

SYNTHESIS OF 1,2,3,4-TETRAHYDRODIBENZO[b,g][1,8]NAPHTHYRIDINES.

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Abstract : 2-Chloro-3-formylquinoline 1 and its derivatives were prepared and aminated by dry ammonia gas in ethanol. The 2-amino-3-formylquinolines 2 so obtained were then condensed with cyclohexanone in presence of acetic acid and sulphuric acid to give 1,2,3,4-tetrahydrodibenzo[b,g][1,8]naphthyridines 3.

Introduction : Interesting pharmacological properties have been associated with [1,8]naphthyridine and its derivatives.¹⁻⁴ Available literature showed the synthesis of dibenzo[b,g][1,8]naphthyridines by the reaction of dimethyl bis(methylthiomethylidene)malonate with anilines.⁵ Here-in we report a new method for the synthesis of 1,2,3,4-tetrahydrodibenzo[b,g][1,8]naphthyridine starting from 2-chloro-3-formylquinoline as shown in scheme.1

Experimental: Melting points were determined on a Boetius Microheating table and are uncorrected. IR Spectra were recorded on a Perkin-Elmer-597 Infrared Spectrophotometer as KBr pellets. ¹H NMR spectra were recorded on a Bruker WH-270 (270 MHz) NMR spectrometer or on an EM-390 (90MHz) NMR spectrometer in CDCl₃ unless otherwise specified. Mass spectra were recorded on a Jeol-D300 mass spectrometer or on Finnigan MAT 8230 GC/mass spectrometer. Elemental analyses were performed by Carlo-Ermer 1106 and Perkin-Elmer model 1240 CHN analyser.

Typical Procedure. 2-Chloro-3-formylquinolines (1a-e).- The starting compound 2-chloro-3-formylquinoline 1 was synthesized by Vilsmeier-Haack reaction of acetanilide with POCl₃/DMF⁶.

Typical Procedure. 2-Amino-3-formylquinolines (2a-e).- To a stirred solution of 1 (1.5 mole) in 40 ml ethanol was passed dry ammonia gas for 3-4 hrs at 0-20°C. It was left aside for 12 hrs. The product separated was filtered and purified using column chromatography over silica gel (60-120 mesh: 50g) using pet.ether-ethyl acetate mixture (98:2v/v) as eluant. The product was recrystallised from pet.ether-ethyl acetate (50:50v/v) mixture. Table (1).

Typical Procedure. 1,2,3,4-Tetrahydrodibenzo[b,g][1,8]naphthyridines(3a-e).- Compound 2 (0.01 mole) was dissolved in a mixture of cyclohexanone (2g,0.02mole) and acetic acid, and then sulphuric acid (0.1 mole) was added and refluxed for 4 hrs. The cold solution was poured on to a mixture of conc aq-ammonia (40mL) in (20g) of ice, which gave a brown tarry product. After extraction with chloroform, drying, evaporation and addition of diethylether, the brown solid obtained was purified by chromatography over silica gel (60-120 mesh:50g) using pet.ether-ethyl acetate (95:5v/v) as eluant. The product was recrystallised from ethyl acetate. (Table II).

Result and discussions

Amination of 2-chloro-3-formyl-7-methylquinoline 1c in ethanol by passing dry ammonia gas gave a product with m.p. 194°C in 86% yield (Lit m.p 194°C).⁷ The IR spectrum of this compound showed peaks at 1680cm⁻¹(CHO) and 3200-3300 cm⁻¹ (NH₂). The mass spectrum gave molecular ion peak at m/z 172. It was identified as 2-amino-3-formyl-7-methylquinoline 2c.

The compound 2c on condensation with cyclohexanone with acetic acid and sulphuric acid at 120°C for 8 hrs, gave a product which on purification furnished a brown compound (m.p.230°C) in 80% yield. Its IR spectrum showed disappearance of peak at 1680 cm⁻¹. The compound showed negative tests for aldehyde and amino groups.

The ¹H-NMR spectrum of the compound showed a signals at 2.7(s,3H,C₈-CH₃);2.09-2.56(m,4H, C₁-2H and C₄-2H);1.25-1.62(m,4H,C₂-2H and C₃-2H);7.7(m,2H,C₇-H&C₈-H);8.5(s,1H,C₁₀-H);9.2(s,1H,C₆-H) and 8.9(s,1H,C₅-H). The mass spectrum gave molecular ion peak at m/z 248. The compound was identified as 1,2,3,4-tetrahydrodibenzo[b,g][1,8]naphthyridine 3c.

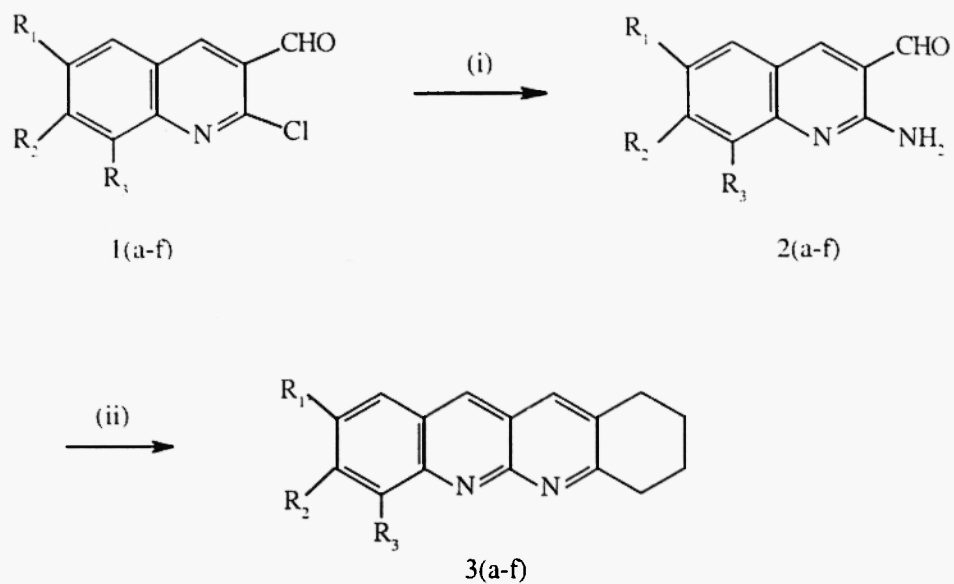
The reaction sequence leading to 3c was then extended to synthesise hitherto unknown compounds 3a,3b,3d-3f.

Table-1 Physical and Spectroscopic Data of 1a-f

Compd	mp°C (Yield%)	Elemental Analysis (Found)			IR cm-1	Mass m/z (M ⁺)
		C	H	N		
2a	125 (82)	69.74 (69.72)	4.68 (4.67)	16.27 (16.30)	1680 3300	172
2b	172 (80)	70.93 (70.92)	5.41 (5.40)	15.04 (15.02)	1685 3250	186
2c	194 ^a (86)	70.93 (70.91)	5.41 (5.38)	15.04 (15.01)	1685 3250	186
2d	162 (83)	70.93 (70.87)	5.41 (5.40)	15.04 15.04	1680 3200	186
2e	145 (80)	65.32 (65.27)	4.98 (4.91)	13.85 (13.81)	1689 3340	202
2f	156 (85)	65.32 (65.30)	4.98 (4.95)	13.85 (13.80)	1689 3300	202

a) Recrystallised from pet.ether-ethyl acetate (50:50v/v).

SCHEME - 1

i). Dry NH_3 gas. Ethanolii). Cyclohexanone. $\text{CH}_3\text{COOH}/\text{H}_2\text{SO}_4$

- a. $\text{R}_1=\text{R}_2=\text{R}_3=\text{H}$
- b. $\text{R}_1=\text{CH}_3$; $\text{R}_2=\text{R}_3=\text{H}$
- c. $\text{R}_1=\text{R}_3=\text{H}$; $\text{R}_2=\text{CH}_3$
- d. $\text{R}_1=\text{R}_2=\text{H}$; $\text{R}_3=\text{CH}_3$
- e. $\text{R}_1=\text{R}_2=\text{H}$; $\text{R}_3=\text{OCH}_3$
- f. $\text{R}_1=\text{R}_2=\text{H}$; $\text{R}_3=\text{OCH}_3$

Table II Physical and spectroscopic Data of 3a-f

Compd	mp, °C (Yield%)	Elemental Analysis (Found)			IR (ν)cm ⁻¹	¹ H NMR (δ)ppm	MS m/z (M ⁺)
		C	H	N			
3a	205 (80)	82.01 (82.01)	6.02 (6.00)	11.96 (11.91)	1446 3024	1.59-1.94(m, 4H, C ₁ -2H & C ₁ -2H); 1.26-1.42(m, 6H, C ₅ -H, C ₆ -H, C ₇ -H, C ₈ -H, C ₉ -H, C ₁₀ -H).	234
3b	211 (72)	82.21 (82.13)	6.49 (6.41)	11.28 (11.26)	1440 3030	—	248
3c	230 (75)	82.21 (82.18)	6.49 (6.45)	11.28 (11.26)	1450 3025	2.7(s, 3H, C ₉ -CH ₃); 2.09-2.56(m, 4H, C ₁ -2H & C ₄ -2H); 1.25-1.62 (m, 4H, C ₂ -2H & C ₃ -2H); 7.7(m, 2H, C ₇ -H & C ₈ -2H); 8.5(s, 1H, C ₁₀ -H); 9.2(s, 1H, C ₆ -H); 8.9(s, 1H, C ₅ -H)	248
3d	197 (76)	82.21 (82.18)	6.49 (6.46)	11.28 (11.23)	1445 3030	2.17(s, 3H, C ₁₀ -CH ₃); 1.59-2.01 (m, 4H, C ₁ -2H & C ₄ -2H); 1.42-1.84 (m, 4H, C ₂ -2H & C ₃ -2H); 7.19-7.77 (m, 6H, C ₅ -H, C ₆ -H, C ₇ -H, C ₈ -H & C ₉ -H)	248
3e	196 (76)	77.23 (77.20)	6.10 (6.06)	10.60 (10.57)	1440 3030	3.9(s, 3H-OCH ₃); 2.17-2.44 (m, 4H, C ₁ -2H & C ₄ -2H); 1.25-1.59(m, 4H, C ₂ -2H & C ₃ -2H); 7.26(m, 3H, C ₇ -H, C ₈ -H & C ₁₀ -H); 7.51(s, 1H, C ₅ -H); 8.7(s, 1H, C ₆ -H)	264
3f	156 (70)	77.23 (77.20)	6.10 (6.08)	10.60 (10.55)	1440 3030	---	264

a. Recrystallised from Ethyl acetate.

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