. These methods suffer from certain limitations. The application of these methods for the preparation of 4-aryl derivatives is restricted by the availability of

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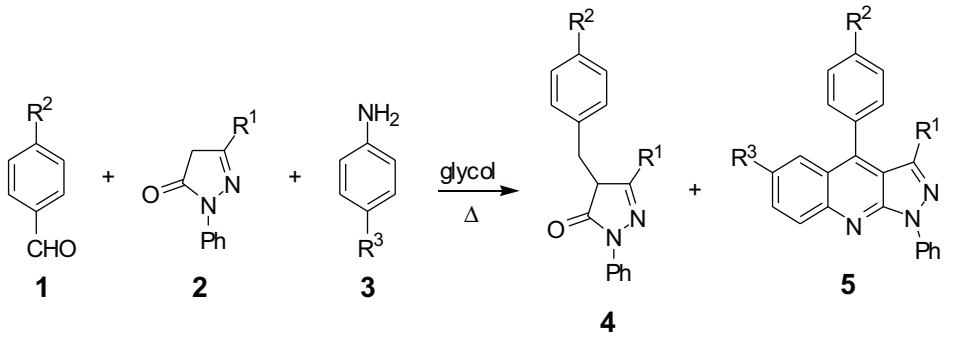
2-aminobenzophenones and aroylpyrazoles, respectively. Mostly, multi-step syntheses are required for their preparation. Recently, an improved synthesis of 4-aryl-1*H*-pyrazolo[3,4-*b*]quinolines has become available from aromatic amines with 4-benzylidene-4,5-dihydro-1*H*-pyrazol-5-ones [19]. In this paper an alternative, one-pot synthesis of 4-aryl-1*H*-pyrazolo[3,4-*b*]quinolines is presented.

RESULTS AND DISCUSSION

The synthesis of 1*H*-pyrazolo[3,4-*b*]quinolines **5** was achieved by heating the mixture of (4-substituted) aniline **3**, (4-substituted) benzaldehyde **1** and 3-methyl- or 3-phenyl-substituted 1-phenyl-4,5-dihydro-1*H*-pyrazol-5-one **2a**,**b** in diethylene glycol. Heating the three component reaction mixture in a microwave oven reduced the reaction time from 60–90 min to 10–20 min. On cooling the resulting 1*H*-pyrazolo[3,4-*b*]quinolines **5** crystallized.

Scheme 1



1-5	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r
R^1	Me	Ph	Me	Ph	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me
R^2	OMe	OMe	H	H	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me	Br	Br
R^3	Me	OMe	Cl	Cl	H	Me	Et	*n*-Bu	*t*-Bu	*n*-$C_{10}H_{21}$	CPh_3	F	Cl	Br	OMe	OPh	Me	Et

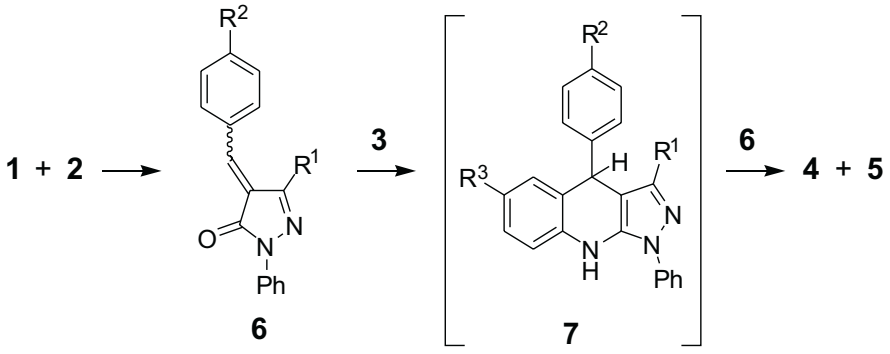
Despite moderate yields (30–33%) this one-pot procedure utilizing commercially available materials is advantageous. The 4-aryl-substituted 1*H*-pyrazolo[3,4-*b*]quinolines may be available from the Friedländer condensation of pyrazolin-5-ones with 2-aminobenzophenones but the latter, except 2-aminobenzophenone and 2-amino-5-chlorobenzophenone, are available only in multistep, time consuming procedures. The formation of 1*H*-pyrazolo[3,4-*b*]quinolines **5** was accompanied by 4-(arylmethyl)-4,5-dihydro-1*H*-pyrazol-5-ones **4** isolated in yields comparable to those of 1*H*-pyrazolo[3,4-*b*]quinolines **5**.

The first step of this reaction is considered to involve the condensation of the aromatic aldehyde **1** with pyrazolin-5-one **2**. Subsequently, the resulting 4-(aryl-methylene)-4,5-dihydro-1*H*-pyrazol-5-one [19] reacts with the aromatic amine **3** affording 4-aryl-1*H*-pyrazolo[3,4-*b*]quinoline **5.** Aniline provided only low yields (10–15%) of the desired 1*H*-pyrazolo[3,4-*b*]quinoline **5e.** Anilines with *para*-substituents R^4 exerting a positive resonance effect performed better (25–33%); the reaction failed with strong electron withdrawing substituents (NO_2 and CF_3).

The structure of all compounds has been confirmed by ^{1}H NMR, and in addition, **5c** and **5d** match samples obtained from the Friedländer condensation of 2-amino-5-chlorobenzophenone with pyrazolin-5-ones **2a** and **2b,** respectively. The by-products **4** accompanying the synthesis of **5e** and **5f** have not been isolated. Compounds **4a, 4b,** and **4q** result from a redox reaction that involves benzylidene intermediates **6** as oxidants. This suggestion is supported by the reported conversion of benzylidene compounds with aniline into 1*H*-pyrazolo[3,4-*b*]quinolines [19]. Furthermore, in the very preliminary stage of the reaction benzylidene compounds **6** were detected in the reaction mixture by TLC (identical R_f with authentic samples **6**).

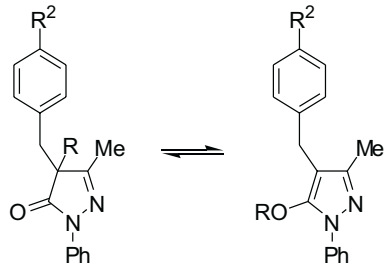
Thus, it is tentatively proposed that aldehyde **1** first reacts with pyrazolin-5-one **2** forming the benzylidene compound **6**. Conversion of the latter with aniline **3** into 4,9-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline **7** is followed by oxidation with **6** resulting in the formation of **5** and **4**, respectively.

Scheme 2



Inspection of the ^{1}H NMR spectra of $CDCl_3$ solutions of **4a** and **4q** revealed the presence of mixtures of the tautomers pyrazolin-5-one **4** and 5-hydroxypyrazole **8**. The structures of both tautomers have been assigned with reference to 3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-one and the predominant tautomer 5-hydroxypyrazole [20]. The tautomer ratios **4a**:**8a** and **4q**:**8q** as determined from the integration of specific signals were 1:3 and 1:2, respectively. Tautomer **8b** could not be detected in the $CDCl_3$ solution of compound **4b**. The failure to observe a tautomeric equilibrium **4b** ⇔ **8b** is reminiscent of 1,3-diphenylpyrazolin-5-one, reportedly existing predominantly in the keto-form [20].

Scheme 3



4a,q (R = H) **8a,q** (R = H)

4D-**4a,q** (R = D) 5-OD-**8a,q** (R = D)

Addition of D_2O to the $CDCl_3$ solutions resulted in the formation of deuterated tautomer species 4D-**4a**/5-OD-**8a** and 4D-**4q**/5-OD-**8q** as observed by the ^1H NMR spectra, with ratios of approximately 1:2 and 1:1, respectively (deduced from signal integration).

In conclusion, a one-pot synthesis of 4-aryl-1*H*-pyrazolo[3,4-*b*]quinolines has been developed. Scope, limitations and the pathway of this reaction are under investigation.

EXPERIMENTAL

Melting points (uncorrected) were determined on a Mel-Temp Apparatus II (capillary). NMR spectra were recorded on a Varian (Mercury 300) spectrometer at 25°C. Mass spectra were recorded on Finnigan MAT 95S. Column chromatography was carried out on Merck silica gel 60 (70–230 mesh) and Merck aluminum oxide 90 (70–230 mesh, II–III activity according to Brockman). Materials were purchased from Merck and Aldrich. A household microwave oven Whirlpool AKL 535 (800W) was used operating at 2450 MHz and at 20% of full power. TLC monitoring of the reactions was performed on silica gel 60 F_{254} plates (Merck) developed with ethyl acetate/toluene 1:3.

6-Methoxy-4-(4-methoxyphenyl)-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5b) and 4-(4-methoxybenzyl)-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-one (4b): Typical Procedure: A mixture of 4-methoxybenzaldehyde (**1b**; 1.36 g, 0.01 mol), 1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-one (**2b**; 2.36 g, 0.01 mol), and anisidine (3**b**; 1.23 g, 0.01 mol) in diethylene glycol (20 mL) was heated at 190°C for 2 h. The cold reaction mixture was treated with methanol (50 mL) to give a yellow precipitate **5b**, which was subjected to column chromatography (Merck Silica Gel 60; toluene). The methanol solution was poured into NaOH (10%, 100 mL), boiled with charcoal and acidified with diluted HCl. The precipitate was filtered off, dried and crystallized from EtOH/water yielding **4b**.

4b: Beige crystals (1.1 g, 31%), m.p. 165–6°C (ethanol/water). ^1H NMR (300 MHz, $CDCl_3$): δ 7.79 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}), 7.73–7.69 (2H, m, 2,6-H_{2Ph}), 7.49–7.40 (2H, m, 3,5-H_{2Ph}), 7.37 (2H, t, J = 7.9 Hz, 3,5-H_{Ph}), 7.25–7.15 (2H, m, 4-H_{Ph}, 4-H_{2Ph}), 6.83, 6.81 (AA', 2,6-H_{ar}), 6.62, 6.60 (BB', 3,5-H_{ar}), 4.06 (1H, t, J = 4.9Hz, 4-H), 3.68 (3H, s, OMe), 3.46 (1H, dd, J = 13.9, 4.67 Hz, C$\mathbf{H_A}H_B$), 3.30 (1H, dd, J = 13.7, 5.22 Hz, $CH_A\mathbf{H_B}$). Anal. Calcd. for $C_{23}H_{20}N_2O_2$: (356.43): C, 77.51; H, 5.66; N, 7.86. Found: C, 77.34; H, 5.45; N, 7.67.

5b: Yellow crystals (1.3 g, 30%), m.p. 251–2°C (ethanol/water). ^1H NMR (300 MHz, $CDCl_3$): δ 8.61 (2H, d, J = 8.3 Hz, 2,6-$H_{1\text{-}Ph}$), 8.14 (1H, d, J = 9.4 Hz, 8-H), 7.57 (1H, t, J = 7.4 Hz, 3,5-H_{Ph}), 7.47 (1H, dd, J = 9.4, 2.75 Hz, 7-H), 7.31 (1H, t, J = 7.4 Hz,4-H_{Ph}), 7.25–7.01 (7H, m, 2,3,4,5,6-H_{2Ph}, 2,6-H_{4Ph}), 6.77,

6.75 (BB', 3,5-H_{4Ph}), 3.82 (3H, s, OMe), 3.77 (3H, s, OMe). Anal. Calcd. for $C_{30}H_{23}N_3O_2$ (457.54): C, 78.76; H, 5.07; N, 9.18; Found: C, 78.65; H, 4.89; N, 9.01.

Utilizing a microwave oven for this procedure allowed for reaction times of 10–20 min. This procedure was applied for the synthesis of **4a**, **5a**, **5c**–**5p**, **4q**, **5q**, and **5r**.

4-(4-Methoxybenzyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-one (4a): Colourless crystals (0.85 g, 29%), m.p. 166–8°C (EtOH /water). ^{1}H NMR (300 MHz, $CDCl_3$; mixture of tautomers **4a** and **4-(4-methoxybenzyl)-3-methyl-1-phenyl-1*H*-pyrazol-5-ol, 8a**): δ 7.78 (2H, d, J= 7.8 Hz, 2,6-H_{Ph}, **8a**), 7.59 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}, **4a**), 7.36 (2H, t, J = 7.0 Hz, 3,5-H_{Ph}, **8a**), 7.25 (2H, t, J = 7.0 Hz, 3,5-H_{Ph}, **4a**), 7.20–7.07 (m, 4-H_{Ph}, AA', 2,6-H_{ar}, **4a**, **8a**), 6.80–6.76 (BB', 3,5-H_{ar}, **4a**, **8a**), 3.76 (3H, s, OMe, **4a**), 3.75 (3H, s, OMe, **8a**), 3.57–3.46 (2H, s, t overlapping, OH-**8a**, 4-H-**4a**,), 3.21–3.19 (2H, s, d overlapping, CH_2- **4a**, CH_2- **8a**), 2.04 (3H, s, Me, **8a**), 2.01 (3H, s, Me, **4a**). ^{1}H NMR (300 MHz, $CDCl_3$ + D_2O) (mixture of tautomers 4D-**4a** and 5-OD-**8a**): δ 7.77 (2H, d, J = 7.8 Hz, 2,6-H_{Ph}, 5-OD-**8a**), 7.66 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}, 4D-**4a**), 7.30–7.40 (4H, m, 3,5-H_{Ph}, 4D-**4a**, 5-OD-**8a**), 7.01–7.19 (3H, m, 4-H_{Ph}, AA', 2,6-H_{ar}, 4D-**4a**, 5-OD-**8a**), 6.76–6.80 (BB', 3,5-H_{Ph}, 4D-**4a**, 5-OD-**8a**), 3.75 (3H, s, OMe, 4D-**4a**), 3.74 (3H, s, OMe, 5-OD-**8a**), 3.55 (2H, s, CH_2, 4D-**4a**), 3.19 (2H, s, CH_2, 5-OD-**8a**), 2.05 (3H, s, Me, 4D-**4a**), 2.04 (3H, s, Me, 5-OD-**8a**). Anal. Calcd. for $C_{18}H_{18}N_2O_2$ (294.36): C, 73.45; H, 6.16; N, 9.52. Found: C, 73.24; H, 5.91; N, 9.27.

4-(4-Methoxyphenyl)-3,6-dimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5a): Yellow crystals (1.21 g, 31%), m.p. 184°C (toluene; lit. [21] m.p. 184°C).

6-Chloro-3-methyl-1,4-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5c): Yellow crystals (1.03 g, 28%), m.p. 193–4°C (lit. [18] m.p. 199–202°C).

6-Chloro-1,3,4-triphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5d): Pale yellow crystals (1.25 g, 29%), m.p. 168–9°C (toluene). ^{1}H NMR vide infra.

3-Methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5e): Yellow needles (0.52 g, 15%), m.p. 206–7°C (lit. [19,21] m.p. 206–7°C).

3,6-Dimethyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5f): Yellow needles (1.12 g, 30%), m.p. 196–7°C (lit. [21] m.p. 197–8°C).

6-Ethyl-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5g): Yellow needles (1.13 g, 30%), m.p. 158–9°C (lit. [19] m.p. 158–9°C).

6-*n*-Butyl-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5h): Yellow needles (1.22 g, 30%), m.p. 246–7°C (lit. [19] m.p. 246–7°C).

6-*tert*-Butyl-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5i): Yellow needles (1.12 g, 30%), m.p. 246–7°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (2H, d, J = 8.7 Hz, 2,6-H_{Ph}), 8.12 (1H, d, J = 9.07 Hz, 8-H), 7.83 (1H, d, J = 9.07, 2.2 Hz, 7-H), 7.65 (1H, s, J = 2.2 Hz, 5-H), 7.53 (2H, t, J = 8.05 Hz, 3,5-H_{Ph}), 7.38, 7.35 (AA', 2,6-$H_{4\text{-}Ph}$), 7.34, 7.31 (BB', 3,5-H_{ar}), 7.24 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 2.51 (3H, s, CH_3), 2.14 (3H, s, 3-CH_3), 1.30 (9H, s, 6-C$(CH_3)_3$). MS FAB**:** Calcd. for $C_{28}H_{27}N_3$: 405.2205. Found: 405.2205. Anal. Calcd.: C, 82.93; H, 6.71; N, 10.36. Found: C, 83.18; H, 6.75; N, 10.64.

6-*n*-Decyl-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5j): Yellow needles (1.03 g, 21%), m.p. 89–90°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (2H, d, J = 8,75 Hz, 2,6-H_{Ph}), 8.13 (1H, d, J = 8.8 Hz, 8-H), 7.61 (1H, d, J = 8.8, 1.9 Hz, 7-H), 7.57 (2H, t, J = 8 Hz, 3,5-H_{Ph}), 7.47 (1H, s, J =1.9 Hz, 5-H), 7.41, 7.38 (AA', 2,6-$H_{4\text{-}Ph}$), 7.36, 7.33 (BB', 3,5-$H_{4\text{-}Ph}$), 7.25 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 2.68 (2H, t, 6-C$\mathbf{H_2}(CH_2)_7CH_2CH_3$), 2.54 (3H, s, CH_3), 2.15 (3H, s, 3-CH_3), 1.62 (2H, pent, 6-$CH_2C\mathbf{H_2}(CH_2)_7CH_3$), 1.38–1.20 (14H, m, 6-$CH_2CH_2(C\mathbf{H_2})_7CH_3$), 0.85 (3H, t, 6-$CH_2CH_2(CH_2)_7C\mathbf{H_3}$). MS FAB: Calcd. for $C_{34}H_{39}N_3$: 489.3144. Found: 489.3134. Anal. Calcd.: C, 83.39; H, 8.03; N, 8.58. Found: C, 83.55; H, 7.88; N, 7.12.

3-Methyl-4-(4-methylphenyl)-1-phenyl-6-trityl-1*H*-pyrazolo[3,4-*b*]quinoline (5k): Yellow needles (1.54 g, 26%), m.p. 278–9°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (2H, d, J = 8.7 Hz, 2,6-H_{Ph}), 8.23 (1H, d, J = 8.8 Hz, 8-H), 7.64 (1H, d, J = 8.8 Hz, 7-H), 7.55 (2H, t, J = 8 Hz, 3,5-H_{Ph}), 7.45 (1H, s, 5-H), 7.38, 7.35 (AA', 2,6-H_{ar}), 7.33, 7.31 (BB', 3,5-H_{ar}), 7.27 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 7.22–7.09 (15H, m, 6-CPh_3), 2.53 (3H, s, C$\mathbf{H_3}C_6H_4$), 2.14 (3H, s, 3-CH_3). MS FAB: Calcd. for: $C_{43}H_{33}N_3$: 591.2674. Found: 591.2669. Anal. Calcd.: C, 87.28; H, 5.62; N, 7.10. Found: C, 87.43; H, 7.26; N, 7.03.

6-Fluoro-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5l): Yellow needles (1.10 g, 30%), m.p. 185–7°C (lit. [19] m.p. 185–7°C).

6-Chloro-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5m): Yellow needles (1.15 g, 30%), m.p. 201–3°C (lit. [19] m.p. 201–3°C).

6-Bromo-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5n): Yellow needles (1.28 g, 30%), m.p. 205–6°C (lit. [19] m.p. 205–6°C).

6-Methoxy-3-methyl-4-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5o): Yellow needles (1.14 g, 30%), m.p. 201–3°C (lit. [19] m.p. 201–3°C).

3-Methyl-4-(4-methylphenyl)-6-phenoxy-1-pheny-1*H*-pyrazolo[3,4-*b*]quinoline (5p): Yellow needles, (1.32 g, 30%), m.p. 158–9°C (lit. [19] m.p. 158–9°C).

4-(4-Bromobenzyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazolin-5-one (4q): Colourless crystals (0.96 g, 28%), m.p. 189–190°C. ^{1}H NMR (300 MHz, $CDCl_3$; mixture of tautomers **4q** and **4-(4-bromobenzyl)-3-methyl-1-phenyl-1*H*-pyrazol-5-ol, 8q**): δ 7.78 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}, **8q**), 7.62 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}, **4q**), 7.40–7.34 (AA'3,5-H_{Ph}, **4q**, **8q**), 7.20–7.13 (m, 4-H_{Ph}, **4q**, **8q**), 7.10–7.07 (BB', 3,5-H_{ar}, **4q**, **8q**), 3.60 (s,2H,CH_2, **4q**), 3.51 (t, J = 5.6 Hz, 4-H, **4q**), 3.23–3.21 (3H, s, d overlapping, OH-**8q**, CH_2-**4q**), 2.09 (3H, s, Me, **4q**), 2.06 (3H, s, Me, **8q**).

^{1}H NMR (300 MHz, $CDCl_3$ + D_2O) (mixture of tautomers 4D-**4q** and 5-OD-**8q**): δ 7.77 (2H, d, J = 7.7 Hz, 2,6-H_{Ph}, 5-OD-**8q**), 7.67 (2H, d, J = 7.7 Hz; 2,6-H_{Ph}, 4D-**4q**), 7.30–7.45 (AA', 3,5-H_{ar}, 4D-**4q**, 5-OD-**8q**), 7.17–7.15 (2H, 2×t overlapping, 4-H_{Ph}, 4D-**4q**, 5-OD-**8q**), 7.06–7.14 (BB', 3.5-H_{ar}, 4D-**4q**, 5-OD-**8q**), 3.51 (2H, s, CH_2, 4D-**4q**), 3.21 (2H, s, CH_2, 5-OD-**8q**), 2.12 (3H, s, Me, 5-OD-**8q**), 2.05 (3H, s, Me, 4D-**4q**). Anal. Calcd. for $C_{17}H_{15}BrN_2O$ (343.23): C, 59.49; H, 4.41; N, 8.16. Found: C, 59.31; H, 4.23; N, 7.86.

4-(4-Bromophenyl)-3,6-dimethyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5q): Yellow needles (1.41 g, 33%), m.p. 202–3°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.52 (2H, d, J = 8.6 Hz, 2,6-H_{Ph}), 8.06 (1H, d, J = 8.8 Hz, 8-H), 7.65, 7.63 (AA', 2,6-$H_{4\text{-}Ph}$), 7.55 (1H, d, J = 8.8 Hz, 7-H), 7.50 (2H, t, J = 8.0 Hz, 3,5-H_{Ph}), 7.48, 7.45 (BB', 3,5-$H_{4\text{-}Ph}$), 7.36 (1H, s, 5-H), 7.27 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 2.43 (3H, s, 6-CH_3), 2.13 (3H, s, 3-CH_3). Anal. Calcd. for $C_{24}H_{18}BrN_3$ (428.34): C, 67.30; H, 4.24; N, 9.81. Found: C, 67.78; H, 3.97; N, 9.65.

4-(4-Bromophenyl)-6-ethyl-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5r): Yellow needles (1.5 g, 34%), m.p. 197–9°C (toluene). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (2H, d, J = 8.6 Hz, 2,6-H_{Ph}), 8.10 (1H, d, J = 8.8 Hz, 8-H), 7.63, 7.60 (AA', 2,6-H_{ar}), 7.60 (1H, d, J= 8.8 Hz, 7-H), 7.54 (2H, t, J = 8.0 Hz, 3,5-H_{ar}), 7.48, 7.45 (BB', 3,5-H_{ar}), 7.36 (1H, s, 5-H), 7.27 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 2.72 (2H, q, 6-C**H$_2$**CH_3), 2.13 (3H, s, 3-CH_3), 1.24 (3H, t, 6-CH_2C**H$_3$**). Anal. Calcd. for $C_{25}H_{20}BrN_3$ (442.36): C, 67.88; H, 4.56; N 9.50. Found: C, 67.92; H, 4.68; N, 9.35.

Friedländer synthesis of 6-chloro-3-methyl-1,4-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5c) [22].

Typical procedure: A mixture of 2-amino-5-chlorobenzophenone (2.31g, 0.01 mol) and 3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-one (**2a**; 1.73g, 0.01 mol) in diethylene glycol (5 mL) was heated at 180–190°C for 24 h. The cold reaction mixture was digested with ethanol (15 mL) to give a yellow precipitate, which was purified by column chromatography (aluminum oxide/toluene) to give yellow crystals **5c** (1.66 g, 45%), m.p. 193–4°C (toluene; lit. [18] m.p. 199–202°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (2H, d, J = 8.7 Hz, 2,6-H_{Ph}), 8.05 (1H, d, J = 8.9 Hz, 8-H), 7.62–7.54 (5H, m, 5-H, 7-H, 3,4,5-H_{2Ph}), 7.51 (2H, t, J = 7.1 Hz, 3,5-H_{Ph}), 7.42–7.40 (2H, m, 2,6-H_{2Ph}), 7.25 (1H, t, J = 7.4 Hz, 4-H_{Ph}), 2.06 (3H, s, 3-Me). Anal. Calcd. for $C_{23}H_{16}ClN_3$ (369.86): C, 74.69; H, 4.36; N, 11.36. Found: C, 74.56; H, 4.02; N, 11.23.

6-Chloro-1,3,4-triphenyl-1*H*-pyrazolo[3,4-*b*]quinoline (5d): Following the preceding procedure 2-amino-5-chlorobenzophenone (2.31 g, 0.01 mol) and 1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-one (**2b**; 2.36 g, 0.01 mol) afforded pale yellow crystals **5d** (2.70 g, 70%), m.p. 168–9°C (toluene). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (2H, d, J = 7.9 Hz, 2,6-$H_{1\text{-}Ph}$), 8.16 (1H, d, J = 9.2 Hz, 8-H), 7.84 (1H, d, J = 2.3 Hz, 5-H), 7.66 (1H, dd, J = 9.2, 2,3 Hz, 7-H), 7.56 (2H, t, J = 7.1 Hz, 3,5-$H_{1\text{-}Ph}$), 7.30–7.35 (2H, m, 4-$H_{1\text{-}Ph}$, 4-$H_{3\text{-}Ph}$), 7.23 (2H, t, J = 7.6 Hz, 3,5-$H_{2\text{-}Ph}$), 7.15–7.19 (m, 3H, 4-$H_{2\text{-}Ph}$, 2,6-$H_{2\text{-}Ph}$), 7.1 (d, J = 6.8 Hz, 2H,

2,6-$H_{3\text{-Ph}}$), 7.05 (2H, t, J = 7.4 Hz, 3,5-$H_{3\text{-Ph}}$). Anal. Calcd. for $C_{28}H_{18}ClN_3$ (431,93): C, 77.86; H, 4.20; N, 9.73. Found: C, 77.78; H, 4.24; N, 9.65.

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