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Efficient and green synthesis of 2-amino-4*H*-chromenes

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ABSTRACT

Herein we report an efficient and green protocol for the synthesis of 2-amino-4H-chromenes from three-component condensation of aldehydes, malononitrile and α or β-naphthol in water as the eco-friendly solvent using ionic liquid [EMIM][OH] as a catalyst at room temperature as well as under microwave irradiation.

Keywords: 2-Amino-4*H*-chromenes, [EMIM] [OH], Microwave irradiation, Ionic liquid, Water

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INTRODUCTION

In these environmentally conscious days there is a need to use eco-friendly 'greener' technologies such as solvent-free, microwave irradiation, sonication, grinding, use of room temperature ionic liquids, water as reaction media, photochemical, electrochemical etc reactions. Microwaves have been emerged as extensively useful non-conventional energy source for performing organic synthesis. Ionic liquids are green catalysts because of their unique chemical and physical properties of non-volatility, non inflammability, thermal stability and controlled miscibility. Ionic liquids, being polar and ionic in character when coupled with mw irradiation, can be used as efficient reaction media as well as catalyst [1].

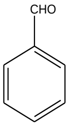
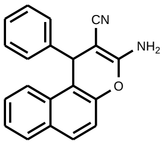
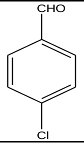
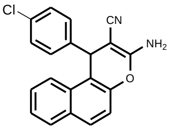
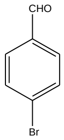
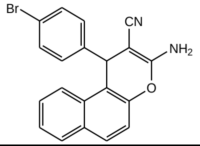
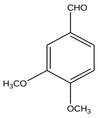
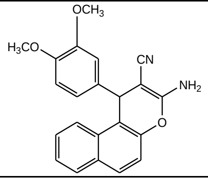
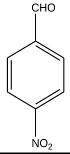
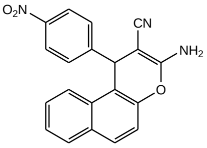
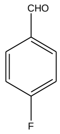
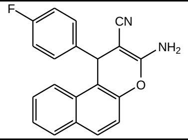
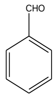
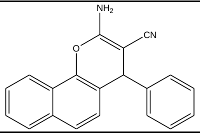
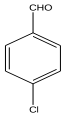
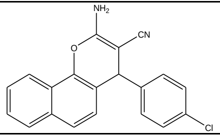
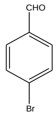
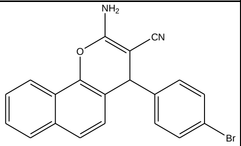
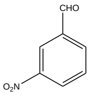
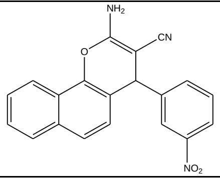
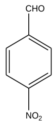
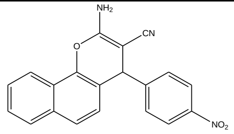
Chromenes constitute an important class of compounds present in plants, including edible vegetables and fruits [2]. These compounds exhibit health promoting and disease preventing effects [3]. 2-Amino-4*H*-chromenes are biologically active compounds with a wide spectrum of pharmacological properties such as antimicrobial [4], antiproliferative [5], anticoagulant, spasmolytic, diuretic, anticancer and antianaphylactic characteristics [6].

As 2-amino-4*H*-chromenes belong to privileged medicinal scaffold. Several synthetic approaches for the synthesis of these compounds were reported. Recently 2-amino-4*H*-chromenes are synthesized by the condensation of aldehyde, activated phenol and malononitrile in presence of catalysts such as silica gel supported polyamine catalyst [7], ammonium acetate [8], $CuSO_4. 5H_2O$ [9], DBU [10], HMTAB [11], MgO [12], DABCO [13], *p*-toluenesulfonic acid [14] etc.

EXPERIMENTAL SECTION

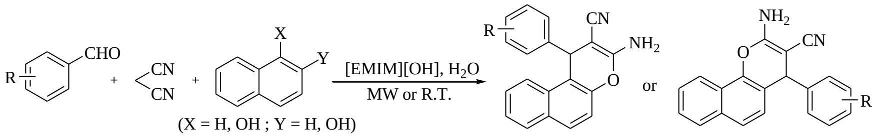
Chemical reagents used were SD Fine made. All the materials were of commercial grade reagent. Melting points were determined in open capillaries using Electrothermal Mk3 apparatus. Infrared (IR) spectra in KBr were recorded using a Perkin-Elmer FT-IR spectrometer. ^{1}H NMR spectra were recorded on an 400 MHz FT-NMR spectrometer in DMSO and $CDCl_3$ as a solvent and chemical shift values were recorded in δ ppm relative to tetramethylsilane (Me_4Si) as an internal standard. The microwave irradiation was carried out in a scientific microwave oven (CATA-4R-Model No. QW-99, India makes), 2450 MHz Frequency, with power output of 140-700 W. The progresses of the reactions were monitored by TLC (Thin Layer Chromatography).

Table 1: [EMIM][OH] catalyzed synthesis of 2-amino-4H-chromenes

Entry	Aldehydes	Naphthol	Products	Mw Time in sec/ Yield (%)	RT Time in min/ Yield in %	m.p. found (Lit.)	m.p. reported (Lit.)
1		β-naphthol		180/85	180/84	278-280	280[13]
2		β-naphthol		120/92	150/90	205-208	206-208[15]
3		β-naphthol		150/87	150/88	241-244	242-244[16]
4		β-naphthol		180/84	180/82	206-208	210-211[17]
5		β-naphthol		120/92	150/90	184-186	185-186[17]
6		β-naphthol		120/88	160/88	232-234	233-235[16]
7		α-naphthol		180/92	180/88	175-177	178-180[17]
8		α-naphthol		120/93	150/84	230-232	231-232[15]
9		α-naphthol		150/87	160/86	240-241	241-243[13]
10		α-naphthol		150/83	170/82	210-212	212-213[14]
11		α-naphthol		120/90	150/88	240-242	239-241[17]

General procedure for synthesis of 2-amino-4*H*-chromene using ionic liquid in H_2O under microwave irradiation:
A mixture of malononitrile (1mmol), aromatic aldehyde (1mmol), α- or β-naphthol (1mmol), water (5 ml) and [EMIM][OH] (10 mol%), was mixed properly and irradiated in a microwave oven at the power of 140W for 2-4 min (**Table 1**). The progress of reaction was monitored by TLC (ethyl acetate: hexane 4:1). After completion of reaction, the reaction mixture was cooled to room temperature, poured onto crushed ice and filtered. The residue was dried and recrystallized from ethanol to get the corresponding 2-amino-4H-chromene. The products were confirmed by comparison with authentic samples, IR, ^{1}H NMR and melting points. The filtrate was concentrated to recover the ionic liquid.

General procedure for synthesis of 2-amino-4H-chromene using ionic liquid in H_2O at room temperature:
A mixture of malononitrile (1 mmol), aromatic aldehyde (1 mmol), α-naphthol or β-naphthol (1 mmol), water (5 ml) and [EMIM][OH] (10 mol%), was stirred at room temperature for appropriate time as mentioned in (**Table 1**) till the reaction was completed (monitored by TLC, ethyl acetate: hexane 4:1). After completion of reaction, the reaction mixture was poured on ice-cold water and filtered. The residue was dried and recrystallized from ethanol to get the corresponding 2-amino-4H-chromene. The products were confirmed by comparisons with authentic samples, IR, ^{1}H NMR and melting points.



Scheme 1

RESULTS AND DISCUSSION

Three-component condensation between malononitrile, p-chlorobenzaldehyde and α- or β-naphthol was chosen as model reaction to obtain 2-amino-4*H*-chromenes. Following the green chemistry approach we decided to use eco-friendly, non-hazardous ionic liquid as catalyst and water as solvent. Initially, the reaction was tested at room temperature by stirring with 2 mol% of catalyst. Reaction was completed within 6 to 7 hours with 45-50% yield. The reaction was optimized by varying molar ratios of catalyst. 10 mol% of [EMIM][OH] gave 2-amino-4*H*-chromenes within 2.5 h with 92-93% yield (**Table 2**). Further increase in amount of [EMIM][OH] did not affect the time or yield of the reaction.

As ionic liquid couple with microwaves very efficiently, we cannot stop ourselves to take advantage of this protocol in this reaction. Surprisingly, this protocol also gave an excellent yield of 2-amino-4H-chromenes using 10 mol% of [EMIM][OH] in water as solvent at 140 W under microwave irradiation.

After optimizing the reaction conditions, different aldehydes were investigated to check the feasibility of this protocol whose results are tabulated in (Table 1). Almost all the employed aldehydes showed good to excellent yield of the corresponding products. Studies revealed that aldehydes with electron-withdrawing substituents reacted faster and gave better yields of the products as compared to the aldehydes with electron-donating substituents. Thus, this protocol provides an easy access of pure products without using any chromatographic techniques. Filtrate that is aqueous layer kept for evaporation on rota evaporator to obtain [EMIM][OH] for further use. The catalyst can be recycled several times without significant loss of its catalytic activity (**Table 3**). A plausible reaction mechanism for this condensation is shown in **Scheme 2**.

Table 2: Optimization of catalyst for synthesis of 2-amino-4H-chromene

Entry	Catalyst (mol %)	mw Time in sec		RT Time in hours		mw Yield in %		RT Yield in %	
		A*	B*	A*	B*	A*	B*	A*	B*
1	2	240	300	6	6.5	50	45	50	44
2	5	180	210	3.5	4	75	70	74	70
3	**10**	**120**	**150**	**2.5**	**3**	**93**	**92**	**91**	**90**
4	15	120	150	2.5	3	93	92	94	93

A synthesis of 2-amino-4H-chromene from 4-chloro benzaldehyde, malononitrile and α-naphthol*
B synthesis of 2-amino-4H-chromene from 4-chloro benzaldehyde, malononitrile and β-naphthol*

Table 3. Recycling of catalyst

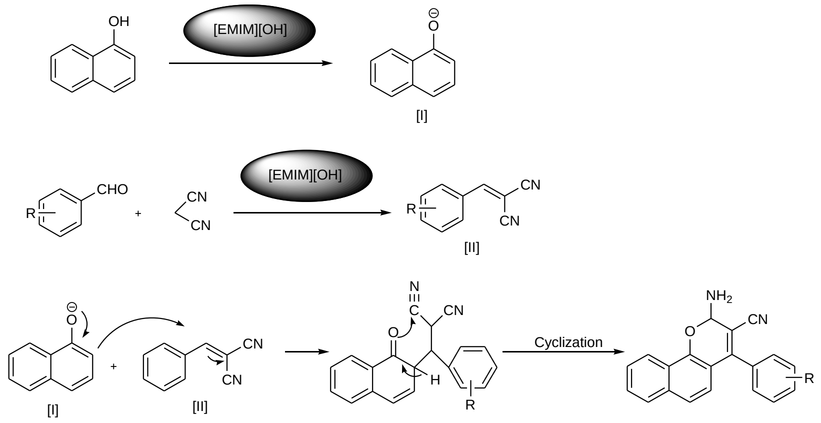
Entry	No. of cycles	Yield in %
1	1	95
2	2	92
3	3	90
4	4	90

Spectral data:

3-Amino-2-cyano-4-(4-chlorphenyl)-4*H*-benzochromene: IR (KBr): cm^{-1} 3411, 3326, 2193, 1643, 1591, 1488, 1404, 1234, 1093; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ ppm: 5.31 (s, 1H, CH), 6.95 (s, 2H, NH$_2$), 7.18-7.20 (d, 2H, ArH), 7.27-7.29 (m, 3H, ArH), 7.30-7. 32 (m, 2H, ArH), 7.76-7.78 (d, 1H, ArH), 7.87-7.89 (m, 2H, ArH).

2-Amino-3-cyano-4-(4-bromophenyl)-4*H*-benzochromene: IR (KBr): cm^{-1} 3415,3327, 2190, 1641, 1590, 1490, 1408, 1233, 1092; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ ppm 4.82 (s, 1H, CH), 6.92 (s, 2H, NH$_2$), 7.03-7.05 (d, 1H, ArH),7.18-7.20 (d, 2H, ArH), 7.44-7.46 (d, 2H, ArH)**,** 7.51-7.60 (m, 3H, ArH), 7.80-7.82 (d, 1H, ArH), 8.26-8.28 (d, 1H, ArH)

Mechanism for synthesis of 2-amino-4*H*-chromene from aldehydes, malononitrile and α-naphthol:



Scheme 2

CONCLUSION

In the present work; we have used microwave irradiation as energy source with water as the eco-friendly reaction medium for the synthesis of 2-amino-4*H*-chromenes. In short this method offers simple, clean, fast, efficient and economic technique for synthesis following the principles of green chemistry.

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REFERENCES

[1] MP Rafael. *J Mex Chem Soc*, **2007**, *51(4)*, 252.
[2] M Curini; G Cravotto; F Epifano; G Giannone. *Curr Med Chem*, **2006**, *13*(2), 199-222.
[3] PO Kennedy; RD Thornes. *J Wiley & Sons Chichester U.K*, **1997**.
[4] MM Khafagy; AH E-Wahas; FA Eid; AM El-Agrody. *Farmaco*, **2002**, 57(9), 715.
[5] G Bianchi; A Tava. *Agric Biol Chem*, **1987**, 51(7), 2001-2002.
[6] K Singh; J Singh; H Singh. *Tetrahedron*, **1996**, 52(45), 14273-14280.
[7] RL Magar; PB Thorat; VB Jadhav; SU Tekale; SA Dake; BR Patil; RP Pawar. *Journal of Molecular Catalysis A: Chemical*, **2013**, 374-375, 118-124.
[8] NK Shah; NM Shah; MP Patel; RG Patel. *J Chem Sci*, **2013**, 125(3), 525-530.
[9] KB Farahnaz; M Sadeghi. *Journal of the Korean Chemical Society*, **2013**, 57(3), 357-360.
[10] Z Afsaneh; M Roghieh; S Maliheh; K Sussan; SE Ardestani**;** F Alireza. *Iranian Journal of Pharmaceutical Research*, **2013**, 12, 679.
[11] TS Jin; AQ Wang; X Wang; JS Zhang; TS Li. *Synlett*, **2004**, 2004(5), 871-873.

[12] D Kumar; VB Reddy; BK Mishra; GR Rana; N Mallikarjuna; R Nadagouda; S Varma. *Tetrahedron*, **2007**, 63(15), 3093-3097.
[13] S Balalaie; S Ramezanpour; M Bararjanian; JH Gross. *Synth Commun*, **2008**, 38(7), 1078-1089.
[14] B Baghernejad; M Majid; A Heravi. *Journal of the Korean Chemical Society*, **2009**, 53(6), 631-634.
[15] R Maggi; R Ballini; G Sartori; R Sartorio. *Tetrahedron Lett*, **2004**, 45(11), 2297-2299.
[16] J Albadi; A Mansournezhad; M Darvishi-Paduk. *Chin Chem Lett*, **2013**, 24(3), 208-210.
[17] R Ballini; G Bosica; ML Conforti; R Maggi. *Tetrahedron*, **2001**, 57(7), 1395-1398.