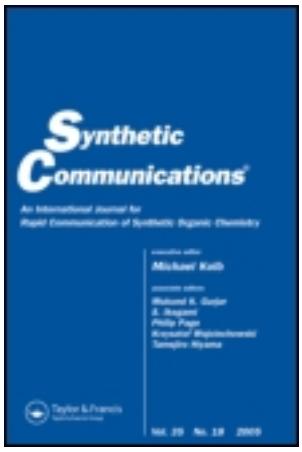


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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

N. Sampathkumar [a], N. Venkatesh Kumar [a] & S. P. Rajendran [a]

[a] Department of Chemistry, Bharathiar University, Coimbatore, Tamil Nadu, 641046, India

Version of record first published: 20 Aug 2006.

To cite this article: N. Sampathkumar, N. Venkatesh Kumar & S. P. Rajendran (2004): A Simple Synthesis of Dibenzo[b,g][1,8]naphthyridines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:11, 2019-2024

To link to this article: http://dx.doi.org/10.1081/SCC-120037914

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 11, pp. 2019–2024, 2004

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

N. Sampathkumar, N. Venkatesh Kumar, and S. P. Rajendran*

Department of Chemistry, Bharathiar University, Coimbatore, Tamil Nadu, India

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

*Correspondence: S. P. Rajendran, Department of Chemistry, Bharathiar University, Coimbatore, Tamil Nadu 641046, India; E-mail: rajendransp@yahoo.com.

DOI: 10.1081/SCC-120037914 0039-7911 (Print); 1532-2432 (Online)

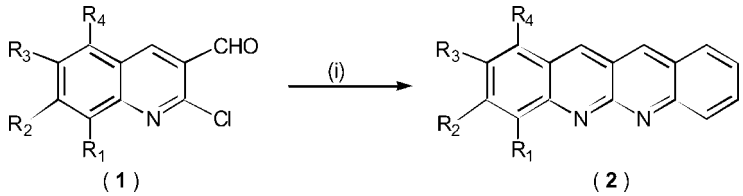
of dimethyl *bis*(methylthio)methylene malonate with anilines.[5] Kidwai and Kohli[6] synthesised dibenzo[*b*,*g*]-5-methyl-1,8-naphthyridines in a three-step process from 2-hydroxy-4-methyl quinoline and aniline. Recently, we have reported the synthesis of 1,2,3,4-tetrahydro dibenzo[*b*,*g*][1,8]naphthyridines[7]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

RESULTS AND DISCUSSION

The reaction of 2-chloro-3-formyl-quinoloine with aniline was attempted in DMF at 75°C. The resulting product was analysed by IR, ^{1}H 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% $CaSO_4$ as binder. IR spectra were recorded on a Perkin–Elmer-597 infrared spectrophotometer as KBr pellets. ^{1}H NMR spectra were recorded on an AMX-400 MHz NMR spectrophotometer using Me_4Si 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) R_1=R_2=R_3=R_4=H; (b) R_1=R_2=H, R_3=CH_3, R_4=H; (c) R_1=CH_3, R_2=R_3=R_4=H; (d) R_1=CH_3, R_2=H, R_3=CH_3, R_4=H; (e) R_1=R_2=H, R_3=OCH_3, R_4=H; (f) R_1=H, R_2=OCH_3, R_3=R_4=H; (g) R_1=OCH_3, R_2=R_3=R_4=H; (h) R_1=OCH_3, R_2=R_3=H, R_4=OCH_3; (i) R_1= − CH=CH − CH=CH − R_2, R_3=R_4=H.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

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

Compound	M.p. (°C) (yield %)	Calculated (found, %) C	H	N	IR ν (cm^{-1})	^{1}H NMR (δ, ppm)	MS $M/z(M^+)$
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*)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 1. Continued.

Compound	M.p. (°C) (yield %)	Calculated (found, %) C	H	N	IR ν (cm^{-1})	^{1}H NMR (δ, ppm)	MS $M/z(M^+)$
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

[a]Recrystallised from ethyl acetate–light petroleum (50 : 50).

MARCEL DEKKER, INC. 270 Madison Avenue, New York, New York 10016

2-Chloro-3-formyl-quinolines (1a–i). 2-Chloro-3-formyl-quinoline derivatives were synthesised by Vilsmeier–Haack reaction of acetanilide with $POCl_3$/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).

ACKNOWLEDGMENTS

We thank the services rendered by the "Sophisticated Instrumentation Facility" at Indian Institute of science, Bangalore, "Indian Institute of Chemical Technology," Hyderabad in recording the ^{1}H NMR and mass spectra.

REFERENCES

1. Lowe, P.A. Naphthyridines pyridoquinolines, anthyridines and similar compounds. In *Comprehensive Heterocyclic Chemistry, Part 2A; Six Membered Rings with One Nitrogen Atom*; Pregamon Press: New York, 1984; Vol. 2, 581–627.
2. Ferrarini, P.L.; Mori, C.; Badwneh, M.; Calderone, V.; Calzolari, L.; Loffredo, T.; Martinotti, E.; Saccomanni, G. Synthesis of 1,8-naphthyridine derivatives: potential antihypertensive agents—part 7. Eur. J. Med. Chem. **1998**, *33*, 383–387.
3. Ferrani, P.L.; Manera, C.; Mori, C.; Badwneh, M.; Saccomanni, G. Synthesis and evaluation of antimycobacterial activity of 4-phenyl-1,8-naphthyridine derivatives. IL Farmaco **1998**, *53*, 741–746.
4. Nyce, P.L.; Gala, D.; Steinman, M. An efficient synthesis of 1,8-naphthyridin-2(1H)-ones: synthesis of leukotriene inhibitors SCH 37244. Synthesis **1991**, *7*, 571–574.
5. Tominaga, Y.; Michioka, T.; Moriyama, K.; Hosomi, A. Synthesis of quinoline derivatives using ketene dithioacetal. J. Heterocyclic. Chem. **1990**, *27*, 1217–1225.
6. Kidwai, M.; Kohli, S. Synthesis of dibenzo(*b,g*)-5-methyl-1,8-naphthyridines. Indian J. Chem. **2001**, *40B*, 248–249.
7. Prakash, G.A.; Rajendran, S.P. Synthesis of 1,2,3,4-tetrahydro dibenzo [*b*,*g*][1,8]naphthyridines. Heterocyclic Commun. **2000**, *6* (1), 63–66.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

8. Meth-Cohn, O.; Narine, B.; Tarnowski, B. A versatile new synthesis of quinolines and related fused pyridines. Part-5. The synthesis of 2-chloroquinoline-3-carbaldehydes. J. Chem. Soc. Perkin Trans-I **1981**, 1520–1530.

Received in India January 5, 2004

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016