Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2014, 6(2):733-735

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives in water using microwave irradiation

Xiaojuan Yang

College of Chemistry and Chemical Engineering, Xinxiang University, Xinxiang, Henan, P. R. China

---

ABSTRACT

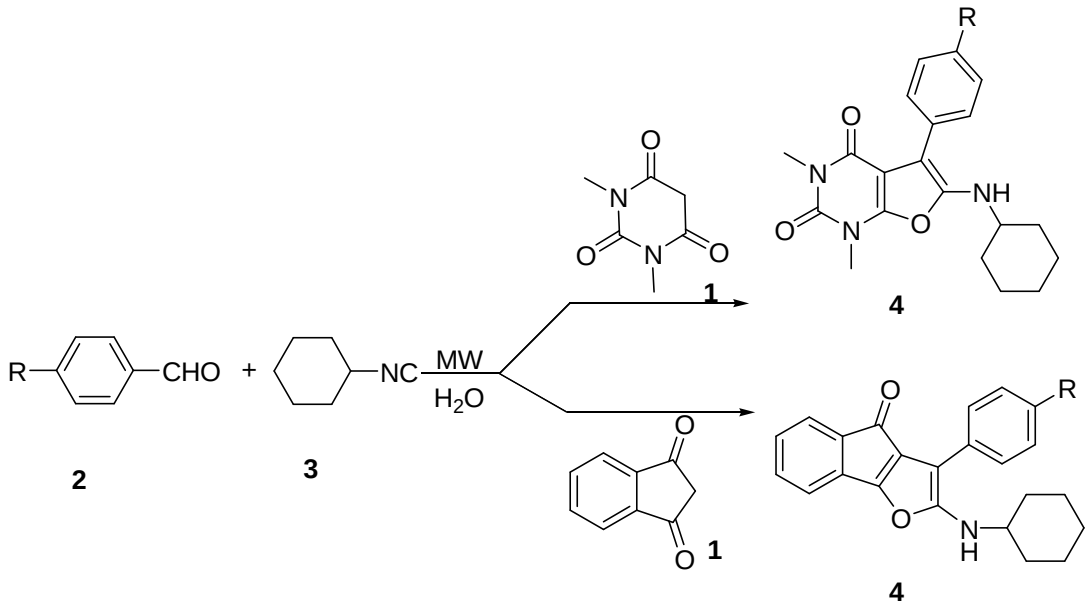
The environment-friendly one-pot three-component condensation reactions of N, N- dimethylbarbituric acid or 1, 3-indandione, aldehyde and cyclohexyl isocyanide to afford furo[2,3-d]pyrimidine and indeno[1,2-b]furan derivatives in water using microwave irradiation in good yields after about 10-12 min are reported.

Keywords: Furo[2,3-*d*]pyrimidines; Indeno[1,2-*b*]furan; Microwave irradiation; Multicomponent reactions

---

INTRODUCTION

Furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives exhibit a large range of biological activities. For example, furo[2,3-*d*]pyrimidines act as sedatives, antihistamines, diuretic, muscle relaxants, and antiulce ragent [1], and indeno[1,2-*b*]furans have antibacterial activity [2]. Therefore, active studies for the synthetic development of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives have been carried out [3-6]. However, many of the synthesis protocol reported so far suffer from disadvantages, such as relying on multi-step reactions, generating by-products, low yields, use of metal-containing reagents, and special starting materials. Thus, there is still need of a simple and general procedure for one-pot synthesis of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives under mild conditions.



Scheme 1

The use of microwave irradiation to enhance organic reactions in environmentally benign solvents such as water, which is inexpensive and not dangerous, represents very powerful green chemical technology both from economic and synthetic points of view. This not only reduces the burden of organic solvent disposal but also enhances the rate of the reaction [7-8]. We now report a simple and efficient route to synthesis of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives in water using microwave irradiation (Scheme 1).

EXPERIMENTAL SECTION

NMR spectra were determined on Bruker AV-400 spectrometer at room temperature using TMS as internal standard, coupling constants (*J*) were measured in Hz; Elemental analysis were performed by a Vario-III elemental analyzer; Melting points were determined on a XT-4 binocular microscope and were uncorrected; Commercially available reagents were used throughout without further purification unless otherwise stated.

General procedure for the preparation of 4

A mixture of N, N-dimethylbarbituric acid or 1, 3-indandione (**1**, 1 mmol), aldehyde (**2**, 1 mmol) and cyclohexyl isocyanide (**3**, 1 mmol) were mixed together in water (2 mL) in a tightly closed tube and subjected to microwave irradiation in a microwave oven at 300 W for 10-12 min (Table 3). After completion of the reaction (TLC), the product was extracted in diethyl ether (2 × 20 mL), solvent removal of the solid residue was crystallized from CH_2Cl_2: EtOH (1:2) to yield desired product **4**. The structures of products were identified through comparison of these spectra data with those in the known literatures [4, 6]. Spectral data for new compounds are as follows.

5-(4-chlorophenyl-6-cyclohexylamino-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**4b**). Cream powder, m.p. 126-128 ^oC; IR (KBr) ν_{max}/cm^{-1}: 3420, 1680, 1626; ^1H NMR ($CDC1_3$, 300 MHz) δ: 7.64 (d, J = 8.2 Hz, 2H, ArH), 7.06 (d, J=8.2 Hz, 2H, ArH), 5.60 (s, 1H, NH), 3.60 (s, 3H, NCH_3), 3.32 (s, 3H, NCH_3), 3.15-3.06 (m, 1H, NCH), 2.02-1.15 (m, 10H, CH_2); Anal. calcd for $C_{20}H_{22}N_3O_3Cl$: C 61.93; H 5.72; N 10.83. found: C 61.85; H 5.78; N 10.92.

2-(cyclohexylamino)-3-(4-bromophenyl)-indeno[1,2-*b*]furan-4-ones **(4i).** Red crystals, m.p. 224-225 ^oC; IR (KBr) ν_{max}/cm^{-1}: 3420, 1646; ^1H NMR ($CDC1_3$, 300 MHz) δ: 7.78-7.16 (m, 8H, ArH), 5.72 (s, 1H, NH), 3.05-2.98 (m, 1H, NCH), 2.16-1.12 (m, 10H, CH_2); Anal. calcd for $C_{23}H_{20}NOBr$: C 65.41; H 4.77; N 3.32. found: C 65.54; H 4.82; N 3.50.

RESULTS AND DISCUSSION

First, to find the optimal solvent for this reaction, the reaction of N, N-dimethylbarbituric acid **1**, benzaldehyde **2a**, and cyclohexyl isocyanide **3** was studied in different solvent using microwave irradiation. The best result was obtained by carrying out the reaction in water using microwave irradiation (see Table 1).

Table 1. Solvent optimization for synthesisof 4a in different solvent using microwave irradiation[a]

Entry	Solvent	Yield (%)
1	ethanol	42
2	glycol	63
3	DMF	65
4	DMSO	52
5	Solvent-free	68
6	water	85
7[b]	water	46

[a]*Reaction time: 10 min; Microwave Power: 300 W*

The power of microwave irradiation was optimized by carrying out the same reaction at powers of 100, 200, 300, 400 and 500 W respectively, using water as solvent (Table 2). When the power was at 300 W, the highest yield was obtained. Therefore, microwave power of 300 W was chosen as the optimum power.

Table 2. Power optimization for synthesisof 4a in water using microwave irradiation[a]

Entry	Power (W)	Yield (%)
1	100	54
2	200	76
3	300	85
4	400	85
5	500	83

[a]*Reaction time: 10 min.*

Based on the optimized reaction conditions, a range of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives was synthesized efficiently in excellent yield by the reaction of N, N-dimethylbarbituric acid or 1, 3-indandione, aldehyde and cyclohexyl isocyanide in water under microwave irradiation for a suitable time (10-12 min) in a tightly closed tube. The results are shown in Table 3. All products in this study were characterized by IR, ^{1}H NMR spectroscopy, as well as by elemental analyses.

Table 3. Preparation of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives in water using microwave irradiation[a]

Entry	R	Material **1**	Product	Time (min)	Yield (%)	m.p.(°C) (lit. m.p.)[ref.]
1	H	N,N-dimethylbarbituric acid	**4a**	10	85	124-126 (122-124)[4]
2	Cl	N,N-dimethylbarbituric acid	**4b**	12	88	126-128
3	OCH_3	N,N-dimethylbarbituric acid	**4c**	12	86	120-121 (122-124)[4]
4	NO_2	N,N-dimethylbarbituric acid	**4d**	10	92	134-136
5	H	1, 3-indandione	**4e**	10	89	199-200 (201)[6]
6	Cl	1, 3-indandione	**4f**	12	90	215-216 (218)[6]
7	OCH_3	1, 3-indandione	**4g**	12	87	208-209 (210)[6]
8	NO_2	1, 3-indandione	**4h**	10	93	218-220 (222)[6]
9	Br	1, 3-indandione	**4i**	12	88	224-225

CONCLUSION

In summary, we have develop a three-component the reaction of N, N-dimethyl barbituric acid or 1, 3-indandione, aldehyde and cyclohexyl isocyanide in water under microwave irradiation, and have shown its application to the synthesis of a number of furo[2,3-*d*]pyrimidine and indeno[1,2-*b*]furan derivatives. This green procedure offers several advantages including operations simplicity, clean reactions, increased safety for small-scale high-speed synthesis, and minimal environmental impact that make it useful and attactive process for the synthesis of these compounds.

Acknowledgements
We are pleased to acknowledge the financial support from Xinxiang University

REFERENCES

[1] R. G. Melik-Ogandzhanyan, V. E. Khachatryan, A. S. Gapoyan, *Russ. Chem. Rev.*, **1985**, 54, 450.
[2] C. A. Obafemi, P. O. Adelani, O. A. Fadare, D. A. Akinpelu, S. O. Famuyiwa, *J. Mol. Struct.*, **2013**, 1049, 429.
[3] A. Ramazani, N. Noshiranzadeh, A. Ghamkhari, K. Slepokura, T. Lis, *Helv. Chim. Acta*, **2008**, 91, 2252 (2008)..
[4] A. Shaabani, M. B. Teimouri, S. Samadi, K. Soleimani, *Synth. Commun.*, **2005**, 35, 535.
[5] I. Yavari, M. Adib, M. H. Sayahi, *Tetrahedron Lett.*, **2008**, 43, 2927.
[6] M. M. Heravi, B. Baghernejad, H. A. Oskooie, *Mol. Diver.*, **2009**, 13, 385.
[7] S. J. Tu, Q. Q. Shao, D. X. Zhou, L. J. Cao, F. Shi, C. M. Li, *J. Heterocycl. Chem.*, **2007**, 44, 1401.
[8] N. M. Abd El-Rahman, A. A. El-Kateb, M. F. Mady, *Synth.c Commun.*, **2007**, 37,