Aluminum Chloride–Iron Promoted Coupling of Sulfonyl Chlorides with Alkyl Halides in Aqueous Media

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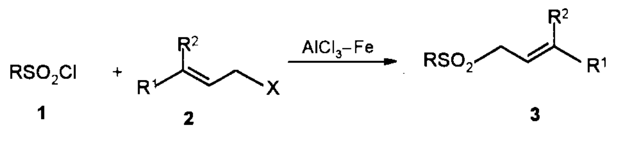
A simple and inexpensive procedure for the coupling of sulfonyl chlorides and alkyl halides with aluminum chloride–iron system at ambient temperature in high yield is achieved in aqueous media.

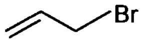
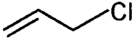
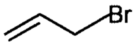
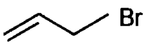
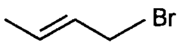
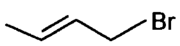
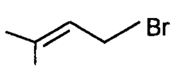
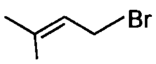
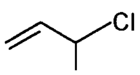
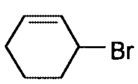
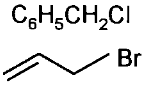
Sulfones have attracted considerable interest in organic synthesis as a useful functionality and its utilisation in the synthesis of medicinally important molecules.[1] Many procedures can be used for the preparation of sulfones while the most commonly employed methods involve the oxidation of sulfides with peracids or with tetra-*n*-butylammonium oxone, sulfonylation of aromatic hydrocarbons in the presence of a Lewis acid and treatment of alkyl halides with alkali metal salts of arene sulfinates.[2,3] These methods are however, not always free from some drawbacks such as unpleasant odor, long reaction times, competing side reactions or insufficient conversion. The main hurdle of the oxidation method is that the foul smelling thiols are the basic starting materials and other groups such as carbon–carbon double bonds are involved in the reaction, while the sulfinate method requires rather long reaction times, anhydrous conditions and usually results only in moderate yields.[4] Therefore, there is still merit in developing a procedure for the preparation of sulfones using efflcient and inexpensive reagents. Moreover, in recent years metal-mediated organic reactions in aqueous media have attracted considerable interest in organic synthesis.[5] Such reactions in aqueous media offer a number of advantages over conventional organometallic reactions in organic solvents; that is, the practical convenience, possible environmentally friendliness and no need to use anhydrous organic solvents.[6] We report herein a novel inexpensive system consisting of aluminum chloride–iron in aqueous media for the coupling of sulfonyl chlorides with alkyl halides under mild conditions to provide alkylic sulfones. The reaction proceeds efficiently in high yields and there is no evidence of any side-reactions such as self-coupling or desulfonylation as reported by earlier workers.[7]



R = $CH_3C_6H_4$, C_6H_5, 4-ClC_6H_4
$R^1 = R^2$ = H, CH_3
X = Br, Cl, I

In a typical case, *p*-toluenesulfonyl chloride (1.9 g, 10 mmol) and iron powder[8] (0.9 g, 10 mmol) were added to water (15 mL) and then allyl bromide (1.3 mL 15 mmol) was added to it. To the reaction mixture was then added $AlCl_3$ (140 mg, 1 mmol) and stirred at room temperature for 4 h. After completion of the reaction (confirmed by TLC) 2 M HCl (10 mL) was added and the mixture was stirred for 5 min, filtered and extracted with ether (25 mL × 2). The organic layer was separated, washed with brine and dried over anhydrous sodium sulfate. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel to get the corresponding allyl *p*-tolyl sulfone (Entry 1) in 85% yield exclusively. It is clear from Table 1 that aromatic sulfonyl chlorides react with active alkyl halides such as allyl bro-

Table 1. $AlCl_3$–Fe mediated coupling of sulfonyl chlorides

Entry	R	Alkyl Halides	Time /h	Yield[a] /%
1	4-$CH_3C_6H_4$		4	85
2	4-$CH_3C_6H_4$		5	80
3	C_6H_5		5	85
4	4-Cl-C_6H_4		4.5	90
5	4-$CH_3C_6H_4$	$C_6H_5CH_2Cl$	5	90
6	4-$CH_3C_6H_4$		4.5	80
7	C_6H_5		5	75
8	4-$CH_3C_6H_4$		5	70
9	C_6H_5		5	70
10	4-$CH_3C_6H_4$		6	70
11	4-$CH_3C_6H_4$		5	75
12	C_6H_5	$C_6H_5CH_2Cl$	4.5	80
13	CH_3	$C_6H_5CH_2Cl$	6	70
14	CH_3		8	50
15	4-$CH_3C_6H_4$	C_2H_5I	7	40
16	4-$CH_3C_6H_4$	CH_3I	8	35
17	4-$CH_3C_6H_4$	$C_2H_5OOCCH_2Br$	8	75
18	4-$CH_3C_6H_4$	$C_6H_5COCH_2Br$	8	75

[a] Yields refer to pure isolated products, fully characterised by ^1H NMR and IR spectroscopy or by direct comparison with authentic samples.

mide, crotyl bromide, benzyl chloride, 2-bromoacetophenone and ethyl bromoacetate. When crotyl bromide was used in place of allyl bromide, the corresponding (*E*)-isomer (2-butenyl *p*-tolyl sulfone, Entry 6) was obtained in 80% yield, without the formation of any rearranged product (1-methyl-2-propenyl *p*-tolyl sulfone). This was checked by employing a secondary allylic halide viz. 3-chloro-1-butene in lieu of crotyl bromide in the above reaction and observed the formation of corresponding coupled product (1-methyl-2-propenyl *p*-tolyl sulfone, Entry 10). The present procedure was not satisfactorily applicable to an alkane sulfonyl chloride, a similar reaction of methanesulfonyl chloride with allyl bromide led to allyl methyl sulfone in 50% yield (Table 1). The same reaction was also not equally effective when alkyl halides were used in place of allyl halides and needs 7–8 h with 35–40% conversion only (Entries 15 and 16). Further increasing the reaction time gave no signiflcant improvement in yields but rather decomposition occurred. Similar treatment of other sulfonyl chlorides gave the corresponding β,γ-unsaturated sulfones in 70–90% yields and the typical results are summerised in Table 1. Although the detailed mechanism of this reaction is not clear at this stage, it is likely that this procedure features in situ activation of metal to generate allyl metal which reacted with sulfonyl chloride to form allylic sulfones after acidic quenching. We have employed iron and aluminum because these metals are cheap and readily available. All the compounds obtained were characterised by infrared and ^{1}H NMR spectroscopy and finally by comparison with authentic samples.

In conclusion this new aluminum chloride–iron system constitutes a useful alternatilve to the commonly accepted procedure for the synthesis of various sulfones of potentially high synthetic utility. The main advantages of this new method are mild reaction conditions, tolerence to olefinic double bonds, simple operation, no polluting solvents and excellent yields of the products.

References and Notes

l B. M. Trost, *Bull. Chem. Soc., Jpn.*, **61**, 107 (1988).

2 For a review of sulfone chemistry see: B. M. Trost, "Comprehensive Organic Synthesis," Pergamon Press, Oxford, (1991), Vol. 6, p. 157; P. D. Magnus, *Tetrahedron*, **33**, 2019 (1977).

3 For reports on Pd- and Te-catalyzed coupling reaction of sulfonyl chlorides see: S. S. Labadie, *J. Org. Chem.*, **54**, 2496 (1989); using tetra-*n*-butylammonium oxone see: B. M. Trost, and R. Braslace, *J. Org. Chem.*, **53**, 532 (1988); H. Suzuki, Y. S. I. Nishioka, S. I. Padmanabhan, and T. Ogawa, *Chem. Lett.*, **1988**, 727; using fluorides catalyst see: A. A. Kolomeitsev, V. N. Movchun, N. V. Kondratenko, and Y. L. Yagupolski, *Synthesis*, **1990**, 1151; using Aliquat 336 see: G. Bram, A. Loupy, M. C. Roux-Schmitt, J. Sansoulet, T. Strzalko, and J. Seyden-Penne, *Synthesis*, **1987**, 56; using sodium formaldehyde sulfoxylate see: A. R. Harris, *Synth. Commun.*, **18**, 659 (1988); for a more recent multistep report using (phenylsulfonyl)-1,2-propadiene see: A. Padwa and P. E. Yeske, *J. Org. Chem.*, **56**, 6386 (1991).

4 E. Block, in "The Chemistry of Functional Groups," E. Supplement, Part l, ed. by S. Patai, Wiley, New York (1980), chap. 13; J. Smeek and J. S. Fowler, *J. Org. Chem.*, **33**, 3422 (1968).

5 Y. Yamamoto and N. Asao, *Chem. Rev.*, **93**, 2307 (1993); C. J. Li, *Chem. Rev.*, **93**, 2023 (1993); A. Lubineau. J. Auge, and Y. Queneau, *Synthesis*, **1994**, 741; C. J. Li, *Tetrahedron*, **52**, 5643 (1996).

6 L. A. Paquette and T. M. Mitzel, *J. Am. Chem. Soc.*, **118**, 1931 (1996); L. A. Paquette and P. C. Lobben, *J. Am. Chem. Soc.*, **118**, 1917 (1996); C. J. Li, D. L. Chen, Y. Q. Lu, J. X. Haberman, and J. T. Mague, *J. Am. Chem. Soc.*, **118**, 4216 (1996).

7 L. L. Frye, E. L. Sullivan, K. P. Cusack and J. M. Funaro, *J. Org. Chem.*, **57**, 697 (1992); S. S. Labadie, *J. Org. Chem.*, **54**, 2496 (1989).

8 Aluminum chloride and iron powder used were of commercial grade and procured from Central Drug House (Pvi) Ltd., New Delhi-110 002; sulfonyl chlorides used were obtained commercially and distilled before use.