

# Synthesis of sulfones using sodium perchlorate as a catalyst under neutral conditions

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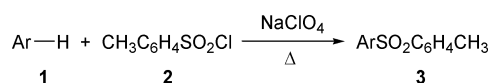
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Letter

**Sulfonylation of aromatics with *p*-toluenesulfonyl chloride in the presence of a catalytic amount of sodium perchlorate gives the corresponding sulfones. Selectivity and neutral condition are the attractive features of this methodology.**

As useful intermediates organosulfones have become increasingly important in organic synthesis<sup>1</sup> as well as in industrial applications.<sup>2</sup> The most widely used procedure for the preparation of sulfones is the oxidation of sulfides and sulfoxides or by a displacement reaction using sodium arene sulfinate. A drawback of the former method is that foul-smelling thiols are the basic starting materials, while the sulfinate method requires rather long reaction times, anhydrous conditions and usually results only in moderate yields of sulfones.<sup>3,4</sup> Friedel–Crafts sulfonylation provides a direct route but traditionally relies on the use of stoichiometric promoters such as aluminium(III) chloride, which are associated with purification problems.<sup>1a</sup> Various efficient catalytic protocols have emerged including the use of zeolites,<sup>5</sup> Fe(III) exchanged montmorillonite clay<sup>6</sup> and bismuth(III) triflate.<sup>7</sup> Very recently, indium(III) triflate<sup>8</sup> has been reported to catalyze sulfonylation of arenes. Although several methods are available for the preparation of sulfones in acidic conditions,<sup>1–8</sup> the synthesis of sulfones under neutral conditions is not reported so far in the literature. The increasing demand for the development of new improved methods prompted us to employ sodium perchlorate for the sulfonylation of arenes. In this paper we wish to highlight our results on the synthesis of diaryl sulfones using sodium perchlorate as a catalyst under almost neutral conditions (pH 6.9) here.



Various catalysts such as sodium perchlorate, sodium periodate, and sodium perborate were tested for this transformation and we found that there was no reaction with sodium perborate catalyst, even after heating the reaction mixture for longer times (15 h). The starting material was recovered even when using a stoichiometric amount of catalyst under the reaction conditions (Table 1, entry 2), whereas sodium

perchlorate and sodium periodate worked equally well (Table 1, entries 3 and 4). A plausible mechanism may involve the formation of *p*-toluenesulfonyl perchlorate or *p*-toluenesulfonyl periodate when sodium perchlorate or sodium periodate are used as catalysts. It was decided to use sodium perchlorate as the preferred catalyst for further study of sulfonylation.

The catalytic activity of the sodium perchlorate was then investigated with respect to the catalyst loading. After many studies on the sulfonylation of toluene (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) under reflux conditions, we found that when less than 20 mol % of sodium perchlorate was applied lower yields of the corresponding product (Table 2, entries 2–4) resulted, whereas use of more than 20 mol % did not improve the yield (Table 2, entries 6 and 7). When attempts were made to carry out the sulfonylation of toluene (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) in the absence of sodium perchlorate catalyst, the substrate was recovered almost quantitatively (Table 2, entry 1). The sulfonylation of toluene in the presence of 20 mol % of sodium perchlorate under mild condition (25 °C) failed, even after stirring the reaction mixture for a longer period of time (20 h).

The sulfonylation of various aromatics were carried out and the results are summarized in Table 3. It was observed that the sulfonylation of activated aromatics required shorter reaction times (Table 3, entries a–e) as compared to the heterocyclic and unactivated aromatics (Table 3, entries f–l). It is important to note that the selectivity of the reaction is impressive in the reported examples wherein exclusively para isomers of diaryl sulfones are obtained in good yields, without the detection or isolation of ortho/meta isomers in trace amounts. On the other hand, the recently reported indium(III) triflate<sup>8</sup> catalyzed sulfonylation of activated aromatics (*e.g.*, anisole, toluene) yields a mixture of isomers with the composition ortho : meta : para = 38 : 0 : 62. Aluminium chloride<sup>9</sup> also gives mixtures of isomers (*e.g.*, ditolyl sulfones) with the composition ortho : meta : para = 29 : 7 : 65 and it generates enormous amounts of solid waste. Similarly, bismuth(III) triflate<sup>7</sup> gives a mixture

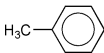
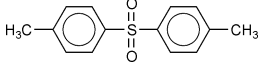
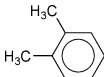
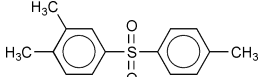
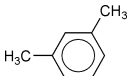
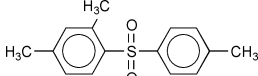
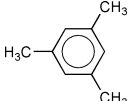
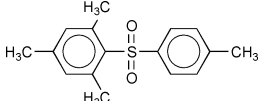
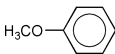
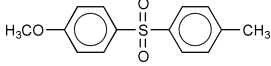

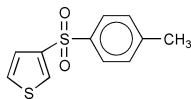

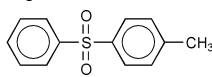
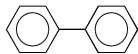
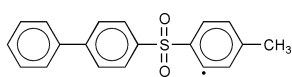

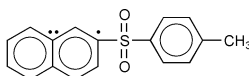

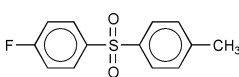

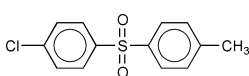

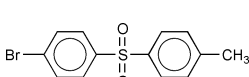
**Table 1** Sulfonylation of toluene (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) at reflux temperature

Entry	Catalyst (mol %)	Time/h	Yield/%
1	NaBO <sub>3</sub> (20)	15	—
2	NaBO <sub>3</sub> (600)	15	—
3	NaClO <sub>4</sub> (20)	6	80
4	NaIO <sub>4</sub> (20)	6.5	79

**Table 2** A catalytic study of NaClO<sub>4</sub> during sulfonylation of toluene (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) at reflux temperature

Entry	NaClO <sub>4</sub> /mol%	Time/h	Yield/%
1	—	6	—
2	5	6	60
3	10	6	65
4	15	6	68
5	20	6	80
6	25	6	77
7	30	6	77

**Table 3** NaClO<sub>4</sub> catalyzed sulfonylation of aromatics

Entry	Arene	Product	Time/h	Yield <sup>a,b</sup> %
a			6	80
b			6	82
c			6	80
d			5	85
e			4	88
f			9	75
g			8	73
h			8	75
i			9	76
j			8	82
k			8	82
l			8	81

<sup>a</sup> Yields are of pure isolated products. <sup>b</sup> Products are characterized by their physical constants and spectral analysis.

of isomers (*e.g.*, ditolyl sulfones) with the composition ortho : meta : para = 29 : 5 : 66. In this regard the present method is superior because it gives selectively *p*-ditolyl sulfones only in good yields (Table 3, entry a). Furthermore, an improvement in regioselectivity is also observed using sodium perchlorate in the sulfonylation of naphthalene with *p*-toluenesulfonyl chloride, giving only the  $\beta$ -isomer without formation of the  $\alpha$ -isomer in trace amounts. On the other hand, sulfonylation of naphthalene using Fe(III) exchanged montmorillonite clay<sup>6</sup> catalyst gave a mixture of  $\alpha$ - and  $\beta$ -isomers.

In conclusion, the present results demonstrate the efficiency of sodium perchlorate as an catalyst for sulfonylation of activated, heterocyclic and unactivated aromatics under almost neutral conditions and constitutes a useful alternative to the commonly accepted sulfonylation procedures. The effectiveness of this protocol is manifested in its selectivity.

## Experimental

### Typical experimental procedure

A mixture of toluene (10 ml), *p*-toluenesulfonyl chloride (5 mmol) and sodium periodate (1 mmol) was refluxed for 6 h.

On completion of the reaction (TLC), the reaction mixture was cooled and toluene was removed under reduced pressure. To the residue chloroform (10 ml) and water (10 ml) were added. The aqueous layer was washed with chloroform (3  $\times$  5 ml). The combined organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and removal of the solvent under vacuum furnished crude product, which was further purified by column chromatography (petroleum ether–ethyl acetate = 8 : 2). In the case of solid substrates, nitrobenzene (10 ml) was used as a solvent.

**Di-*p*-tolyl sulfone (3a).** M.p. = 156 °C (lit. 156 °C).<sup>10</sup> IR (KBr, cm<sup>-1</sup>): 630, 765, 816, 990, 1035, 1100, 1180, 1360, 1460, 1500, 1600, 3421; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.39 (s, 6H, 2 Ar-CH<sub>3</sub>), 7.27 (d, 4H, *J* = 5 Hz, 4 Ar-H), 7.80 (d, 4H, *J* = 5 Hz, 4 Ar-H). EI-MS: *m/z* = 246 (M<sup>+</sup>). Anal. calcd. for C<sub>14</sub>H<sub>14</sub>SO<sub>2</sub> (246.27): C, 68.28%; H, 5.73%; S, 12.99%. Found: C, 68.33%; H, 5.69%; S, 13.02%.

**(3,4-Dimethylphenyl)-*p*-tolyl sulfone (3b).** M.p. = 55 °C. IR (KBr, cm<sup>-1</sup>): 1017, 1123, 1342, 1447, 1515, 1603; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  2.3(s, 3H, ArCH<sub>3</sub>), 2.36 (s, 3H, Ar-CH<sub>3</sub>) 2.43 (s, 3H, Ar-CH<sub>3</sub>), 7.1 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.8 (d, 1H, *J* = 1.5 Hz, Ar-H), 8.0 (dd, 1H, *J* = 1.5 Hz, 7.5 Hz, Ar-H) 7.5 (d, 2H, *J* = 8.6 Hz, Ar-H), 8.1 (d, 2H, *J* = 8.6 Hz, Ar-H)

7.5 (d, 2H,  $J = 8.6$  Hz, Ar-H). EI-MS:  $m/z = 260$  ( $M^+$ ). Anal. calcd. for  $C_{15}H_{16}SO_2$  (260.30): C, 69.92%; H, 6.20%; S, 12.30%. Found: C, 69.88%; H, 6.24%; S, 12.26%.

**(2,4-Dimethylphenyl)-*p*-tolyl sulfone (3c).** M.p. = 49 °C (lit. 48–49 °C).<sup>10</sup> IR (KBr,  $cm^{-1}$ ): 1028, 1110, 1175, 1355, 1455, 1505, 1610;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.34 (s, 3H, Ar-CH<sub>3</sub>), 2.38 (s, 3H, Ar-CH<sub>3</sub>), 2.41 (s, 3H, Ar-CH<sub>3</sub>), 7.01 (d, 1H,  $J = 1.7$  Hz, Ar-H), 7.16 (dd, 1H,  $J = 1.7$  Hz, 7.7 Hz, Ar-H), 7.25 (d, 2H,  $J = 8.8$  Hz, Ar-H), 7.77 (d, 2H,  $J = 8.8$  Hz, Ar-H), 8.08 (d, 1H,  $J = 7.7$  Hz, Ar-H). EI-MS:  $m/z = 260$  ( $M^+$ ). Anal. calcd. for  $C_{15}H_{16}SO_2$  (260.30): C, 69.92%; H, 6.20%; S, 12.30%. Found: C, 69.88%; H, 6.24%; S, 12.26%.

**(2,4,6-Trimethylphenyl)-*p*-tolyl sulfone (3d).** M.p. = 122 °C (lit. 123 °C).<sup>10</sup> IR (KBr,  $cm^{-1}$ ): 810, 1011, 1150, 1350, 1460, 1522, 1611;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.32 (s, 3H, Ar-CH<sub>3</sub>), 2.35 (s, 3H, Ar-CH<sub>3</sub>), 2.45 (s, 6H, 2 Ar-CH<sub>3</sub>), 7.03 (s, 2H, Ar-H), 7.62 (d, 2H,  $J = 8.4$  Hz, Ar-H), 8.2 (d, 2H,  $J = 8.4$  Hz, Ar-H). EI-MS:  $m/z = 274$  ( $M^+$ ). Anal. calcd. for  $C_{16}H_{18}SO_2$  (274.32): C, 70.06%; H, 6.61%; S, 11.67%. Found: C, 69.98%; H, 6.57%; S, 11.73%.

**(4-Methoxyphenyl)-*p*-tolyl sulfone (3e).** M.p. = 105 °C; (lit. 104 °C).<sup>10</sup> IR (KBr,  $cm^{-1}$ ): 683, 838, 1007, 1360, 1599, 2910, 3300;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.36 (s, 3H, CH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 6.95 (d, 2H,  $J = 7.2$  Hz, Ar-H), 7.91 (d, 2H,  $J = 7.2$  Hz, Ar-H), 7.15 (d, 2H,  $J = 8.8$  Hz, Ar-H), 8.14 (d, 2H,  $J = 8.8$  Hz, Ar-H). EI-MS:  $m/z = 262$  ( $M^+$ ). Anal. calcd. for  $C_{14}H_{14}SO_3$  (262.27): C, 64.12%; H, 5.38%; S, 12.20%. Found: C, 64.09%; H, 5.45%; S, 12.11%.

**(Thiophene)-3-*p*-tolyl sulfone (3f).** M.p. = 110 °C. IR (KBr,  $cm^{-1}$ ): 1160, 1310, 1500, 1610;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  7.8 (d, 2H,  $J = 8.1$  Hz, Ar-H), 8.02 (d, 2H,  $J = 8.1$  Hz, Ar-H), 8.12–8.3 (m, 3H, Ar-H). EI-MS:  $m/z = 238$  ( $M^+$ ). Anal. calcd. for  $C_{11}H_{10}S_2O_2$  (238.1): C, 55.44%; H, 4.23%; S, 26.89%. Found: C, 55.51%; H, 4.19%; S, 26.94%.

**(Phenyl)-*p*-tolyl sulfone (3g).** M.p. = 126 °C (lit. 127 °C).<sup>10</sup> IR (KBr,  $cm^{-1}$ ): 1153, 1303, 1500, 1604;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.4 (s, 3H, Ar-CH<sub>3</sub>), 7.2 (d, 2H,  $J = 7.8$  Hz, Ar-H), 7.4–7.8 (m, 5H, Ar-H), 8.01 (d, 2H,  $J = 7.8$  Hz, Ar-H). EI-MS:  $m/z = 232$  ( $M^+$ ). Anal. calcd. for  $C_{13}H_{12}SO_2$  (232.24): C, 67.23%; H, 5.21%; S, 13.78%. Found: C, 67.19%; H, 5.26%; S, 13.84%.

**(Bisphenyl)-*p*-tolyl sulfone (3h).** M.p. = 155 °C. IR (KBr,  $cm^{-1}$ ): 1160, 1312, 1512, 1601;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.36 (s, 3H, Ar-CH<sub>3</sub>), 7.11–7.24 (m, 5H, Ar-H), 7.75 (d, 2H,  $J = 8.2$  Hz, Ar-H), 7.89 (d, 2H,  $J = 7.9$  Hz, Ar-H), 8.1 (d, 2H,  $J = 7.9$  Hz, Ar-H), 8.3 (d, 2H,  $J = 8.2$  Hz, Ar-H). EI-MS:  $m/z = 296$  ( $M^+$ ). Anal. calcd. for  $C_{18}H_{16}SO_2$  (296.33): C, 72.96%; H, 5.44%; S, 10.80%. Found: C, 72.96%; H, 5.39%; S, 10.85%.

**( $\beta$ -Naphthyl)-*p*-tolyl sulfone (3i).** M.p. = 164 °C. IR (KBr,  $cm^{-1}$ ): 1155, 1305, 1509, 1607;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):

$\delta$  2.33 (s, 3H, Ar-CH<sub>3</sub>), 7.06–7.15 (m, 4H, Ar-H), 7.7 (d, 2H,  $J = 7.7$  Hz, Ar-H), 7.8 (d, 1H,  $J = 8.1$  Hz, Ar-H), 8.1 (dd, 1H,  $J = 1.3$  Hz, 8.1 Hz, Ar-H), 8.2 (d, 1H,  $J = 1.3$  Hz, Ar-H), 8.3 (d, 2H,  $J = 7.7$  Hz, Ar-H). EI-MS:  $m/z = 306$  ( $M^+$ ). Anal. calcd. for  $C_{19}H_{14}SO_2$  (306.32): C, 74.50%; H, 4.60%; S, 10.45%. Found: C, 74.56%; H, 4.56%; S, 10.51%.

**(4-Fluorophenyl)-*p*-tolyl sulfone (3j).** M.p. = 93 °C (lit. 95 °C).<sup>11</sup> IR (KBr,  $cm^{-1}$ ): 629, 775, 816, 880, 1050, 1110, 1175, 1355, 1590, 3390;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.42 (s, 3H, Ar-CH<sub>3</sub>), 7.20 (m, 2H, Ar-H), 7.35 (d, 2H,  $J = 8.4$  Hz, Ar-H), 7.85 (d, 2H,  $J = 8.4$  Hz, Ar-H), 7.91–7.98 (m, 2H, Ar-H). EI-MS:  $m/z = 250$  ( $M^+$ ). Anal. calcd. for  $C_{13}H_{11}SO_2F$  (250.23): C, 62.40%; H, 4.4%; S, 12.79%; F, 7.59%. Found: C, 62.37%; H, 4.39%; S, 12.84%; F, 7.65%.

**(4-Chlorophenyl)-*p*-tolyl sulfone (3k).** M.p. = 124 °C (lit. 123 °C).<sup>10</sup> IR (KBr,  $cm^{-1}$ ): 626, 772, 885, 816, 990, 1040, 1100, 1175, 1353, 1599, 3397;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.38 (s, 3H, Ar-CH<sub>3</sub>), 7.34 (d, 2H,  $J = 7.7$  Hz, Ar-H), 7.43–7.52 (m, 2H, Ar-H), 7.82 (d, 2H,  $J = 9.0$  Hz, Ar-H), 7.86–7.92 (m, 2H, Ar-H). EI-MS:  $m/z = 267$  ( $M + 1$ )<sup>+</sup>. Anal. calcd. for  $C_{13}H_{11}SO_2Cl$  (266.68): C, 58.55%; H, 4.1%; S, 12.00%; Cl, 13.29%. Found: C, 58.61%; H, 4.21%; S, 11.94%; Cl, 13.35%.

**(4-Bromophenyl)-*p*-tolyl sulfone (3l).** M.p. = 136–137 °C (lit. 135–136 °C).<sup>11</sup> IR (KBr,  $cm^{-1}$ ): 626, 772, 816, 895, 1030, 1120, 1175, 1360, 1580, 3410;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  2.49 (s, 3H, Ar-CH<sub>3</sub>), 7.48 (d, 2H,  $J = 8.5$  Hz, Ar-H), 7.76–7.91 (m, 4H, 4 Ar-H), 7.98 (d, 2H,  $J = 8.5$  Hz, Ar-H). EI-MS:  $m/z = 312$  ( $M + 1$ )<sup>+</sup>. Anal. calcd. for  $C_{13}H_{11}SO_2Br$  (311.13): C, 50.19%; H, 3.56%; S, 10.29%; Br, 25.68%. Found: C, 50.25%; H, 3.62%; S, 10.27%; Br, 25.67%.

## References

- (a) F. R. Jensen and G. Goldman, in *Friedel–Crafts and Related Reactions*, ed. G. Olah, Wiley Interscience, New York, 1964, vol. III, pp 1319–1367; (b) N. S. Simpkins, *Sulfones in Organic Synthesis*, Pergamon Press, Oxford, 1993 and references cited therein.
- K. M. Roy, in *Ullmann's Encyclopedia of Industrial Chemistry*, ed., W. Gerhartz, VCH, Weinheim, 1985, vol. A 25, pp 487–501 and references cited therein.
- C. M. Suter, *The Organic Chemistry of Sulfur*, John Wiley and Sons, New York, 1948, p. 568–773.
- J. Smeek and J. S. Fowler, *J. Org. Chem.*, 1968, **33**, 3422.
- K. Smith, G. M. Ewart and K. R. Randles, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1085.
- B. M. Choudary, N. S. Chowdari, M. L. Kantam and R. Kannan, *Tetrahedron Lett.*, 1994, **40**, 2859.
- S. Rapichet, C. Le Roux and J. Dubac, *J. Org. Chem.*, 1999, **64**, 6479.
- C. G. Froast, J. P. Hartley and A. J. Whittle, *Synlett*, 2000, **6**, 830.
- G. A. Olah, S. Kobayashi and J. Nishimura, *J. Am. Chem. Soc.*, 1973, **95**, 564.
- M. Ueda, K. Uchiyama and T. Kano, *Synth. Commun.*, 1984, 323.
- B. M. Choudary, N. S. Chowdari and M. L. Kantam, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2689.