

Regioselective Sulfonation of Aromatic Compounds over 1,3-Disulfonic Acid Imidazolium Chloride under Aqueous Media

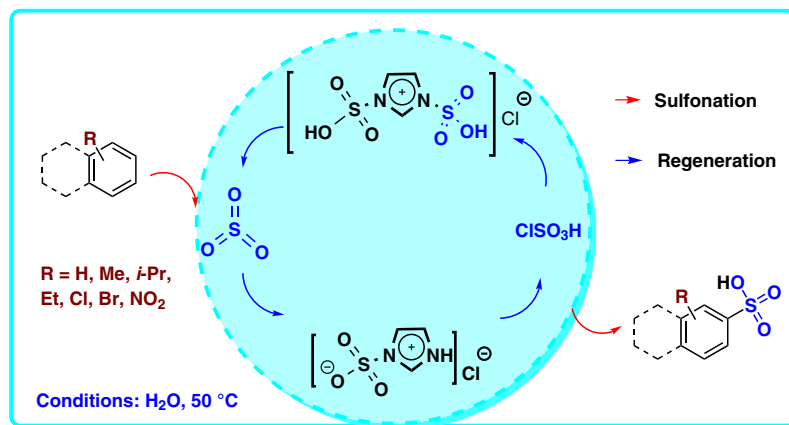
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Abstract 1,3-Disulfonic acid imidazolium chloride ([Dsim]Cl), as a Brønsted acidic ionic liquid, is introduced for the sulfonation of aromatic compounds by in situ generation of sulfuric acid at 50 °C under mild conditions and in aqueous medium.

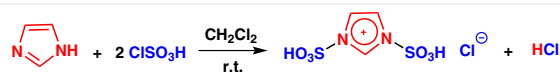
Key words sulfonation, ionic liquid, sulfonic acid functionalized imidazolium salt (SAFIS), aqueous medium

The sulfonation of aromatic compounds is one of the most important reactions in the synthesis of intermediates vital for the preparation of many useful pharmaceutical, industrial, and agrochemicals.¹ Reagents that have been reported for the sulfonation reaction of aromatic compounds include sulfuric acid,^{2,3} trifluoroacetic acid–sulfuric acid,⁴ sulfur trioxide in dichloromethane,⁵ silica–sulfuric acid,⁶ sulfur trioxide–dioxane complex,⁷ oleum,⁸ and sulfur trioxide in nitrobenzene.¹ Other protocols such as sulfonation of Grignard and lithium reagents⁹ and nucleophilic aromatic substitution with sodium sulfite,¹⁰ Vilsmeier–Haack conditions in acetonitrile medium,¹¹ destructive oxidation of S-aryl thioglycolate esters,¹² and oxidation of thiols and disulfides to sulfonic and sulfinic acids using HOF·MeCN¹³ have also been reported. Nevertheless, many of these previous methods for the sulfonation of aromatic compounds are associated with one or more drawbacks, including use of volatile organic solvents, extended reaction times, high temperatures, and low yields.

Recently, sulfonic acid functionalized imidazolium salts (SAFIS) have been prepared and characterized as a new group of acidic ionic liquids and applied as solvents, cata-

lysts, and reagents in organic transformations for the preparation of bis(indolyl)methanes,¹⁴ *N*-sulfonyl imines,¹⁵ 1-amidoalkyl-2-naphthols,¹⁶ xanthene derivatives,¹⁷ 1-carbamatoalkyl-2-naphthols,¹⁸ 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s,¹⁹ *N*-Boc-protected amines,²⁰ hexahydroquinolines,²¹ nitroaromatic compounds,^{22,23} 1,2,4,5-tetrasubstituted imidazoles,²⁴ 6-amino-4-(4-methoxyphenyl)-5-cyano-3-methyl-1-phenyl-1,4-dihydropyran[2,3-*c*]pyrazoles,²⁵ benzylated aromatic compounds,²⁶ β-acetamido ketones,²⁷ benzimidazoles,²⁸ and amido-alkyl phenols.²⁹

Herein, we introduce 1,3-disulfonic acid imidazolium chloride ([Dsim]Cl), by simple reaction of imidazole (1 equiv) with chlorosulfonic acid (2 equiv) at room temperature (Scheme 1) as a sulfonic acid functionalized imidazolium salt (SAFIS)^{14–16} and a highly efficient reagent for the sulfonation of aromatic compounds at 50 °C in aqueous medium.



Scheme 1 The preparation of 1,3-disulfonic acid imidazolium chloride ([Dsim]Cl)

The reaction of [Dsim]Cl with water and chlorobenzene was selected as a model reaction and examined at various temperatures, resulting in successful sulfonation at 50 °C in high yield and very short reaction time. After the optimization of reaction conditions, sulfonation of a range of aromatic substrates was investigated. All of the sulfonated products were successfully synthesized under these reaction conditions (Table 1). For the regeneration of [Dsim]Cl,

the sulfonic acid imidazolium chloride was separated, dried, and reacted with chlorosulfonic acid. The regenerated [Dsim]Cl was used within the limits of the experimental error for three successive recycle runs (Table 2).

Table 1 The Sulfonation of Aromatic Compounds Using [Dsim]Cl at 50 °C

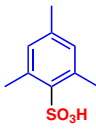
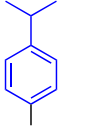
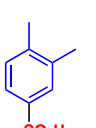
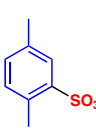
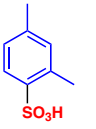
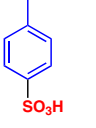
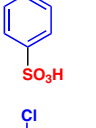
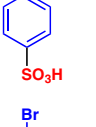
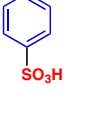

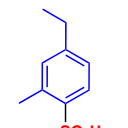
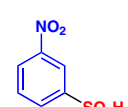
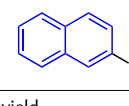
Entry	Product	Time (min)	Yield (%) ^a
1		5	80
2		5	78
3		5	85
4		2	82
5		3	78
6		3	72
7		3	75
8		5	82
9		7	85

Table 1 (continued)

Entry	Product	Time (min)	Yield (%) ^a
10		3	72
11		3	85
12		8	38
13		13	72

^a Isolated yield.

Table 2 Regenerating Experiments for [Dsim]Cl

Cycle	Time (min)	Yield (%) ^a
1st run	2	82
2st run	2	80
3st run	3	80

^a Isolated yield.

To compare the applicability and the efficiency of our reagent with other reported reagents for the sulfonation of aromatic compounds, we have tabulated the results with these reagents in the reaction of benzene with [Dsim]Cl in Table 3. As shown [Dsim]Cl, remarkably improved the sulfonation yield.

Table 3 Comparison of the Results of the Reaction of Benzene with [Dsim]Cl with those Obtained by the Recently Reported Reagents

Reagent	Time (min)	Yield (%) ^a
silica sulfuric acid, 80 °C	30	80 ⁶
H ₂ SO ₄ , ultrasound, r.t.	45	28 ³
[Dsim]Cl, 50 °C	3	75 ^b

^a Isolated yield.

^b Our work.

To establish the applicability of our protocol on a larger scale, we examined the sulfonation of different quantities of chlorobenzene (1–20 mmol) using [Dsim]Cl (Table 4). As shown, the reactions were successfully performed at the larger scales without significant loss of yields.

Table 4 The Large-Scale Sulfonation of Chlorobenzene Using [Dsim]Cl at 50 °C under Aqueous Media

Entry	Amount of chlorobenzene (mmol)	Time (min)	Yield (%) ^a
1	1	2	82
2	5	2	82
3	10	2	80
4	15	4	79
5	20	10	70

^a Isolated yield.

In summary, we have introduced a novel and interesting SAFIS ([Dsim]Cl) as a green and highly efficient reagent for the sulfonation of aromatic compounds at 50 °C in aqueous medium. The acidic catalyst and the source of in situ generation of H₂SO₄ are present in a single compound that also serves as the solvent and ionic liquid.³⁰

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- (30) **General Sulfonation Procedure (Table 1)**
To a round-bottomed flask (10 mL) containing of 1,3-disulfonic acid imidazolium chloride ([Dsim]Cl) (2 mmol, 0.513 g) were added water (2 mmol, 0.036 g) and the aromatic substrate (2 mmol). The reaction mixture was stirred at 50 °C for the requisite time. After the reaction was complete (monitored with TLC), CH₂Cl₂ (10 mL) was added and the reaction mixture stirred for 2 min. The organic solvent was removed, and the product was purified by short column chromatography.
2,4,6-Trimethylbenzenesulfonic Acid (1)
R_f = 0.39 (EtOAc–n-hexane, 2:8); mp 73–75 °C (lit.⁶ 74–76 °C). IR (KBr): 3394, 3092, 3060, 2923, 1653, 1592, 1374, 1188 cm⁻¹. ¹H NMR (90 MHz, DMSO-d₆): δ = 2.13 (s, 3 H), 2.57 (s, 6 H), 6.74 (s, 2 H), 11.34 (s, 1 H) ppm.
3,4-Dimethylbenzenesulfonic Acid (3)
R_f = 0.34 (EtOAc–n-hexane, 2:8); mp 80–82 °C (lit.⁶ 80–84 °C). IR (KBr): 3390, 2989, 2946, 1671, 1452, 1220 cm⁻¹. ¹H NMR (90 MHz, DMSO-d₆): δ = 2.17 (s, 6 H), 7.02–7.37 (m, 3 H), 14.52 (s, 1 H) ppm.
4-Bromobenzenesulfonic Acid (9)
R_f = 0.62 (EtOAc–n-hexane, 2:8); mp 102–104 °C (lit.⁶ 103–105 °C). IR (KBr): 3382, 3136, 3090, 1567, 1006 cm⁻¹. ¹H NMR (90 MHz, DMSO-d₆): δ = 7.15 (s, 4 H), 13.6 (s, 1 H) ppm.