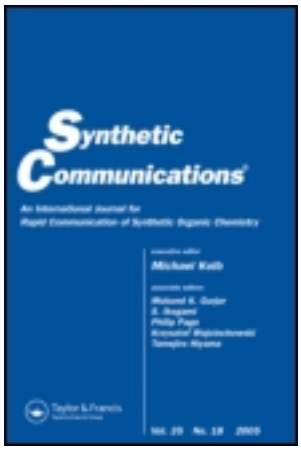


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

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

One-Step Synthesis of Pyridine and 4 H -Pyran Derivatives from Bisarylidenecyclohexanone and Malononitrile Under Microwave Irradiation

Jian-Feng Zhou [a b]

[a] Department of Chemistry, Huaiyin Normal College, Huaiyin, P.R., China

[b] Department of Chemistry, Huaiyin Normal College, Huaiyin, P.R., China

Version of record first published: 29 Jun 2011

To cite this article: Jian-Feng Zhou (2003): One-Step Synthesis of Pyridine and 4 H -Pyran Derivatives from Bisarylidenecyclohexanone and Malononitrile Under Microwave Irradiation, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:1, 99-103

To link to this article: http://dx.doi.org/10.1081/SCC-120015564

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 1, pp. 99–103, 2003

One-Step Synthesis of Pyridine and 4*H*-Pyran Derivatives from Bisarylidenecyclohexanone and Malononitrile Under Microwave Irradiation

Jian-Feng Zhou*

Department of Chemistry, Huaiyin Normal College,
Huaiyin, P.R. China

ABSTRACT

The 3-cyano-2-methoxylpyridine and 2-amino-3-cyano-4H-pyran derivatives were synthesized by one-step reaction of 2,6-bisarylidene-cyclohexanone with malononitrile in sodium hydroxide/methanol or piperidine/ethanol under microwave irradiation with good yields.

The 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. 2-Amino-3-cyano-4*H*-pyrans possess photochemical activity.[2] Polyfunctionalized 4*H*-pyrans are a common structural unit in a number of natural products,[3] 4*H*-pyrans ring can

*Correspondence: Jian-Feng Zhou, Department of Chemistry, Husiyin Normal College, Huaiyin, P.R. China. E-mail: jfchow@sohu.com.

DOI: 10.1081/SCC-120015564 0039-7911 (Print); 1532-2432 (Online)

be transformed to pyridine systems related to pharmacologically important calcium antagonists of the DHP type.[4–6]

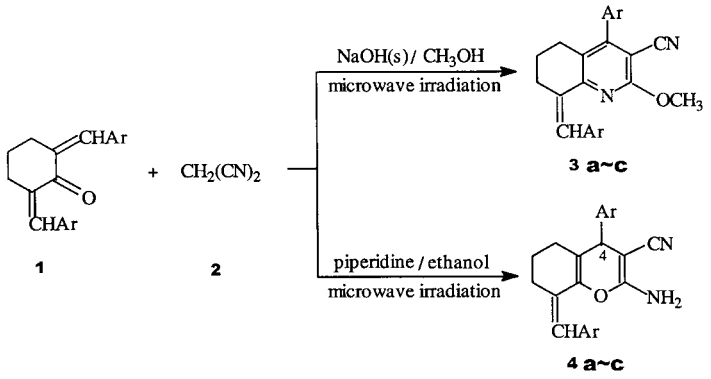
Since the reaction of malononitrile and α,β-unsaturated ketones in presence of ammonium acetate to give pyridines was first reported by Sakurai and Midorikawa,[7] the use of malononitrile and α,β-unsaturated ketones for the synthesis of pyridine and pyran derivatives has attracted much attention.[8–11] However, the most of reaction times were long by classical methods.

Recently, the wide applicability of microwave irradiation in chemical reaction enhancement is due to high reaction rate with formation of cleaner products and the operation simplicity.[12,13] Continuing our interest in the development of efficient and simple procedures for the synthesis of heterocyclic compounds, we have recently reported that a facile synthesis of 4-arylpolyhydroquinolines under microwave irradiation.[14] In this communication, we would like to report a facile synthesis of 3-cyano-2-methoxylpyridine and 2-amino-3-cyano-4*H*-pyran derivatives by one-step reaction of 2,6-bisarylidenecyclohexanone with malononitrile in sodium hydroxide/methanol or piperidine/ethanol under microwave irradiation. The reactions were generally finished in 5–10 min with 70–92% yields and easy work-up.

The synthesis route is shown in Sch. 1.

The results obtained are shown in Table 1.

All of title compounds were established by their melting points, IR, ^{1}H NMR and elemental analysis. The formation of compounds **4** was assumed to proceed vis formation of an Michecal adduct intermediate followed by cyclization according to Sch. 2.

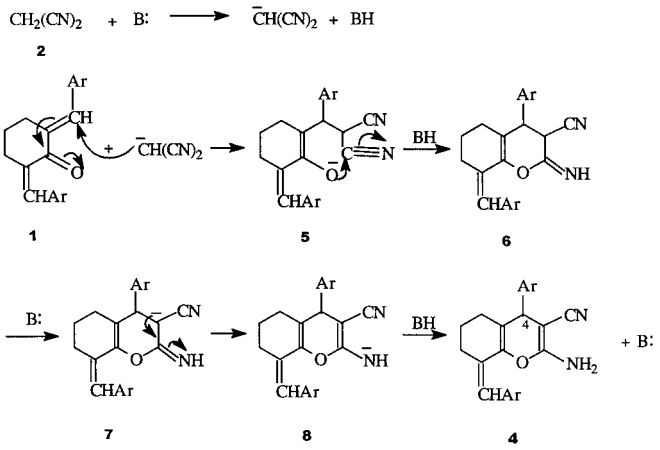


Scheme 1.

Table 1. Comparisons between classic heating and microwave irradiation synthesis of **3a**–**c** and **4a**–**c**.

		Classic heating		MWI	
Entry	Ar	Time (h)	Yield (%) (lit.)	Time (min)	Yield (%)[a]
3a	C_6H_5	3	80 (10)	5	92
3b	4-ClC_6H_4	3	70 (10)	8	91
3c	4-$CH_3OC_6H_4$	3	85 (10)	10	88
4a	C_6H_5	4	60[a]	5	70
4b	4-ClC_6H_4	4	67[a]	9	71
4c	3-$O_2NC_6H_4$	4	70[a]	5	71

[a]Yields of the isolated products.



Scheme 2.

EXPERIMENTAL

Melting points were determined in open capillaries and uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX instrument. ^{1}H NMR was measured on a Bruker 300 MHz spectrometer in $CDCl_3$ with TMS as internal standard. Elemental analyzer were determined using Perkin–Elmer 240C elemental analyzer. The reactions were carried out with a modified commercial microwave oven (Sanle WP650D 650 W) under atmospheric pressure.

2,6-bisArylidenecyclohexanones were prepared according to literature procedure.[15]

General Procedure for 3-Cyano-2-methoxylpyridine and 2-Amino-3-cyano-4*H*-pyran Derivatives

Into an Erlenmeyer flask (25 mL) equipped with reflux condenser were introduced the bisarylidnecyclohexanone **1** (1 mmol), malononitrile **2** (1 mmol), sodium hydroxide (0.05 g) and dry methanol (3 mL) or piperidine (0.05 mL) and dry ethanol (3 mL). After irradiation with microwaves for 5–10 min (monitored by TLC), the reaction mixture was cooled. The precipitate was collected by suction filtration and washed with cold ethanol. The crude product was recrystallized from ethanol to give a pure sample.

3a: M.p. 212–214°C (210°C).[10] **3b:** M.p. 206–208°C (221–223°C).[10] **3c:** M.p. 221–223°C (225°C).[10] **4a:** M.p. 228–230°C. ^{1}H NMR (CD_3Cl) δ: 1.60–1.69 (m, 2H, CH_2), 1.90–2.04 (m, 2H, CH_2), 2.56–2.79 (m, 2H, CH_2), 3.99 (s, 1H, H-4), 4.54 (br, 2H, NH_2), 7.25–7.63 (m, 11H, $2 \times C_6H_5$ and ylidene CH). IR (KBr, cm^{-1}): 3410, 3310, 3020, 2850, 2200, 1670, 1620, 1600, 1410, 1125. Anal. Calcd. for $C_{23}H_{20}N_2O$ (%): C, 81.18; H, 5.88; N, 8.24. Found: C, 80.77; H, 5.85; N, 8.18. **4b:** M.p. 217–219°C. ^{1}H NMR (CD_3Cl) δ: 1.62–1.69 (m, 2H, CH_2), 1.83–2.06 (m, 2H, CH_2), 2.52–2.72 (m, 2H, CH_2), 3.97 (s, 1H, H-4), 4.89 (s, 2H, NH_2), 7.18–7.63 (m, 9H, $2 \times C_6H_4$ and ylidene CH). IR (KBr, cm^{-1}): 3450, 3300, 2800, 2210, 1690, 1585, 1490, 1405, 1180, 1090. Anal. Calcd. for $C_{23}H_{18}Cl_2N_2O$ (%): C, 67.48; H, 4.40; N, 6.84. Found: C, 67.10; H, 4.36; N, 6.80. **4c:** M.p. 238–240°C. ^{1}H NMR (CD_3Cl) δ: 1.61–1.70 (m, 2H, CH_2), 1.88–2.10 (m, 2H, CH_2), 2.55–2.76 (m, 2H, CH_2), 4.02 (s, 1H, H-4), 4.76 (br, s, 2H, NH_2), 7.52–8.08 (m, 11H, $2 \times C_7H_6$ and ylidene CH). IR (KBr, cm^{-1}); 3440, 3320, 3090, 2820, 2200, 1680, 1610, 1520, 1420, 1350, 1130. Anal. Calcd. for $C_{23}H_{18}N_4O_5$ (%): C, 64.19; H, 4.19; N, 13.02. Found: C, 63.86; H, 4.16; N, 12.94.

REFERENCES

1. Temple, C.; Rener, G.A., Jr.; Raud, W.R.; Noker, P.E. J. Med. Chem. **1992**, *35*, 3686.
2. Ocallaghan, C.N.; Mcmurry, T.B.H. J. Chem. Res. (S) **1999**, 457.

3. Martin, L.N.; Quinteiro, M.; Seoane, C.; Soto, J.L. Liebigs. Ann. Chem. **1990**, 101.
4. Martin, N.; Martin, G.; Secoane, A.C.; Marco, J.L.; Albert, A.; Cano, F.H. Liebigs. Ann. Chem. **1993**, 801.
5. Marco, J.L.; Martin, N.; Grau, A.M.; Seoane, C.; Albert, A.; Cano, F.H. Tetrahedron **1994**, *50*, 3509.
6. Albert, D.A.; Cano, F.H.; Martin, N.; Ramos, A.; Rodriguez, M.; Segura, J.L.; Seoane, C. J. Chem. Soc. Perkin Trans. (I) **1997**, 3401.
7. Sakurai, A.; Midorikawa, N. Bull. Chem. Soc. Japn. **1968**, *41*, 430.
8. Al-Arab, M.M. J. Heterocyclic Chem. **1989**, *26*, 1665.
9. Al-Arab, M.M.; Atfeh, F.S.; Mayoof, S.M. J. Heterocyclic Chem. **1998**, *35*, 1473.
10. Elgemeie, G.H.; Abdelaal, F.A.; Abou, K. J. Chem. Res. (S) **1991**, 128.
11. Tyndall, T.; Nakib, A.; Meegan, M.J. Tetrahedron Lett. **1988**, *29*, 2703.
12. Caddick, S. Tetrahedron **1995**, *51*, 10403.
13. Galema, S.A. Chem. Soc. Rev. **1997**, *26*, 233.
14. Tu, S.J.; Zhou, J.F.; Deng, X.; Cai, P.J.; Wang, H.; Feng, J.C. Chin. J. Org. Chem. **2001**, *21*, 313.
15. Zhou, J.F.; Xu, J.M.; Wei, H.; Zhang, L.L. Chin. J. Org. Chem. **2001**, *21*, 322.

Received in Japan August 7, 2001

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016