THE SYNTHESIS OF SALICYLATE PROMPTED BY BRØNSTED ACIDIC IONIC LIQUIDS

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ABSTRACT

Brønsted acidic ionic liquids based on imidazolium cation were employed as a series of efficient and environmentally benign catalysts and solvents for the synthesis of salicylate, the yields could reach 76%-96%. The optimal reaction conditions were determined. The results showed that Brønsted acidic ionic liquids were efficient catalysts and solvents which could be recycled easily without obvious decline in catalytic activities.

Key words: Ionic liquid, esterification, salicylate

INTRODUCTION

Salicylate was a kind of very useful organic compound, which could be used as essence, medicine, solvent and so on. The traditional catalysts used for the synthesis of salicylate were concentrated sulfuric acid and phosphoric acid which were strongly corrosive, harmful to environment and unreusable. When using concentrated sulfuric acid and phosphoric acid as catalysts, it also brought difficulty to the final treatment of the synthesis of salicylate[1]. Toluene-p-sulfonic acid, sodium acid sulfate and solid acid had been used as substitute catalysts for the synthesis of salicylate, but the recovery of them was difficult[1-3].

Brønsted acidic ionic liquids (ILs) 1-butyl-3-methyl-imidazolium hydrogen sulphate ([bmim]HSO_4), 1-butyl-3-methyl-imidazolium dihydogen phosphate ([bmim]H_2PO_4), 1-methyl-3-hydro-imidazolium tetrafluoroborate ([Hmim]BF_4), 1-methyl-3-(3-sulfopropyl)-imidazolium hydrogen sulphate ([HSO_3-pmim]HSO_4), 1-methyl-3-(3-sulfopropyl)-imidazolium tetrafluoroborate ([HSO_3-pmim]BF_4) and 1-methyl-3-(3-sulfopropyl)-imidazolium 4-methylbenzenesulfonate ([HSO_3-pmim][pTSA]) had received vast research interests in recent years which had been used as satisfactory acidic catalysts and solvents for many organic reactions[4-6], due to their particular properties, such as high thermal stability, reusability, miscibility with organic compounds and so on[7-9]. In this paper, an efficient and feasible procedure for the synthesis of salicylate was reported, using Brønsted acidic ILs [bmim]HSO_4, [bmim]H_2PO_4, [Hmim]BF_4, [HSO_3-pmim]HSO_4, [HSO_3-pmim]BF_4 and [HSO_3-pmim][pTSA] (Figure 1) as recyclable catalysts and solvents (Scheme 1). The optimal reaction conditions were determined and the results showed that Brønsted acidic ILs were efficient catalysts and solvents for the synthesis of salicylate. ILs used could be recycled easily without obvious decline in catalytic activities.

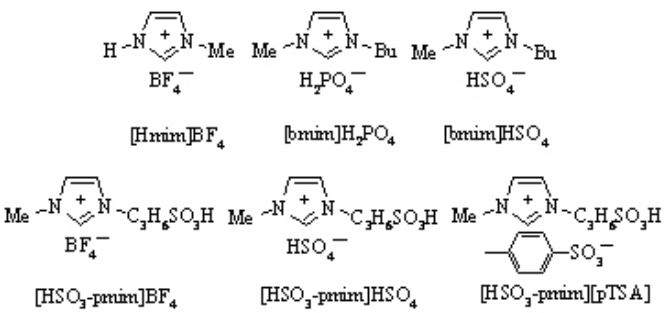
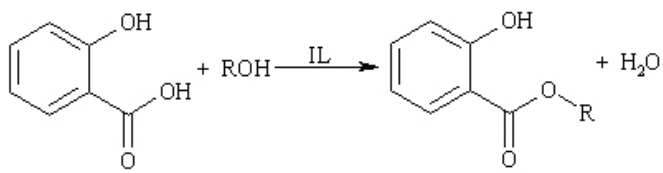


Figure 1 ILs synthesized for the synthesis of salicylate



Scheme 1 The synthesis of salicylate

EXPERIMENTAL

N-methylimidazole and 1-butylbromide were purchased and distilled before using. All the other reagents used were purchased and used without any further purification.

The synthesized salicylates were characterized by FT-IR (Nicolet Nexus 670) and GC (Agilent 6890-5973N). The results of GC showed that the purities of salicylates were higher than 99%[10-14].

Preparation of ILs: ILs used were synthesized according to the previously published papers[4-6, 15].

Typical esterification procedure: Alcohol (20 mmol), salicylic acid (20 mmol) and IL (20 mmol) were added into a flask and stirred at 115°C for 10h. Upon completion of the reaction, the reaction mixture became biphasic. The upper phase was salicylate and the lower phase was IL. The upper phase was separated, washed with water and saturated solution of sodium hydrogen carbonate, and dried over anhydrous sodium sulfate. Then salicylate was characterized by FT-IR and GC. The lower phase was rotatory evaporated and IL was reused after removal of water under vacuum (0.01Torr) at 80°C for 6h.

RESULTS AND DISCUSSION

1. The optimization of reaction conditions

The results of the optimization of reaction conditions were listed in Table 1. The effect of reaction temperature on the yield was shown in entries 1, 2 and 3. When the reaction temperature was 100°C, the yield was only 28% (entry 1). However, when the reaction temperature was higher than 115°C, the increase in the yield was slightly, 51% for 115°C and 53% for 130°C (entries 2 and 3). So the optimal reaction temperature was 115°C.

The effect of molar ratio on the yield was shown in entries 2, 4 and 5, the optimal molar ratio (acid: alcohol: IL) was 1: 1: 1. When the molar ratio was higher than 1: 1: 1, the increase in the yield was also slightly, 51% for 1: 1: 1 and 52% for 1: 1: 1.5 (entries 2 and 5).

As can be seen, the yields of salicylate for 4h and 7h were not satisfactory, 51% for 4h and 64% for 7h (entries 2 and 6). When the reaction time reached 10h, the yield could reach 86% (entry 7). Then prolonging the reaction time, there was no obvious increase in the yield, 88% for 12h (entry 8). So the optimal reaction time was 10h.

Therefore, the optimal reaction conditions were: molar ratio (acid: alcohol: IL), 1: 1: 1; reaction time, 10h; reaction temperature, 115°C.

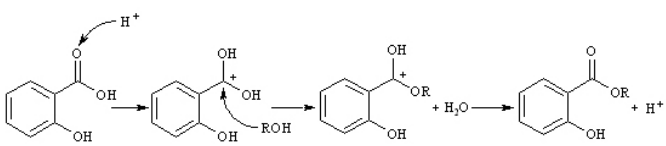
Table 1 The results of the optimization of reaction conditions

Entry	Alcohol	IL	Reaction time (h)	Reaction temperature (°C)	Molar ratio (acid: alcohol: IL)	Yield (%)
1	ethyl alcohol	[Hmim]BF_4	4	100	1: 1: 1	28
2			4	115	1: 1: 1	51
3			4	130	1: 1: 1	53
4			4	115	1: 1: 0.5	44
5			4	115	1: 1: 1.5	52
6			7	115	1: 1: 1	64
7			10	115	1: 1: 1	86
8			12	115	1: 1: 1	88

2. The synthesis of salicylate in Brønsted acidic ILs

The synthesis of salicylate was carried out in Brønsted acidic ILs [bmim]HSO_4, [bmim]H_2PO_4, [Hmim]BF_4, [HSO_3-pmim]HSO_4, [HSO_3-pmim]BF_4 and [HSO_3-pmim][pTSA]. The results were listed in Table 2 showing good yields. The reactants had good solubilities in Brønsted acidic ILs while salicylate was almost immiscible with ILs. Therefore, the esterification started as a homogeneous process and ended as biphasic which could facilitate the separation of salicylate from the reaction mixture and promote the forward reaction of the synthesis of salicylate. Upon completion of the reaction, the upper phase was salicylate and the lower phase was IL, so salicylate could be separated easily. No volatile ILs as catalysts and solvents for the synthesis of salicylate could be reused easily after removal of water under vacuum.

The results of the synthesis of salicylate in Brønsted acidic ILs were shown in Table 2, the catalytic activities of Brønsted acidic ILs were decreased over the following series: [bmim]HSO_4> [Hmim]BF_4> [bmim]H_2PO_4; [HSO_3-pmim]HSO_4> [HSO_3-pmim]BF_4> [HSO_3-pmim][pTSA]. Y. L. Gu had indicated that the acidity sequence of Brønsted acidic ILs [bmim]HSO_4, [Hmim]BF_4 and [bmim]H_2PO_4 was [bmim]HSO_4> [Hmim]BF_4> [bmim]H_2PO_4[16]. The acidity sequence and the catalytic activity sequence of [bmim]HSO_4, [Hmim]BF_4 and [bmim]H_2PO_4 revealed that the catalytic activities of Brønsted acidic ILs were related to their acidities, the strong acidic IL had higher catalytic activity than the weak acidic IL. From the mechanism of the synthesis of salicylate (Scheme 2), it also could find that when using the strong acidic IL as catalyst and solvent, the synthesis of salicylate from alcohol and salicylic acid was easier. For the catalytic activity sequence of Brønsted acidic ILs containing sulfonic acid groups was [HSO_3-pmim]HSO_4> [HSO_3-pmim]BF_4> [HSO_3-pmim][pTSA], the acidity sequence of them should be [HSO_3-pmim]HSO_4> [HSO_3-pmim]BF_4> [HSO_3-pmim][pTSA].



Scheme 2 The mechanism of the synthesis of salicylate

In the synthesis of salicylate using Brønsted acidic ILs as catalysts and solvents, the yields increased from methyl alcohol to n-octyl alcohol orderly (82%, 85%, 86%, 88% and 90%, entries 1-5). For the boiling points of alcohols increased from methyl alcohol to n-octyl alcohol orderly, the amounts of alcohols in the gas phase decreased from methyl alcohol to n-octyl alcohol during the reaction process. Therefore, the yield of salicylate using the high-boiling alcohol was higher than that using the low-boiling alcohol.

Table 2 The results of the synthesis of salicylate in Brønsted acidic ILs

Entry	IL	Alcohol	Yield (%)
1	[HSO_3-pmim]HSO_4	methyl alcohol	82
2		ethyl alcohol	85
3		n-butyl alcohol	86
4		n-hexyl alcohol	88
5		n-octyl alcohol	90
6	[HSO_3-pmim]BF_4	methyl alcohol	80
7		ethyl alcohol	83
8		n-butyl alcohol	85
9		n-hexyl alcohol	86
10		n-octyl alcohol	88
11	[HSO_3-pmim][pTSA]	methyl alcohol	76
12		ethyl alcohol	78
13		n-butyl alcohol	81
14		n-hexyl alcohol	83
15		n-octyl alcohol	84
16	[bmim]HSO_4	methyl alcohol	86
17		ethyl alcohol	90
18		n-butyl alcohol	91
19		n-hexyl alcohol	93
20		n-octyl alcohol	96
21	[Hmim]BF_4	methyl alcohol	84
22		ethyl alcohol	86
23		n-butyl alcohol	88
24		n-hexyl alcohol	91
25		n-octyl alcohol	92
26	[bmim]H_2PO_4	methyl alcohol	7
27		ethyl alcohol	9
28		n-butyl alcohol	12
29		n-hexyl alcohol	15
30		n-octyl alcohol	16

One important advantage of using Brønsted acidic ILs as efficient catalysts and solvents was the possibility of recycling. We examined the synthesis of n-butyl salicylate in [Hmim]BF_4. The results of recycling experiments were summarized in Table 3. For each cycling reaction, n-butyl alcohol (20mmol), salicylic acid (20mmol) and recovered [Hmim]BF_4 were added into a flask successively and stirred at 115°C for 10h. Upon completion of the reaction, salicylate was separated and [Hmim]BF_4 was reused after removal of water. The results of recycling use of [Hmim]BF_4 revealed that Brønsted acidic ILs as catalysts and solvents for the synthesis of salicylate were recyclable. The slightly decline in the yield should be ascribed to the slightly lose of IL.

Table 3 The results of recycling use of [Hmim]BF_4 in the synthesis of n-butyl salicylate

Entry	1	2	3	4	5
Yield (%)	88	86	85	85	82

CONCLUSIONS

In summary, a procedure for the synthesis of salicylate in Brønsted acidic ILs has been developed. The synthesis of salicylate, using Brønsted acidic ILs [bmim]HSO_4, [bmim]H_2PO_4, [Hmim]BF_4, [HSO_3-pmim]HSO_4, [HSO_3-pmim]BF_4 and [HSO_3-pmim][pTSA] as catalysts and solvents, has several advantages: (1) ILs as catalysts show good catalytic activities, the yields could reach 76%-96%, except [bmim]H_2PO_4; (2) For salicylate could not dissolve in ILs, ILs as solvents could promote the forward reaction and facilitate the separation of salicylate from the reaction mixture; (3) ILs could be reused easily after removal of water without obvious decline in catalytic activities.

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