Sodium Periodate Catalyzed Selective Sulfonylation of Aromatics

B. P. Bandgar* and V. T. Kamble
Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded 431 606, India

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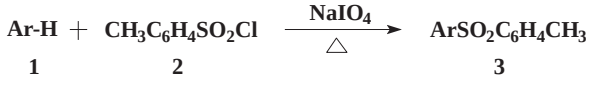
Sodium periodate catalyzed sulfonylation of aromatics with *p*-toluenesulfonyl chloride gives the corresponding sulfones in good yield under neutral conditions.

As a useful intermediate, sulfones have received considerable attention in organic synthesis,[1] as well as in industrial application.[2] A well known procedure for the preparation of sulfones is the oxidation of sulfides and sulfoxides or by a displacement reaction using sodium arenesulfinate. The former method suffers by foul smelling of the starting material while the sulfinate method requires longer reaction times, anhydrous conditions and moderate yield of sulfones.[3,4] Other methods such as aluminium(III) chloride[1a] which relies on its stoichiometric use are associated with purification problems. Sulfones are also prepared by the catalytic use of zeolites,[5] Fe(III) exchanged montmorillonite clay[6] and bismuth(III) triflate.[7] For the sulfonylation of unactivated aromatics, the most effective reported catalyst is bismuth(III) triflate but this is not commercially available and has to be prepared from triphenyl bismuth and triflic acid. More recently, indium(III) triflate[8] have been reported to catalyze the sulfonylation of activated and unactivated aromatics. Although several methods are reported for the preparation of sulfones under acidic conditions[1–3,5–8] and basic conditions,[4] the synthesis of sulfones under neutral conditions has not been reported so far in the literature. Therefore, synthesis of diaryl sulfones using inexpensive and neutral reagent is highly desirable. In this communication, we wish to disclose our preliminary results on the synthesis of diaryl sulfones using sodium periodate as a catalyst under neutral conditions (Scheme 1).

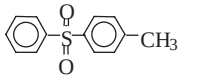
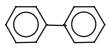
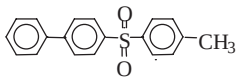
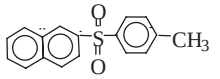
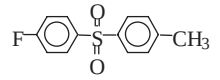
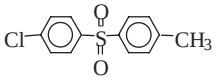
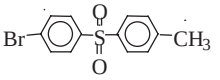
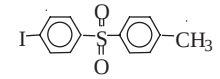
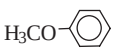
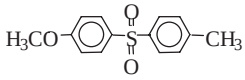
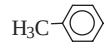
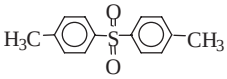
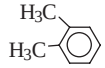
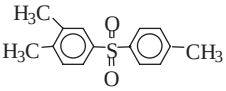
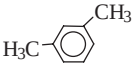
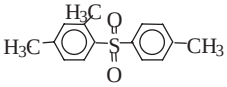
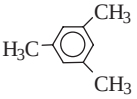
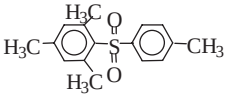
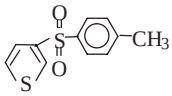


Scheme 1.

Table 1. A catalytic study of $NaIO_4$ during sulfonylation of anisole (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) at reflux temperature

Entry	$NaIO_4$/mol%	Time/h	Yield/%
1	—	3	—
2	5	3	55
3	10	3	60
4	15	3	65
5	20	3	89
6	25	3	85
7	30	3	85

Table 2. $NaIO_4$ catalyzed sulfonylation of aromatics

Entry	Arene	Product	Time /h	Yield[a,b] %
a			7	75
b			7	76
c			9	79
d			7	84
e			7	86
f			7	83
g			7	83
h			3	89
i			5	82
j			5	83
k			4.5	82
l			4	82
m			9	75

[a]Yields are of pure isolated products. [b] Products are characterized by their physical constants and spectral analysis.

The catalytic activity of the sodium periodate was then investigated with respect to the loadings. After much studies on sulfonylation of anisole (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) under reflux conditions, we found that when less than

20 mol% of sodium periodate was applied, it resulted in low yield of the corresponding product (Table 1, entries 2–4), whereas use of more than 20 mol% did not improve the yield (Table 1, entries 6–7). When attempts were made to carry out sulfonylation of anisole (10 ml) with *p*-toluenesulfonyl chloride (5 mmol) in the absence of catalyst, sodium periodate, it resulted in almost quantitative recovery of the substrate (Table 1, entry 1). The sulfonylation of anisole in the presence of 20 mol% of sodium periodate under mild conditions (25 °C) was failed even after stirring the reaction mixture for 15 h. A plausible mechanism may involve the formation of *p*-toluenesulfonyl periodate when sodium periodate is used as a catalyst.

The sulfonylation of various aromatics were carried out[9] and the results are summarized in Table 2. It was observed that for the sulfonylation of activated aromatics less reaction time was required (Table 2, entries h–l) as compared to the unactivated and heterocyclic aromatics (Table 2, entries a–g and m). 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 detection or isolation of ortho/meta isomers in trace amounts. On the other hand, recently reported indium(III) triflate[8] catalyzed sulfonylation of activated aromtics (e.g. anisole, toluene) yields a mixture of isomers with the composition of ortho : meta : para = 38 : 0 : 62. Also aluminium(III) chloride[10] gives mixtures of isomers (e.g. ditolyl sulfones) with the composition of ortho : meta : para = 29 : 7 : 65 and it generates an enormous amount of solid waste. Similarly bismuth(III) triflate[7] gives a mixture of isomers (e.g. ditolyl sulfones) with the composition of ortho : meta : para = 29 : 5 : 66. In this regard the present method is superior because it gives selectively *p*-ditolyl sulfones in good yield (Table 2, entry i). Further, the improvement in regioselectivity is also observed using sodium periodate in sulfonylation of naphthalene with *p*-toluenesulfonyl chloride giving only β-isomer without formation of α-isomer in trace amounts. On the other hand sulfonylation of naphthalene using the Fe(III) exchanged montmorillonite clay[6] catalyst gave a mixture of α- and β-isomers.

In summary, we have described a novel and highly selective procedure for the sulfonylation of activated and unactivated aromatics using sodium periodate under almost neutral conditions.

References and Notes

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9 Typical experimental procedure: A mixture of anisole (10 ml), *p*-toluenesulfonyl chloride (5 mmol) and sodium periodate (1 mmol) was refluxed for 3 h. On completion of the reaction (TLC), the reaction mixture was cooled and anisole was removed under reduced pressure. To the residue chloroform (10 ml) and water (10 ml) was added. The aqueous layer was washed with chloroform (3 × 5 ml). The combined organic layer was dried with anhydrous Na_2SO_4 and removal of the solvent under vacuum furnished crude product which was further purified by column chromatography (petroleum ether : ethyl acetate = 8 : 2). In case of solid substrates, nitrobenzene (10 ml) was used as a solvent. **3a**: (Phenyl)-*p*-tolyl sulfone: mp = 126 °C (lit. 127 °C);[12] IR (KBr, cm^{-1}): 1153, 1303, 1500, 1604; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.4 (s, 3H, Ar-CH_3), 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). **3b**: (Biphenyl)-*p*-tolyl sulfone: mp 155 °C; IR (KBr, cm^{-1}) 1160, 1312, 1512, 1601; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (s, 3H, Ar-CH_3), 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). **3c**: (β-Naphthyl)-*p*-tolyl sulfone: mp = 164 °C; IR (KBr, cm^{-1}): 1155, 1305, 1509, 1607; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H, Ar-CH_3) 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). **3d**: (4-Fluorophenyl)-*p*-tolyl-sulfone: mp = 93 °C; (lit. 95 °C);[12] IR (KBr, cm^{-1}): 629, 775, 816, 880, 1050, 1110, 1175, 1355, 1590, 3390,; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.42 (s, 3H, Ar-CH_3), 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). **3e**: (4-Chlorophenyl)-*p*-tolyl sulfone: mp = 124 °C; (lit-123 °C);[11] IR (KBr, cm^{-1}): 626, 772, 885, 816, 990, 1040, 1100, 1175, 1353, 1599, 3397; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H, Ar-CH_3), 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). **3f**: (4-Bromophenyl)-*p*-tolyl sulfone: mp = 136–137 °C; (lit. 135–136 °C);[12] IR (KBr, cm^{-1}): 626, 772, 816, 895, 1030, 1120, 1175, 1360, 1580, 3410; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.49 (s, 3H, Ar-CH_3), 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). **3g**: (4-Iodophenyl)-*p*-tolyl sulfone: mp 140 °C; IR (KBr, cm^{-1}): 621, 778, 801, 904, 1050, 1107, 1160, 1355, 1518, 1600; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.4 (s, 3H, Ar-CH_3), 7.76 (d, 2H, J = 7.7 Hz, Ar-H), 7.72 (d, 2H, J = 8.4 Hz, Ar-H), 8.1 (d, 2H, J = 8.4 Hz, Ar-H), 8.21 (d, 2H, J = 7.7 Hz, Ar-H). **3h**: (4-Methoxyphenyl)-*p*-tolyl sulfone: mp = 105 °C; (lit. 104 °C);[11] IR (KBr, cm^{-1}): 683, 838, 1007, 1360, 1599, 2910, 3300; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 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). **3i**: Di-*p*-tolyl sulfone: mp = 156 °C; (lit. 156 °C)[11] IR (KBr, cm^{-1}): 630, 765, 816, 990, 1035, 1100, 1180, 1360, 1460, 1500, 1600, 3421; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 6H, 2 × Ar-CH_3), 7.27 (d, 4H, J = 5 Hz, 4 × Ar-H), 7.80 (d, 4H, J = 5 Hz, 4 × Ar-H). **3j**: (3,4-Dimethylphenyl)-*p*-tolyl sulfone: mp 55 °C; IR (KBr, cm^{-1}): 1017, 1123, 1342, 1447, 1515, 1603; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.3 (s, 3H, ArCH_3), 2.36 (s, 3H, Ar-CH_3) 2.43 (s, 3H, Ar-CH_3), 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). **3k**: (2,4-Dimethylphenyl)-*p*-tolyl sulfone: mp = 49 °C (lit. 48–49 °C)[11] IR (KBr, cm^{-1}): 1028, 1110, 1175, 1355, 1455, 1505, 1610; ^{1}H NMR(300 MHz, $CDCl_3$): δ 2.34 (s, 3H, Ar-CH_3), 2.38 (s, 3H, Ar-CH_3) 2.41 (s, 3H, Ar-CH_3), 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). **3l**: (2,4,6-Trimethylphenyl)-*p*-tolyl sulfone: mp = 122 °C (lit. 123 °C).[11] IR (KBr, cm^{-1}): 810, 1011, 1150, 1350, 1460, 1522, 1611; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, Ar-CH_3), 2.35 (s, 3H, Ar-CH_3), 2.45 (s, 6H, 2 × Ar-CH_3), 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). **3m**: (Thiophene)-3-*p*-tolyl sulfone: mp 110 °C IR (KBr, cm^{-1}): 1160, 1310, 1500, 1610; ^{1}H NMR (300 MHz, $CDCl_3$): δ 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).

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