Contents lists available at Avicenna Publishing Corporation (APC)

Asian Journal of Green Chemistry

journal homepage: http://ajgreenchem.avicenna.pub/

Original Research article

Microwave-assisted multicomponent reaction for the synthesis of 2-amino-4*H*-chromene derivatives using ilmenite ($FeTiO_3$) as a magnetic catalyst under solvent-free conditions

Saeid Taghavi Fardood[a,b,*], Ali Ramazani[a,*], Pegah Azimzadeh Asiabi[a], Yousef Bigdeli Fard[c], Behrooz Ebadzadeh[a]

[a] *Department of Chemistry, University of Zanjan, P.O. BOX 45195-313, Zanjan, Iran*

[b] *Young Researchers Club, Zanjan Branch, Islamic Azad University, Zanjan, Iran*

[c] *Department of Chemistry, Payame Noor University, P.O. Box 19395-3697, Tehran, Iran*

ARTICLE INFORMATION

Received: 12 July 2017
Received in revised: 22 July 2017
Accepted: 23 July 2017
Available online: 25 July 2017

DOI:10.22631/ajgc.2017.93142.1006

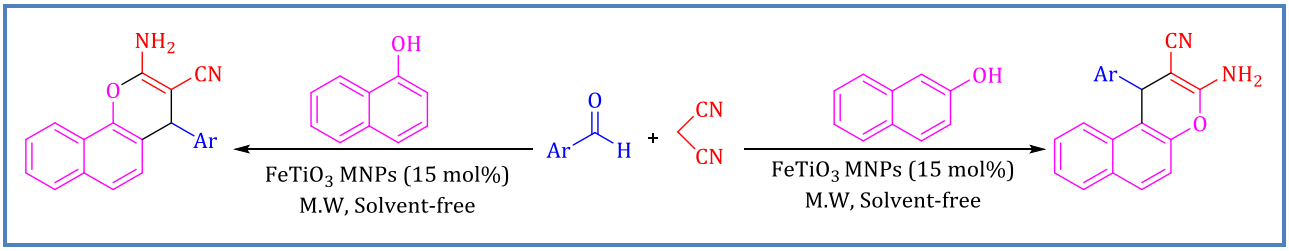
KEYWORDS

2-Amino-4*H*-Chromenes
Ilmenite
Three-component reaction
Microwave irradiation

ABSTRACT

A green and highly efficient method has been developed for the synthesis of 2-amino-4*H*-chromene derivatives in the presence of $FeTiO_3$ as magnetic catalyst *via* one-pot three-component condensation reaction of aromatic aldehydes, malononitrile and *α*- or *β*-naphthol without solvent under microwave irradiation. Mild reaction conditions, short reaction times, simple work-up, use of an economically convenient catalyst, and excellent product yields are the advantageous features of this method. The catalyst can be easily recovered by a simple magnetic separation and can be recycled six times with no significant loss of catalytic activity.

Graphical Abstract



Corresponding author, email: aliramazani@gmail.com (A. Ramazani); saeidt64@gmail.com (S. Taghavi Fardood).
Tel.: +9824 33052635; Fax: +9824 33583203.

Introduction

Multicomponent reaction (MCR) is a reaction in which three or more reactants react together and form product that has all features of the starting materials. MCRs have been recognized for over 160 years. The first MCR was reported in 1850 by *Strecker* [1-4]. Many basic MCRs are name reactions for instance, Passerini, Gewald, van Leusen, Hantzsch, Ugi, Biginelli, Strecker, or one of their many variations [5-10]. MCRs are the efficient tools in modern synthetic organic chemistry due to their significant features such as atom economy and the straight forward reaction designing. MCRs facilitate the synthesis of compounds of biological and pharmacological importance by introducing several steps in one pot reaction [11].

2-Amino-4*H*-chromene derivatives are important class of heterocyclic compounds with an array of biological and pharmacological properties such as antimicrobial [12], antiviral [13, 14], mutagenicity [15], antiproliferative [16], sex hormone [17], antitumour [18], cancer therapy [19, 20], and central nervous system activities [20]. 2-Aminochromenes were also used as biodegradable agrochemicals and components of many natural products [21]. Thus, introduction of efficient procedures with easily separable, green approach and reusable catalysts for the synthesis of these derivatives is needed.

Microwave (MW) irradiation which is a new and efficient technique for reagent activation in the synthesis of organic compounds [22-24], has been successfully applied for the synthesis of heterocyclic compounds under mild reaction condition. This method has gained great popularity compared to traditional heating and conventional reactions because of its ability to reduce reaction times, improving yields, having environmental and economic advantages, and also simplifieng the work-up processes [25-28].

In this work, we have reported an efficient and simple synthesis of highly functionalized 2-amino-4*H*-chromene derivatives using three-component reaction of various aldehydes (**1**), malononitrile (**2**), and *α*-, or *β*-naphthol (**3**) in the presence of $FeTiO_3$ magnetic nanoparticles (MNPs) as an efficient and reusable catalyst under solvent free conditions (Scheme 1).

Experimental

Matreials and methodes

Starting materials were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. The microwave-assisted procedures were carried out in a Milestone Microwave Oven operating at 1600 W. All obtained products are known compounds identified by

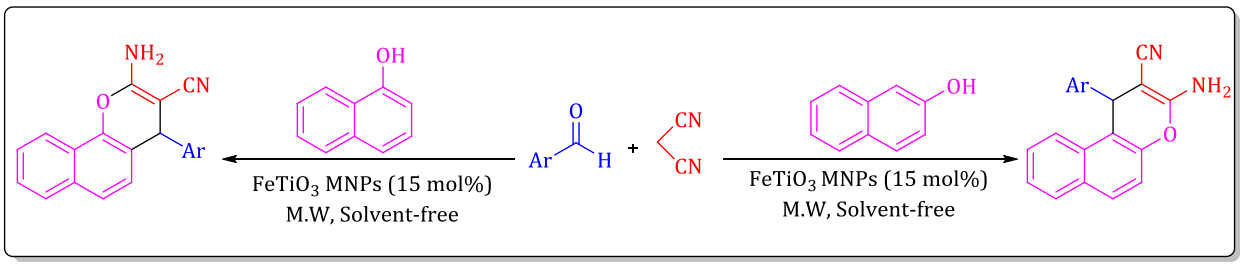
comparing their Melting points with those reported in the literature. The progress of reactions was monitored by thin layer chromatography (TLC).

General procedure for the synthesis of 2-amino-4*H*-chromene derivatives

A mixture of aldehydes (1 mmol), malononitrile (1 mmol), α- or *β*-naphthol (1 mmol) and 15 mol% of $FeTiO_3$ nanoparticles were taken in a round bottom flask (50 mL) and irradiated with microwave (500w). The progress of the reaction was checked by TLC (petroleum ether/EtOAc, 10:1). After completion, the resulting product was heated in ethanol. The catalyst was magnetically removed from the mixture and washed several times with ethanol for reuse. Then, the residue was poured into crushed ice and stirred for several minutes. The solid product was filtered and was recrystallized from ethanol to afford the pure 2-amino-4H-chromene derivatives.

Results and discussion

In the present paper, magnetic $FeTiO_3$ was investigated as a catalyst in the synthesis of 2-amino-4*H*-chromene derivatives under microwave irradiation and under solvent-free conditions. We optimized the reaction conditions such as catalyst amount and reaction times. First, the efficiency and amount of the $FeTiO_3$ MNPs catalyst was investigated in a model reaction of 4-chlorobenzaldehyde **1b** (1 mmol), malononitrile **2** (1 mmol), and *β*-naphthol **3a** (1 mmol) for the synthesis of compound **4b** (Table 2, entry 2). As shown in Table 1, the optimum yield of the product was obtained when 20 mg of the catalyst (15 mol %) was used. It was found that in the absence of a catalyst, the desired product **4b** was obtained in 12% yield within 10 min (Table 1, entry 1).



Scheme 1. Synthesis of 2-amino-4*H*-chromene derivatives.

Using these optimized conditions, a wide range of aldehydes, malononitrile, and α- or *β*-naphthol were subjected to undergo three-component condensation in the presence of $FeTiO_3$ MNPs under solvent free conditions (Table 2). Then, various aromatic aldehydes carrying electron-donating and electron-withdrawing groups on the aromatic ring in the ortho, meta, and para positions and heterocyclic aldehydes were evaluated. Yields of the all reactions were good to excellent. It was

found that the presence of electrondonating groups on the aromatic aldehydes resulted in low yields of the corresponding products and the reaction was sluggish. The presence of electronwithdrawing groups, however, resulted in shorter reaction times and higher yields. Using α-naphthol or *β*-naphthol had no effect on the reaction time or yield of the corresponding products. (Table 2).

Table 1. Effect of the catalyst amount for the synthesis of **4b**[a]

Entry	Catalyst (mol%)	Microwave power (W)	Time (min)	Yield (%)[b]
1	None	500	10	12
2	5	500	10	72
3	10	500	10	84
4	15	500	10	93
5	20	500	10	93

[a] Reaction conditions: 4-chlorobenzaldehyde (1 mmol), malononitrile (1 mmol), *β*-naphthol (1 mmol)

[b] Isolated yields

The $FeTiO_3$ MNPs were studied in this system. For this purpose, the reaction of *β*-naphthol (1 mmol) with 4-chlorobenzaldehyde (1 mmol) and malononitrile (1 mmol), was performed in the presence of $FeTiO_3$ MNPs under microwave irradiation (500 W) in solvent-free conditions. After the magnetic separation of the catalyst from the reaction mixture, the catalyst was washed with ethanol, dried in air to remove any remaining ethanol, and reused in the further reactions for several times. The average chemical yield for six consecutive runs was 90%, which clearly demonstrates the practical recyclability of this catalyst (Table 3).

Table 2. $FeTiO_3$ MNPs catalyzed the synthesis of 2-amino-4*H*-chromene derivatives.[a]

Entry	Ar	Phenol	Product	Time (min)	Yield (%)[b]	M.P. (°C)	M.P. (°C) [Ref.]
1	Ph	*β*- Naphthol	**4a**	9	90	287-288	288-289 [29]
2	4-Cl–C_6H_4	*β*- Naphthol	**4b**	10	93	207-209	209-210 [30]
3	3-Cl–C_6H_4	*β*- Naphthol	**4c**	10	94	210-212	211-213 [24]
4	2-Cl–C_6H_4	*β*- Naphthol	**4d**	10	91	272-274	272-273 [29]
5	4-Me–C_6H_4	*β*- Naphthol	**4e**	13	88	268-270	270-272 [31]
6	3-NO_2–C_6H_4	*β*- Naphthol	**4f**	12	91	229-231	233-235 [32]
7	4-NO_2–C_6H_4	*β*- Naphthol	**4g**	10	93	185-187	186-187 [31]
8	4-Br-C_6H_4	*β*- Naphthol	**4h**	11	92	227-229	228-231 [33]
9	4-OMe-C_6H_4	*β*- Naphthol	**4i**	12	87	186-188	190-191 [30]
10	Ph	*α*- Naphthol	**5a**	9	91	208-210	210-211 [34]
11	4-Cl–C_6H_4	*α*- Naphthol	**5b**	10	94	231-232	231-232 [30]
12	3-Cl–C_6H_4	*α*- Naphthol	**5c**	10	94	210-212	211-213 [24]
13	2-Cl–C_6H_4	*α*- Naphthol	**5d**	10	91	235-237	236-237 [35]
14	4-Me–C_6H_4	*α*- Naphthol	**5e**	13	87	204-206	204-206 [36]
15	3- NO_2–C_6H_4	*α*- Naphthol	**5f**	12	90	214-216	214-215 [30]

16	4- NO_2–C_6H_4	*α*- Naphthol	**5g**	10	93	239-241	240-241 [30]
17	4-Br–C_6H_4	*α*- Naphthol	**5h**	11	91	240-242	241-243 [37]
18	4-OH–C_6H_4	*α*- Naphthol	**5i**	13	85	245-247	245-247 [36]

[a] Reaction conditions: aldehyde **1a–i** (1 mmol), malononitrile (1 mmol), α- or *β*-naphthol (1 mmol) and 20 mg of catalyst (15 mol%) under microwave irradiation (500 w) in solvent-free conditions

[b] Isolated yields

Table 3. Reusability and recovery of the $FeTiO_3$ MNPs catalyst in the synthesis of **4b**

Run	Yield (%)[a]	Recovery of $FeTiO_3$MNPs (%)
1	93	99
2	93	97
3	92	96
4	91	94
5	90	93
6	90	92

[a] Isolated yields

Conclusion

In summary, we have developed a simple, inexpensive and effective method for the synthesis of 2-amino-4H-chromene derivatives using α- or *β*-naphthol, malononitrile, various aldehydes and $FeTiO_3$ as magnetic catalyst without solvent under microwave irradiation. The catalyst is inexpensive and easily available. Moreover, mild reaction conditions, simple procedure, short reaction times, easy workup, high yields of products and ease of separation and recyclability of the catalyst are salient features of the presented work.

Acknowledgments

This research was supported by the University of Zanjan, Iran National Science Foundation: INSF and Research Council of Islamic Azad University of Zanjan.

References

[1]. Kazemizadeh A.R., Ramazani A. *Curr. Org. Chem*., 2012, **16**:418

[2]. Ramazani A., Jafari A., Joo S.W., Ahmadi Y., Sadri F., Azimzadeh Asiabi P. *Iran. Chem. Commun*., 2016, **4**:42

[3]. Poor Heravi M.R., Amirloo M. *Iran. Chem. Commun*., 2014, **3**:73

[4]. Bahrami M., Ramazani A., Hanifehpour Y., Fattahi N., Taghavi Fardood S., Asiabi P.A., Joo S.W. Phosphorus, *Sulfur Silicon Relat. Elem*., 2016, **191**:1368

[5]. Dömling A., Ugi I. *Angew. Chem*., 2000, **112**:3300

[6]. Ramazani A., Ahmadi Y., Fattahi N., Ahankar H., Pakzad M., Aghahosseini H., Rezaei A., Taghavi Fardood S., Joo S.W. Phosphorus, *Sulfur Silicon Relat., Elem*, 2016, **191**:1057

[7]. Rahmani S., Amoozadeh A. *J. Nanostruct*., 2014, **4**:91

[8]. Ramazani A., Farshadi A., Mahyari A., Sadri F., Joo S.W., Asiabi P.A., Taghavi Fardood S., Dayyani N., Ahankar H. *Int. J. Nano Dimens*., 2016, **7**:41.

[9]. Domling A., Wang W., Wang K. *Chem. Rev*., 2012, **112**:3083

[10]. Kiasat A.R., Hamid S., Saghanezhad S.J. *Nanochem. Res*., 2016, **1**:157

[11]. Kamble V., Saleh B., Sadaf M. *Iran. Chem. Commun*., 2017, **5:**192

[12]. Khafagy M.M., El-Wahab A.H.A., Eid F.A., El-Agrody A.M. *IlFarmaco*, 2002, **57**:715

[13]. Smith P.W., Sollis S.L., Howes P.D., Cherry P.C., Starkey I.D., Cobley K.N., Weston H., Scicinski J., Merritt A., Whittington A. *J. Med. Chem*., 1998, **41**:787

[14]. Martínez-Grau A., Marco J. *Bioorg. Med. Chem. Lett*., 1997, **7**:3165

[15]. Hiramoto K., Nasuhara A., Michikoshi K., Kato T., Kikugawa K., Mutat. Res. Genet. Toxicol. Environ. *Mutagen*., 1997, **395**:47

[16]. Bianchi G., Tava A. *Agric. Biol. Chem*., 1987, **51**:2001

[17]. Mohr S.J., Chirigos M.A., Fuhrman F.S., Pryor J.W. *Cancer Res*., 1975, **35**:3750

[18]. Anderson D.R., Hegde S., Reinhard E., Gomez L., Vernier W.F., Lee L., Liu S., Sambandam A., Snider P.A., Masih L. *Bioorg. Med. Chem. Lett*., 2005, **15**:1587

[19]. Skommer J., Wlodkowic D., Mättö M., Eray M., Pelkonen J. *Leukemia Res*., 2006, **30**:322

[20]. Wang J.L., Liu D., Zhang Z.J., Shan S., Han X., Srinivasula S.M., Croce C.M., Alnemri E.S., Huang Z. *Proc. Natl. Acad. Sci*., 2000, **97**:7124

[21]. Hafez E.A.A., Elnagdi M.H., Elagamey A.G.A., El-Taweel F.M.A.A. *Heterocycles*, 1987, **26**:903

[22]. Taghavi Fardood S., Ramazani A., Moradi S. *J. Sol-Gel Sci. Technol*., 2017, **82**:432

[23]. Zhu S.L., Ji S.J., Zhao K., Liu Y. *Tetrahedron Lett*., 2008, **49**:2578

[24]. Mehrabi H., Kamali N. *J. Iran. Chemi. Soc*., 2012, **9**:599

[25]. Lidström P., Tierney J., Wathey B., Westman J. *Tetrahedron*., 2001, **57**:9225

[26]. Kappe C.O. *Angew. Chem. Int. Ed*., 2004, **43**:6250

[27]. Imanzadeh G., Kabiri S., Taghavi S., Zamanloo M., Mansoori Y. *J. Chil. Chem. Soc.*, 2013, **58**:1888

[28]. Taghavi Fardood S., Ramazani A., Golfar Z., Joo S.W. *Appl. Organomet. Chem.*, 2017, DOI: 10.1002/aoc.3823

[29]. Zhang A.Q., Zhang M., Chen H.H., Chen J., Chen H.Y. *Synth. Commun*., 2007, **37**:231

[30]. Gong K., Wang H.L., Fang D., Liu Z.L. *Catal. Commun*., 2008, **9**:650

[31]. Jin T.S., Xiao J.C., Wang S.J., Li T.S. *Ultrason. Sonochem*., 2004, **11**:393

[32]. Rao M.S., Chhikara B.S., Tiwari R., Shirazi A.N., Parang K., Kumar A. *Chem. Biol. Interfaces*., 2012, **2**:362

[33]. Mobinikhaledi A., Moghanian H., Sasani F. *Synth. React. Inorg. Met. Org. Chem*., 2011, **41**:262

[34]. Jin T.S., Xiao J.C., Wang S.J., Li T.S., Song X.R. *Synlett*, 2003, **2003**:2001

[35]. Ballini R., Bosica G., Conforti M.L., Maggi R., Mazzacani A., Righi P., Sartori G. *Tetrahedron*, 2001, **57**:1395

[36]. Ren Y.M., Cai C. *Catal. Commun*., 2008, **9**:1017

[37]. Maggi R., Ballini R., Sartori G., Sartorio R. *Tetrahedron Lett*., 2004, **45**:2297

How to cite this manuscript: Saeid Taghavi Fardood, Ali Ramazani, Pegah Azimzadeh Asiabi, Yousef Bigdeli Fard, Behrooz Ebadzadeh. Microwave-assisted multicomponent reaction for the synthesis of 2-amino-4*H*-chromene derivatives using ilmenite ($FeTiO_3$) as a magnetic catalyst under solvent-free conditions. *Asian Journal of Green Chemistry*, 2017, 1, 34-40. DOI:10.22631/ajgc.2017.93142.1006