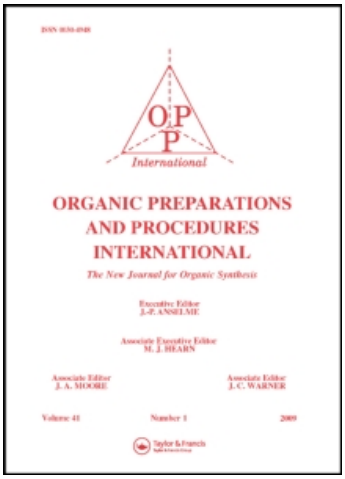

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SYNTHIESIS OF PYRAZOLO (3,4-b)QUINOLINES AND THEIR 1-PHENYL DERIVATIVES

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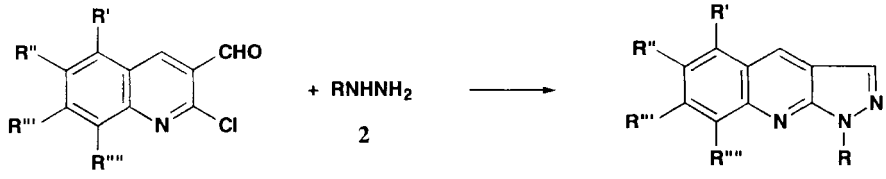
Pyrazolo[3,4-b]quinolines are of interest as possible antiviral agents.[1] Some of their derivatives exhibit parasiticidic properties[2] and were studied as potential antimalarials.[3] Since several members of this ring system fluoresce, they have been proposed as optical brightners for polyester fibers.[4] Herein, we report the synthesis of 1H-pyrazolo-[3,4-b]quinolines (**3a-d**) and 1-phenylpyrazolo[3,4-b]quinolines (**3e-h**) from the reaction of 2-chloro-3 formyl-quinolines (**1**)[5] with hydrazine and phenylhydrazine respectively. Though a few reports have appeared already on the synthesis of derivatives of pyrazolo[3,4-b]quinolines,[6,7] our synthesis constitutes a simple route from 2-chloro-3-formyl-quinolines (**1**).



1 3

a) R = R' = R" = R"' = R"" = H
b) R = R' = R"' = R"" = H, R" = CH_3
c) R = R' = R"' = R"" = H, R" = OCH_3
d) R = R' = R" = R"" = H, R"' = OCH_3
e) R = Ph, R' = R" = R"' = R"" = H
f) R = Ph, R' = R"' = R"" = H, R" = CH_3
g) R = Ph, R' = R"' = R"" = H, R" = OCH_3
h) R =Ph, R' = R" = R"" = H, R"' = OCH_3

EXPERIMENTAL

Melting points were taken on mettler-FP5 apparatus and are uncorrected. IR Spectra were recorded on a Perkin-Elmer 597 spectrophotometer PMR Spectra on a FX90 QNMR spectrometer using TMS as internal reference and mass spectra on a Jeol JMD-D 300 mass spectrometer. 2-chloro-3-formyl quinolines **1a-d** were prepared from the appropriate acetanilides by the procedure of Meth-Cohn *et al.*[5]

1H-Pyrazolo [3,4-b]quinolines (3a-d). General Procedure.- Compound **1** (0. 001 mole) was added to a solution of hydrazine hydrate (0.01 mole) in ethanol (10 mL) and refluxed on a water bath for about 5 hrs. Excess ethanol was removed under reduced pressure and the cooled mixture was poured onto crushed ice. The separated solid was recrystallized from ethanol (Table 1).

TABLE 1. Physical and Spectroscopic Data of **3a-h**[a]

Cmpd	Yield (%)	mp. (°C)	Elemental Analysis (Found) C	H	N	IR[b] (cm^{-1})	^1H NMR[c] (δ) ppm	MS m/z (M^+)
3a	63	203-204	70.99 (70.75)	4.17 (4.28)	24.82 (24.80)	3400 (NH) 1640 (–C=N–)	7.5-8.29 (m, 4H, H_5, H_6, H_7 & H_8); 8.35(s, 1H, H_3), 8.72 (s, 1H, H_4); 12.61 (bs, 1H, NH)	169
3b	77	175 (d)	72.00 (72.21)	4.95 (4.84)	22.31 (22.33)	3300 (NH) 1630 (–C=N–)	2.52 (s,3H, CH_3); 7.55 (dd, 1H, H_7,$J_{7,8}$ = 8cps, $J_{7,5}$ = 1.5cps); 7.70 (d, 1H, H_5, $J_{5,7}$ = 1.5cps); 7.93 (d, 1H,H_8, $J_{8,7}$ = 8cps); 8.23 (s, 1H, H_3); 8.6 (s, 1H, H_4)[e]	183
3c	78	217-218	66.32 (66.52)	4.55 (4.45)	21.08 (21.02)	3400 (NH) 1640 (–C=N–)	3.93 (s, 3H, OCH_3); 7.04 (dd, 1H,H_7,$J_{7,8}$ = 8cps, $J_{7,5}$ =2 cps); 7.36 (d, 1H, H_5, $J_{5,7}$ = 2cps); 8.13 (s, 1H, H_3); 8.5 (s, 1H, H_4)[e]	199
3d	44	243-244	66.32 (66.50)	4.55 (4.55)	21.08 (21.04)	3150 (NH) 1640 (–C=N–)	3.93 (s,3H, OCH_3); 6.90-8.30 (m,4H, H_3, H_5, H_6 & H_8); 8.57 (s, 1H, H_4)[e]	199
3e	44	172 (d)	78.35 (78.59)	4.53 (4.51)	17.14 (17.18)	1640 (–C=N–)	7.00-8.20 (m, 8H, H_5, H_6, H_7, H_8, H_2', H_3', H_4' & H_5'); 8.30 (s, 1H, H_3); 8.40-8.50 (m, 2H, H_4 & H_1')	245
3f	82	176-178	78.74 (78.54)	5.05 (5.15)	16.19 (16.21)	1640 (–C=N–)	2.93 (s,3H, CH_3); 7.10-7.80 (m,5H, H_5, H_7, H_2',H_3' & H_4'); 8.03 (d, 1H, H_8, $J_{8,7}$ = 8cps); 8.27 (s, 1H, H_3); 8.30-8.53 (m, 3H, H_4, H_1' & H_5')	259
3g	81	150 (d)	74.14 (74.43)	4.76 (4.87)	15.25 (15.20)	1600 (-C=N–)	3.98 (s,3H, OCH_3); 6.90-8.00 (m,7H, H_5, H_7, H_8, H_2', H_3', H_4' & H_5'); 8.26 (s, 1H, H_3); 8.30-8.50 (m, 2H, H_4 & H_1')[e]	275
3h	68	201 (d)	74.14 (74.30)	4.76 (4.65)	15.25 (15.22)	1610 (–C=N–)	4.01 (s, 3H, OCH_3); 7.00-7.90 (m, 7H, H_5, H_6,H_8, H_2', H_3', H_4' & H_5'); 8.35-8.59 (m, 3H, H_3, H_4 & H_1')	275

a) Recrystallized from ethanol. b) As KBr pellet. c) In $CDCl_3$ unless otherwise specified. d) Decomposed.
e) In $CDCl_3$ + DMSO-d_6.

1-Phenylpyrazolo[3,4-b]quinolines (3e-h). General Procedure.- Compound **1** (0.001 mole) was added to a solution of phenylhydrazine hydrochloride (0.001 mole) in absolute ethanol (10 mL) and refluxed on a water bath for 7 hrs. Excess ethanol was removed under reduced pressure and the cooled mixture was poured onto crushed ice. The separated solid was recrystallized from ethanol (Table 1).

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