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# Tandem Knoevenagel–Michael–cyclocondensation reaction of malononitrile, various aldehydes and 2-naphthol over acetic acid functionalized ionic liquid

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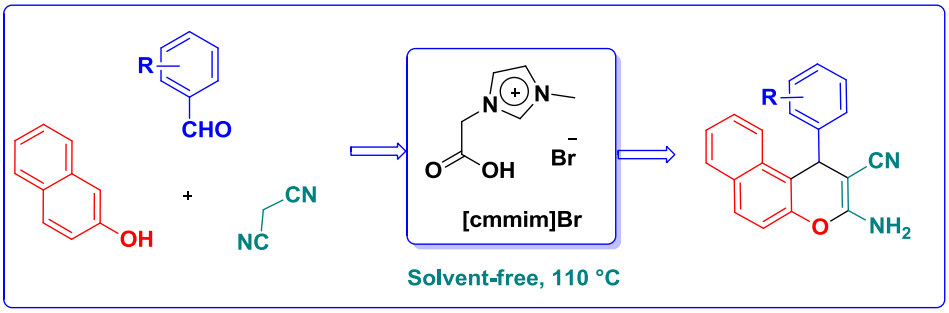
## HIGHLIGHTS

- Introducing efficient catalysts for the synthesis of 2-amino benzo[h]chromenes.
- Study of TGA, XRD and calculation of size and inter planer distance of the catalysts.
- Generality of the catalysts, high yields and short reaction times.

## GRAPHICAL ABSTRACT

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## ABSTRACT

An efficient solvent-free approach for the synthesis of 2-amino benzo[h]chromene derivatives from the condensation of malononitrile, 2-naphthol and various aldehydes using acetic acid functionalized imidazolium salt (1-carboxymethyl-3-methylimidazolium bromide {[cmmim]Br} as a reusable catalysts is reported. In addition, thermal gravimetric analysis (TGA), differential thermal gravimetry (DTG), powder X-ray diffraction (PXRD) and calculation of size and inter planer distance of the catalyst have been studied in this work.


## 1. Introduction

Ionic liquids based on imidazolium and other organic cations have received considerable interest as eco-friendly solvents, reagents and catalysts in organic synthesis because of their special properties, including low volatility, high thermal stability, non-flammability, negligible vapor pressure and ability to dissolve a wide range of materials [1–9]. Among them, Brønsted acidic ionic liquids, with the useful characteristics of solid acids and mineral liquid acids, have been designed to replace the traditional mineral liquid acids such as sulfuric acid and hydrochloric acid in chemical transformations [10–25].

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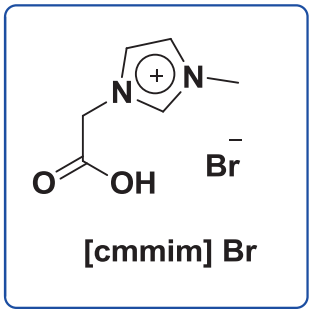



**Fig. 1.** The structure of 1-carboxymethyl-3-methylimidazolium bromide {[cmmim]Br}.

The Knoevenagel condensation and Michael reaction are significant C–C bond forming reaction which are commonly employed for the synthesis of important chemical intermediates and products such as 4H-chromene derivatives as well as pharmaceuticals [26–29]. Also, recently, these mentioned reactions have been performed in microreactor using different catalysts [26–28].

The synthesis of 4H-chromenes and fused 4H-chromene derivatives is an important concept because of their significant antimicrobial, anti-fungal [30], anti-oxidant [31], anti-leishmanial [32], anti-tumor [33], hypotensive [34] and antiproliferation properties [35]. Also, they can be widely applied in central nervous system (CNS) activities and effects [36] as well as treatment of Alzheimer's disease [37] and Schizophrenia disorder [38]. In addition, substituted 4H-chromenes act as inhibitors of influenza virus sialidases [39,40]. Several protocols have been introduced for the preparation of 2-amino benzo[h]chromene derivatives [29,41–47]. However, they are mostly suffer from one or more drawbacks including the use of toxic metals, the use of volatile organic solvents, high cost and low product yields.

Having the above facts, herein we would like to introduce acetic acid functionalized imidazolium salt (1-carboxymethyl-3-methylimidazolium bromide {[cmmim]Br} as a highly efficient and reusable catalyst for the synthesis of 2-amino benzo[h]chromene derivatives via the one-pot three component condensation reaction of various aldehydes, 2-naphtol and malononitrile at 110 °C under solvent-free conditions (Fig. 1 and Scheme 1).

## 2. Experimental section

### 2.1. Materials

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literature. Acetic acid functionalized ionic liquid was prepared according to previous literature reports [48,49]. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The $^{1}$H NMR (400) and $^{13}$C NMR (100 MHz) were recorded on a Bruker Avance DPX-250 FT-NMR spectrometer ($\delta$ in ppm). Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

### 2.2. General procedure for the synthesis of 2-amino benzo[h]chromenes

A mixture of 2-naphtol (1 mmol), malononitrile (1 mmol), aldehyde (1 mmol) and and catalyst ([cmmim]Br) (0.1 mmol, 10 mol%) was added to a 10 mL round-bottomed flask connected to a reflux condenser and stirred in an oil-bath at 110 °C. After the completion of the reaction, which was monitored by TLC, $H_2O$ (1 mL) was added to the reaction mixture and then stirred and refluxed for 3 min. In the next step, for the separation of the catalyst from crude product, the reaction mixture was filtered by sintered glass funnel. The catalyst was soluble in water and crude products were insoluble. Then, the solvent of the filtrate ($H_2O$) was removed under reduced pressure to recover the catalyst. The solid residue (crude product) on sintered glass funnel was triturated by hot EtOH (95%) to afford the pure product. The recovered catalyst was washed with ethyl acetate and dried under reduced pressure and then reused for the next run. The catalyst was recovered and reused for four times without any significant changes in the yields and the reaction times.

## 3. Results and discussion

### 3.1. Preparation of the catalysts

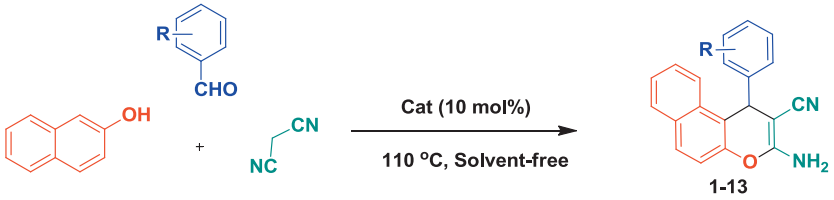
In the first step, 1-carboxymethyl-3-methylimidazolium bromide {[cmmim]Br} was synthesized according to the literature reports [45,46]. The structures of acetic acids functionalized ionic liquid were characterized by $^{1}$H NMR, $^{13}$C NMR and IR as well as mass spectroscopy and the resulting characterization data are consistent with literature reports [48,49].

### 3.2. Thermal gravimetric analysis (TGA) of the catalyst

Thermal gravimetric analysis (TGA) of the acetic acid functionalized imidazolium salt was also studied at the range of 25–600 °C, with a temperature ramp rate of 10 °C min$^{-1}$ under nitrogen atmosphere (Fig. 2). As TG (thermal gravimetry) and DTG (differential thermal gravimetric) diagrams indicates, [cmmim]Br was decomposed in one step after 230 °C. The TG patterns of [cmmim]Br is similar to single stage decomposition in which no intermediate was exactly identified.

### 3.3. Powder X-ray diffraction analysis (PXRD) of the catalyst

PXRD pattern of [cmmim]Br was investigated in a domain of 10–90° (Fig. 3). As shown at Fig. 3, PXRD patterns of 1-carboxymethyl-3-methylimidazolium bromide {[cmmim]Br} illustrated diffraction lines of a high crystalline nature at $2\theta \approx 13.0°$, 15.7°,




**Scheme 1.** The synthesis of 2-amino benzo[h]chromenes catalyzed by acetic acid functionalized imidazolium salts.