Asian Journal of Chemistry Vol. 14, Nos. 3–4 (2002), 1303–1306

Synthesis of Cyclopenta[*b*]Benzo[*g*][1,8]Naphthyridines

G. ARUL PRAKASH, N. SAMPATH KUMAR and S.P. RAJENDRAN*
Department of Chemistry, Bharathiar University
Coimbatore-641 046, India

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 cyclopentanone in presence of acetic acid and sulphuric acid to give benzo[g]cyclopenta[b][1,8]naphthyridines **3**.

Key Words: Synthesis, Cyclopenta[b]benzo[g][1,8] naphthyridines.

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 dimethylbis (methylthiomethyledene) malonate with anilines.[5] We have already reported the synthesis of 1,2,3,4-tetrahydro dibenzo[*b,g*][1,8] naphthyridine[6]. Herein we report a method for the synthesis of benzo[*g*]cyclopental[*b*][1,8]naphthyridines starting from 2-chloro-3-formyl-quinoline 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. ^{1}H NMR spectra were recorded on a Bruker WH-270 (270 MHz) NMR spectrometer or on an EM-390 (90 MHz) NMR spectrometer in $CDCl_3$ unless otherwise specified.

Typical Procedure, 2-Chloro-3-formylquinolines (1a–g): The starting compound 2-chloro-3-formylquinoline **1** was synthesized by Vilmeter-Haack reaction of acetanilide with $POCl_3$/DMF[7].

Typical Procedure, 2-Amino-3-formylquinolines4 (2a-g): To a stirred solution of 2-chloro-3-formylbenzo[7,8-*h*]quinoline **1g** (1.5 mole) in 40 mL ethanol was passed dry ammonia gas for 3–4 h at 0–20°C. It was left aside for 12 h. The product separated was filtered and purified using column chromatography over silica gel (60–120 mesh, 50g) using pet. ether-ethyl acetate mixture (98 : 2 v/v) as eluant. The product was recrystallised from pet.ether- ethyl acetate (50 : 50 v/v) mixture.

Compound 2g: Yield 63%; m.p. 224–226°C; IR = 3300, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.1–7.2 (t, 2H, C_8-H and C_9-H), 7.44–7.55 (m, 4H, C_5-H, C_6-H,

C_7-H and C_{10}-H), 8.3 (s, 1H, C_4-H), 6.62 (d, 2H, NH_2), 10.51 (s, 1H, CHO); m/z = 222 (M^+). Elemental analaysis: found (calcd.): [C = 75.66 (75.65), H = 4.53 (4.51), N = 1260 (12.59)].

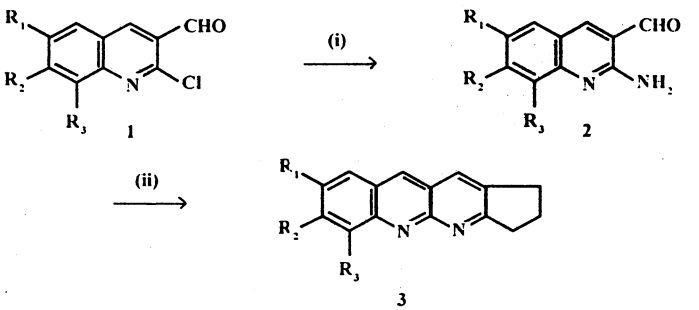
Typical Procedure: Cyclopenta[*b*]benzo[*g*][1,8]naphthyridines (3a–g): Compound **2** (0.01 g) was dissolved in a mixture of cyclopentanone, 2 g (0.02 mole) and acetic acid and then sulphuric acid (0.1 mol) was added and refluxed for 4 h. The cold solution was poured on to a mixture of conc. aq. ammonia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

RESULTS AND DISCUSSION

The compound **2a** on condensation with cyclopentanone with acetic and sulphuric acids at 120°C for 8 h, gave a product which on purification furnished a brown compound (m.p. 192–193°C) in 70% 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 signal at δ 3.10 (m, 4H, C_1-2H and C_3-2H); 2.18 (m, 2H, C_2-2H); 7.6–8.42 (m, 6H, Ar-H). The mass spectrum gave moleular ion peak at m/z 220. The compound was identified as cyclopenta[*b*]benzo[*g*][1,8]naphthyridine, **3a**.

The reaction sequence leading to **3a** was then extended to synthesis of hitherto unknwon compounds **3b–3g.**



Scheme-1

(i) Dry ammonia gas, ethanol

(ii) Cyclopentanone, acetic acid, sulphuric acid

(a) $R_1 = R_2 = R_3 = H$; (b) $R_1 = CH_3$; $R_2 = R_3 = H$;

(c) $R_1 = R_3 = H$; $R_2 = CH_3$; (d) $R_1 = R_2 = H$; $R_3 = CH_3$

(e) $R_1 = OCH_3$; $R_2 = R_3 = H$; (f) $R_1 = R_3 = H$; $R_2 = OCH_3$

(g) $R_1 = H$; $R_2 = R_3 =$ —CH=CH—CH=CH—

TABLE-1
PHYSICAL AND SPECTROSCOPIC DATA OF **3a–G**[a]

Compd.	m.p. (°C) (Yield %)	Elemental analysis %, found (Calcd.)			IR (ν) (cm^{-1})	^{1}H NMR (δ) ppm	MS m/z (M^+)
		C	H	N			
3a	192–193 (70)	81.78 (81.76)	5.49 (5.45)	12.72 (12.70)	1446 1610 3024	3.10 (m, 4H, C_1-2H and C_3-2H); 2.18 (m, 2H, C_2-2H) ; 7.6–8.42 (m, 6H, Ar-H)	220
3b	155–157 (70)	82.01 (82.00)	6.02 (6.02)	11.95 (11.94)	1440 1600	—	234
3c	164–166 (68)	82.01 (82.00)	6.02 (6.01)	11.95 (11.94)	1440 1600 3024	2.7 (s, 3H, C_8-CH_3); 3.00(m, 4H, C_1-2H and C_3-2H); 2.09 (m, 2H,C_2-2H); 7.7 (m, 2H, C_6-H and C_7-H); 8.2 (s, 1H, C_9-H); 8.7 (s, 1H, C_4-H) ; 9.1 (s,1H, C_5-H)	234
3d	202–203 (65)	82.01 (82.01)	6.02 (6.01)	11.95 (11.93)	1440 1600 3024	2.17 (s, 3H, C_9-CH_3); 3.10 (m,4H, C_1-2H and C_3-2H); 2.01 (m, 2H, C_2-2H); 7.29–7.54 (m, 3H, C_6-H,C_7-H and C_8-H); 8.23 (s,1H,C_4-H); 8.92 (s, 1H, C_5-H)	234
3e	199–201 (64)	76.77 (76.76)	5.64 (5.62)	11.19 (11.15)	1440 1610 3025	—	250
3f	182–184 (65)	76.77 (76.75)	5.64 (5.63)	11.19 (11.17)	1440 1600 3024	3.91 (s, 3H, C_8-OCH_3); 3.15 (m, 4H, C_1-2H and C_3-2H); 2.17 (m, 2H, C_2-2H); 7.26-7.55 (m, 2H, C_6-H and C_7-H); 8.1 (s,1H, C_9-H); 8.61 (s, 1H, C_4-H); 8.91 (s, 1H, C_5-H)	234
3g	225–226 (58)	84.41 (84.38)	5.21 (5.19)	10.37 (10.33)	1440 1600 3024	3.1 (m, 4H, C_1-2H and C_3-2H); 2.91 (m.2H, C_2-2H); 7.45-7.65 (m, 3H, C_6-H, C_7-H and C_8-H); 7.31 (t,2H, C_9-H, C_{11}-H); 7.05 (t, 1H, C_{10}-H); 8.3 (s, 1H, C_4-H); 8.9 (s.1H, C_5-H	270

ACKNOWLEDGEMENTS

We thank CSIR, New Delhi for the award of SRF to one of us (GA). We also thank the services rendered by the "Sophisticated Instrumentation Facility" at Indian Institute of Science, Bangalore, "Regional Sophisticated Instrumentation Centre", IIT, Chennai; CDRI Lucknow and SPIC Science Foundation, Chennai, in recording ^{1}H NMR and mass spectra. We thank Aruljothi Computer Centre, Coimbatore for the computational work.

REFERENCES

1. P.A. Lowe, in: A.R. Katritzky and C.W. Rees (Eds.), Comprehensive Heterocyclic Chemistry, Vol II, Pergamon Press Ltd., Oxford-New York, pp. 581–627 (1984).
2. N.P. Buu-Hoi, P. Jacquignon, D.C. Thang and T. Bartnik, *J. Chem. Soc., Perkin-Trans.-1*, 263 (1972).
3. K.G. Gupta, S.V. Kessar and B. Singh, *Appl. Microbiol.*, **19**, 1017 (1970).
4. P.L. Nyce, D. Gala and M. Strinman, *Synthesis*, 571 (1991).
5. Y. Tominaga, T. Michioka and A. Hosomi, *J. Heterocyclic Chem.*, **27**, 1217 (1990).
6. G. Arul Prakash and S.P. Rajendran, *Heterocyclic Communications*, **6**, 63 (2000).
7. O. Meth-Cohn, B. Narine and B. Tarnowski, *J. Chem. Soc., Perkin-1*, 1520 (1981).

(*Received:* 21 February 2002; *Accepted:* 6 May 2002) AJC-2686