

Synthesis of β -keto-sulfones using alkyl/aryl sulphinates in ionic liquids [bmim-BF₄] as an efficient and reusable reaction medium

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ABSTRACT

Synthesis of β -keto-sulfones using alkyl/aryl sulphinates in ionic liquids as an efficient and reusable medium is described. Reaction of α -haloketones with sodium alkyl/aryl sulphinates in ionic liquid afforded the corresponding sulfones in excellent yields. Obtained products were characterized using IR, HNMR, CNMR and Mass Spectroscopy.

Keywords:

β -Keto-sulfones,
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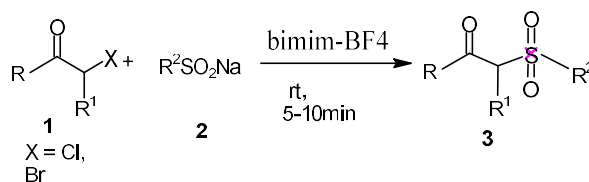
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Introduction

β -keto-sulfones are of great importance in organic synthesis. The presence of sulfone group, in an organic compound adds variety to its chemical architecture¹ and also enhances the biological activity of the compound. The methylene and methyl sulfones are very good α -carbanion-stabilizing substituents because strong $-IE$ by the sulfone, but they do not involve conjugation with α -protons. However, the presence of keto group at 3rd position to the sulfone group, adds variety to its functionalities, known as β -keto-sulfones, which are very important group of intermediates as they are used in Michael and Knoevenagel reactions,^{2,3} in the preparation of acetylenes, allenes, chalcones,⁴⁻⁹ vinylsulfones¹⁰ and polyfunctionalized 4H-pyrans.¹¹ In addition, they are useful for the synthesis of optically active β -hydroxysulfones¹³ and α -halo methylsulfones.¹⁴ This has led to development of novel synthetic methodologies for these compounds. Although several methods of synthesis of ketosulfones have been reported in literature, which includes alkylation of metallic arene sulphinates with either α -haloketone¹⁵ or α -tosyloxy ketones,¹⁶ acylation of alkyl sulfones,¹⁷ reactions of diazo sulfones with aldehydes catalyzed by SnCl₂,¹⁸ reaction of an acid ester with α -sulfonyl carbanions,¹⁹ reaction of an acid anhydride with α -sulfonyl carbanions, addition of aldehydes to α -sulfonyl carbanions followed by oxidation of the resulting β -hydroxysulfones,²⁰ oxidation of β -ketosulphides,²¹ oxidation of β -ketosulfoxides.²² The direct and straightforward method is the treatment of metallic arene

sulphinates with α -haloketone.¹⁵ However, the low solubility of metal sulphinate salts in organic solvents is the inadequacy.

In recent years, the use of ionic liquids (ILs) as green solvents in organic synthetic processes has gained considerable importance due to their solvating ability, negligible vapor pressure, easy recyclability and reusability.²³ Recently, we have reported the direct synthesis of α -iodo β -ketosulfones and their base-induced cleavage to afford α -iodo methyl sulfones.²⁴ In continuation of our work, although not novel, we envisaged the synthesis of ketosulfones using sodium alkyl/aryl sulphinates in bmim-BF₄ as a ionic liquid, as efficient and reusable reaction medium



Scheme 1.

In this report (Scheme 1) we describe an efficient method for the synthesis of sulfones using sodium alkyl/aryl sulphinate in $bmim-BF_4$. This method does not need expensive reagents or special care to exclude the moisture from the reaction medium. We chose $bmim-BF_4$, which are inexpensive and readily available for the preparation of ionic liquid. The resulting salt $bmim-BF_4$ being a liquid at room temperature $bmim-BF_4$. We

first examined the reaction of phenacyl bromide 1 with sodium *p*-toluenesulphinate 2 in bmim-BF₄ at room temperature to yield the corresponding sulfone 3 in 98 % yield (Table 2, Entry 1). This result encouraged us to carry out the reaction in ionic liquids. In order to optimize the reaction conditions, we carried out the reaction in different solvents (Table 1). The poor yields in hydroxylic solvents and less polar solvents are probably due to the lower solubility of the sulphinate salt in these solvents, coupled with the fact that the nucleophile (*p*-MeC₆H₄SO₂⁻) is solvated in hydroxylic solvents thereby reducing its effective nucleophilicity. It was observed that bmim-BF₄ ability to act as a phase transfer catalyst for this transformation and the reaction was complete very fast (Scheme 2). Reaction of different α -haloketones with alkyl/aryl sulphinates proceeded efficiently and smoothly and the products were obtained in good to excellent yields. Various sulfones have been synthesized in facile manner using ionic liquids as an efficient reaction medium (Scheme 1,

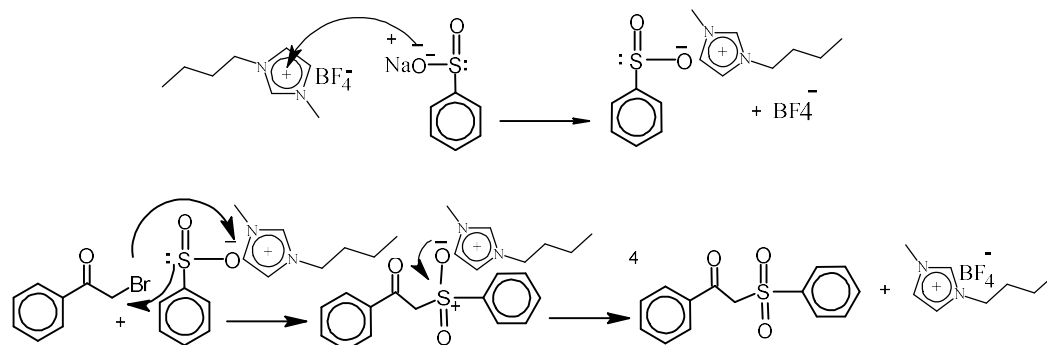
Table 2). From the foregoing results, it is evident that the bmim-BF₄ is an efficient reaction medium for the synthesis of sulfones. Further, it is noticed that the ionic liquid can be recovered and reused for next run without loss of its activity.

The formation of the product ketosulfones rather than ketosulphinate ester can be explained by soft hard acid base (SHAB) terminology and it follows a reductive dehalogenation followed by nucleophilic attack of sulphinate sulphur in a concerted manner (Scheme 2).

In conclusion we have described synthesis of ketosulfones using sodium sulphinates in bmim-BF₄ as an ionic liquid, as efficient and reusable reaction medium. The present procedure for the synthesis of β -ketosulfones has the advantage of high efficient reaction medium with high yields of products and simple work-up procedure, which makes it, is a useful and important addition to the present existing methods.

Table 1: Solvent effect on the reaction of phenacyl bromide with sodium *p*-toluenesulphinate at room temperature

Entry	Solvent	Time	Yield (%)
1	bmim-BF ₄	5 min	99
2	CH ₃ CN	25 min	95
3	THF	24 h	96
4	1,4 Dioxane	24 h	85
5	EtOH	24 h	50
6	CH ₃ CN	24 h	50
7	IPA	24 h	40
8	C ₆ H ₆	24 h	Nil
9	CHCl ₃	24 h	Nil
10	DCM	24 h	Nil



Scheme 2 Plausible Mechanism

Table 2. Synthesis of β -keto-sulfones using ionic liquid.

Entry	Substrate				Product	Time (min)	Yield ^a (%)
	R	R ¹	X	R ²			
1	-Ph	H	Br	<i>p</i> -Toluyyl	3a	5	98
2	-Me	H	Br	<i>p</i> -Toluyyl	3b	5	98
3	<i>p</i> -Toluyyl	H	Br	<i>p</i> -Toluyyl	3c	5	95
4	<i>p</i> -Cl(C ₆ H ₅)	H	Br	<i>p</i> -Toluyyl	3d	5	98
5	-Ph	H	Br	-Ph	3e	5	95
6	-Me	H	Br	-Ph	3f	6	98
7	<i>p</i> -Toluyyl	H	Br	-Ph	3g	5	98
8	<i>p</i> -Cl(C ₆ H ₅)	H	Br	-Ph	3h	5	96
9	-Ph	H	Br	-Me	3i	6	96
10	-Me	H	Br	-Me	3j	6	98
11	<i>p</i> -Toluyyl	H	Br	-Me	3k	8	98
12	<i>p</i> -Cl(C ₆ H ₅)	H	Br	-Me	3l	10	98
13	-Ph	H	Cl	<i>p</i> -Toluyyl	3m	5	98
14	-Me	H	Cl	<i>p</i> -Toluyyl	3n	5	98
15	<i>p</i> -Toluyyl	H	Cl	<i>p</i> -Toluyyl	3o	5	95
16	<i>p</i> -Cl(C ₆ H ₅)	H	Cl	<i>p</i> -Toluyyl	3p	5	98
17	-Ph	H	Cl	-Ph	3q	5	95
18	-Me	H	Cl	-Ph	3r	6	98
19	<i>p</i> -Toluyyl	H	Cl	-Ph	3s	5	98
20	<i>p</i> -Cl(C ₆ H ₅)	H	Cl	-Ph	3t	5	96
21	-Ph	H	Cl	-Me	3u	10	96
22	-Me	H	Cl	-Me	3v	6	98
23	<i>p</i> -Toluyyl	H	Cl	-Me	3w	8	98
24	<i>p</i> -Cl(C ₆ H ₅)	H	Cl	-Me	3x	10	98
25	-Ph	Me	Br	<i>p</i> -Toluyyl	3y	10	98
26	-Ph	CN	Br	<i>p</i> -Toluyyl	3z	10	95

^aThe reaction was conducted using ionic liquid.^bThe yields are calculated after column purification.

Typical experimental procedure: A mixture of α -haloketone (10 mmol) and sodium alkyl/aryl sulphinate (11 mmol) in bmim-BF₄ (5 mL). The reaction was stirred at RT for an appropriate time (Table 1). After completion of the reaction, as monitored by TLC, the product was extracted into diethyl ether (3 x 20 mL). The combined organic extract was evaporated under reduced pressure to give crude product, which was purified by silica column chromatography. The ionic liquid was recovered and for next run without loss of its activity.

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