# Straightforward and Solvent-Free Synthesis of 2-Amino-4*H*-chromenes in the Presence of a Choline-Based Magnetic Ionic Liquid as Catalyst<sup>1</sup>

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**Abstract**—Choline tetrachloroferrate with a magnetic response property is applied in multicomponent one-pot synthesis of 2-amino-4*H*-chromenes as effective catalyst. The catalyst is characterized by the UV–Vis and Raman spectroscopies and by the electrospray ionization mass spectrometry.

**Keywords:** magnetic ionic liquid, 2-amino-4*H*-chromene derivatives, multicomponent reactions, choline chloride, choline tetrachloroferrate

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### **INTRODUCTION**

The sequencing of multicomponent reactions (MCRs) and subsequent cyclization reactions provide powerful tools for the synthesis of biologically active complex molecules and natural products, which are the very important compounds for many chemical areas, including medicinal and pharmaceutical chemistry [1–3].

2-Amino-4*H*-chromenes are a class of privileged heterocycles that show a variety of activities, such as antibacterial, mutagenic, antiviral, antitumoral, anticoagulant, and antianaphylactic activity. These compounds are also applied in cosmetics and pigments and are potential biodegradable agrochemicals [4–6]. Commonly, they are synthesized by three-component condensation of aldehyde, malononitrile, and activated phenol under catalytic conditions. However, most of the reported methods have such drawbacks as low yield, long reaction time, harsh reaction conditions, hard work-up procedure, complex reaction pathway, and proceed in the presence of expensive or toxic catalysts [7–9].

Since the first synthesis and application of a magnetic ionic liquid (MIL) [10, 11], a wide variety of interests has been focused on this class of compounds.

Magnetic ionic liquids combine general properties of room-temperature ionic liquids with the properties associated with incorporation of a metal ion into their structure, such as strong response to an external magnetic field and photophysical/optical or catalytic properties [12].

As part of our ongoing studies of green synthetic approaches [13–16] and in continuation of our previous study on the application of MILs in multi-component reactions [17], we study here the catalytic behavior of choline tetrachloroferrate in the synthesis of 2-amino-4*H*-chromenes.

## **RESULTS AND DISCUSSION**

Choline chloride, (2-hydroxyethyl) trimethylammoniumchloride, is commercially available, cheap, bio-

**Scheme 1.** Preparation of choline chloride-based paramagnetic ionic liquid.



<sup>&</sup>lt;sup>1</sup> The text was submitted by the authors in English.



Fig. 1. Response of choline [FeCl<sub>4</sub>] to an external magnetic field.



Fig. 3. Raman spectrum of the MIL.

degradable, non-toxic, and non-explosive quaternary ammonium salt. It can be synthesized from fossil reserves in large-scale quantities through the process with a very high atom economy [18, 19].

Choline tetrachloroferrate is prepared by mixing choline chloride and iron(III) chloride hexahydrate (molar ratio 1 : 1.2) under ambient conditions (Scheme 1).

The magnetic properties of the ionic liquid were screened at the magnetic field strength of 1 T supplied with an NdFeB magnet. As seen, the properties of choline [FeCl<sub>4</sub>] can be manipulated through the application of a strong magnetic field (Fig. 1).

The paramagnetic ionic liquid was characterized by several methods. The absorption spectrum has bands in



**Fig. 4.** (a) Positive and (b) negative ion spectra of choline [FeCl<sub>4</sub>]<sup>-</sup>.

the visible region, which can be attributed to the  $[FeCl_4]$  anion (Fig. 2).

Raman spectra of ammonium tetrachloroferrate salts have strong peak attributable to stretch vibrations of the totally symmetric Fe–Cl bond at approximately 330 cm<sup>-1</sup> and peaks attributable to the  $(CH_3)_3N^+CH_2$ · CH<sub>2</sub>OH cation in the regions 1400–1600 and 2800–3050 cm<sup>-1</sup> (Fig. 3).

The above results were also confirmed by data on the electrospray ionization mass spectrometry: peaks at m/e = 104.10 and 197.80 in the ESI-MS spectra are due to (CH<sub>3</sub>)<sub>3</sub>N<sup>+</sup>CH<sub>2</sub>CH<sub>2</sub>OH and FeCl<sub>4</sub>, respectively (Fig. 4).

We found that choline [FeCl<sub>4</sub>] has a significant catalytic performance in multicomponent synthesis of 2-amino-4H-chromenes. The condensation of p-nitro benzaldehyde, malononitrile, and  $\beta$ -naphthol (1 : 1 : 1 mmol) was used as a model reaction in order to optimize the reaction conditions. For this purpose, the reaction was carried out at varied amounts of MIL (0.05, 0.1, and 0.2 mmol) and different temperatures (room temperature, 40, and 60°C). In the absence of the catalyst, trace amounts of the product were detected. The best result was obtained when the reaction was carried out with 20 mol % of choline [FeCl<sub>4</sub>] at 60°C to give 1H-naphtho[2,1-b]pyran-2-carbonitrile,3-amino-1-(4-nitrophenyl) (Table 1, run no. 4). Fortunately, the desired chromenes in high yield are obtained by this procedure in the presence of different substituted aromatic benzaldehydes and no by-products is formed (Table 2).

A probable mechanistic rationale portraying sequence of events for this coupling reaction is postulated in Scheme 2. In the first step, the carbonyl group is activated via the positive part of MIL, facilitating the nucleophilic attack of malononitrile, by the Knoevenagel condensation mechanism. After  $\beta$ -

| Run<br>no. | Catalyst,<br>mol % | Temperature,<br>°C | Time,<br>min | Yield <sup>b</sup> ,<br>% |
|------------|--------------------|--------------------|--------------|---------------------------|
| 1          | _                  | 60                 | 120          | Trace                     |
| 2          | 5                  | 60                 | 30           | >20                       |
| 3          | 10                 | 60                 | 30           | 65                        |
| 4          | 20                 | 60                 | 30           | 94                        |
| 5          | 20                 | 40                 | 30           | 55                        |
| 6          | 20                 | Room temperature   | 30           | 35                        |

Table 1. Screening of the reaction conditions<sup>a</sup>

<sup>a</sup> *p*-Nitro benzaldehyde (1 mmol), malononitrile (1 mmol), and βnaphthol (1 mmol). <sup>b</sup> Isolated yield.

naphthol is deprotonated with tetrachloroferrate, the subsequent Michael addition occurs. The final step, following enol formation, is the intramolecular cyclization with the replacement of hydrogen to give the product.

# **EXPERIMENTAL**

All compounds were synthesized from commercial sources and used without further purification. Melting

| $\begin{array}{cccc} Ar - CHO & NC & CN \\ 1 & 2 \\ & &$ |                               |           |                        |                   |            |  |  |  |
|--|-------------------------------|-----------|------------------------|-------------------|------------|--|--|--|
| Product <sup>a</sup>   | Ar                            | Time, min | Yield <sup>b</sup> , % | mp, °C            | References |  |  |  |
| <b>4</b> a   | C <sub>6</sub> H <sub>5</sub> | 40        | 96                     | 277–279 (280)     | [4]        |  |  |  |
| 4b   | $4-NO_2-C_6H_4$               | 30        | 94                     | 185–186 (188–189) | [4]        |  |  |  |
| 4c   | $4-Cl-C_6H_4$                 | 35        | 87                     | 205–206 (206–208) | [9]        |  |  |  |
| 4d   | $4-Br-C_6H_4$                 | 35        | 96                     | 240–243 (241–243) | [9]        |  |  |  |
| <b>4e</b>  | $4-\text{MeO-C}_6\text{H}_4$  | 30        | 95                     | 182–183 (182–183) | [4]        |  |  |  |
| <b>4</b> f   | $4-\text{Me-C}_6\text{H}_4$   | 40        | 96                     | 269–271 (270–271) | [20]       |  |  |  |
| 4g   | $3-NO_2-C_6H_4$               | 35        | 95                     | 235–236 (232–235) | [9]        |  |  |  |
| 4h   | $3-\text{MeO-C}_6\text{H}_4$  | 70        | 86                     | 259–260 (262–263) | [21]       |  |  |  |
| <b>4i</b>  | $2-Cl-C_6H_4$                 | 60        | 92                     | 258–261 (259–261) | [9]        |  |  |  |

Table 2. Synthesis of 2-amino-4H-chromene derivatives in the presence of MIL as catalyst under solvent-free conditions

<sup>a</sup> The products are known and were identified by comparison of their melting points and spectral data with those reported in the literature.

<sup>b</sup> Yield is given for isolated not-purified products.



points are given uncorrected. The visible absorption spectra of the samples (0.1 M acetonitrile solutions) were recorded on a Jenway Genova Plus UV–Vis spectrometer in the region 500–1000 nm. The Raman spectra were measured on an Almega Thermo Nicolet Dispersive Raman spectrometer at the wavelength 532 nm delivered by a Nd:YLF laser. The electrospray ionization-mass (ESI-MS) spectrometry was done on an Agilent 6410 Triple Quadrupole LC/MS mass spectrometer.

General procedure for the synthesis 2-amino-4*H*-chromenes. Into a test tube, aldehyde (1 mmol),  $\beta$ naphthol (1 mmol), malononitrile (1 mmol), and choline tetrachloroferrate (0.2 mmol) were introduced and the resulting solution was heated on a thermostatic oil bath to 60°C for the required time (Table 2). The mixture was cooled to room temperature, then 10 mL of water was added to it, and the mixture was stirred for 5 min. The aqueous layer was decanted and dried under vacuum in order to recover the catalyst. The crude product was purified by recrystallization from hot ethanol.

## CONCLUSIONS

In conclusion, choline tetrachloroferrate magnetic ionic liquid was prepared and its properties were determined by the UV-visible and Raman spectroscopies and by the electrospray ionization mass spectrometry. After successful characterization, the catalytic activity of MIL was evaluated in the one-pot preparation of 2-amino-4*H*-chromenes. Advantages of using this catalyst are simple work-up procedure, eco-friendly reaction conditions, short reaction time, and high yield of the products.

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