JOURNAL OF CHEMICAL RESEARCH 2004 APRIL, 267–269 **RESEARCH PAPER** 267

Organic reactions in ionic liquids: an efficient method for the synthesis of aryl sulfones by alkylation of sodium arenesulfinates with alkyl halides

Yi Hu[a,b], Zhen-Chu Chen[a,b]*, Zhang-Gao Le[b] and Qin-Guo Zheng[c]

[a]*Ningbo Institute of Technology Zhejiang University, Ningbo, 315104, P.R. China*

[b]*Department of Chemistry, Zhejiang University (Xi Xi Campus), Hangzhou,310028, P.R. China*

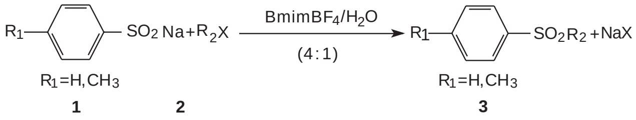
[c]*Pharmaceutical Science Research Institute, Aston University, Aston Triangle, Birmingham B4 7ET,UK*

An ionic liquid based on 1-butyl-3-methylimidazolium tetrafluoroborate ($BmimBF_4$) is used as a reusable reaction medium for the alkylation of sodium arenesulfinates with alkyl halides. This procedure is convenient, efficient and generally gives rise to the *S*-alkylated product with high selectivity when applied to active halides.

Keywords: ionic liquids, sulfones, alkylation, arenesulfinate, alkyl halides

---

Alkyl aryl sulfones have been widely used as useful intermediates in organic synthesis; of particular interest are the applications of the sulfonyl group as an activating function that can be subsequently be removed under mild conditions.[1] Aryl sulfones are generally prepared either by substitution reaction of alkyl halides with alkali-metal salts of arenesulfinates[2] or by oxidation of alkyl aryl sulfides.[3] Recently, metal-mediated coupling reactions of arenesulfonyl chlorides with alkyl halides have been developed.[4] The main drawback of the oxidation method is that the foul smelling and poorly available thiols are the basic starting materials, while the coupling method requires active halides and usually results only in moderate yields of sulfones. As far the substitution method is concerned, traditional reaction conditions using alcohols or dipolar aprotic solvents in which the two reactants have at least some solubility are often inconvenient and the method requires rather long reaction times and usually gives moderate yields of sulfones.[1] The use of preformed tetra-*n*-butylammonium *p*-toluenesulfinate salts[5] or the benzenesulfinate form of a polystyrene anionic exchange resin[6] allows the reaction to be performed rapidly in typical nonpolar solvents, but the reagent must be prepared in a separate step. As a consequence, a number of modifications of the substitution method have been reported. For example, the reaction can be performed more efficiently using a phase transfer catalyst (PTC) process[7] in which a volatile organic solvent is used and the recovery of the catalyst is a considerable challenge. Besides, microwaves or ultrasound have been applied to facilitate this substitution reaction[8], but in general these methods are limited and sometimes low yields are obtained. Therefore, preparation of aryl sulfones using a facile and efficient method with environmentally benign technology is still a challenge in organic synthesis.



Scheme 1

In recent years, room temperature ionic liquids (RTILs) have attracted increasing interest as green and reusable reaction media for synthetic organic chemistry.[9] There are many reports of great improvements in the reaction yields and rates[10] and these prompted us to investigate the alkylation of arenesulfinate salts with alkyl halides in ionic liquids.

Here, we have examined the alkylation of sodium benzenesulfinate and sodium *p*-toluenesulfinate with various alkyl halides in a mixture of 1-butyl-3-methylimidazolium tetrafluoroborate ($BmimBF_4$) and water (4:1) (Scheme 1).

The results are summarised in Table 1. The products were characterised by ^1H NMR, IR, and melting points that were consistent with the literature data.

As can be seen from Table 1 this procedure was found to be efficient when activated chlorides and bromides (allylic, benzyl and α-carbonyl) and primary iodides are used as alkylation agents, the reaction exhibited high selectivity, the

Table 1 Alkylation of sodium arenesulfinate with alkyl halides

Entry[a]	Alkyl halide	R_1	Product	Temp./°C	Time/h	Yield[b]/%	M.p.[c]/°C	Lit. m.p./°C
1	$PhCH_2Br$	H	3a	60	1	95	147–148	146–147[4a]
2	$PhCH_2Cl$	H	3a	60	2	96	147–148	
3	$BrCH_2COPh$	H	3b	60	3	94	93–94	94–95[4a]
4	$CH_2{=}CHCH_2Br$	H	3c	60	3	92	Oil[d]	Oil[4a]
5	$ClCH_2COOEt$	H	3d	60	4	91	45–46	45–47[7f]
6	CH_3I	H	3e	25	24	88	87–88	87[8a]
7	$PhCH_2Br$	CH_3	3f	60	1	96	144–145	144–145[4a]
8	$PhCH_2Cl$	CH_3	3f	60	2	97	144–145	
9	$BrCH_2COPh$	CH_3	3g	60	2	94	107–108	109–110[4a]
10	$CH_2{=}CHCH_2Br$	CH_3	3h	60	3	90	50–51	50–52[4a]
11	$ClCH_2COOEt$	CH_3	3i	60	4	92	33–34	34–35[7d]
12	CH_3I	CH_3	3j	25	24	87	87–88	88–89[5]
13	$CH_3(CH_2)_2CH_2Br$	CH_3	3k	80	6	70[e]	Oil[d]	Oil[7d]
14	$CH_3(CH_2)_2CH_2Cl$	CH_3	3k	70	18	65[f]	Oil[d]	
15	$(CH_3)_2CHBr$	CH_3	3l	50	24	54[g]	80–81	78.5–80[5]

[a]All reactions were run with sodium arenesulfinate hydrate (1.5mmol),alkyl halide(1.0mmol) in 2ml $BmimBF_4$ and 0.5ml H_2O. [b]Isolated yields based on alkyl halides. [c]Melting points were uncorrected. [d]Purities were >98% by GC. [e]Isolated yield of butyl *p*-toluenesulfinate was 20%, oil (lit[15], oil). [f]Isolated yield of butyl *p*-toluenesulfinate was 26%. [g]Isolated yield of i-propyl *p*-toluenesulfinate was 17%, oil (lit[16], oil).

---

* Correspondence. zhenchuc@mail.hz.zj.cn

O-alkylation side product could be negligible and high yields of sulfones were obtained. When primary and secondary bromides were used, moderate yields were obtained. Primary chlorides could be also reacted to give moderate yields of sulfones using the present method, while the literature[7a] reported that no product was obtained when primary chlorides were reacted using the phase transfer catalyst process. During the isolation of **3k** and **3l** the alkylsulfinates formed by *O*-alkylation of *p*-toluenesulfinate ion were obtained.

The recyclability of the ionic liquid $BmimBF_4$ solvent was investigated. Upon completion of the reaction, the product was extracted with diethyl ether first or directly filtered from the reaction mixture (for preparation of **3a**, **3f** and **3g)**. The ionic liquid was dried for 2h under vacuum to evaporate the water, followed by filtration the suspension to remove residual arenesulfinate and formed sodium halide. As a result the recovered ionic liquid could be reused with no appreciable decrease in yield and reaction rate. The representative results are summarised in Table 2. In order to compare with the traditional methods, some representative literature data are summarised in Table 3.

In conclusion, we have demonstrated that the alkylation of sodium arenesulfinates can be effectively performed with alkyl halides in ionic liquid $BmimBF_4$ mixed with water (4**:**1). The present method has many obvious advantages compared to those methods reported in the literature, including environmental friendliness, generality, simplicity of the methodology, ease of product isolation, higher yield, shorter reaction times, higher selectivity and potential for recycling of the ionic liquid.

Experimental

Melting points were determined on digital melting point apparatus and were uncorrected. Infrared spectra were recorded on a VECTOR22 (Bruker), ^{1}HNMR spectra were recorded on a BRUKER-400MHz spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. Gas chromatographic analyses were performed on a Agilent 6890 gas chromatograph. The ionic liquid $[bmim]BF_4$ was synthesised as in the literature.[14] The other materials are commercially available and were used without further purification.

General procedure for the alkylation of sodium arenesulfinates: Sodium benzenesulfinate dihydrate or sodium *p*-toluenesulfinate tetrahydrate 1 (1.5mmol) and alkyl halide 2 (1.0mmol) were taken in $BmimBF_4$ (2 ml) mixed with H_2O (0.5ml). The mixture was stirred magnetically under reaction conditions listed in Table 1 and the course of the reaction was generally monitored by TLC or GC. After completion of the reaction, the product 3 was extracted with diethyl ether (3 × 10ml) or filtered directly from the reaction mixture (for preparation of **3a**, **3f** and **3g**). The ethereal solvent was removed by evaporation and the residue was purified by preparative thin-layer chromatography (silica gel). After isolation of the product, the remainder of the ionic liquid could be typically recovered by drying for 2h under vacuum and filtering the suspension to remove residual sodium arenesulfinates and formed sodium halide.

Received 16 December 2003; accepted 3 March 2004
Paper 03/2258

Reference

1 (a) P.D. Magnus, *Tetrahedron*, 1977, 33, 2019; (b) N-S. Simpkins, Sulfones in Organic Synthesis in Tetrahedron Organic Chemistry Series Vol. 10, J.E. Baldwin and P.D. Magnus, Ed. Pergamon Press, Oxford, 1993; (c) C. Najer and M. Yus, *Tetrahedron*, 1999, **55**, 10547.
2 B.M. Trost and N.R. Schmuff, *J. Am. Chem. Soc.*, 1985, **107**, 396 and references cited therein.
3 (a) B.M. Trost and R. Braslau, *J. Org. Chem.*, 1988, 53, 532; (b) K. Sato, M. Hyodo, M. Aoki, X.- Q. Zheng and R. Noyori, *Tetrahedron*, 2001, **57**, 2469.
4 (a) X.H. Sun, L. Wang and Y.M. Zhang, *Synth. Commun.*, 1998, **28**, 1785; (b) H.B. Li, H. Wang, Y. Pan and Y.Z. Shi, *Synth. Commun.*, 1998, **28**, 409.
5 G.E. Vennstra and B. Zwanenburg, *Synthesis*, 1975, 519.
6 F. Manescalchi, M. Orena and D. Savoia, *Synthesis*, 1979, 445.
7 (a) J.K. Crandall and C. Pradat, *J. Org. Chem.*, 1985, **50**, 1327; (b) G. Bram, A. Loupy, M.C. Roux-Schmit, J. Sansoulet, T. Strzalk and S.-P. Jacqueline, *Synthesis*, 1987, 56; (c) K. Ramaiah, P.K. Dubey, J. Ramanatham, J.S. Grossert and D.L. Hooper, *Ind. J. Chem., Sect., B* 1999, 38B(3), 297; (d) J. Wildeman and A.M.V. Leusen, *Synthesis*, 1979, 733; (e) G.K. Biswas, M. Chakrabarty and P. Bhattacharyya, *Ind. J. Chem., Sect., B* 1991, **30B**(11), 1059; (f) Y.Q. Li, *Chem. Res. Appl.*, 1997, 9, 311; (g) T. Murakami and K. Furusawa, *Synthesis*, 2002, 479.
8 (a) D. Villemin and A.B. Alloum, *Synth. Commun,*. 1990, 20, 925; (b) G.K. Biswas, S.S. Jash and P. Bhattacharyya, *Ind. J. Chem., Sect., B* 1990, 29B(5), 491.

Table 2 Recycling of $BmimBF_4$ for the benzylation of sodium arenesulfinate with benzyl chloride

Cycle	Time/h	Product	Yield[a]/%	Cycle	Time/h	Product	Yield[a]/%
1	2	3a	96	1	2	3f	97
2	2	3a	94	2	2	3f	95
3	2	3a	95	3	2	3f	97

[a] Isolated yields based on benzyl chloride.

Table 3 Synthesis of aryl sulfones under different reaction conditions

Product	Yield (%)		
	This work		Literature work
3a	95/96	52[12]	Benzyl chloride, ethanol, 7–8h, 76°C
		95[7b]	Benzyl bromide, phase transfer catalyst Aliquat 336, 24h, 60°C
		15[7f]	Benzyl chloride, 1,4-dioxane, 1h, 100°C
3e	88	52[8a]	Microwave irradition, 5min, 160W
		60[13]	DMSO, r.t.
3f	96/97	85[7b]	Benzyl bromide, phase transfer catalyst Aliquat 336, 2h, 85°C
		85[7e]	Benzyl chloride, polysorbate – 80 as phase transfer catalyst, reflux 5 hours in water : benzene : acetone (2:1:1)
3i	92	52[8b]	Ultrasound, DMF-H_2O mixt (1:2), 10min
		85[7f]	Tetrabutylammonium bromide as phase transfer catalyst, 1,4-dioxane, 1h, 100°C
3j	87	50[11]	DMF, 22h, 25°C
		77[11]	Methanol, 23h, reflux
		43[13]	DMSO, r.t.
3k	70	45[7e]	Polysorbate – 80 as phase transfer catalyst, reflux 10 hours in water : benzene : acetone (2:1:1)
		43[8b]	Ultrasound, DMF-H_2O mixt (1:2), 15min

9 (a) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (b) P. Wasserscheid and W. Keim, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 3772; (c) R. Sheldon, *Chem. Commum.*, 2001, 2399; (d) D. Jairton, F. Robeerto and A.Z.S. Paulo, *Chem. Rev.*, 2002, **102**, 3667; (e) D. Zhao, M. Wu, Y. Kou and E. Min, *Catal Today*, 2002, **74**, 157.

10 P. Wasserscheid and T. Welton, (eds) *Ionic Liquids in Synthesis*, VCH Wiley, Weinheim, Germany, 2002.

11 J.S. Meek and J.S. Fowler, *J. Org. Chem.*, 1968, 33, 3422.

12 R.L. Shriner, H.C. Struck and W.J. Jorison, *J. Am. Chem. Soc.*, 1930, 52, 2069.

13 J.L. Kice and K S. Lidia, *J. Org. Chem.*, 1991, 56, 1424.

14 G.S. Owens and M.M. Abu-Omer, *J. Mol. Catal. A: Chem.*, 2002, **187,** 211.

15 M. Furukawa, T. Ohkawara, Y. Noguchi, M. Isoda and T. Hitoshi, *Synthesis*, 1980, 937.

16 D.A. Evans, M.M. Faul, L. Colombo, J.J. Bisaha, J. Clardy and D. Cherry, *J. Am. Chem. Soc.* 1992, **114**, 5977.