Biginelli reaction in ionic liquids: synthesis and application of a novel iron catalyst with dual activation

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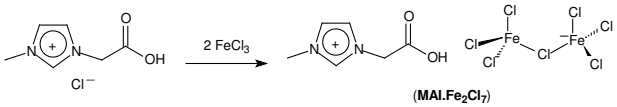
INTRODUCTION

The Biginelli reaction is an elegant and efficient protocol applied in the synthesis of 3,4-dihydropyrimidine-2-(1H)-ones (DHPs).[1] The interest in this class of compounds is due to their potential as biological active compounds.[2] In this sense, many methodologies are found in the literature as attempts to a more efficient condition to obtain DHPs derivatives. Based in our interest in catalysis and ionic liquids (ILs),[3] herein we present a study on the use of a novel ionically-tagged iron catalyst as the promoter of the Biginelli reaction.

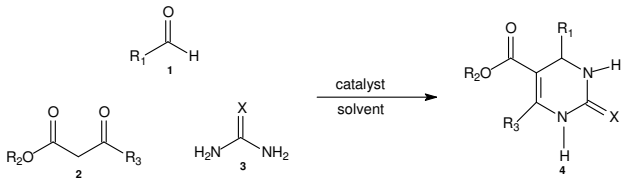
RESULTS AND DISCUSSION

The novel iron catalyst was prepared as shown in Scheme 1.



Scheme 1. Synthesis of the novel iron catalyst (MAI.Fe_2Cl_7).

The iron catalyst was supported in ILs and applied in the Biginelli reaction (Scheme 2).



Scheme 2. The Biginelli reaction in ILs promoted by MAI.Fe_2Cl_7.

Many conditions were tested to achieve the desired adduct. The best condition was obtained at 80 °C using 5 mol% of the catalyst, 9.00 mmol of benzaldehyde, 3.00 mmol ethyl acetoacetate, 3.00 mmol of urea, 1.0 mL of BMI. BF_4 in 2 h of reaction. Under the developed condition, the desired DHP derivative was isolated in 99% yield.

It is worth noting the presence of a Bronsted acid and a Lewis acid in the same structure of the catalyst, allowing a dual activation to promote the reaction. The reaction profile is shown in Figure 1.

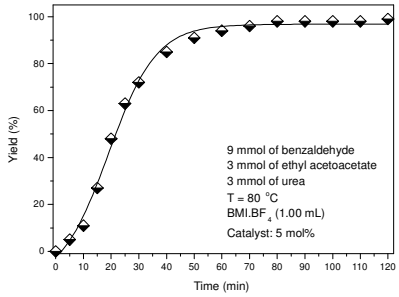


Figure 1. Reaction profile of the Biginelli reaction.

The catalyst was tested with different aldehydes, 1,3-dicarbonyl compounds and urea (or thiourea) resulting in the desired DHPs in excellent yields (85-99%).

Recycling reactions were also tested and at least 8 recharges were performed with no lost of activity (Figure 2).

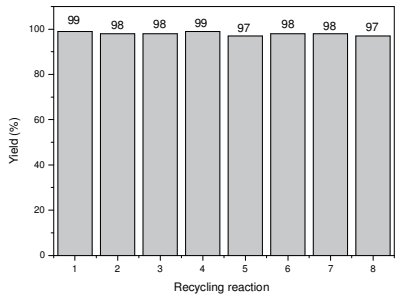


Figure 2. Recycle reactions using MAI.Fe_2Cl_7.

CONCLUSION

A promising iron catalyst has been developed and efficiently tested as the promoter of the Biginelli reaction.

ACKNOWLEDGEMENTS

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