SHORT PAPER

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One-step synthesis of pyridine derivatives from malononitrile with bisarylidenecycloalkanone under microwave irradiation†

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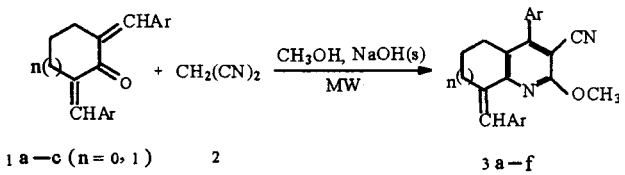
Six pyridine derivatives were synthesised by one-step reaction of malononitrile with 2,5-bisarylidenecyclopentanones or 2,6-bisarylidenecyclohexanones in methanol / sodium hydroxide under microwave irradiation in 75~92% yields.

Keywords: pyridine derivatives, malonitrile, bisarylidene cycloalkanone

Pyridine derivatives have shown important biological activities as pharmaceuticals and potential agrochemicals such as herbicides.[1] Some other pyridines possess fluorescent properties and have been used in the liquid-crystal industry. For example, the molecular design of liquid crystalline 2,5-disubstituted pyridine derivatives for twisted nematic and super twisted nematic liquid crystal displays and the correlation between the molecular structure of pyridine derivatives and their physical-chemical properties has been reported.[2]

Since the reaction of malononitrile and α,β-unsaturated ketones in presence of ammonium acetate to give pyridines was first reported by Sakurai and Midorikawa,[3] the use of malononitrile and α,β-unsaturated ketones for the synthesis of pyridine derivatives has attracted much attention. For example, reaction of malononitrile with 1,3-diaryl-2-propen-1-ones using sodium alkoxide in ethanol or methanol at room temperature to afford 2,4-diaryl-5-cyano-6-alkoxypyridines (R=CH_3, C_2H_5),[4] malononitrile with 1,3-diphenylpropenone and other α,β-unsaturated ketones in refluxing methanol / sodium hydroxide to afford 1,4-dipheny-3-cyano-2-methoxypyridines and phenyl-substituted [1]benzopyrano-[4,3-b]pyridines, [1]benzothiopyrano[4,3-b]pyridines, pyrido[3,2-b] [1,4]benzothiazines (1-azaphenothiazines) (the yields of 3a and 3d were 59% and 23% respectively),[5] malononitrile with 2,5-bisarylidenecyclopentanones and 2,6-diarylidenecyclohexanones using sodium ethoxide in absolute ethanol at room temperature or in refluxing methanol / sodium hydroxide to give 3-cyano-2-alkoxypyridine derivatives.[6–7]



1 a–c (n = 0, 1) 2 3 a–f

	Ar
a:	C_6H_5
b:	4-ClC_6H_4
c:	4-$CH_3OC_6H_4$

	n	Ar
3a:	0	C_6H_5
3b:	0	4-ClC_6H_4
3c:	0	4-$CH_3OC_6H_4$
3d:	1	C_6H_5
3e:	1	4-ClC_6H_4
3f:	1	4-$CH_3OC_6H_4$

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

However, reaction times were long and yields were low by classical methods.

Recently, the wide applicability of microwave irradiation in chemical reaction enhancement is due to high reaction rates with the formation of cleaner products and operational simplicity.[8,9] Because of our continued interest in the condensation reactions of active methylene compounds with aldehydes and ketones under microwave irradiation,[10–12] we would like to report a facile synthesis of arylidenecycloalka[b]-4-aryl-3-cyano-2-methoxypyridine by one-step reaction of malononitrile with 2,5-bisarylidenecyclopentanone or 2,6-bisarylidenecyclohexanone in methanol / sodium hydroxide under microwave irradiation. The reactions were generally finished in 5–12 minutes with 75–92% yields and easy work-up.

Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX instrument. ^{1}HNMR spectra were measured on a Bruker 300 MHz spectrometer in $CDCl_3$ with TMS as internal standard. The reactions were carried out with a modified commercial microwave oven (Sanle WP650D 650w) under atmospheric pressure.

2,5-Bisarylidenecyclopentanones and 2,6-bisarylidenecyclohexanones were prepared according to literature procedures.[13]

General procedure: Into an Erlenmeyer flask (50ml) equipped with reflux condenser were introduced the bisarylidenecycloalkanone **1** (1 mmol), malononitrile **2** (1 mmol), dry methanol (2 ml) and a catalytic quantity of sodium hydroxide. After irradiation with microwaves for 5–12 minutes (reaction followed by TLC), the reaction mixture was cooled. The precipitate was collected by suction filtration and washed with cold ethanol, then washed with water. The crude product was recrystallised from ethanol to give a pure sample. Specific details on each product are as follows:

3a: Yield 78%. m.p. 176–178°C. IR (KBr): 3045, 2940, 2210, 1610, 1590, 1140. ^{1}HNM δ: 1.86 (m, 2H, CH_2), 2.80–2.64 (m, 2H, CH_2), 4.20 (s, 3H, OCH_3), 7.60–7.33 (m, 11H, $2\times C_6H_5$ and ylidene CH). Anal. Calcd. for $C_{23}H_{18}N_2O$ (%): C, 81.65; H, 5.32; N, 8.28. Found: C, 81.25; H, 5.06; N, 7.85.

3b: Yield 75%. m.p. 202–204°C. IR (KBr):3035, 2945, 2210, 1610, 1580, 1140. ^{1}HNMR δ: 1.85 (m, 2H, CH_2), 2.77–2.61 (m, 2H, CH_2), 4.19 (s, 3H, OCH_3), 7.56–7.35 (m, 9H, $2\times C_6H_4$ and ylidene CH). Anal. Calcd. for $C_{23}H_{16}Cl_2N_2O$ (%): C, 58.82; H, 4.09; N, 7.16. Found: C, 59.03; H, 4.32; N, 6.56

3c: Yield 76%. m.p. 186–188°C. IR (KBr):3050, 2935, 2210, 1625, 1585, 1140. ^{1}HNMR δ: 1.87 (m, 2H, CH_2), 2.65 (m, 2H, CH_2), 3.73 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.18 (s, 3H, OCH_3), 7.61–7.43 (m, 9H, $2\times C_6H_4$ and ylidene CH). Anal. Calcd. for $C_{25}H_{22}N_2O_3$ (%): C, 69.95; H, 5.53; N, 7.04. Found: C, 70.08; H, 5.25; N, 6.81

3d: Yield 92%. m.p. 212–214°C (Lit.[7] 210°C). IR (KBr): 3040, 2940, 2210, 1620, 1585, 1140. ^{1}HNMR δ: 1.53 (m, 2H, CH_2), 1.85 (m, 2H, CH_2), 2.78–2.63 (m, 2H, CH_2), 4.18(s, 3H, OCH_3), 7.55–7.30

(m, 11H, $2 \times C_6H_5$ and ylidene CH). Anal. Calcd. for $C_{24}H_{20}N_2O$ (%): C, 81.80; H, 5.70; N, 8.00. Found: C, 81.40; H, 5.44; N, 7.60.

3e: Yield 91%. m.p. 206–208°C (Lit.[7] 210°C). IR (KBr):3040, 2940, 2210, 1610, 1590, 1140. ^{1}HNMR δ: 1.54 (m, 2H, CH_2), 1.86 (m, 2H, CH_2), 2.78–2.60 (m, 2H, CH_2), 4.17 (s, 3H, OCH_3), 7.58–7.35 (m, 9H, $2 \times C_6H_4$ and ylidene CH). Anal. Calcd. for $C_{24}H_{18}Cl_2N_2O$ (%): C, 68.40; H, 4.30; N, 6.70. Found: C, 68.65; H, 4.55; N, 6.22.

3f: Yield 88 %. m.p. 221–223 °C (Lit[7] 225°C). IR (KBr):3030, 2940, 2210, 1620, 1590, 1140. ^{1}HNMR δ:1.59 (m, 2H, CH_2), 1.90 (m, 2H, CH_2), 2.67–2.48 (m, 2H, CH_2), 3.61 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 7.41–7.20 (m, 9H, $2 \times C_6H_4$ and ylidene CH). Anal. Calcd. for $C_{26}H_{24}N_2O_3$ (%): C, 75.7; H, 5.80; N, 6.80. Found: C, 75.56; H, 5.60; N, 6.55.

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References

1 C. Temple, Jr. G.A. Rener, W.R. Raud and P.E. Noker, *J. Med. Chem.*, 1992, **35**, 3686.
2 A.I. Pavluchenko, V.F. Petrov and N. I. Smirnova, *Liquid Crystals*, 1995, **9**, 811.
3 A. Sakurai, and N. Midorikawa, *Bull. Chem. Soc. Japn.*, 1968, **41**, 430.
4 M.M. Al-Arab, *J. Heterocyclic Chem*., 1989, **26**, 1665.
5 D.V. Tyndall, T. Al Nakib, M.J. Al Meegan, *Tetrahedron Lett.*, 1988, **29**, 2703.
6 M.M. Al-Arab, F.S. Atfeh, and S.M. Mayoof, *J. Heterocyclic Chem.*, 1998, **35**, 1473.
7 G.H. Elgemeie, F.A. Abdelaal, and K. Abou, *J. Chem. Res.(S)*,1991, 128.
8 S. Caddick, *Tetrahedron*, 1995, **51**, 10403.
9 S.A. Galema, *Chem. Soc. Rev*., 1997, **26**, 233.
10 S-J.Tu, H. Wang, J-Q. Feng, A-L. Tang, and J-C. Feng, *Synth.Commun.*, (in press).
11 S-J. Tu, Q-H.Wei, H-J. Ma, D-Q. Shi, Y. Gao and G-Y. Cui, *Synth.Commun.*, (in press).
12 S-J. Tu, J-F.Zhou, X. Deng, P-J. Cai, H. Wang and J-C. Feng, *Chinese J. Org. Chem*., (in press).
13 B.A. Hathaway, *J. Chem. Educ.*, 1987, **64**, 367.