

Polymer-supported basic ionic liquid as an efficient heterogeneous catalyst system for straightforward synthesis of flavanones

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Received 20 October 2015; received in revised form 22 January 2016; accepted 25 February 2016

ABSTRACT

Aromatic aldehydes are efficiently condensed with 2'-hydroxyacetophenone by polymer-supported basic ionic liquid as an excellent heterogeneous catalyst utilizing the Claisen–Schmidt reaction. Microwave irradiation has been employed, providing flavanone in good yield and short reaction time.

Keywords: Polymer-supported catalyst, Immobilization, Basic ionic liquid, Flavanone.

1. Introduction

Over the past decade, ionic liquids (ILs) have drawn considerable interest for their roles as catalyst or reaction medium in various organic reactions [1,2]. Among acidic, neutral and basic type ionic liquids, the latter has been utilized efficiently in many base-catalyzed processes such as Michael addition, Heck reaction, Knoevenagel condensation, Henry reaction, Mannich reaction, synthesis of heterocyclic compounds and *etc* [3]. From the view point of green chemistry, the use of basic ILs to replace conventional basic catalysts such as NaOH, KOH and K₂CO₃ in organic synthesis could eliminate numerous disadvantages such as waste production, corrosion and no catalyst recovery [4].

On the other hand, supported ionic liquid catalysis combines the advantages of ionic liquids with those of heterogeneous supported materials. It has been reported that supported ILs led to more improvements in efficiency than homogenous ionic liquids. Otherwise, the required amount of the ionic phase can be significantly reduced and it opens the possibility to use fixed-bed reactor systems [5-8].

Flavanones and its derivatives are a class of natural products that have been characterized as “privileged

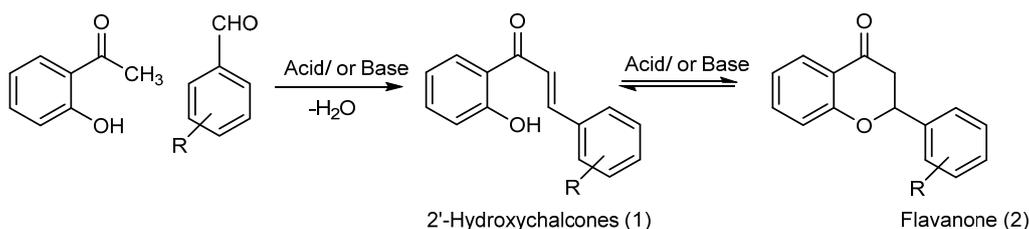
structures,” due to their ability to interact with a number of different receptors in the body, thereby precipitating a wide range of biological responses [9]. Several beneficial biological effects of these compounds including anticancer, antitumor, antibacterial, antimicrobial, antioxidant, estrogenic and anti-estrogenic properties have been ascertained in several previous studies [10-14].

The straightforward method for the synthesis of flavanone is *via* the Claisen–Schmidt condensation of benzaldehyde and 2'-hydroxyacetophenone and the subsequent isomerization of the produced 2'-hydroxychalcone intermediates under homogeneous or heterogeneous conditions (Scheme 1) [15-20].

Recently, many useful methods have been proposed for the synthesis of flavanone, but some of these suffer from disadvantages such as low yield, long reaction time, strong acidic medium leading to environmental pollution, use of expensive catalysts, no catalyst recovery and reusability. Furthermore, in some cases a mixture of products is obtained [21]. Consequently, development of efficient methods for rapid synthesis of flavanone has stimulated considerable interest.

In this study, our interest in developing an environmentally benign and heterogeneous catalytic system [22-25] leads us to investigate use of polystyrene-supported basic imidazolium-based ionic liquid (PSBIL, Scheme 2) in synthesis of flavanone.

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Scheme 1.

2. Experimental

2.1. General

Merrifield resin (Mesh 200-400, 2% cross-linked with divinylbenzene, 2-4 mol capacity) was purchased from Alfa Aesar chemical company. Other compounds were purchased from Merck chemical company and was used as received without further purification. The purity of the products and reaction monitoring were followed by thin layer chromatography on Merck DC-Alufolien plates pre-coated with silica gel F₂₅₄. The microwave reactions were performed in a Milestone MW apparatus model MicroSynth (2500 W) equipped with a condenser. Products were characterized by comparison of their physical data, IR and ¹H NMR spectra with known samples. NMR spectra were recorded in CDCl₃ on a Bruker Advance DPX 400 MHz instrument spectrometer using TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer RX1 FTIR spectrometer. SEM images were obtained from a Philips XL30 instrument.

2.2. Preparation of polystyrene-supported 1-methylimidazolium hydroxide

A mixture of commercial Merrifield resin (2.0 g) and 1-methylimidazole (120 mL, 1.5 mol) was refluxed for 36 h. After cooling to room temperature, the reaction mixture was filtered and the solid was washed successively with dichloromethane, methanol, and finally acetone, followed by drying under reduced pressure. Then, the resin was added to 100 mL solution of KOH (0.5 M) and stirred vigorously at room temperature for 48 h. After that, the mixture was filtrated and washed with distilled water (3×25 mL). This was followed by drying under reduced pressure to give the pale brown Polystyrene-Supported basic ionic liquid; anal. (%) found: N 5.72 (2.06 mmol of the ionic liquid portion per gram of PS[MIm]OH).

2.3. General experimental procedure for the synthesis of flavanones

A mixture of aldehyde (1.0 mmol), 2'-hydroxyacetophenone (1.0 mmol) and PS[MIm]OH (0.05/ or 0.1 g) in dichloromethane (5.0 mL) was magnetically stirred and heated by microwave radiation (300W) under reflux condition for the time shown in Table 2. The reaction was monitored by TLC. After completion, the insoluble resin was filtered off and the filtrate was

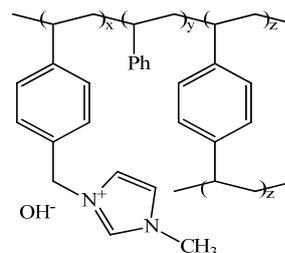
dried over Mg₂SO₄. Then, the organic solvent evaporated in vacuum to give the products in 60-90% isolated yields. Further purification was achieved by preparative TLC or by silica gel column chromatography.

3. Results and Discussion

PS[MIm]Cl was prepared using the method reported by Chi et al. with some changes [8]. A further treatment of the resin with KOH solution afforded PS[MIm]OH. The concentration of hydroxide ions was estimated to be 0.70 mmol/g from acid-base titration. In heterogeneous reactions, using organic polymer-supported catalysts, it is crucial to find an appropriate solvent due to the influence on the resin swelling and reaction rate [26-27]. The solvent absorbance of a resin is a fundamental property of polymeric beads with 1-2% cross-link of divinylbenzene.

FT-IR spectroscopy was employed to confirm the successful functionalization of the resin. The spectrum of the catalyst showed a broad peak at ~3430 cm⁻¹, which could be related to OH vibration. The weak bands located at ~2830-2950 cm⁻¹ correspond to C-H asymmetric and symmetric stretching vibration modes. The strong peak ~1630 cm⁻¹ is mainly from the bending vibration of adsorbed H₂O. Moreover, the two peaks observed at ~1560 cm⁻¹ and ~1641 cm⁻¹ correspond to the C=C and C=N vibrations of the imidazole moiety (Fig. 1).

Scanning electron microscopy (SEM) has been used to characterize the structure and morphology of the catalyst. These images show Merrifield resin had spherical structures, but the polystyrene microspheres have been destroyed when the imidazole ring supported on resins (Fig. 2).



Scheme 2. Structure of the polystyrene-supported basic imidazolium-based ionic liquid (PS[MIm]OH).

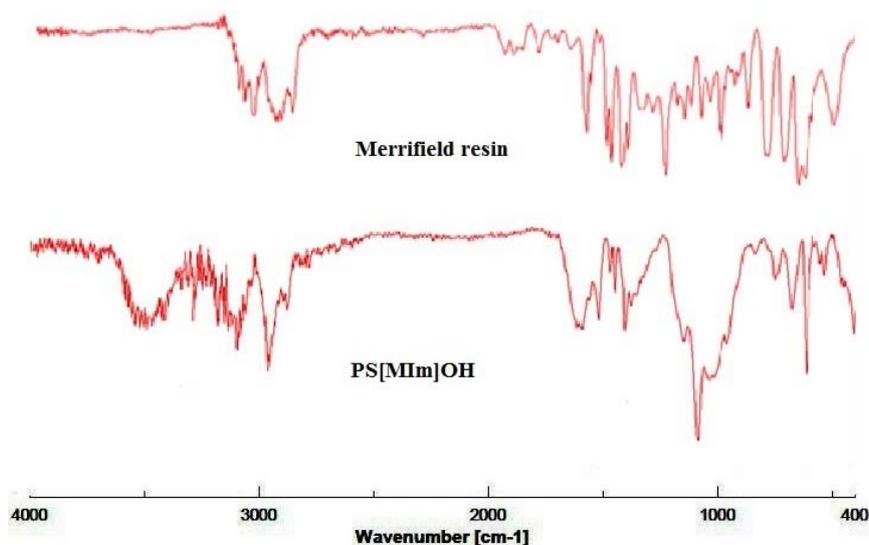


Fig. 1. FT-IR spectra of Merrifield resin and PS[MIm]OH.

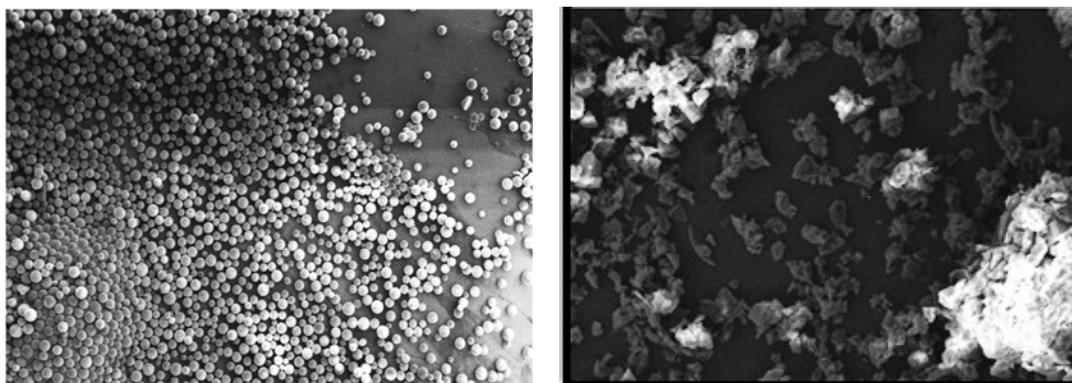


Fig. 2. SEM images of Merrifield resin (left) and PS[MIm]OH (right).

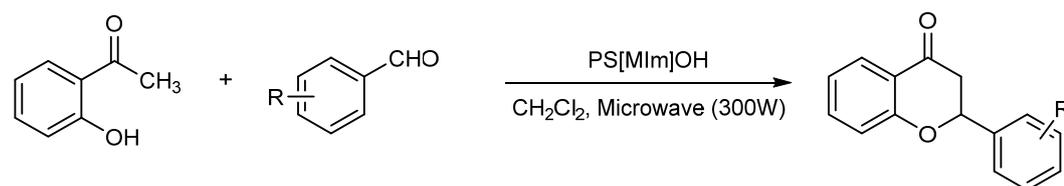
In order to seek the optimal condition and to investigate the catalytic activity of PS[MIm]OH, equimolar mixture of benzaldehyde (1 mmol) and 2'-hydroxyacetophenone (1 mmol) was chosen as model, and was subjected to microwave irradiation in different solvents such as methanol, water, acetonitrile and dichloromethane. As outlined in Table 1, comparatively high yields (91%) were obtained by carrying out the reaction in the presence of PS[MIm]OH (0.05 g) and refluxing in CH₂Cl₂, giving turn over number and frequency up to 26 and 780 h⁻¹, respectively (Table 1, Entry 5). It is worth noting that the results are consistent with the swelling behavior of Merrifield resin [28].

Encouraged by the observation of high efficiency of the procedure and to enlarge the application of this method for synthesis of different flavanones, reactions of a verity of aromatic benzaldehyde bearing electron-donating or electron-withdrawing substituent were surveyed. In all cases, condensation reactions afforded the corresponding product in good to relatively high yield in short time under optimization condition

(Table 2). It should be noted that in this reaction the resins do not suffer from extensive mechanical degradation after operating. After completion of the reaction, the catalyst was separated by filtration, washed with CH₂Cl₂, CH₃OH and dried. The recycled catalyst was then used for at least up to four times. Although a decrease of activity is observed upon recycling, by increasing the reaction time (from 5 min to 7 min), this limitation is compensated in fifth cycle.

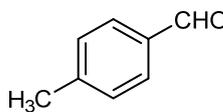
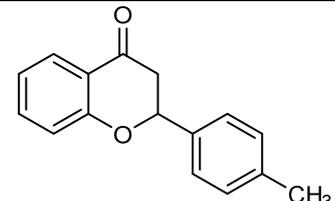
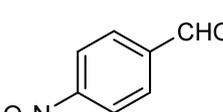
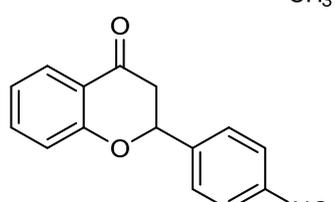
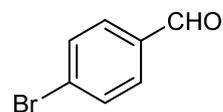
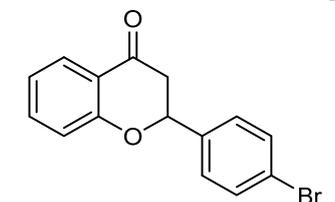
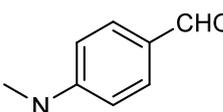
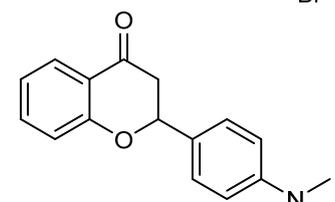
Table 1. Optimization of the reaction conditions.

Entry	Solvent	Cat (g)	Time (min)	Result
1	CH ₃ OH	0.1	15	Trace
2	H ₂ O	0.1	15	15% Yield
3	CH ₃ CN	0.1	15	26% Yield
4	CH ₂ Cl ₂	0.1	5	Completed
5	CH ₂ Cl ₂	0.05	2	Completed
6	CH ₂ Cl ₂	-	15	Trace

Table 2. Synthesis of Flavanones catalyzed by PS[MIm]OH.

Entry	Aldehyde	Product ^a	Time (min)	Yield (%) ^b	m.p. (°C)	
					Found	Reported
1			2	91	74-75	76-77
2			10	79	147-148	147-148
3			4	84	113-114	113-114
4			6	81 ^c	78-80	78-79
5			5	84	96-98	96-98
6			12	71 ^c	93-94	95-97
7			5	70 ^c	95-96	93-95

Table 2. (Continued).

8			6	78 ^c	82-83	77-78
9			6	60 ^c	156-157	156-157
10			6	73 ^c	118-120	118-119
11			6	61 ^c	117-118	117-118

^aAll products are known and were identified by comparison of their physical and spectral data with those of authentic samples; the reported data are from refs. [18,20,29].

^bIsolated yield.

^cThe reaction was carried out by 0.1 g of catalyst.

To compare the efficiency of our catalyst with the reported catalysts for the synthesis of flavanones, we compared our results obtained from the reaction of benzaldehyde with 2'-hydroxyacetophenone in the presence of PS[Mim]OH as a heterogeneous catalyst with the results reported in literature. The catalyst amount, reaction times or product yield values showed that our catalyst is more effective than those reported for other catalytic systems (Table 3).

4. Conclusions

In summary, we have shown that polystyrene-supported 1-methylimidazolium hydroxide can be used as an efficient and reusable heterogeneous catalyst for the synthesis of flavanone analogues via straightforward Claisen–Schmidt condensation.

Acknowledgements

The authors acknowledge funding from Mahshahr Branch Research Council, Islamic Azad University.

Table 3. Comparison of PS[Mim]OH with other reported catalysts in the reaction of benzaldehyde with 2'-hydroxyacetophenone.

Entry	Catalyst, conditions	Time	Yield (%)	Ref.
1	Iodine, Aniline, CH ₃ OH	15 min	88	[18]
2	Nanocrystalline MgO, EtOH	12 h	90 ^a	[30]
3	Zn–Al (6) CHTlc, 140 °C	6 h	28.2	[31]
4	[LiAl ₂ (OH) ₆](CO ₃) _{0.5} ·nH ₂ O	60 min	56 ^a	[15]
5	PS[Mim]OH, CH ₂ Cl ₂ , MW	2 min	91	This work

^aConversion.

References

- [1] H. Olivier-Bourbigou, L. Magna, D. Morvan, *Appl. Catal. A* 373 (2010) 1-56.
- [2] D.D. Patel, J.M. Lee, *Chem. Rec.* 12 (2012) 329-355.
- [3] A.R. Hajipour, F. Rafiee, *J. Iran. Chem. Soc.* 6 (2009) 647-678.
- [4] S. Abello, F. Medina, X. Rodriguez, Y. Cesteros, P. Salagre, J.E. Sueiras, D. Tichit, B. Coq, *Chem. Commun.* (2004) 1096-1097.
- [5] H. Li, P.S. Bhadury, B. Song, S. Yang, *RSC Adv.* 2 (2012) 12525-12551.
- [6] C.P. Mehnert, *Chem- Eur. J.* 11 (2005) 50-56.
- [7] C. Yuan, Z. Huang, J. Chen, *Catal. Commun.* 24 (2012) 56-60.
- [8] D.W. Kim, D.J. Hong, K.S. Jang, D.Y. Chi, *Adv. Synth. Catal.* 348 (2006) 1719-1727.
- [9] A.E. Nibbs, K.A. Scheidt, *Eur. J. Org. Chem.* 2012 (2012)449-462.
- [10] W. Ren, Z. Qiao, H. Wang, L. Zhu, L. Zhang, *Med. Res. Rev.* 23 (2003) 519-534.
- [11] H. Yoon, T.W. Kim, S.Y. Shin, M.J. Park, Y. Yong, D.W. Kim, T. Islam, Y.H. Lee, K.-Y. Jung, Y. Lim, *Bioorg. Med. Chem. Lett.* 23 (2013)232-238.
- [12] M. Cabrera, M. Simoens, G. Falchi, M.L. Lavaggi, O.E. Piro, E.E. Castellano, A. Vidal, A. Azqueta, A. Monge, A.L. de Ceráin, G. Sagrera, G. Seoane, H. Cerecetto, M. González, *Bioorg. Med. Chem.* 15 (2007) 3356-3367.
- [13] N. Anand, P. Singh, A. Sharma, S. Tiwari, V. Singh, D.K. Singh, K.K. Srivastava, B.N. Singh, R.P. Tripathi, *Bioorg. Med. Chem.* 20 (2012) 5150-5163.
- [14] M. Safavi, N. Esmati, S.K. Ardestani, S. Emami, S. Ajdari, J. Davoodi, A. Shafiee, A. Foroumadi, *Eur. J. Med. Chem.* 58 (2012) 573-580.
- [15] D. French, P. Schifano, J. Cortés-Concepción, S. Hargrove-Leak, *Catal. Commun.* 12(2010) 92-94.
- [16] J. A. Cortes-Concepcion, F. Patcas, M.D. Amiridis, *Appl. Catal. A* 386 (2010) 1-8.
- [17] X. Wang, Y.-H. Tseng, J.C.C. Chan, S. Cheng, *J. Catal.* 233 (2005) 266-275.
- [18] V. Kavala, C. Lin, C.-W. Kuo, H. Fang, C.-F. Yao, *Tetrahedron* 68 (2012) 1321-1329.
- [19] S. Chandrasekhar, K. Vijeender, K.V. Reddy, *Tetrahedron Lett.* 46 (2005) 6991-6993.
- [20] R. Mondal, A.D. Gupta, A.K. Mallik, *Tetrahedron Lett.* 52 (2011)5020-5024.
- [21] R. Sakirolla, M. Yaeghoobi, N. Abd. Rahman, *Monatsh. Chem.* 143 (2012) 797-800.
- [22] A. R. Kiasat, S. Sayyahi, *Mol. Diversity* 14 (2010) 155-158.
- [23] A.R. Kiasat, S. Sayyahi, *Catal. Commun.* 11 (2010) 484-486.
- [24] S. Sayyahi, H.M. Rezaee, F.S. Khalfabadi, M. Gorjizadeh, *J. Chem. Res.* 36 (2012) 396-397.
- [25] S. Sayyahi, J. Saghanezhad, *Chin. Chem. Lett.* 22 (2011) 300-302.
- [26] A. Fauvel, H. Deleuze, Y. Landais, *Eur. J. Org. Chem.* 2005 (2005) 3900-3910.
- [27] B.-H. Jun, J.-H. Kim, J. Park, H. Kang, S.-H. Lee, Y.-S. Lee, *Synlett* (2008) 2313-2316.
- [28] N. Galaffu, G. Sechi, M. Bradley, *Mol. Diversity* 9 (2005) 263-275.
- [29] D. Kumar, G. Patel, A. Kumar, R. K. Roy, *J. Heterocycl. Chem.* 46 (2009) 791-795.
- [30] B.M. Choudary, K.V.S. Ranganath, J. Yadav, M.L. Kantam, *Tetrahedron Lett.* 46 (2005) 1369-1371.
- [31] L.B. Kunde, S.M. Gade, V.S. Kalyani, S.P. Gupte, *Catal. Commun.* 10 (2009) 1881-1888.