

Eco-friendly, Catalyst-free Synthesis of 2-Amino-2-chromenes in Ionic Liquid [bmim]Br

A. DAVOODNIA, A. TAVAKOLI-NISHABURI*, H. BEHMADI,
N. TAVAKOLI-HOSEINI and P. ATTAR

*Department of Chemistry, Faculty of Sciences,
Islamic Azad University, Mashhad Branch, Mashhad, Iran
Fax: (98)(511)8424020; Tel: (98)(511)8416015
E-mail: afsaneh.tavakoli2010@yahoo.com*

A simple and eco-friendly procedure for the synthesis of 2-amino-2-chromene derivatives using [bmim]Br, a neutral ionic liquid, as an efficient medium without any catalysts has been developed. The present methodology offers several advantages, such as simple procedure with an easy work-up, excellent yields, short reaction times, environmentally benign milder reaction conditions.

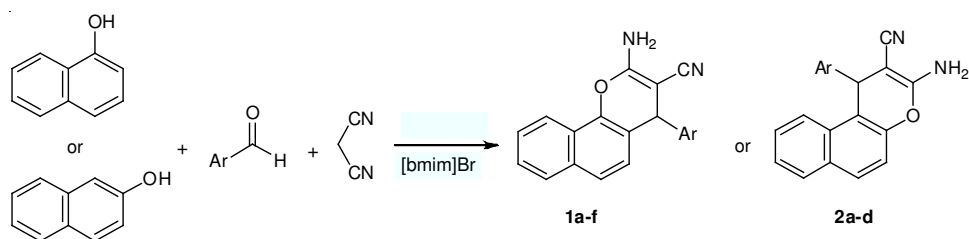
Key Words: [Bmim]Br, Ionic liquids, Catalyst-free, 2-Amino-2-chromenes.

INTRODUCTION

2-Amino-2-chromenes represent an important class of compounds being the main components of many naturally occurring products and are widely employed as food additives, cosmetic agents and utilized as potential biodegradable agro-chemicals¹⁻⁴. Thus the synthesis of 2-amino-2-chromenes is of much importance to organic chemists. The most straightforward synthesis of this compounds involve the three-component condensation of an aldehyde, malononitrile and α (or β)-naphthol in the presence of piperidine using acetonitrile or ethanol as a reaction solvent⁵⁻⁷. Recently, relatively benign catalysts such as cetyltrimethyl ammonium bromide (CTABr), I_2/K_2CO_3 , basic alumina and nano MgO in water have also been used in this reaction⁸⁻¹¹. However, the application of some of these methods is limited due to the moderate yields of the products, longer reaction time and laborious work-up procedure. The increasing attention during the last decades for environmental protection has led both modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost while using non-toxic reagents, solvents and catalysts or solvent-free conditions. Therefore, the development of simple, efficient, clean, high-yielding and environmentally friendly approaches for the synthesis of these compounds is an important task for organic chemists.

Room-temperature ionic liquids, especially those based on 1-alkyl-3-methylimidazolium cations, are the subject of considerable interest as benign reaction media in organic synthesis because of their unique properties, such as non-volatility, non-flammability, recyclability, high thermal stability and ability to dissolve a wide

range of organic and inorganic substrates. During the past decade, a variety of ionic liquids have been demonstrated as efficient and practical alternatives to volatile organic solvents for many important organic reactions^{12,13}. Moreover their polar nature makes them useful for use under solvent-free conditions. As part of our current studies on the development of new routes for the synthesis of organic compounds in ionic liquids¹⁴⁻¹⁷, we now report an efficient and clean synthetic route to 2-amino-2-chromenes in ionic liquid [bmim]Br as a green medium (**Scheme-I**).



Scheme-I: Synthesis of 2-amino-2-chromenes

EXPERIMENTAL

All compounds were known and their physical and spectroscopic data were compared with those of authentic samples and found to be identical. Melting points were recorded on an electrothermal type 9100 melting point apparatus. The IR spectra were obtained on a 4300 Shimadzu spectrophotometer as KBr disks. The ¹H NMR (500 MHz) spectra were recorded on Bruker DRX500 spectrometer.

General procedure for the synthesis of 2-amino-2-chromenes: A mixture of α (or β)-naphthol (2 mmol), aromatic aldehyde (2 mmol), malononitrile (2 mmol) and [bmim]Br (1 mmol) was heated on the oil bath at 100 °C for the indicated time. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and then ethanol was added. The precipitated solid was filtered off and recrystallized from ethanol to give compounds **1a-f** and **2a-d** in high yields.

Recycling of the ionic liquid: [Bmim][Br] is soluble in ethanol and water. Therefore, after filtration of the product, a mixture of water and dichloromethane was added to the filtrate. [Bmim][Br] was recovered by evaporation of the aqueous layer under reduced pressure, dried at 50 °C under vacuum for 1 h and reused in another reaction.

RESULTS AND DISCUSSION

For present investigations, ionic liquid [bmim]Br (Fig. 1) was prepared according to the literature procedure¹⁸. Initially, in order to optimize the reaction conditions, the synthesis of 2-amino-3-cyano-4-phenyl-4*H*-benzo[h]chromene (**1a**) was used as a model reaction. Therefore, a mixture of α -naphthol, benzaldehyde and malononitrile was heated under various reaction conditions (Table-1). At first, we examined the synthesis of compound **1a** without catalyst and solvent at 100 °C for

240 min but under these conditions no product could be detected (entry 1). Increasing the reaction time or temperature did not improve the yield. The reaction was also carried out in various solvents (entries 2-5). As shown, in comparison to conventional solvents, the yield of the reaction in [bmim]Br is higher and the reaction time is shorter. Therefore, it can be suggested that the ionic liquid plays a role as promotor besides the role of the media. The best result was obtained when [bmim]Br was used at 100 °C for 10 min.

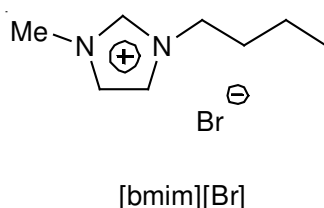


Fig. 1. Structure of ionic liquid

TABLE-1
SYNTHESIS OF COMPOUND **1a** IN DIFFERENT SOLVENTS

Entry	Solvent	Temperature (°C)	Time (min)	Yield (%)*
1	Solvent-free	100	240	None
2	EtOH	78	120	Trace
3	CH ₃ CN	81	240	Trace
4	CHCl ₃	61	60	41
5	[bmim][Br]	100	10	88

*Isolated yields.

The results obtained from α -naphthol with benzaldehyde and malononitrile, a series of 2-amino-2-chromenes were prepared in high yields using various aldehydes, malononitrile and α or β -naphthol in the presence of [bmim]Br at 100 °C. The results are summarized in Table-2. The substituents of aromatic aldehydes affect the reaction time and the yields of 2-amino-2-chromenes. It was found that the aromatic aldehydes with electron-withdrawing groups reacted faster than the aromatic aldehyde with electron-donating groups as would be expected. When aromatic aldehydes with electron-withdrawing groups are reactants, the reaction times are shorter.

Reusability of [bmim]Br was also investigated. After filtration of the product, [bmim][Br] was recovered from the filtrate according to the procedure mentioned in experimental section and reused for next reactions. The obtained results are summarized in Table-3. As it is shown in this table, [bmim]Br could be reused at least three times without appreciable reduction in its activity as promoting medium.

TABLE-2
 SYNTHESIS OF 2-AMINO-2-CHROMENES*

Entry	Naphthol	Ar	Products [†]	Time (min)	Yield (%) [‡]	m.p. (°C)	
						Found	Reported
1	α -Naphthol	C ₆ H ₅	1a	10	88	220-221	210-211 [8]
2	α -Naphthol	4-ClC ₆ H ₄	1b	4	92	236-239	231-232 [8]
3	α -Naphthol	4-MeC ₆ H ₄	1c	20	84	210-212	204-206 [9]
4	α -Naphthol	4-MeOC ₆ H ₄	1d	20	87	120-122	116-117 [8]
5	α -Naphthol	3-O ₂ NC ₆ H ₄	1e	15	84	226-228	212-214 [8]
6	α -Naphthol	4-O ₂ NC ₆ H ₄	1f	5	89	252-254	239-241 [8]
7	β -Naphthol	C ₆ H ₅	2a	15	85	290-292	280-282 [8]
8	β -Naphthol	4-ClC ₆ H ₄	2b	6	92	180-182	206-208 [8]
9	β -Naphthol	4-MeOC ₆ H ₄	2c	35	85	110-112	116-117 [8]
10	β -Naphthol	4-O ₂ NC ₆ H ₄	2d	10	90	170-172	185-186 [8]

*2 mmol α (or β)-naphthol, 2 mmol aromatic aldehyde and 2 mmol malononitrile in 1 mmol [bmim]Br at 100 °C; [†]All the products were characterized by ¹H NMR and IR spectral data and comparison of their melting points with those of authentic samples; [‡]Isolated yields.

 TABLE-3
 COMPARISON OF EFFICIENCY OF [bmim][Br] IN THE SYNTHESIS OF
 2-AMINO-2-CHROMENES AFTER THREE TIMES

Entry	Naphthol	Ar	Yield (%)*run		
			First	Second	Third
1a	α -Naphthol	C ₆ H ₅	88	86	85
1b	α -Naphthol	4-ClC ₆ H ₄	92	89	87
1e	α -Naphthol	3-O ₂ NC ₆ H ₄	84	83	80

*Isolated yields.

Conclusion

In conclusion, a simple and efficient method for the high-yielding synthesis of 2-amino-2-chromenes by one-pot three-component condensations of naphthols, aromatic aldehydes and malononitrile in the presence of [bmim]Br, a neutral ionic liquid, as an efficient promoting medium was developed. The product was easily separated with high yields. The ionic liquid was readily recycled and reused to produce almost identical results. No organic solvent and catalyst were used, resulting in eco-friendly process.

REFERENCES

1. E.A. Hafez, M.H. Elnagdi, A.A. Elagamey and F.M.A.A. El-Taweel, *Heterocycles*, **26**, 903 (1987).
2. M.A. Sofan, F.M.A.A. El-Taweel and M.H. Elnagdi, *Liebigs Ann. Chem.*, 935 (1989).
3. F.M. Abdel Galil, B.Y. Riad, S.M. Sherif and M.H. Elnagdi, *Chem. Lett.*, **8**, 1123 (1982).
4. R.S. Varma and R. Dahiya, *J. Org. Chem.*, **63**, 8038 (1998).
5. J. Bloxham, C.P. Dell and C.W. Smith, *Heterocycles*, **38**, 399 (1994).
6. A.G.A. Elagamey and F.M.A.A. El-Taweel, *Indian J. Chem.*, **B29**, 885 (1990).
7. A.G.A. Elagamey, F.M.A.A. El-Taweel, M.N.M. Khodeir and M.H. Elnagdi, *Bull. Chem. Soc. (Japan)*, **66**, 464 (1993).

8. T.S. Jin, J.C. Xiao, S.J. Wang and T.S. Li, *Ultrason. Sonochem.*, **11**, 393 (2004).
9. Y.M. Ren and C. Cai, *Catal. Commun.*, **9**, 1017 (2008).
10. R. Maggi, R. Ballini, G. Sartori and R. Sartorio, *Tetrahedron Lett.*, **45**, 2297 (2004).
11. D. Kumar, V.B. Reddy, B.G. Mishra, R.K. Rana, M.N. Nadagouda and R.S. Varma, *Tetrahedron*, **63**, 3093 (2007).
12. P. Wasserscheid and T. Welton, *Ionic Liquids in Synthesis*, Wiley-VCH: Weinheim (2003).
13. R.D. Rogers, *Ionic Liquids as Green Solvents, Progress and Prospects*, American Chemical Society, Washington, DC (2005).
14. A. Davoodnia, M.M. Heravi, L. Rezaei-Daghigh and N. Tavakoli-Hoseini, *Monatsh. Chem.*, **140**, 1499 (2009).
15. A. Davoodnia, M. Bakavoli, R. Moloudi, M. Khashi and N. Tavakoli-Hoseini, *Chin. Chem. Lett.*, **21**, 1 (2010).
16. A. Davoodnia, M.M. Heravi, Z. Safavi-Rad and N. Tavakoli-Hoseini, *Synth. Commun.*, (2010) In Press.
17. A. Davoodnia, M.M. Heravi, L. Rezaei-Daghigh and N. Tavakoli-Hoseini, *Chin. J. Chem.*, **28**, 429 (2010).
18. R.S. Varma and V.V. Namboodiri, *Chem. Commun.*, **7**, 643 (2001).

(Received: 15 March 2010;

Accepted: 30 July 2010)

AJC-8927