Fischer indole synthesis catalyzed by novel SO_3H-functionalized ionic liquids in water†

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Novel SO_3H-functionalized ionic liquids bearing two alkyl sulfonic acid groups in the imidazolium cations were designed and successfully applied as catalysts for the one-pot Fischer indole synthesis in water medium. The sequence of the catalytic activity observed in the transformation was in good agreement with the Brønsted acidity order determined by the Hammett method. Various types of indoles from single-carbonyl ketones/aldehydes and cyclohexandiones were provided in 68–96% yields using the catalytic system of $[(HSO_3\text{-p})_2\text{im}][HSO_4]/H_2O$. The indole products could be conveniently separated from the reaction mixture by filtration and the dissolved catalyst could be regenerated by treatment with a strongly acidic cation exchange resin, which meant the whole process was performed in water without using any organic solvents.

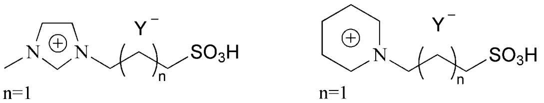
Introduction

The indole scaffold is probably the most ubiquitous heterocycle structure in natural and unnatural compounds that usually have biological activities.[1] The synthesis of indoles has been a major object of research for over hundred years, and a variety of well-established classical methods are now available.[2] Compared with other methodologies for indole synthesis, the Fischer indole reaction of ketones with aryhydrazines remains an extremely useful and important method.[3] In many cases, acid catalysts have been employed to effect the cyclization of enolizable N-arylhydrazones derived from ketones and aryhydrazines. Alternative catalysts, including Brønsted acids (H_2SO_4, HCl, PPA, AcOH, TsOH),[4] Lewis acids ($ZnCl_2$, $TiCl_4$),[5] and solid acids (zeolite, montmorillonite clay),[6] have been reported for the Fischer indole synthesis. Nevertheless, the search for novel environmentally benign and efficient catalysts and catalytic systems is still being actively pursued, because the reported Brønsted and Lewis acids are environmentally unfriendly, hazardous, difficult to reuse, and usually required in large amounts. While solid acids' shortcomings of restricted accessibility and rapid deactivation limit their application to some degree.

Task-specific acidic ionic liquids have been reported offering a new possibility for developing environmentally friendly acidic catalysts owing to the combination of the advantages of liquid acids and ionic liquids (ILs).[7] Rebeiro and Khadikar firstly described the synthesis of indoles with the ionic liquid 1-butyl-pyridinium chloride·$3AlCl_3$ as a dual solvent–catalyst.[8a] Jenkins and co-workers carried out the Fischer indole synthesis with one equivalent of the ionic liquid choline chloride·$2ZnCl_2$ for the exclusive formation of 2,3-disubstituted indoles.[8b]

Although such Lewis acidic ILs present excellent catalytic activities, their application was limited, since they are unstable in air and difficult to reuse. In our previous work, the stable Brønsted acidic ILs, such as $[\text{bmim}][HSO_4]$ and $[\text{bmim}][H_2PO_4]$, were successfully applied to conquer some drawbacks mentioned above and it was found that the acidity of the ILs was an important property relevant to their catalytic activity for indole synthesis.[8c]

In contrast, the alkane sulfonic acid group functionalized ILs emerged, which as strong Brønsted acidic ILs exhibited great potential in replacement of conventional homogeneous/heterogeneous acidic catalysts (examples shown in Fig. 1).[9] In this work, we investigated the catalytic ability of such acidic ILs in the Fischer indole synthesis. For enhancing the acidity and catalytic performance of these ILs, novel SO_3H-functionalized ILs which have two alkyl sulfonic acid groups in the imidazolium cation were designed and applied (Fig. 2). Moreover, water, as a readily available, safe, non-toxic, and cheap solvent,[10] was found to be a good medium for the Fischer indole synthesis, which could afford a more green, practical, and scalable method for the large-scale preparation of indoles.



n=1	n=1
$[HSO_3\text{-pmim}][Cl]$, Y=Cl	$[HSO_3\text{-pPydin}][Cl]$, Y=Cl
$[HSO_3\text{-pmim}][H_2PO_4]$, Y=$H_2PO_4$	$[HSO_3\text{-pPydin}][H_2PO_4]$, Y=$H_2PO_4$
$[HSO_3\text{-pmim}][HSO_4]$, Y=$HSO_4$	$[HSO_3\text{-pPydin}][HSO_4]$, Y=$HSO_4$
n=2	n=2
$[HSO_3\text{-bmim}][Cl]$, Y=Cl	$[HSO_3\text{-bPydin}][Cl]$, Y=Cl
$[HSO_3\text{-bmim}][H_2PO_4]$, Y=$H_2PO_4$	$[HSO_3\text{-bPydin}][H_2PO_4]$, Y=$H_2PO_4$
$[HSO_3\text{-bmim}][HSO_4]$, Y=$HSO_4$	$[HSO_3\text{-bPydin}][HSO_4]$, Y=$HSO_4$

Fig. 1 Brønsted acidic ILs bearing one alkyl sulfonic acid group.

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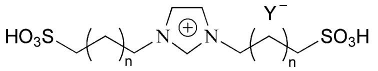
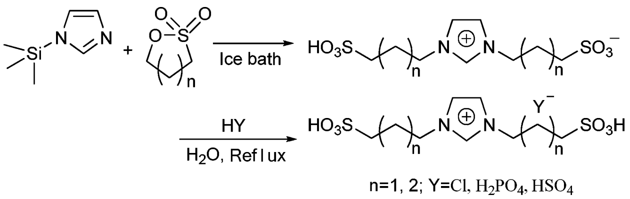


n=1	n=2
$[(HSO_3\text{-p})_2im][Cl]$, Y=Cl	$[(HSO_3\text{-b})_2im][Cl]$, Y=Cl
$[(HSO_3\text{-p})_2im][H_2PO_4]$, $Y=H_2PO_4$	$[(HSO_3\text{-b})_2im][H_2PO_4]$, $Y=H_2PO_4$
$[(HSO_3\text{-p})_2im][HSO_4]$, $Y=HSO_4$	$[(HSO_3\text{-b})_2im][HSO_4]$, $Y=HSO_4$

Fig. 2 Novel Brønsted acidic ILs bearing two alkyl sulfonic acid groups.

Results and discussion

To begin with, the novel SO_3H-functionalized acidic ILs bearing two alkyl sulfonic acid groups were prepared from the reaction of *N*-trimethylsilylimidazole with 1,3-propane or 1,4-butane sultone, respectively, followed by the acidification of the afforded zwitterions with strong acids (Scheme 1). The obtained acidic ILs are water-stable, nonvolatile, and immiscible with non-polar organic solvents. The other types of Brønsted acidic ILs, such as SO_3H-functionalized ILs shown in Fig. 1, $[bmim][HSO_4]$ and $[bmim][H_2PO_4]$, were synthesized according to the literature.[8,9]



Scheme 1 Synthesis of the novel Brønsted acidic ILs bearing two alkyl sulfonic acid groups.

The Brønsted acidity of the above typical ILs was evaluated from the determination of the Hammett acidity functions using UV-visible spectroscopy with 3-nitroanline as the indicator in ethanol.[11] As shown in Fig. 3, the maximal absorbance of the unprotonated form of the indicator was observed at 374 nm, which decreased with added acid.[12] The decreasing order of the absorbance of the $[HSO_4]$-type ILs was observed as follows: $[bmim][HSO_4] > [HSO_3\text{-bmim}][HSO_4] > [HSO_3\text{-pmim}][HSO_4] > H_2SO_4 > [(HSO_3\text{-b})_2im][HSO_4] > [(HSO_3\text{-p})_2im][HSO_4]$, indicating the acidity order of ILs to be as follows: $[(HSO_3\text{-p})_2im][HSO_4] > [(HSO_3\text{-b})_2im][HSO_4] > H_2SO_4 > [HSO_3\text{-pmim}][HSO_4] > [HSO_3\text{-bmim}][HSO_4] > [bmim][HSO_4]$. It is obvious that the Brønsted acidity of the ILs depended both on the nature of the cations and anions. ILs bearing two alkyl sulfonic acid groups on the cations have stronger acidity than those of bearing one such group, which showed further stronger acidity than those of bearing no such group ($[(HSO_3\text{-b})_2im][HSO_4]$ *vs.* $[HSO_3\text{-bmim}][HSO_4]$ and $[bmim][HSO_4]$), suggesting the significant effect of the alkyl sulfonic acid group on the acidity of the ILs. The acidity of the ILs with the conjugate base of $[HSO_4]^-$ was stronger than that of the corresponding ILs with the conjugate base of $[Cl]^-$ and $[H_2PO_4]^-$ ($[HSO_3\text{-pmim}][HSO_4]$ *vs.* $[HSO_3\text{-pmim}][Cl]$; $[(HSO_3\text{-b})_2im][HSO_4]$ *vs.* $[(HSO_3\text{-b})_2im][H_2PO_4]$). Ultimately, $[(HSO_3\text{-p})_2im][HSO_4]$ exhibited a stronger Brønsted acidity than the other tested ILs and even stronger than H_2SO_4. The Brønsted acidity of $[(HSO_3\text{-b})_2im][HSO_4]$ was slightly weaker as compared with $[(HSO_3\text{-p})_2im][HSO_4]$, but was also stronger than H_2SO_4.

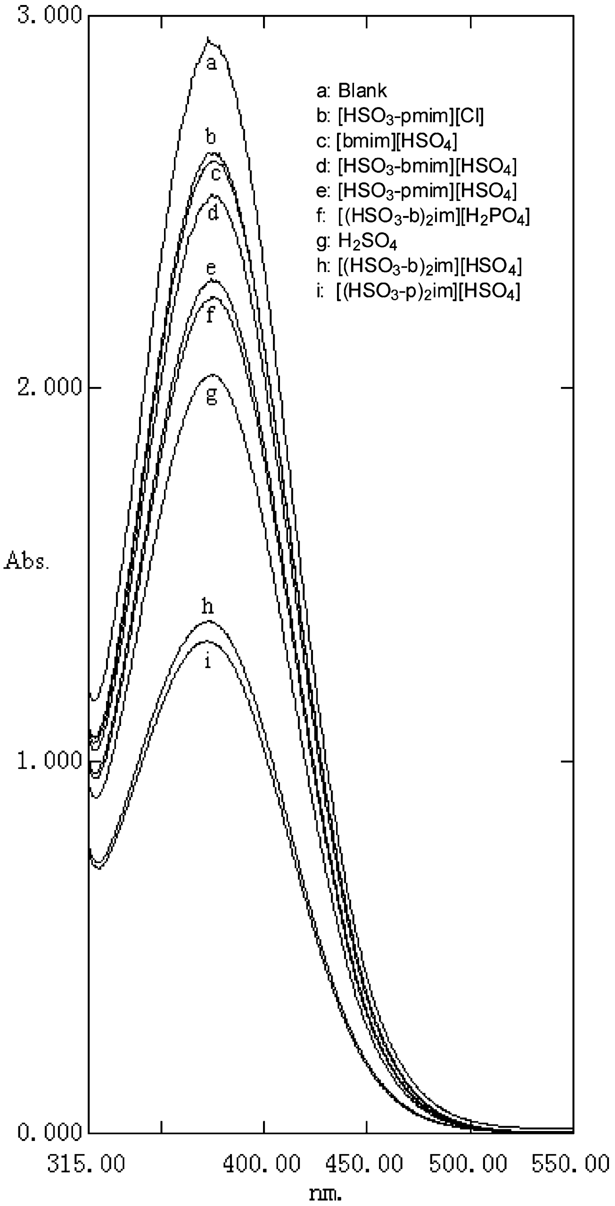
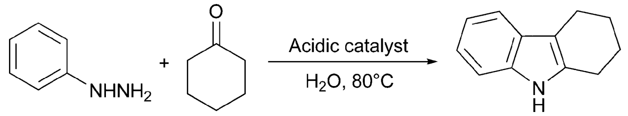


Fig. 3 Absorption spectra of 3-nitroaniline for various Brønsted acidic ILs in ethanol.

The one-pot Fischer indole synthesis of cyclohexanone with phenylhydrazine was focused on as a model reaction for the evaluation of the catalytic activity of the above Brønsted acidic ILs in water medium. To the best of our knowledge, there have been few reports on the application of SO_3H-functionalized ILs as Brønsted acid catalysts in aqueous organic reactions and also few on the Fischer indole synthesis in aqueous media. We envisioned that as the above mentioned SO_3H-functionalized Brønsted acidic ILs are not only water stable but also miscible with water, they could give full play to the acid-catalysis in water. Initially, the model reaction was carried out in water at 80 °C. As shown in Table 1, the acid resin of Dowex-50 and organic acid of p-TsOH proved to be less active than strong inorganic acids of HCl and H_2SO_4 (Entry 1–3 and 5), and the nature of ILs showed a greatly significant effect on the catalytic activity. The ILs bearing no or only one alkyl sulfonic acid group on the cations exhibited worse activity than their corresponding inorganic Brønsted acids of HCl, H_3PO_4 and H_2SO_4

Table 1 The Fischer indole synthesis of cyclohexanone with phenylhydrazine catalyzed by different ILs and acids in water[a]



Entry	Acidic catalyst	Time/h	Conversion (%)	Isolated yield (%)
1	Dowex-50 acid resin	10	32	—
2	p-TsOH	2	90	80
3[b]	HCl	3	92	77
4	H_3PO_4	3	83	70
5[b]	H_2SO_4	1	98	84
6	[bmim][Cl]	10	30	—
7	[bmim][H_2PO_4]	8	68	40
8	[bmim][HSO_4]	5	80	68
9	[HSO_3-pmim][Cl]	10	60	30
10	[HSO_3-pmim][H_2PO_4]	8	80	60
11	[HSO_3-pmim][HSO_4]	3	89	77
12	[HSO_3-bmim][HSO_4]	3	86	74
13	[HSO_3-pPydin][HSO_4]	3	85	73
14	[HSO_3-bPydin][HSO_4]	3	83	71
15[b]	[(HSO_3-p)$_2$im][Cl]	7	86	75
16[b]	[(HSO_3-p)$_2$im][H_2PO_4]	4	97	86
17[b]	**[(HSO_3-p)$_2$im][HSO_4]**	**0.5**	**99**	**93**
18[b]	[(HSO_3-b)$_2$im][Cl]	7	84	72
19[b]	[(HSO_3-b)$_2$im][H_2PO_4]	4	98	83
20[b]	[(HSO_3-b)$_2$im][HSO_4]	0.5	99	90
21[c]	[(HSO_3-p)$_2$im][HSO_4]	0.5	99	90
22[d]	[(HSO_3-p)$_2$im][HSO_4]	6	55	30
23[c]	H_2SO_4	10	65	42
24[e]	[(HSO_3-p)$_2$im][HSO_4]	12	99	89
25[b,f]	[(HSO_3-p)$_2$im][HSO_4]	3	96	84

[a] Reaction conditions: cyclohexanone (5 mmol), phenylhydrazine (5 mmol), acidic catalyst (5 mmol), water (15 mL). [b] The amount of catalyst: 2.5 mmol. [c] The amount of catalyst: 1.5 mmol. [d] The amount of catalyst: 1 mmol. [e] The reaction was carried out at room temperature. [f] 2.5 mmol NH_4OH was previously added into the reaction system.

(Entries 3–5 *vs.* Entries 6–14). While the activity of [Cl]-type ILs bearing two alkyl sulfonic acid groups were still inferior as compared with that of HCl (Entries 15, 18 *vs.* Entry 3), those of [H_2PO_4]- and [HSO_4]-type ILs exhibited more activity than H_3PO_4 and H_2SO_4, respectively (Entry 16, 19 *vs.* Entry 4; Entry 17, 20 *vs* Entry 5). When the amount of the acid catalyst was reduced from 50 mol% to 30 mol%, [(HSO_3-p)$_2$im][HSO_4] led to only a slightly decreased yield from 93% to 90%; in contrast, H_2SO_4 gave a yield from 84% to 42% under the same reaction conditions (Entry 17 *vs.* Entry 21; Entry 5 *vs.* Entry 23). The [(HSO_3-p)$_2$im][HSO_4] catalyzed reaction could also be performed at room temperature, leading to 89% yield of the desired product after 12 hours, and [(HSO_3-p)$_2$im][HSO_4] previously treated with NH_3 afforded 84% yield after reaction for 3 hours at 80 °C (Entry 24–25). It was noteworthy that the sequence of the catalytic activity observed in the Fischer indole synthesis was in good agreement with the acidity order determined by the Hammett method. Increasing the Brønsted acidity of ILs improved the catalytic activity, and [(HSO_3-p)$_2$im][HSO_4] should be a suitable catalyst for the Fischer indole synthesis.

Apart from the efficient and environmentally benign reaction system, the simplicity of the product separation and the possibility to recycle the [(HSO_3-p)$_2$im][HSO_4]/H_2O system offer significant advantages, which was central to its application. Because the indole products are insoluble in water, the products could be conveniently separated out by filtration without using any organic solvents after the reaction completed. According to the mechanism of the Fischer indole synthesis,[2] 1 equivalent of NH_3 was produced in the reaction and coordinated with acidic [(HSO_3-p)$_2$im][HSO_4] to form the corresponding ammonium salt in water. But [(HSO_3-p)$_2$im][HSO_4] could be readily recovered by a strongly acid cation exchange resin Dowex-50 to remain its catalytic ability. After the cation exchanged resin was removed by filtration, the remaining [(HSO_3-p)$_2$im][HSO_4]/H_2O system could be reused for the subsequent catalytic cycle of the aqueous reaction directly. The cation exchanged resin could also be regenerated by treatment with hydrochloric acid. Therefore, an overall process for the one-pot Fischer indole synthesis in [(HSO_3-p)$_2$im][HSO_4]/H_2O system can be envisaged as shown in Fig. 4. The recycling procedure was very simple, and the results are summarized in Table 2. Apparently, the regenerated [(HSO_3-p)$_2$im][HSO_4]/H_2O system could be reused without an obvious decrease in the reaction performance after twelve recycles in terms of the rate and the yield, and the untreated catalytic system led to rapid deactivation, implying that the removal of the accumulated NH_3 is vital.

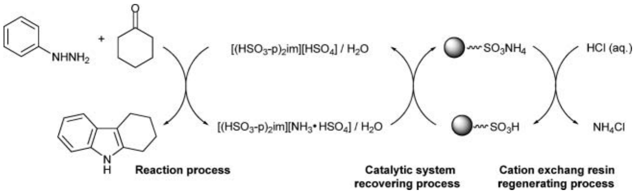


Fig. 4 The overall process for the one-pot Fischer indole synthesis in [(HSO_3-p)$_2$im][HSO_4]/H_2O.

Encouraged by the above results, the generality of the reaction in [(HSO_3-p)$_2$im][HSO_4]/H_2O was investigated for the synthesis of various indole products. As shown in Table 3, the [(HSO_3-p)$_2$im][HSO_4]/H_2O system exhibited very high activity

Table 2 Recycling of the [(HSO_3-p)$_2$im][HSO_4]/H_2O system in the Fischer indole synthesis of 1,2,3,4-tetrahydrocarbazole[a]

Run	1	2	3	4	5	6	7	8	9	10	11	12
Time[b]/h	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Isolated yield[b] (%)	93	90	89	90	88	87	88	87	89	88	89	87
Time[c]/h	0.5	1.5	4	6	—	—	—	—	—	—	—	—
Isolated yield[c](%)	93	88	76	40	—	—	—	—	—	—	—	—

[a] Reaction conditions: cyclohexanone (5 mmol), phenylhydrazine (5 mmol), [(HSO_3-p)$_2$im][HSO_4] (2.5 mmol), water (15 mL). [b] [(HSO_3-p)$_2$im][HSO_4] was reused after treatment with Dowex-50. [c] [(HSO_3-p)$_2$im][HSO_4] was reused without treatment with Dowex-50.

Table 3 One-pot synthesis of Fischer indoles from ketones/aldehydes with arylhydrazines in $[(HSO_3\text{-p})_2im][HSO_4]/H_2O^a$

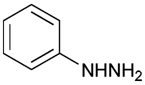
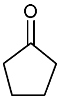
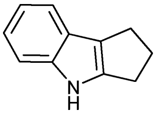
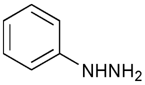
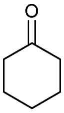
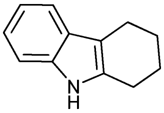
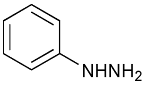
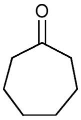
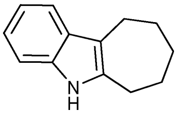
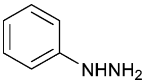
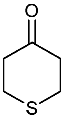
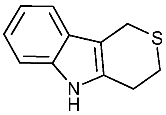
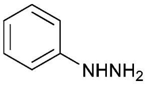
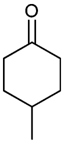
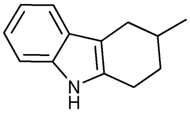
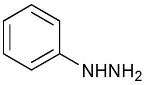
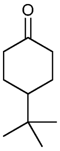
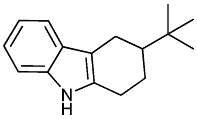
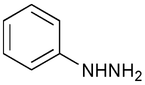
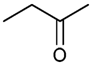
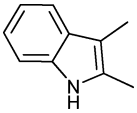
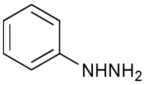
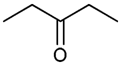
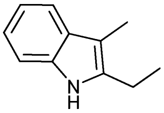
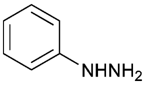
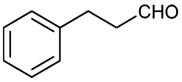
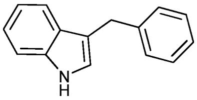
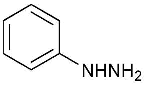
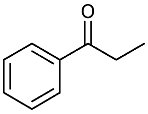
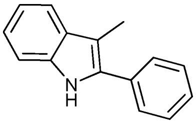
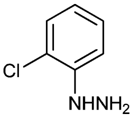
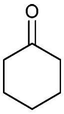
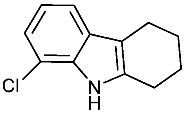
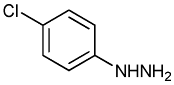
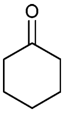
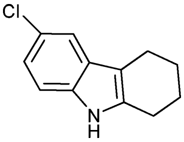
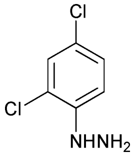
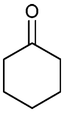
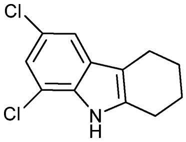
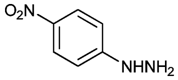
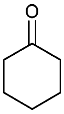
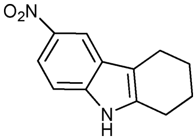
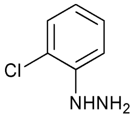
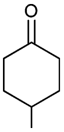
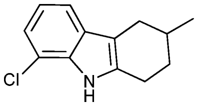
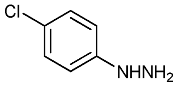
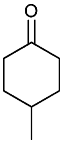
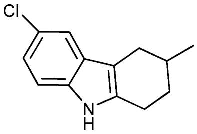
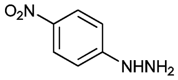
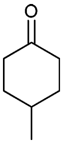
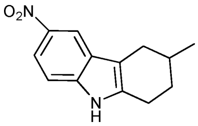
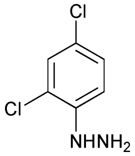
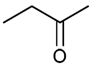
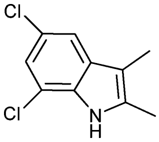
Entry	Arylhydrazines	Ketones/aldehydes	Indoles	*T*/°C	Time/h	Isolated yield (%)
1				80	1	87
2				80	0.5	93
3				80	1	88
4				80	1	95
5				100	1	90
6				100	1	96
7				100	1	90
8				80	1	88
9				80	2	86
10				80	3	83
11				100	1	91
12				100	1	92

Table 3 *(Contd.)*

Entry	Arylhydrazines	Ketones/aldehydes	Indoles	T/°C	Time/h	Isolated yield (%)
13				100	4	87
14				100	1.5	84
15				100	1	87
16				100	1	87
17				100	4	85
18				100	6	83

[a] Reaction conditions: ketones/aldehydes (5 mmol), arylhydrazines (5 mmol), $[(HSO_3\text{-p})_2im][HSO_4]$ (2.5 mmol), water (15 mL).

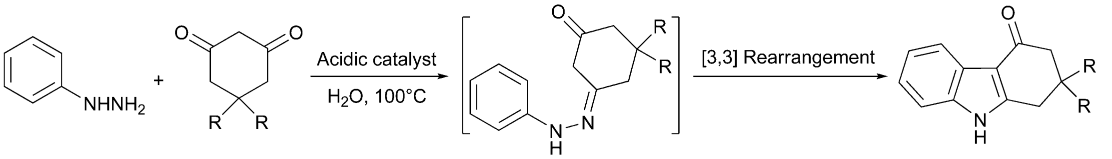
for the Fischer indole synthesis. 87–93% yields were obtained for the reactions of phenylhydrazine with 5–7-carbon cycloketones or tetrahydrothiopyran-4-one within 1 hour at 80 °C (Entries 1–4). Enhancing the reaction temperature to 100 °C, 4-alkylcyclohexanones also gave the corresponding indoles in excellent yields (Entries 5–6). Moreover, linear aldehyde/ketones and the aryl-ketone of propiophenone were proved as adoptive reactants for the Fischer indole synthesis (Entries 7–10). Less activated phenylhydrazines with election-withdrawing groups substituted could also complete the reaction within 1–6 hours at 100 °C, providing the corresponding indoles in 83–92% yields (Entries 11–18).

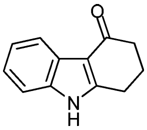
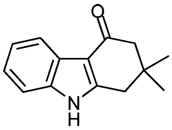
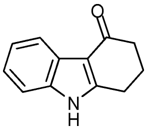
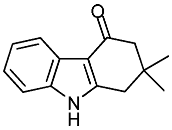
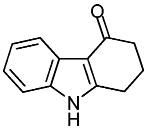
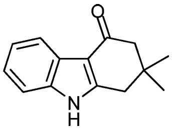
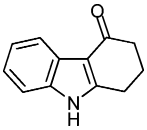
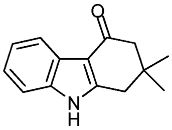
To extend the scope of the one-pot Fischer indole synthesis in $[(HSO_3\text{-p})_2im][HSO_4]/H_2O$ system, the reaction of 1,3-cyclohexanediones with phenylhydrazine was investigated and the results are listed in Table 4. Compared with single-carbonyl ketones, the *N*-phenylhydrazone intermediate from 1,3-cyclohexanedione with phenylhydrazine is more stable and more difficult to activate to continue the next [3,3] sigmatropic rearrangement reaction. However, the 70% isolated yield of the indole product 2,3-dihydro-1*H*-carbazol-4(9*H*)-one, an important pharmaceutical intermediate, could be achieved using $[(HSO_3\text{-p})_2im][HSO_4]$ as catalyst in water, which was much higher than those obtained using other types of Brønsted acids (Entries 1–4). Similarly, the reaction of 5,5-dimethyl-1,3-cyclohexanedione with phenylhydrazine gave a higher yield of 68% in $[(HSO_3\text{-p})_2im][HSO_4]/H_2O$ than those in other catalytic systems (Entries 5–8).

Conclusions

In this paper, an environmentally benign process for the one-pot Fischer indole synthesis in water medium was established, using novel designed SO_3H-functionalized Brønsted acidic ILs bearing two alkyl sulfonic acid groups of the imidazolium cations. The catalytic activity of the SO_3H-functionalized ILs depend mostly on their Brønsted acidity determined from the Hammett method, while the two alkyl sulfonic acid groups of

Table 4 One-pot Fischer indole synthesis of phenylhydrazine with 1,3-cyclohexanedione/5,5-dimethyl-1,3-cyclohexanedione in water[a]



Entry	Acidic catalyst	R	Product	Time/h	Isolated yield (%)	Entry	Acidic catalyst	R	Product	Time/h	Isolated yield (%)
1	[bmim][HSO$_4$]	H		8	30	5	[bmim][HSO$_4$]	CH$_3$		8	29
2	H_2SO_4	H		6	57	6	H_2SO_4	CH$_3$		6	58
3	[(HSO$_3$-b)$_2$im][HSO$_4$]	H		4	66	7	[(HSO$_3$-b)$_2$im][HSO$_4$]	CH$_3$		4	64
4	[(HSO$_3$-p)$_2$im][HSO$_4$]	H		4	70	8	[(HSO$_3$-p)$_2$im][HSO$_4$]	CH$_3$		4	68

[a] Reaction conditions: ketone (5 mmol), phenylhydrazine (5 mmol), acidic catalyst (5 mmol), water (20 mL).

the cations played an important role in the ILs acid strength and the Brønsted acidity of [(HSO$_3$-p)$_2$im][HSO$_4$] was proved to be stronger than the other Brønsted acidic ILs investigated and to be even stronger than H_2SO_4, and thus [(HSO$_3$-p)$_2$im][HSO$_4$] was the most efficient for the transformation in water. Compared with previous attempts, the developed methodology offered significant improvements: (1) the whole process for the Fischer indoles was performed in water without using any organic solvents; (2) the reaction–separation–recycle process was quite convenient and the catalytic system of [(HSO$_3$-p)$_2$im][HSO$_4$]/H_2O could be reused at least twelve times without an obvious decrease in catalytic activity; (3) the novel catalytic system could be successfully applied in the indole synthesis from both single-carbonyl ketones and cyclohexanediones to afford good to excellent yields. Further investigations involving the effectiveness of the benign catalytic system for other reactions are currently underway.

Experimental

General remarks

UV-Vis spectra were recorded on a SHIMADZU UV-2550 diode-array spectrophotometer. NMR data were obtained on Bruker AVANCE III 500 MHz for ^{1}H at 500 MHz and for ^{13}C at 125 MHz with TMS as the internal standard. GC-MS experiments were performed on an Agilent 6890 N GC system with a 5973 N mass selective detector. HRMS data were measured on an Agilent 6120 LC/TOF-MS with ESI source or Waters Premier GC/TOF-MS with EI source. Chemicals were used without purification as commercially available.

Representative procedure for the preparation of the Brønsted acidic ILs

The already reported Brønsted acidic ILs, such as SO$_3$H-functionalized ILs shown in Scheme 1, [bmim][HSO$_4$] and [bmim][H$_2$PO$_4$], were synthesized according to the literature.[7,8]

[HSO$_3$-pmim][HSO$_4$]. ^{1}H NMR (500 MHz, D$_2$O, δ ppm): 2.17–2.23 (m, 2H), 2.79–2.82 (t, 2H, $J = 7.5$ Hz), 3.78 (s, 3H), 4.24–4.27 (t, 2H, $J = 7$ Hz), 7.33–7.34 (t, 1H, $J = 2$ Hz), 7.41 (t, 1H, $J = 2$ Hz), 8.64 (s, 1H).

[HSO$_3$-bmim][HSO$_4$]. ^{1}H NMR (500 MHz, DMSO, δ ppm): 1.51–1.55 (m, 2H), 1.84–1.90 (m, 2H), 2.43–2.46 (t, 2H, $J = 7.5$ Hz), 3.85 (s, 3H), 4.17–4.20 (t, 2H, $J = 7$ Hz), 7.70-7.71 (t, 1H, $J = 2$ Hz), 7.78 (t, 1H, $J = 2$ Hz), 9.14 (s, 1H).

[HSO$_3$-pPydin][HSO$_4$]. ^{1}H NMR (500 MHz, D$_2$O, δ ppm): 2.34–2.40 (m, 2H), 2.87–2.90 (t, 2H, $J = 7.5$ Hz), 4.66–4.70 (d, 2H, $J = 7.5$ Hz), 7.98–8.00 (t, 4H, $J = 7.5$ Hz), 8.45–8.48 (t, 1H, $J = 8$ Hz), 8.79–8.80 (d, 1H, $J = 5.5$ Hz).

[HSO$_3$-bPydin][HSO$_4$]. ^{1}H NMR (500 MHz, D$_2$O, δ ppm): 1.62-1.68 (m, 2H), 1.99-2.05 (m, 2H), 2.80-2.83 (t, 2H, J = 7.5 Hz), 4.49-4.52 (t, 2H, J = 7.5 Hz), 7.91-7.94 (d, 2H, J = 7 Hz), 8.38-8.41 (t, 1H, J = 8 Hz), 8.71-8.72 (d, 1H, J = 5.5 Hz).

Under vigorous stirring, 1,3-propane or 1,4-butane sultone (0.2 mol) was added slowly to trimethylsilylimidazole (0.1 mol), while the flask was cooled in an ice bath. After the reaction had finished, the reaction mixture was stirred for half an hour and then water was added dropwise. The reaction mixture was then dried under vacuum to remove water and the byproduct trimethylsilanol, giving the requisite precursor zwitterions. Next, a stoichiometric amount of acid H_2SO_4 (or HCl or H_3PO_4) was added slowly to the aqueous solution of the zwitterions and the mixture stirred for six hours at reflux. The mixture was then dried under vacuum to afford the final products of the desired novel SO_3H-functionalized ILs bearing two alkyl sulfonic acid groups. The products were obtained with 92–95% yields and in high purities, as assessed by NMR and HRMS spectroscopy.

[(HSO$_3$-p)$_2$im][HSO$_4$]. ^{1}H NMR (500 MHz, D$_2$O, δ ppm): 2.12–2.18 (m, 4H), 2.75–2.78 (t, 4H, J = 7.5 Hz), 4.18–4.21 (t, 4H, J = 7.5 Hz), 7.39–7.40 (d, 2H, J = 1.5 Hz), 8.70 (s, 1H). ^{13}C NMR (125 MHz, D$_2$O, δ ppm): 27.6, 49.8, 50.4, 125.1, 138.3. HRMS: calcd for $C_9H_{17}N_2O_6S_2$: 313.0528 [M-HSO$_4$]$^+$, found: 313.0527 [M-HSO$_4$]$^+$.

[(HSO$_3$-b)$_2$im][HSO$_4$]. ^{1}H NMR (500 MHz, D$_2$O, δ ppm): 1.48–1.54 (m, 4H), 1.76–1.82 (m, 4H), 2.69–2.72 (m, 4H), 3.99–4.02 (t, 4H, J = 7.5 Hz), 7.29 (d, 2H, J = 2 Hz), 8.59 (s, 1H). ^{13}C NMR (125 MHz, D$_2$O, δ ppm): 20.9, 28.0, 48.9, 50.0, 122.4, 135.2. HRMS: calcd for $C_{11}H_{21}N_2O_6S_2$: 341.0841 [M-HSO$_4$]$^+$, found: 341.0844 [M-HSO$_4$]$^+$.

UV-VIS acidity evaluation

Tested ethanol solutions were prepared from dried ethanol, 3-nitroanline and ILs, or 98% H_2SO_4, 85% H_3PO_4 and 37% HCl. All the spectra were recorded on a SHIMADZU UV-2550 spectrophotometer at room temperature.

Representative procedure for the one-pot Fischer indole synthesis

Cyclohexanone (0.49 g, 5.0 mmol) was mixed with [(HSO$_3$-p)$_2$im][HSO$_4$] (2.5 mmol) in water (15 mL), and phenylhydrazine (0.54 g, 5.0 mmol) was added. The mixture was then stirred at 80 °C for about 0.5 h. Reaction progress was monitored by GC-MS. After completion, the reaction mixture was cooled to room temperature, and 1,2,3,4-tetrahydrocarbazole was obtained by filtration and drying without further purification. The remaining mixture of [(HSO$_3$-p)$_2$im][HSO$_4$]/H$_2$O was treated by a strongly acidic cation exchange resin (Dowex-50) at room temperature and was then reused for the subsequent catalytic cycle after filtering off the cation exchanged resin. The cation exchanged resin was then regenerated by treatment with 3 mol L^{-1} hydrochloric acid aqueous solution. ^{1}H NMR (500 MHz, CDCl$_3$, δ ppm): 1.86–1.93 (m, 4H), 2.70–2.74 (m, 4H), 7.05–7.12 (m, 2H), 7.27-7.29 (d, 1H, J = 7.5 Hz), 7.45-7.47 (d, 1H, J = 7.5 Hz), 7.67 (s, 1H). MS (EI): m/z 171 [M]$^+$.

Notes and References

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