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A Simple Synthesis of Dibenzo[*b,g*][1,8]naphthyridines

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ABSTRACT

2-Chloro-3-formyl quinoline and its derivatives on reaction with anilines in DMF afforded the dibenzo[*b,g*][1,8]naphthyridines.

KeyWords: Dibenzo[*b,g*][1,8]naphthyridines; Anilines; 2-Chloro-3-formyl quinolines; DMF.

INTRODUCTION

Interesting pharmacological properties have been associated with [1,8]naphthyridine and its derivatives.^[1–4] Available literature showed the reports on the synthesis of dibenzo[*b,g*][1,8]naphthyridines by the reaction

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Sampathkumar, Venkatesh Kumar, and Rajendran

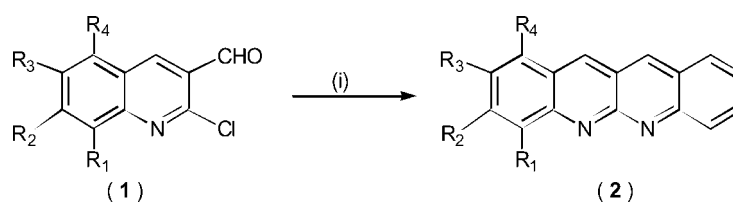
of dimethyl *bis*(methylthio)methylene malonate with anilines.^[5] Kidwai and Kohli^[6] synthesised dibenzo[*b,g*]-5-methyl-1,8-naphthyridines in a three-step process from 2-hydroxy-4-methyl quinoline and aniline. Recently, we have reported the synthesis of 1,2,3,4-tetrahydro dibenzo[*b,g*][1,8]naphthyridines^[7] from 2-amino-3-formyl quinoline and cyclohexanone.

RESULTS AND DISCUSSION

The reaction of 2-chloro-3-formyl-quinoline with aniline was attempted in DMF at 75°C. The resulting product was analysed by IR, ¹H NMR, mass spectroscopy, and elemental analysis and assigned the structure dibenzo[*b,g*][1,8]naphthyridine. A number of 2-chloro-3-formyl-quinolines were reacted with aniline to produce substituted dibenzo[*b,g*][1,8]naphthyridines, which revealed the generality of this protocol (Sch. 1).

EXPERIMENTAL SECTION

Melting points were determined on a Boetius microheating table and are uncorrected. Thin-layer chromatography were performed on glass plates coated with silica gel-G incorporating 13% CaSO₄ as binder. IR spectra were recorded on a Perkin-Elmer-597 infrared spectrophotometer as KBr pellets. ¹H NMR spectra were recorded on an AMX-400 MHz NMR spectrophotometer using Me₄Si as internal standard and chemical shifts are quoted in ppm. Mass spectra were recorded on an Autospec mass spectrophotometer. Elemental analyses were performed by Cario-Elmer 1106 and Perkin-Elmer analyser.



Scheme 1. (i) Aniline, DMF, 75°C/stirring, 2 hr; (a) R₁=R₂=R₃=R₄=H; (b) R₁=R₂=H, R₃=CH₃, R₄=H; (c) R₁=CH₃, R₂=R₃=R₄=H; (d) R₁=CH₃, R₂=H, R₃=CH₃, R₄=H; (e) R₁=R₂=H, R₃=OCH₃, R₄=H; (f) R₁=H, R₂=OCH₃, R₃=R₄=H; (g) R₁=OCH₃, R₂=R₃=R₄=H; (h) R₁=OCH₃, R₂=R₃=H, R₄=OCH₃; (i) R₁=-CH=CH-CH=CH-R₂, R₃=R₄=H.



Table 1. Physical and spectroscopic data of compounds (**2a–2i**).^a

Compound	M.p. (°C)	M.p. (yield %)	Calculated (found, %)			IR ν (cm ⁻¹)	¹ H NMR (δ , ppm)	MS $M/z(M^+)$
			C	H	N			
2a	128 (82)		83.46 (83.42)	4.38 (4.40)	12.16 (12.12)	1,610	8.95–7.30 (m, 10H, C ₁ -H, C ₂ -H, C ₃ -H, C ₄ -H, C ₇ -H, C ₈ -H, C ₉ -H, C ₁₀ -H, C ₁₁ -H, and C ₁₂ -H)	230
2b	117 (86)		83.58 (83.55)	4.95 (4.90)	11.47 (11.42)	1,618	2.5 (s, 3H, C ₂ -CH ₃), 8.96 (s, 1H, C ₁₂ -H), 8.94 (s, 1H, C ₁₁ -H), 7.94–7.30 (m, 7H, C ₁ -H, C ₃ -H, C ₄ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	244
2c	115–116 (85)		83.58 (83.52)	4.95 (4.93)	11.47 (11.46)	1,621	2.71 (s, 3H, C ₄ -CH ₃), 8.8 (s, 1H, C ₁₁ -H), 8.9 (s, 1H, C ₁₂ -H), 8.0–7.4 (m, 7H, C ₂ -H, C ₃ -H, C ₁ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	244
2d	94 (86)		83.69 (83.68)	5.46 (5.47)	10.85 (10.84)	1,600	2.4 (s, 3H, C ₂ -CH ₃), 2.7 (s, 3H, C ₄ -CH ₃), 8.5 (s, 1H, C ₁₁ -H), 8.7 (s, 1H, C ₁₂ -H), 7.9–7.3 (m, 6H, C ₃ -H, C ₁ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	258
2e	182 (81)		78.44 (78.42)	4.65 (4.67)	10.76 (10.74)	1,616	3.95 (s, 3H, C ₂ -OCH ₃), 8.95 (s, 1H, C ₁₂ -H), 8.94 (s, 1H, C ₁₁ -H), 7.9–7.4 (m, 7H, C ₁ -H, C ₃ -H, C ₄ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	260

(continued)

Table 1. Continued.

Compound	M.p. (°C)	Calculated (found, %)			IR ν (cm ⁻¹)	¹ H NMR (δ , ppm)	MS $M/z(M^+)$
		C	H	N			
2f	160–161 (85)	78.44 (78.42)	4.65 (4.62)	10.76 (10.74)	1,620	3.97 (s, 3H, C ₃ -OCH ₃), 8.9 (s, 1H, C ₁₂ H), 8.94 (s, 1H, C ₁₁ -H), 7.8–7.1 (m, 7H, C ₁ -H, C ₂ -H, C ₄ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	260
2g	134 (85)	78.44 (78.40)	4.65 (4.61)	10.76 (10.75)	1,614	3.98 (s, 3H, C ₄ -OCH ₃), 8.91 (s, 1H, C ₁₂ -H), 8.8 (s, 1H, C ₁₁ -H), 7.9–7.3 (m, 7H, C ₂ -H, C ₃ -H, C ₁ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	260
2h	135 (80)	74.47 (74.45)	4.86 (4.88)	9.65 (9.64)	1,618	4.1 (s, 3H, C ₄ -OCH ₃), 3.95 (s, 3H, C ₁ -OCH ₃), 8.8 (s, 1H, C ₁₁ -H), 8.7 (s, 1H, C ₁₂ -H), 8.1–7.3 (m, 6H, C ₂ -H, C ₃ -H, C ₇ -H, C ₈ -H, C ₉ -H, and C ₁₀ -H)	290
2i	151–152 (82)	85.69 (85.64)	4.32 (4.30)	9.99 (9.95)	1,620	9.4–7.7 (m, 12H, C ₁ -H, C ₂ -H, C ₃ -H, C ₄ -H, C ₅ -H, C ₆ -H, C ₇ -H, C ₈ -H, C ₉ -H, C ₁₀ -H, C ₁₁ -H, and C ₁₂ -H)	280

^aRecrystallised from ethyl acetate–light petroleum (50:50).

2-Chloro-3-formyl-quinolines (1a–i). 2-Chloro-3-formyl-quinoline derivatives were synthesised by Vilsmeier–Haack reaction of acetanilide with POCl₃/DMF.^[8]

Dibenzo[*b,g*][1,8]naphthyridines (2). Compound **1** (0.01 mol), aniline (0.0125 mol) in DMF (20 mL) were stirred at (75°C) for 2 hr. The reaction was monitored by TLC. DMF was removed under reduced pressure, the residue washed with 2 N NaOH solution (50 mL), water and then chromatographed on silica gel (60–120) using light petroleum–ethyl acetate (98:2) as eluant to give **2** (86%), recrystallised from ethyl acetate–light petroleum (Table 1).

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2024

Sampathkumar, Venkatesh Kumar, and Rajendran

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