Advanced Synthesis & Catalysis

Accepted Article

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To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201900246

Link to VoR: http://dx.doi.org/10.1002/adsc.201900246

10.1002/adsc.201900246

Very Important Publication

FULL PAPER

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

A Sulfone-Containing Imidazolium-Based Brønsted Acid Ionic Liquid Catalyst Enables Replacing Dipolar Aprotic Solvents with Butyl Acetate

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Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract: Replacing dipolar and aprotic solvents with environmentally benign media has emerged as a new facet of green chemistry. In this paper, a sulfone-containing imidazolium-based Brønsted acid ionic liquid was prepared and used as a recyclable acid catalyst. The ionic liquid catalyst enables the use of an industrially acceptable and environmentally benign solvent, butyl acetate, as the reaction medium. The ionic liquid/butyl acetate biphasic system was successfully utilized in many organic reactions, which generally relied heavily on dipolar and aprotic solvents.

Keywords: Brønsted acid; Ionic liquid; Biphasic reaction; Dipolar aprotic solvent; Green solvent

Introduction

A crucial problem in modern organic chemistry is the large use of toxic, hazardous, and flammable solvents both as reaction media and for the isolation and purification steps of the desired products.[1] Among the plethora of chemicals used as solvents, dipolar aprotic media such as dimethylformamide (DMF), *N*-methyl pyrrolidone (NMP), and nitromethane, are commonly used in several useful organic transformations.[2] In fact, these solvents are able to create a unique solvation environment that can stabilize or destabilize reaction intermediates, thus facilitating the control of both reaction rate and selectivity. However, most of these solvents are toxic. For example, DMF is teratogenic, and 1,4-dioxane is carcinogenic. Some of them are very difficult to recycle due to their high boiling points and hydrophilicity. For these reasons, in all the solvent selection guides[3, 4] most of the dipolar aprotic solvents are classified as not-recommended-solvents, and one of the main goals of current research in green chemistry is to replace them with green, environmentally friendly alternatives.[4]

In recent years, several efforts have been made to find chemical efficiency and safer alternatives to classic dipolar aprotic solvents. In 2011, we proposed the use of a NO_2-functionalized imidazolium-based ionic liquid as a solvent (or component) to replace nitromethane, which is an explosive polar solvent.[5] Some interesting options have been found in the world of bio-based chemicals and in fact, cyrene ((–)-dihydrolevoglucosenone),[6] *N*-butylpyrrolidinone,[7] γ-valerolactone,[8] 2-methyltetrahydrofuran (2-MeTHF)[9] have been proposed obtaining relevant results. Other possibilities have been envisaged in the use of solvent-pair mixtures composed of hydrogen bond donor/acceptor (HBD−HBA)[10] couples that have been proposed again to replace polar aprotic solvents. An alternative approach has been suggested by Lipshutz who proposed the use of water as the solvent in a combination of TPGS-750-M, bio-based nonionic surfactant,[11] showing that with the constructed micellar system, some organic reactions no longer need the use of dipolar aprotic media.

Despite the achievements gained by the aforementioned methods, it is still very challenging the individuation of generally efficient media to replace dipolar aprotic solvents. For instance, in many acid-catalyzed reactions, classic dipolar aprotic media can be hardly replaced in the efficient stabilization of the generated carbocation intermediate, and chemical stability of bio-based solvents toward acids is generally limited. To solve this problem, Xiao and Sun have recently used a mesoporous material that has a high density of polar

moieties as support to anchor sulfonic acid.[12] The solvation environment in the inside pore of this material to some extent may be similar to that of DMSO, enabling the synthesis of 5-hydroxyfurfural from glucose, which is a typical solvent-dependent reaction, to be performed in tetrahydrofuran.

This work demonstrated explicitly that by means of catalyst design, it is possible to avoid the use of toxic polar aprotic solvents. Inspired by this elegant approach, and in order for the catalyst to significantly affect the reaction in a concerted solvation environment, we envisioned that a strongly polar liquid should be an ideal choice for the catalyst support. With proper liquid support, the catalyst can be designed to be insoluble in the reaction system, while being sufficiently able to stabilize the carbocation intermediate, therefore, allowing to perform a reaction in an industrially and environmentally acceptable solvent as an ester (**Figure 1**).

We previously reported that a sulfone-containing Brønsted acid ionic liquid, can act as a unique solvent-conserving catalyst, allowing acid-catalyzed reactions to be performed under solvent-free conditions (**Figure 1**).[13] The ionic liquid was poorly soluble in the organic phase (Table S1 in supporting information) while the presence of the highly polar sulfone fragment was able to create a unique dipolar aprotic microenvironment, allowing the reaction to proceed smoothly and efficiently. However, a major drawback is that this ionic liquid is highly viscous, and could only be efficiently utilized in a few reactions until now.[13] In addition, the triflic acid component is not always steadily combined with the zwitterionic salt. And in the presence of an organic solvent able to dissolve triflic acid, the acidic component can thus be extracted, hampering the recyclability of the ionic liquid.

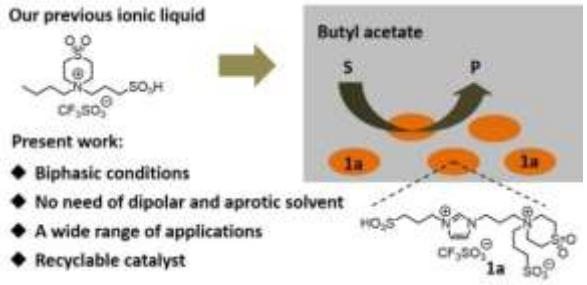


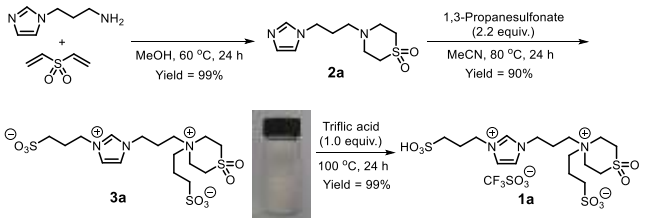
Figure 1. Our previous ionic liquid and a biphasic system and our new ionic liquid **1a**.

To solve all these issues, we designed a new imidazolium-based sulfone-containing Brønsted acid ionic liquid, **1a** (**Figure 1**). This compound can be used as an acid catalyst in many organic reactions in combination with butyl acetate as a reaction medium. Intriguingly, without this ionic liquid, the reactions generally require the use of toxic and hazardous dipolar aprotic solvents to proceed efficiently.

Results and Discussion

The ionic liquid **1a** was synthesized using a three-step procedure as shown in **Scheme 1**. It involved (i) the heating equimolar amounts of 1-(3-aminopropanyl)imidazole and divinylsulfone in methanol at 60 °C for 24 h that after removal of volatile methanol, allowed **2a** to be obtained in nearly quantitative yield; (ii) the synthesis of **3a** via quaternization of **2a** with 1,3-propanesulfonateto give **3a** as a white solid (see **Scheme 1**) after filtration and washing with acetone; and (iii) acidification of **3a** with triflic acid to finally give **1a** as a yellow-pale viscous liquid. Using this three-step synthetic strategy, ionic liquid **1a** was synthesized in an overall 88% yield.

It is noteworthy that ionic liquid **1a** is immiscible with many organic solvents, including butyl acetate, 1,2-dichloroethane, and toluene. Importantly, these solvents are not able to extract triflic acid from **1a**. Therefore, this tailor-made ionic liquid should bring all the features to be a recyclable catalyst when used in an organic solvent.



Scheme 1. Preparation of ionic liquid **1a**.

The catalytic activity of ionic liquid **1a** was examined in a representative reaction of 4-chloroaniline (**4a**) and ethyl pyruvate (**5a**) to synthesize the corresponding 1,2-dihydroquinoline **6a**. This is a typical acid-catalyzed reaction, and previous studies have indicated that iodine, [14] $MgBr_2$, [15] $AuCl_3$,[16] $(p\text{-}BrC_6H_4)_3N{\cdot}SbCl_6$,[17] $Bi(OTf)_3$,[18] and $In(OTf)_3$[19] are effective catalysts for this process. However, most of the reported catalytic systems required the use of toxic solvents, such as acetonitrile and 1,2-dichloroethane and could not be recycled after the first reaction.

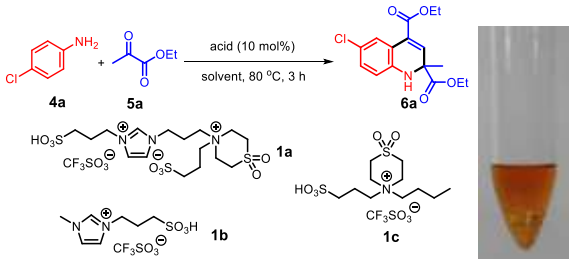
Our preliminary results are listed in **Table 1**. In classic solvents, such as acetonitrile, 1,2-dichloroethane, and 1,4-dioxane, common triflic acid worked well, promoting the formation of **6a** in 55%-75% yields (entries 1–3). In an alternative to these toxic solvents, butyl acetate was also considered as a representative recommended greener solvent.[3] Unfortunately, performing the reaction with triflic acid in this medium, **6a** was obtained in only 44% yield (entry 4).

Most importantly, when ionic liquid **1a** was used as a catalyst, the reaction proceeded very well in butyl acetate, and the yield of **6a** reached the highest value of 96% (entry 5). As the ionic liquid catalyst is insoluble in butyl acetate, the reaction proceeded

under practically biphasic conditions (see the photograph in **Table 1**). However, a similar biphasic system composed of butyl acetate and Forbes's ionic liquid, **1b**, was proven to be only moderately effective for the synthesis of **6a** (entry 6). It is worth mentioning that the acid strength of **1a** and **1b** were scrutinized by Hammett method.[20a,b] No significant difference on their acid strength is observed (Scheme S1 and table S1), which rules out the effect of acid strength on the catalytic activity.[20c] Replacing ionic liquid **1b** by **1c** slightly increased the reaction yield, and **6a** could be only obtained in 76% yield under identical conditions (entry 7).

In the absence of butyl acetate, the reaction with catalyst **1a** hardly proceeded, and **6a** could be prepared in only 24% yield after 3 h under solvent-free conditions (entry 8). 1,2-Dichloroethane was also proven to be a suitable solvent with exploiting the catalytic efficiency of **1a** in the conversion of **4a** and **5a** to **6a** (entry 9). For evident safety and environmental reasons, further investigation on the process and on the efficiency of **1a** was continued using butyl acetate. Temperature and time of the reaction influenced the process significantly and the optimal conditions were found to be 90 °C and 3 h

Table 1. Reaction of **4a** and **5a** under different conditions.[a]



Entry	Solvent	Catalyst	Yield (%)
1	Acetonitrile	Triflic acid	75
2	1,2-Dichloroethane	Triflic acid	55
3	1,4-Dioxane	Triflic acid	57
4	Butyl acetate	Triflic acid	44
5	Butyl acetate	**1a**	96 (95[b])
6	Butyl acetate	**1b**	46
7	Butyl acetate	**1c**	76 (41[c])
8	—	**1a**	24
9	1,2-Dichloroethane	**1a**	94
10	Butyl acetate	**1a**	71[d]
11	Butyl acetate	**1a**	85[e]
12	Butyl acetate	**1a** (5 mol%)	72
13	Butyl acetate	**1a** (15 mol%)	96
14	Butyl acetate	**1a**	93[f]

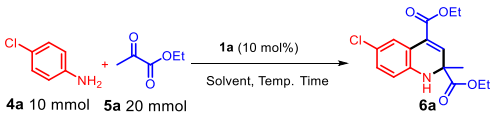
[a] Reaction conditions: **4a**, 0.3 mmol; **5a**, 0.6 mmol, catalyst, 0.03 mmol; solvent, 0.5 mL, 80 °C, 3 h.
[b] 10.0 mmol scale reaction.
[c] Result obtained with recovered **1c** after the first run.
[d] Reaction performed at 60 °C.
[e] After 2 h of reaction time.
[f] Yield obtained with recovered **1a** after the fifth run. The results obtained with recovered **1a** in the 2nd, 3rd, and 4th runs are 96%, 94%, and 94%, respectively.

(entries 10 and 11). Moreover, increasing the amount of catalyst generally led to improving the conversion of **4a**, but using more than 10 mol% of **1a** had no positive effect on the yield of **6a** (entries 12 and 13). It is worth noting that the reaction can also be effectively scaled up with similar efficiency and in a representative 10-mmol-scale process, **6a** could be obtained in 95% yield (3.1 g, entry 5).

One of the main goals to achieve when using an ionic liquid as a catalyst is to test and optimize its recycling and reuse. The synthesis of **6a** was consecutively carried out for representative four runs with only a slight decrease in the isolated yields (Table 1, entry 14). On the contrary, ionic liquid **1c** could not be satisfactorily recovered due to the partial leaching of triflic acid (entry 7). This result proved that a tailored design of the ionic liquid is necessary to perfectly combine all the features of the process and access a process efficiently from chemical, safety, and environmental point of views.

When an ionic liquid is used as a reaction medium or catalyst, the use of a traditional (volatile) organic solvent is generally necessary to extract the product from the ionic liquid. In many cases, ethyl acetate is utilized. However, owing to the high volatility, it is not easy to fully recover the ethyl acetate solvent. The insufficient recovery of ethyl acetate not only increased the cost of synthesis but also generated environmental problems, such as Volatile organic compounds (VOC) emissions and water contaminations. Considering the fact that the polarity of butyl acetate is very close to that of ethyl acetate, we tried to use butyl acetate as a dual reaction medium/extracting solvent in the reaction of **4a** and **5a**. Thus, **4a** (1.28 g, 10 mmol) and **5a** (2.32 g, 20 mmol) was mixed with **1a** (0.64 g, 1 mmol) in butyl acetate (15 mL). The mixture was heated at 80 °C for 3 h. Then, it was cooled to room temperature. The organic phase was decanted out. The ionic liquid phase was extracted by butyl acetate (5 mL × 3). The organic phase was combined together and dried over anhydrous Na_2SO_4, and then subjected to concentration in a rotary evaporator equipped with a circulating water vacuum pump. The residue was subjected to isolation with silica column chromatography. Our attention was paid not only to the synthesis efficiency of **6a** but also the recovery of the solvent. As shown in **Table 2**, after 3 h of reaction at 80°C, the expected product **6a** was isolated in 93% yield. And the solvent, butyl acetate, can be recovered in the rotary evaporator in 94% of recovery ratio. We also used ethyl acetate as the solvent for synthesizing **6a**. However, the yield of **6a** reached only 83% under identical conditions, partially due to the low boiling point of ethyl acetate (77 °C). By increasing the reaction time to 5 h, the yield of **6a** can be increased to 89%. But, a part of ethyl acetate solvent was lost during the reaction, extraction, and concentration. The recovery ratio of ethyl acetate solvent reached only about 70%. Therefore, butyl acetate is an appropriate solvent to cooperate with the ionic liquid **1a**. In the **1a**/butyl

Table 2. Comparison of butyl acetate and ethyl acetate for the synthesis of **6a**.



Solvent	Temp. (°C)	Reaction time (h)	Yield (%)	Recovery of solvent
Butyl acetate	80	3	93	94%
Ethyl acetate	Reflux	3	83	71%
Ethyl acetate	Reflux	5	89	70%

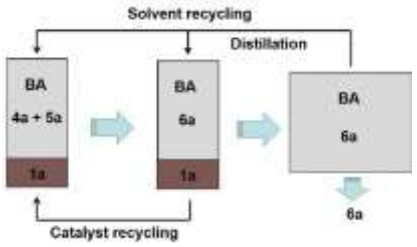
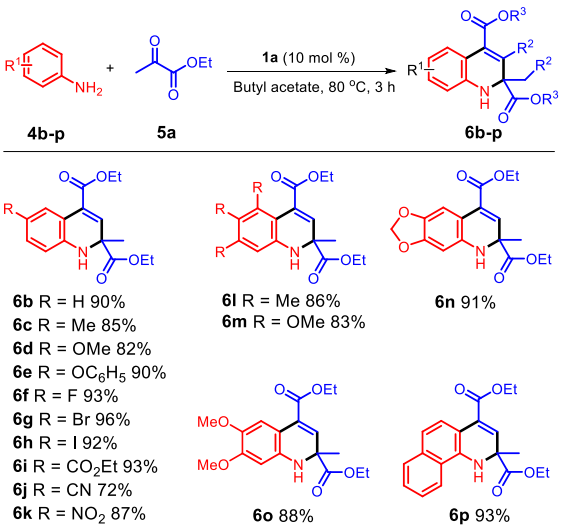


Figure 2. Schematic illustration of recycling **1a** and butyl acetate (BA) in the synthesis of **6a**.

acetate system, the catalyst and the solvent can all be sufficiently recycled (**Figure 2**), strengthening thus the greenness of the synthetic methodology.

Using the optimized conditions defined in Table 1 entry 5, we investigated the scope of the reaction with respect to both the aniline and the pyruvate components. As evidenced by the results in **Scheme 2**, anilines with different substituents smoothly reacted with **5a**, producing the corresponding dihydroquinoline products **6a**–**p** with generally good yields. Both electron-rich (**6c**–**e**, **6n,** and **6o**) and electron-poor (**6i**–**k**) anilines readily reacted. Ester, ether, and cyano groups were all tolerated leading the corresponding products with very satisfactory yields and with no detectable formation of decomposition products (**6d**–**e** and **6i**–**j**). Anilines containing sterically demanding substituents, such as 3,4,5-



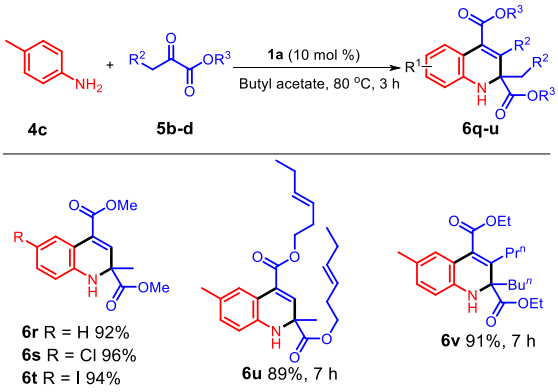
Scheme 2. Scope of substrate with respect to aromatic amines.

trimethylaniline (**4l**) and 3,4,5-trimethoxyaniline (**4m**), also readily reacted, generating the corresponding products, **6l** and **6m**, in 86% and 83% yields, respectively. 1-Aminonaphthalene (**4p**) smoothly reacted with **5a**, producing **6p** in 93% yield.

Catalyst **1a** in combination with butyl acetate allowed also the reaction of indoline (**4q**) with ethyl pyruvate (**5a**), and the resulting tricyclic compound of **6v** was obtained in 78% yield (**Scheme 3**).

Scheme 3. Reaction of **4q** and **5a**.

The scope of the reaction with respect to alkyl pyruvate was also investigated. The reaction of methyl pyruvate (**5b**) confirmed those of ethyl pyruvate allowing the preparation of products **6q–s** in excellent yields ranging from 92 to 94% (**Scheme 4**). *trans*-3-Hexenyl pyruvate (**5c**) also smoothly reacted with *p*-toluidine in butyl acetate using **1a** as a catalyst, and the *trans*-C–C double bond was successfully retained in the isolated product **6t**. While in the literature the synthesis of 1,2-dihydroquinolines **6** is readily accomplished with anilines and alkyl pyruvates, the use of α-substituted pyruvates is very rare and, and until now, only $In(OTf)_3$ has proven to be capable of catalyzing such a reaction.[19] We found that our biphasic system is also applicable in the reaction of *p*-toluidine (**4c**) and ethyl 2-oxohexanoate



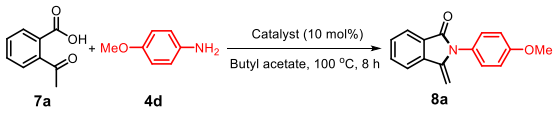
Scheme 4. Scope of substrate with respect to pyruvates.

(**5d**). After 7 h of reaction, the expected product **6u** could be isolated in 91% yield. Obviously, the ionic liquid **1a**/butyl acetate system is applicable in the reactions of structurally distinct anilines **4a–p** and pyruvates **5a–d** with steric bulky and various electronic properties, which provide an efficient and a practical protocol for synthesizing richly decorated 1,2-dihydroquinolines **6a–u**.

The **1a**/butyl acetate system was also used in a reaction of 2-acetylbenzoic acid **7a** and *p*-anisidine **4d**, that can hopefully give a 3-methyleneisoindolin-1-one derivative **8a**. 3-Methyleneisoindolin-1-one a subunit found in a variety of natural and biologically active molecules, such as magallanesine,[21] fumaridine,[22] and narceine imide.[23] Many methods have been developed for their synthesis, such as dehydration of 3-hydroxyisoindolin-1-ones,[24] cycloisomerization of 2-alkynyl substituted benzamides,[25] Pd-catalysed carbonylation-hydroamination reaction of 1-halo-2-alkynylbenzene with amines,[26] domino Heck−Suzuki−Miyaura reactions of ynamides and boronic acids,[27] Rh(III)-catalysed amidation/annulation of aryl ketone oximes with isocyanates,[28] and Cu-promoted coupling of benzamides with nitroalkanes.[29] A Pd-catalysed C–H functionalization approach was also developed by using carboxamides and carboxylic acids or anhydrides as substrates.[30] From the viewpoint of precursor availability and simplicity of operation, direct condensation of 2-acetylbenzoic acids with amines is probably one of the most attractive ways to synthesize 3-methyleneisoindolin-1-ones. However, until now, only the reactions with aliphatic amine were successful.[31] When aromatic amines were used, the reactions had to be performed in toxic organic solvents, such as *o*-dichlorobenzene, at high temperature (180 °C).[32] Nevertheless, the reactions generally gave low yield.[33]

We found that **1a** can effectively catalyze the condensation of **7a** and **4d** in butyl acetate at 100 °C, giving **8a** in 95% yield after 8 h of reaction (**Table 3**, entry 1). Replacing **1a** with triflic acid or PTSA resulted in a dramatic yield decrease, and **8a** was obtained in 42–65% yield (entries 2 and 3). In the absence of the catalyst, the reaction proceeded sluggishly, and the yield of **8a** reached only 14% (entry 4). The solvent, butyl acetate, is necessary, as the reaction under solvent-free conditions is not successful (entry 5). Ionic liquids **1b** and **1c** displayed mild catalytic activities under identical conditions, and **8a** can be isolated in moderate yield (entries 6 and 7). Other organic solvents, such as 1,4-dioxane and toluene, were also used as the reaction media instead of butyl acetate. However, the reaction proceeded slowly in these solvents, and **8a** was obtained in 33–45% yield (entries 8 and 9). In this reaction, **1a** can also be recovered and reused. And in the second run, the recovered ionic liquid

Table 3. Condensation of **7a** and *p*-anisidine **4d**.[a]

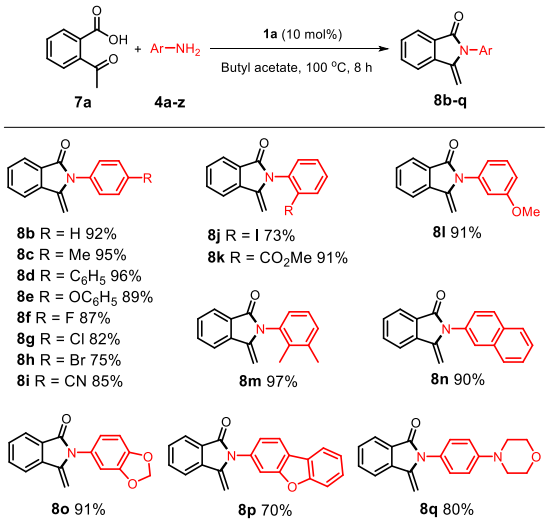


Entry	Catalyst	Yield (%)
1	**1a**	95 (94[e])
2	Triflic acid	42
3	PTSA	65
4	—	14
5	**1a**	15[b]
6	**1b**	55
7	**1c**	72
8	**1a**	33[c]
9	**1a**	45[d]

[a] Reaction conditions: **7a**, 0.3 mmol; **4d**, 0.3 mmol, catalyst, 0.03 mmol, 100 °C, 8 h.
[b] Solvent-free conditions.
[c] 1,4-Dioxane as solvent.
[d] Toluene as solvent.
[e] Recovered **1a** was used as catalyst.

can effectively catalyze the reaction, and **8a** can be isolated in 94% yield (entry 1).

Upon repeating the reaction with **7a** in the **1a**/butyl acetate system, anilines with different functional groups on the arene ring all work well under the standard conditions, efficiently offering the corresponding 3-methyleneisoindolin-1-ones **8b–q** with yields ranging from 70% to 97% (**Scheme 5**). A variety of functional groups, such as methoxy (**8a**, **8l**), phenoxyl (**8e**), cyano (**8i**), ethoxycarboxyl (**8k**), fluoro (**8f**), chloro (**8g**), bromo (**8h**), and iodo (**8j**), can tolerate the acidic conditions well. It should be noted that the reaction efficiency was not significantly affected when electron-deficient anilines



Scheme 5. Reactions of **7a** with different aromatic amines.

were used as substrates (**8i**, **8k**). Heterocycle-anilines, such as 3,4-(methylenedioxy)aniline, 3-dibenzofuranamine, and 4-morpholinoaniline can also be smoothly converted without affecting the stability of these moieties (**8o**−**q**). We thus developed an effective way for synthesizing 3-methyleneisoindolin-1-one derivatives from **7a** and aromatic amines. This reaction demonstrated also that combination of **1a** and butyl acetate is indeed useful for organic synthesis.

Conclusion

A sulfone-containing imidazolium-based Brønsted acid ionic liquid **1a** was prepared. By using this ionic liquid as an acid catalyst, the use of toxic and hazardous dipolar aprotic solvents was avoided. The reactions can be performed in an environmentally benign solvent, butyl acetate, and the ionic liquid is also recyclable. The combined use of **1a** as a catalyst and butyl acetate as a solvent offers a possible means for chemists to minimize the utilization of toxic and hazardous dipolar aprotic solvents in acid-catalyzed reactions. Designing a catalyst that enables the replacement of a less-green solvent with a green one is a promising direction of catalysis research, and this work can hopefully trigger the enthusiasm of researchers to develop more efficient catalytic systems.

Experimental Section

All reactions were determined by microscopic melting point meter (Yu Hua Instrument, X–4). ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AV-400 (400 MHz ^{1}H, 100 MHz ^{13}C, 375 MHz ^{19}F) at room temperature. Fourier transform infrared (FT-IR) spectra were recorded on a FT-IR Bruker (VERTEX 70) using liquid film technology. High-resolution mass spectra (HRMS) was recorded on a Bruker micrOTOF-Q II instrument. Ionic liquid **1b** and **1c** were prepared according to literature's methods with slight modification.[13, 34]

Synthesis of ionic liquid 1a

Brønsted acid ionic liquid **1a** was synthesized through the following three steps: (i) synthesis of **2a**: in 100 ml of around bottomed flask equipped with mechanical stirring, equal amount of divinyl sulfone **2a** (5.0 g, 42.3 mmol) was mixed with 1-(3-aminopropanyl)imidazole (5.2 g, 42.3 mmol) in 75 ml of methanol; the mixture was stirred at 60 °C for 24 h; then, volatile methanol was removed by a rotary evaporator; a yellow-pale oil was obtained, which is **2a**, in nearly quantitative yield. (ii) synthesis of **3a** via quaternization: **2a** (10.0 g, 41.1 mmol), 1,3-propanesulfonate (11.0 g, 90.4 mmol), and acetonitrile (75 ml) were mixed in a 250 ml of around bottomed flask equipped with mechanical stirring; the mixture was stirred at 80 °C for 24 h; a yellow solid was generated; then the solvent was decanted out; the yellow solid was filtrated, and washed with acetone (5.0 ml × 3); **3a** can be obtained as white solid; then, the white solid was dried at 60 °C under vacuum (20 mmHg) for 4 h; and (iii) acidification: **3a** (10.0 g, 20.5 mmol) was mixed with triflic acid (3.1 g, 20.5 mmol) in 25 mL of around bottomed flask; to facilitate the reaction, a small amount of water (0.25 ml) was also added in this step. Then, the mixture was stirred at 100 °C for 24 h. The generated ionic liquid was washed with ethyl acetate (5.0 ml × 3) and diethyl ether (5.0 ml × 3); then, water and volatile solvents were removed under reduced pressure; finally, **1a** was obtained as a yellow-pale viscous liquid. Through all these three-step reactions, the ionic liquid **1a** can be synthesized in 88% yield.

A typical procedure for synthesis of 1,2-dihydroquinolines

All reactions were carried out in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, **1a** (19.1 mg, 0.03 mmol) was mixed with 4-chloroaniline **4a** (38.3 mg, 0.3 mmol) and ethyl pyruvate **5a** (69.7 mg, 0.6 mmol) in 0.5 mL of butyl acetate. The mixture was stirred for 3 h at 80 °C. After the completion of the reaction, the mixture was cooled to room temperature. The butyl acetate was decanted out. The ionic liquid phase was extracted with butyl acetate (0.5 mL × 3). The organic phase was combined and then subjected to isolation with preparative TLC (eluting solution: petroleum ether/ ethyl acetate = $10/1_{v/v}$). The desired product **6a** was obtained in 96 % of yield. Tests for substrate scope were performed according to an analogous procedure. The large scale synthesis of **6a** was performed in a round-bottom flask equipped with an egg-shaped magnetic stirring bar. **1a** (0.6 g, 1.0 mmol) was mixed with 4-chloroaniline **4a** (1.3 g, 10.0 mmol) and ethyl pyruvate **5a** (2.3 g, 20.0 mmol) in 30 mL of butyl acetate. The mixture was stirred for 4 h at 80 °C. After the completion of the reaction, the mixture was cooled to room temperature. The butyl acetate was collected and the ionic liquid phase was extracted with butyl acetate (20.0 mL × 3). The organic phase was combined and evaporated. The residual mixture was submitted to silica column chromatography (eluting solution: petroleum ether/ ethyl acetate = $20/1_{v/v}$). After purification, 3.1 gram (95% yiled) of **6a** was obtained. The recovered ionic liquid was treated at 100 °C under vacuum (10 mmHg) for 30 minutes and then used in the next run.

A typical procedure for reaction of 2-acetylbenzoic acid and *p*-anisidine

All reactions were carried out in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, **1a** (19.1 mg, 0.03 mmol) was mixed with 2-acetylbenzoic (49.2 mg, 0.3 mmol) and *p*-anisidine (36.9 mg, 0.3 mmol) in 0.5 mL of butyl acetate. The mixture was stirred for 8 h at 100 °C. After the completion of the reaction, the mixture was cooled to room temperature. The butyl acetate was decanted out. The ionic liquid phase was extracted with butyl acetate (0.5 mL × 3). The organic phase was combined and then subjected to isolation with preparative TLC (eluting solution: petroleum ether/ ethyl acetate = $10/1_{v/v}$). The desired product **8a** was obtained in 95 % of yield. Tests for substrate scope were performed according to an analogous procedure.

Spectroscopic data of ionic liquid and selected products

4-(3-(*1H*-Imidazol-1-yl) propyl)thiomorpholine 1, 1-dioxide (2a): 10.2 gram, 99% yield, a yellow-pale oil, ^{1}H NMR (400 MHz, D_2O, 25 °C, TMS) δ = 7.56 (s, 1H), 7.05 (s, 1H), 6.91 (s, 1H), 3.96 – 3.75 (m, 2H), 3.41 – 3.23 (m, 2H), 3.10 (s, 3H), 2.91 (s, 3H), 2.38 (t, J = 8.0 Hz, 2H), 1.90 – 1.80 ppm (m, 2H); ^{13}C NMR (100 MHz, D_2O, 25 °C) δ = 140.5, 130.3, 122.6, 54.7, 52.4, 52.1, 47.6, 47.2, 32.4, 29.7 ppm. . IR (cm^{-1}): 3111, 2934, 2827, 1663, 1509, 1451, 1297, 1231, 1190, 1124, 1080, 1042, 910, 855, 751, 667, 667, 525, 436. HRMS-ESI (m/z) calcd for $C_{10}H_{18}N_3O_2S$, $[M + H]^+$ 244.1120, found 244.1154.

3-(1,1-Dioxido-4-(3-(3-(3-sulfonatopropyl)-*1H*-imidazol-3-ium-1-yl)propyl) thiomorpholino-4-ium) propane-1-sulfonate (3a): 18.0 gram, 90% yield, a white solid; ^{1}H NMR (400 MHz, D_2O, 25 °C, TMS) δ = 8.86 – 8.80 (m, 1H), 7.56 – 7.49 (m, 2H), 4.32–4.06 (m, 6H), 3.82 – 3.53 (m, 4H), 3.28 – 3.19 (m, 5H), 2.96 – 2.70 (m, 5H), 2.41 – 2.09 ppm (m, 6H); ^{13}C NMR (100 MHz, D_2O, 25

°C) δ = 136.1, 135.7, 123.1, 122.9, 122.6, 122.4, 57.9, 52.0, 50.1, 49.2, 48.1, 47.9, 47.3, 47.1, 46.6, 45.8, 45.1, 25.9, 25.1, 22.4, 17.5 ppm. IR (cm^{-1}): 3109, 2933, 1638, 1567, 1320, 1194, 1043, 950, 920, 848, 744, 609, 530, 439. HRMS-ESI (m/z) calcd for $C_{16}H_{30}N_3O_8S_3$, $[M + H]^+$ 488.1195, found 488.1180.

3-(1,1-Dioxido-4-(3-(3-(3-sulfopropyl)-*1H*-imidazol-3-ium-1-yl) propyl)thiomorpholino-4-ium)propane-1-sulfonate trifluoromethanesulfonate (1a): 12.9 gram, 99% yield, a yellow-pale viscous ionic liquid; ^{1}H NMR (400 MHz, D_2O, 25 °C, TMS) δ = 8.76 (d, J =10.4 Hz, 1H), 7.45 (t, J = 9.2 Hz, 2H), 4.23 – 3.99 (m, 6H), 3.78 – 3.46(m, 8H), 3.29 – 3.24(m, 2H), 3.04 – 2.76 (m, 2H), 2.33 – 1.81 ppm (m, 7H); ^{13}C NMR (100 MHz, D_2O, 25 °C) δ = 135.9, 122.9, 122.5, 57.9, 53.2, 51.0, 48.1, 47.7, 47.3, 46.6, 46.2, 45.8, 45.1, 25.0, 24.6, 22.4, 17.5 ppm. IR (cm^{-1}): 3460, 3103, 2978, 2932, 1646, 1566, 1462, 1318, 1197, 1139, 1038, 950, 850, 729, 605, 529. HRMS-ESI (m/z) calcd for $C_{16}H_{30}N_3O_8S_3$, [M - CF_3SO_3] 488.1190, found 488.1180.

Diethyl 6-chloro-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (6a):[14] 93.2 mg, 96% yield, a yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.86 (d, J = 1.6 Hz, 1H), 6.94 (dd, J = 1.6, 8.4 Hz, 1H), 6.73 (s, 1H), 6.55 (d, J = 8.4 Hz, 1H), 4.56 (brs, 1H), 4.32 (q, J = 6.9 Hz, 2H), 4.25 – 4.12 (m, 2H), 1.54 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H), 1.26 ppm (t, J = 7.2 Hz, 3H), ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 173.5, 165.2, 141.2, 133.9, 129.3, 127.4, 126.4, 123.3, 117.2, 115.2, 62.0, 61.2, 58.6, 27.3, 14.2, 14.1 ppm. HRMS-ESI (m/z) calcd for $C_{16}H_{19}ClNO_4$, [M + H] 324.1003, found 324.0091.

Diethyl 4-methyl-1,2-dihydro-*4H*-pyrrolo[3,2,1-ij]quinoline-4,6-dicarboxylate (6q):[35] 73.8 mg, 78% yield, a yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.58 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 7.2 Hz, 1H), 6.57 (t, J = 7.6 Hz, 1H), 6.41 (s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 4.16 (q, J = 6.5 Hz, 2H), 3.64 – 3.52 (m, 2H), 3.14 – 2.99 (m, 2H), 1.63 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H), 1.22 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 166.7, 160.8, 143.6, 128.6, 123.5, 121.6, 120.4, 118.8, 113.0, 108.0, 58.6, 56.7, 56.2, 42.8, 23.5, 17.9, 9.5, 9.4 ppm. HRMS-ESI (m/z) calcd for $C_{18}H_{22}NO_4$, [M + H] 316.1549, found 316.1536.

2-(4-Methoxyphenyl)-3-methyleneisoindolin-1-one (8a): 71.6 mg, 95% yield, a gum-like yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.82 (d, J = 7.4 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 5.12 (s, 1H), 4.66 (s, 1H), 3.76 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 166.9, 159.2, 143.6, 136.2, 132.2, 129.7, 129.3, 129.0, 127.1, 123.5, 120.1, 114.7, 90.3, 55.5 ppm. IR (cm^{-1}): 3397, 3068, 3005, 2841, 1893, 1712, 1641, 1512, 1468, 1386, 1298, 1250, 1137, 1026. HRMS-ESI (m/z) calcd for $C_{16}H_{13}NNaO_2$, $[M + Na]^+$ 274.0844, found 274.0841.

Acknowledgements

The authors thank the National Natural Science Foundation of China (2171101076 and 21872060) and the Fundamental Research Funds for the Central Universities of China (2016YXZD033) for the financial support. The Cooperative Innovation Center of Hubei Province is also acknowledged.

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10.1002/adsc.201900246

FULL PAPER

Green Chemistry

A Sulfone-Containing Imidazolium-Based Brønsted Acid Ionic Liquid Catalyst Enables Replacing Dipolar Aprotic Solvents with Butyl Acetate

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