

Highly selective catalytic Friedel–Crafts sulfonylation of aromatic compounds using a FeCl₃-based ionic liquid

Kiumars Bahrami*, Mohammad Mehdi Khodei*, Fomeida Shahbazi

*Department of Chemistry, Razi University, Kermanshah 67149, Iran
Nanoscience and Nanotechnology Research Center (NNRC), Razi University, Kermanshah 67149, Iran*

Received 20 February 2008; revised 21 March 2008; accepted 9 April 2008

Available online 12 April 2008

Abstract

Friedel–Crafts sulfonylation of aromatic compounds was carried out using FeCl₃-based ionic liquid. These liquids serve as efficient media as well as Lewis acid catalyst.

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Keywords: Friedel–Crafts sulfonylation; Lewis acid; Ionic liquid; Aromatic compounds

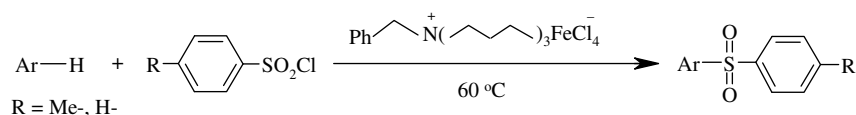
1. Introduction

The wide use of organosulfones as versatile synthons in organic synthesis is well known.¹ Organosulfones are useful intermediates in a wide range of fields such as agrochemicals,² pharmaceuticals^{3,4} and polymers.⁵ The most practical laboratory method for preparing aryl sulfones is via the Friedel–Crafts sulfonylation of arenes using sulfonyl chlorides.^{6,7} Catalysts such as AlCl₃ and SbF₅,⁸ BiCl₃/triflic acid,⁹ metal-exchanged K-10 Montmorillonites,¹⁰ Sn(OTf)₂,¹¹ In(OTf)₃,¹² Nafion-H,¹³ Zn-exchanged zeolites¹⁴ and InCl₃/triflic acid¹⁵ have been used to promote Friedel–Crafts reactions.

A large number of these catalysts suffer from drawbacks such as difficult handling, harsh reaction conditions,

tedious work-up, long reaction times, a need for large amounts of catalyst, lower selectivity for *para/ortho* sulfonylated isomers, incompatibility with other functional groups and generation of environmentally hazardous waste materials, as a result of aqueous extraction procedures. Also, some of these catalysts are expensive and are not commercially available. Therefore, there is still a considerable interest in investigating other convenient and chemoselective synthetic methods for the sulfonylation of aromatic compounds without using organic solvents, in terms of economic benefit, environmental impact and safety.

The design of solvent-free reactions and the use of ionic liquids in organic synthesis have gained significant interest.¹⁶ Some of the unique physical and chemical properties



Scheme 1.

* Corresponding authors. Fax: +98 831 4274559 (K.B.).

E-mail addresses: kbahrami2@hotmail.com (K. Bahrami), mmkhoda@razi.ac.ir (M. M. Khodei).

Table 1
Effect of increasing the amount of FeCl₃ on the sulfonylation reaction of bromobenzene, using [BTBA]Cl–FeCl₃ ionic liquid^a

[BTBA]Cl/[FeCl ₃]	Mole fraction of FeCl ₃ (N)	Yield ^b (%)
1:0.1	0.09	30
1:0.3	0.23	40
1:0.5	0.33	60
1:0.7	0.41	50
1:1	0.5	90

^a Reaction conditions: The reactions were performed with 4-methylbenzenesulfonyl chloride (1 mmol), bromobenzene (1 mmol) and ionic liquid (1 mmol) for 5 min, at 60 °C.

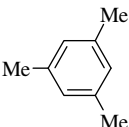
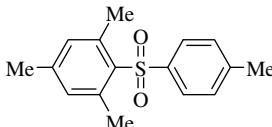
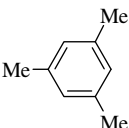
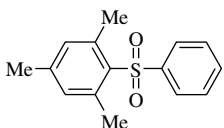
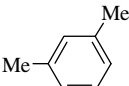
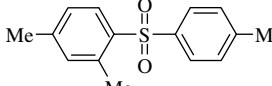
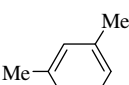
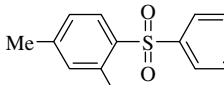
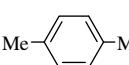
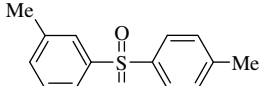
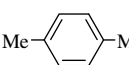
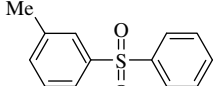
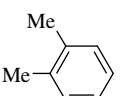
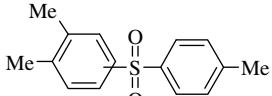
^b Isolated yield.

Table 2
Sulfonylation of bromobenzene with 4-methylbenzenesulfonyl chloride in the presence of several Lewis acids in [BTBA]Cl–Lewis acid, N = 0.5

Entry	[BTBA]Cl–Lewis acid	Time (min)	Yield ^a (%)
1	[BTBA]Cl–ZrCl ₄	5	Trace
2	[BTBA]Cl–ZnCl ₂	5	Trace
3	[BTBA]Cl–AlCl ₃	5	30
4	[BTBA]Cl–FeCl ₃	5	90

^a Isolated yields.

Table 3
Sulfonylation of aromatic compounds using [BTBA]Cl–FeCl₃ ionic liquid (N = 0.5), with benzenesulfonyl chloride and 4-methylbenzenesulfonyl chloride

Entry	Substrate	R	Time (min)	Product ^a	Yield ^b (%) [o:m:p]
1		Me	1		96
2		H	<1		94
3		Me	1		97
4		H	1		95
5		Me	1		94
6		H	1		93
7		Me	1		93 [5:0:95]

of ionic liquids such as thermal stability, negligible vapour pressure, ability to dissolve a large range of organic and inorganic compounds, increased reaction rate, selectivity and tendency to immobilize starting materials and catalysts make them an attractive substitute for various volatile organic solvents.

Many organic transformations have been carried out in ionic liquids, for example, hydrogenation,^{17,18} oxidation,¹⁹ epoxidation²⁰ and hydroformylation²¹ reactions.

In continuation of our recent work on sulfonylation reactions,²² we report a FeCl₃-based ionic liquid as an effective and a highly chemoselective catalyst for the Friedel–Crafts sulfonylation of aromatic compounds under mild reaction conditions (Scheme 1).

To study the effect of increasing the amount of the Lewis acid in the ionic liquid, the sulfonylation of bromobenzene as a model substrate, with 4-methylbenzenesulfonyl chloride was carried out in benzyl tributylammonium chloride (BTBAC) at 60 °C. The best result based on yield and time of the reaction was obtained with [BTBA]Cl–FeCl₃,²³ N = 0.5 (Table 1).

We also investigated the sulfonylation of bromobenzene with 4-methyl benzenesulfonyl chloride in the presence of

Table 3 (continued)

Entry	Substrate	R	Time (min)	Product ^a	Yield ^b (%) [<i>o:m:p</i>]
8		H	1		91 [5:0:95]
9		Me	2		90 [5:0:95]
10		H	2		92 [5:0:95]
11		Me	1		95 [15:0:85]
12		H	1		93 [13:0:87]
13		Me	3		92
14		H	3		93
15		Me	4		90 [5:0:95]
16		H	4		90 [5:0:95]
17		Me	5		91 [5:0:95]
18		H	5		90 [5:0:95]
19		Me	3		91 [$\alpha = 8, \beta = 92$] ^c
20		H	3		90 [$\alpha = 6, \beta = 94$] ^c
21		NO ₂	60	No reaction	—

^a The products were characterized by comparison of their spectroscopic data with those reported in the literature.^{24–27}

^b Isolated yields.

^c Isomers distribution based on ¹H NMR.

several Lewis acids in [BTBA]Cl–Lewis acid, $N = 0.5$. The results showed that only FeCl₃ was effective (Table 2).

To extend the scope of the procedure, we investigated the reactions of a series of aromatic hydrocarbons with

p-toluenesulfonyl chloride and benzenesulfonyl chloride under the optimized reaction conditions (Table 3). It was observed that the presence of electron-donating groups such as alkyl and OMe on the aromatic compound gave

Table 4
Comparison of the sulfonylation of methoxybenzene using [BTBA]Cl–FeCl₃ with methods reported in the literature

Conditions	Yield (%) [o:m:p]
[BTBA]Cl–FeCl ₃ /4-MePhSO ₂ Cl/60 °C/1 min	95 [3:0:97]
[BTBA]Cl–FeCl ₃ /PhSO ₂ Cl/60 °C/1 min	93 [3:0:97]
Crosslinked polystyrene supported AlCl ₃ (Ps–AlCl ₃)/4-MePhSO ₂ Cl/85 °C/1.1 h ²⁸	92 [9:3:88]
BiCl ₃ –TfOH/PhSO ₂ Cl/120 °C/0.5 h ²⁹	82 [47:0:53]
Indium metal/4-MePhSO ₂ Cl/dioxane/100 °C ³⁰	76
Fe-pillared bentonite (Fe–PILC)/4-MePhSO ₂ Cl/120 °C/20 min ²⁷	84 [35.2:0:64.8]
[bmim]Cl–FeCl ₃ /4-MePhSO ₂ Cl/50 °C/5 h ³¹	84 [43:0:57]

excellent yields of the products (entries 10 and 11). Also, deactivated arenes such as chlorobenzene and bromobenzene underwent sulfonylation in excellent yields (entries 16 and 17). Further, an improvement in the regioselectivity was observed in the sulfonylation of naphthalene with benzenesulfonyl chloride and 4-methylbenzenesulfonyl chloride (entries 19 and 20). 4-Nitrobenzenesulfonyl chloride failed to give the sulfonylated product (entry 21). As shown in Table 3, a significant enhancement of *para* selectivity was observed in each case.

To access the feasibility of applying this method in a preparative scale, we carried out the sulfonylation of mesitylene with benzenesulfonyl chloride in 40 mmol scale. As expected, the reaction proceeded smoothly, similar to the case in a smaller scale (Table 3, entry 2), and the desired aryl sulfone was obtained in 96% isolated yield.

In order to show the efficiency of this method, the results of the sulfonylation of methoxybenzene with sulfonylating agents using our method are compared with those reported by other methods. The results show that this method is superior to some previously reported methods in terms of yields, reaction times and the amount of the reagent used for successful sulfonylation (Table 4).

In conclusion, the best results are realized and the utility of the FeCl₃-based ionic liquid both as solvent and catalyst is satisfactorily justified. The advantages of this methodology using a FeCl₃-based ionic liquid are mild reaction conditions, excellent yields, short reaction times, simple work-up procedure, low cost and easy preparation and handling of the catalyst.

2. General procedure for sulfonylation

To [BTBA]Cl–FeCl₃ (*N* = 0.5, 1 mmol), *p*-toluenesulfonyl chloride or benzenesulfonyl chloride (1 mmol) and aromatic compound (1 mmol) were added. The reaction mixture was stirred magnetically, at 60 °C. After complete conversion, as indicated by TLC, the reaction mixture was quenched by adding water (10 mL), extracted with diethyl ether (4 × 10 mL) and the extract dried with anhydrous MgSO₄. The filtrate was evaporated and the corresponding sulfone was obtained in excellent yield (Table 3).

Acknowledgement

The authors are thankful to the Razi University Research Council for financial support for this research.

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