Selective Sulfonylation of Arenes and Benzoylation of Alcohols Using Lithium Perchlorate as a Catalyst Under Neutral Conditions

B. P. Bandgar,* V. T. Kamble, V. S. Sadavarte, L. S. Uppalla

Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University,
Handed-431 606, India
Fax +91(2462)29245; E-mail: vtkd@redifffmail.com

Received 16 October 2001

Abstract: Sulfonylation of aromatics with *p*-toluenesulfonyl chloride and benzoylation of alcohols with benzoyl chloride using lithium perchlorate as a catalyst is described. The remarkable selectivity under neutral conditions is an attractive feature of this method

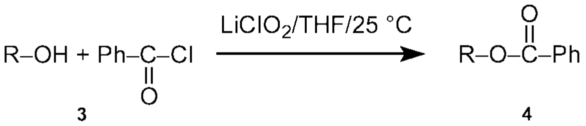
Key words: sulfonylation, benzoylation, lithium perchlorate, catalyst, neutral conditions

Organosulfones are important intermediates in organic synthesis[1] as well as in industrial applications.[2] Sulfones are generally prepared by oxidation of the corresponding sulfides and sulfoxides or by a displacement reaction of sodium arenesulfinate with appropriate alkyl halide.[3] Some metal halides,[1a] zeolites,[4] Bronsted acids[5] and $Bi(OTf)_3$[6] have been reported to catalyze the sulfonylation of arenes. Diaryl sulfones are synthesized using conventional Lewis acid catalysts and are useful intermediates for drug industry (e.g. diphenyl sulfone is used as an intermediate for DAPSONE (4,4′-diamino-diphenyl sulfone, effective for leprosy treatment).[7] More recently indium triflate,[8] Fe(III) exchanged montmorillonite clay[9] and $BiCl_3$-triflic acid[10] has been successfully used for catalytic sulfonylation of arenes. However, many of these procedures generally require strong protic or Lewis acids, prolonged reaction times and high temperatures. Thus, the use of an alternative method under neutral conditions would extend the scope of useful sulfonylation reaction for the synthesis of sulfones.

In recent years lithium perchlorate has received considerable attention as a powerful reaction medium for effecting various transformations[11] such as cycloaddition reactions, sigmatropic rearrangements, ring opening reactions of epoxides, glycosidation reactions, selective carbonyl protection as dithioacetal, Michael reactions and aldol reactions. Lithium perchlorate provides a convenient procedure to carry out the reactions under essentially neutral conditons. In addition, lithium perchlorate is found to retain its activity even in the presence of nitrogen containing compounds. These special properties inherent to lithium perchlorate prompted us to explore this catalyst for the synthesis of sulfones from arenes and benzoates from alcohols. In this communication, we describe a simple and practical method for the sulfonylation of aromatic compounds (Scheme 1) and benzoylation of alcohols (Scheme 2) using a catalytic amount of lithium perchlorate.

$$\underset{\mathbf{1}}{\text{Ar–H} + CH_3C_6H_4SO_2Cl} \xrightarrow[\Delta]{LiClO_4} \underset{\mathbf{2}}{ArSO_2C_6H_4CH_3}$$

Scheme 1



$$\underset{\mathbf{3}}{\text{R–OH} + \text{Ph–}\overset{}{\underset{\|\atop O}{C}}\text{–Cl}} \xrightarrow{LiClO_2/THF/25\ ^\circ C} \underset{\mathbf{4}}{\text{R–O–}\overset{O\atop \|}{C}\text{–Ph}}$$

Scheme 2

The catalytic activity of the lithium perchlorate for sulfonylation of anisole (5 mL) with *p*-toluenesulfonyl chloride (5 mmol) under reflux conditions was studied (Table 1) and it was found that application of less than 20 mol% of lithium perchlorate resulted in low yield of the corresponding sulfone (Table 1, entries 2, 3) whereas use of more than 20 mol% of lithium perchlorate did not improve the yield (Table 1, entries 5–7). When attempts were made to carry out sulfonylation of anisole with *p*-toluenesulfonyl chloride in the absence of catalyst, lithium perchlorate, it resulted in almost qantitative recovery of the substrate (Table 1, entry 1).

Table 1 A Catalytic Study of $LiClO_4$ for Sulfonylation of Anisole (5 mL) with *p*-Toluenesulfonyl Chloride (1 mmol) at Reflux Temperature

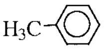
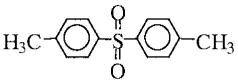
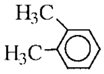
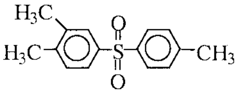
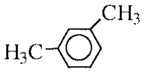
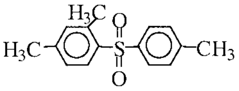
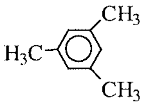
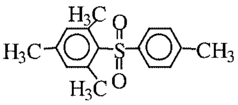
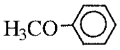
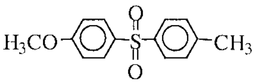
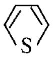
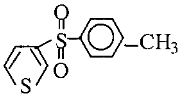
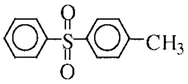
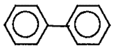
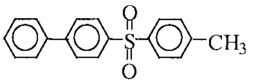
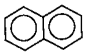
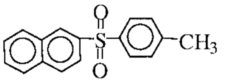
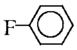
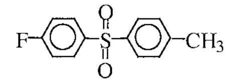
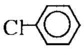
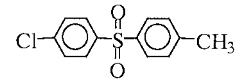
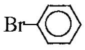
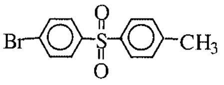
Entry	$LiClO_4$ (mol %)	Time (h)	Yield (%)
1	–	2.5	–
2	0.01	2.5	30
3	0.05	2.5	40
4	0.10	2.5	85
5	0.20	2.5	90
6	0.50	2.5	89
7	1.00	2.5	88

Synlett 2002, No. 5, 03 05 2002. Article Identifier:
1437-2096,E;2002,0,05,0735,0738,ftx,en;D23801ST.pdf.

ISSN 0936-5214

Various activated and unactivated aromatics reacted well under the present reaction conditions to give the corresponding sulfones in good to excellent yield.[12] The results for sulfonylation of aromatics are summarized in Table 2. 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 without detection or isolation of *ortho*/*meta* isomers in trace amount. On the other hand sulfonylation of toluene involving $AlCl_3$[13] or more recently reported protocol of sulfonylation using $Bi(OTf)_3$[6] or $In(OTf)_3$[10] yields a mixture of isomers (e.g. ditolyl sulfones). In this regard the present method is superior because it gives selectively *para* isomer (e.g. *p*-tolyl sulfone) only in good yield (Table 2, entry 1). Further, the improvement in regioselectivity is also observed using $LiClO_4$ in sulfonylation of naphthalene with *p*-toluenesulfonyl chloride giving only β-isomer without formation of α-isomer in trace amount. On the other hand sulfonylation of naphthalene using Fe(III) exchanged montmorillonite clay[9] gave mixture of α-and β-isomers. It is interesting to note that heterocyclic (Table 2, entry 6) and unactivated aromatics (Table 2, entries 6–12) also undergo sufonylation smoothly under these neutral reaction conditions. However, these aromatic substrates require longer reaction time as compared to activated aromatics (Table 2, entries 1–5). But the yields of sulfones obtained from both activated as well as unactivated aromatics are good to excellent (Table 2).

Table 2 $LiClO_4$-catalyzed Sulfonylation of Aromatics Under Reflux Temperature

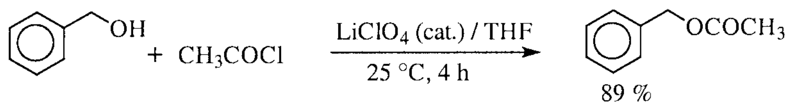
Entry	Arene	Product	Time (h)	Yield[a,b] (%)
1			4	84
2			4	85
3			3.5	84
4			3.5	83
5			2.5	90
6			8	82
7			6	76
8			6	77
9			8	80
10			5	85
11			5	85
12			5	84

[a] Yields are of pure isolated products.

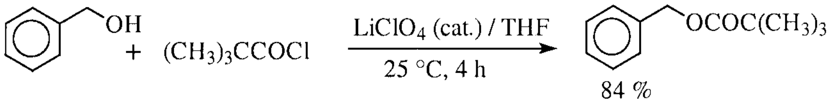
[b] Products are characterized by their physical constants and spectral analysis.

In order to explore the scope and limitations $LiClO_4$ as a catalyst, it has been employed for benzoylation of alcohols under mild and neutral conditions. Benzoylation of alcohols is a very important functional group transformation in synthetic organic chemistry. Benzoylation of alcohols in general is carried out by the treatment of alcohols with acid anhydrides or acid halides under the influence of a base.[14,15] For example, the benzoylation of alcohols with benzoyl chloride[15] or with benzoyl triflate[16] usually proceeds in the presence of pyridine. Several other procedures for benzoylation of alcohols have been reported in the literature.[17] More recently, remarkably fast benzoylation of alcohols with benzoyl chloride in the presence of base, *N*,*N*,*N′*,*N′*-tetramethyl ethylene diamine (TMEDA) at very low temperature (–78 °C) has been described.[18] The development of a new practical methods which allows transformation under essentially neutral conditions should heighten the synthetic potentiality of the reaction. The mild and selective protocol always attracts a great deal of attention of organic chemists. We report here for the first time catalytic benzoylation of alcohols with benzoyl chloride using $LiClO_4$ in THF under mild and neutral conditions (Scheme 2).

A variety of alcohols were converted to the corresponding benzoates[19] using benzoyl chloride in the presence of a catalytic amount of $LiClO_4$ in THF at 25 °C. The results are presented in Table 3. The methodology appears to be chemoselective as only primary alcohols (aliphatic, benzylic, allylic and propargylic) were benzoylated under these reaction conditions whereas the secondary alcohols were inert and tertiary alcohols did not afford corresponding benzoate esters. This may be due to steric hindrance around hydroxyl group of secondary and tertiary alcohols. It should be noted that primary alcoholic OH-group was selectively benzoylated in the presence of secondary alcoholic OH (Table 3, entries 11, 12) and tertiary alcoholic OH (Table 3, entry 13). One of the most noteworthy features of this method is that benzyl alcohols are selectively benzoylated in the presence of phenolic OH-groups where as reported methods involving base are not competitive for benzyl alcohols and phenols. It may be also quite interesting that the presence of an epoxide or a halogen

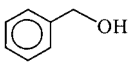
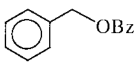
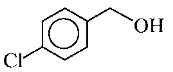
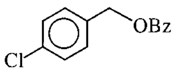
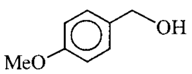
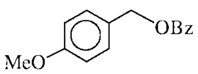
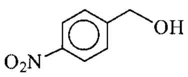
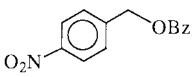
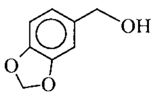
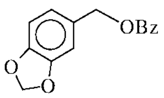
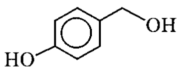
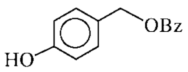
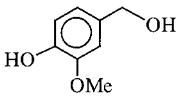
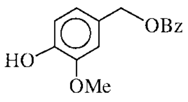
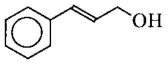
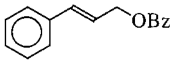
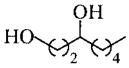
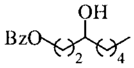
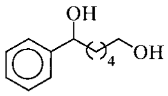
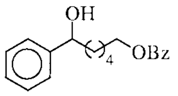
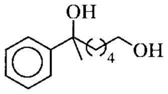
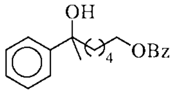
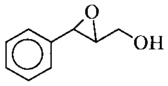
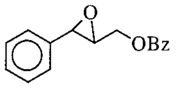
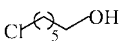
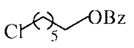
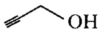
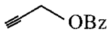


Equation 1



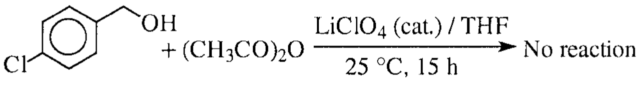
Equation 2

Table 3 $LiClO_4$-catalyzed Chemoselective Benzoylation of Alcohols at 25 °C

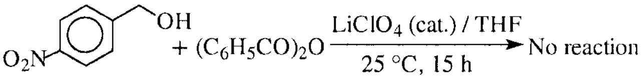
Entry	Alcohol	Product	Time (h)	Yield[a] (%)
1	$CH_3(CH_2)_5OH$	$CH_3(CH_2)_5OBz$	5	73
2	$(CH_3)_2CH(CH_2)_2OH$	$(CH_3)_2CH(CH_2)_2OBz$	6	75
3			7	80
4			7	78
5			6	85
6			7	87
7			7	80
8			6	79
9			6	85
10			7	85
11			5.5	70
12			6	72
13			7	77
14			8	75
15			5	79
16			5	82
17	$(CH_3)_3COH$	$(CH_3)_3COBz$	10	00
18	Ph_3COH	Ph_3COBz	10	00

[a] Pure isolated products are characterized by comparison with authentic samples and spectral analysis.

atom, which may show some reactivity under the basic conditions of conventional methods, did not give any disturbance to the present reaction (Table 3, entries 14, 15). This may be attributed to the fact that the reaction proceeds under neutral conditions. The reaction was equally effective when acetyl or pivaloyl chloride was used instead of benzoyl chloride (Equation 1 and Equation 2). However, acylation or benzoylation of alcohols with acetic anhydride or benzoic anhydride did not proceed even after stirring the reaction mixture for longer time (15 h) and it resulted in almost quantitative recovery of the substrate (Equation 3 and Equation 4).



Equation 3



Equation 4

The present protocol is truly catalytic and more attractive due to convenient and neutral reaction conditions as compared to reported methods of benzoylations involving stoichiometric amount of base. In conclusion, the present results on sulfonylation of arenes and benzoylation of alcohols demonstrate the efficiency of $LiClO_4$ as a catalyst under almost neutral conditions and constitutes a useful alternative to the commonly accepted procedures. The effectiveness of the protocol is manifested in its selectivity.

Acknowledgement

VSS thanks CSIR, New Delhi for fellowship.

References

(1) (a) Jonsen, F. R.; Goldman, G. In *Friedel–Crafts and Related Reactions*, Vol. 3; Olah, G., Ed.; Wiley Interscience: New York, **1964**, 1319. (b) Simpkins, N. S. *Sulfones in Organic Synthesis*; Pergamon Press: Oxford, **1993**.

(2) Roy, K. M. In *Ullamann's Encyclopedia of Industrial Chemistry*, Vol. A-25; Gerhartz, W., Ed.; VCH: Weinheim, **1985**, 487; and references cited therein.

(3) Block, E. In *The Chemistry of Functional Groups*, Suppl. E., Part 1; Patai, S., Ed.; Wiley: New York, **1980**, Chap. 13.

(4) (b)Smeek, I.; Fowler, I. S. *J. Org. Chem.* **1968**, *33*, 3422.

(5) Smith, K.; Ewart, G. M.; Randles, K. R. *J. Chem. Soc., Perkin Trans. 1* **1997**, *1*, 1085.

(6) (a) Sipe, H. J. Jr.; Clary, D. W.; White, S. B. *Synthesis* **1984**, 283. (b) Ueda, M.; Uchiyama, K.; Kono, T. *Synthesis* **1984**, 323.

(7) Repichet, S.; Le Roux, C.; Dubac, J. *J. Org. Chem.* **1999**, *64*, 6429.

(8) Weijlard, J.; Messerly, J. P. US patent 2,385,899 Oct. 2, **1945**; *Chem. Abstr.* **1946**, *40*, p180.

(9) Frost, C. G.; Hartley, J. P.; Whittle, A. J. *Synlett* **2001**, *6*, 830.

(10) Choudary, B. M.; Chowdary, N. S.; Kantam, M. L.; Kannan, R. *Tetrahedron Lett.* **1999**, *40*, 2859.

(11) Repichet, S.; Le Roux, C.; Dubac, J. *Tetrahedron Lett.* **1999**, *40*, 9223.

(12) (a) Gvieco, P. A. *Aldrichimica Acta* **1991**, *24*, 59.
(b) Balasubramanian, K. K. *Acros Org. Acta* **1999**, *6*, 12.

(13) **A Typical Procedure for Sulfonylation of Arenes**: A mixture of anisole (10 mL), *p*-toluene sulfonyl chloride (2 mmol) and lithium perchlorate (0.4 mmol) was refluxed for 2.5 h. On completion of the reaction, the mixture was cooled and excess anisole was removed under reduced pressure. To the residue chloroform (10 mL) and water (10 mL) was added. The aq layer was washed with chloroform (3 × 5mL). The combined organic layer was dried with anhyd Na_2SO_4 and removal of the solvent under vacuum furnished crude product, which was further purified by column chromatography.
Yield = 90%; mp = 149 °C; IR (KBr): 683, 834, 1007, 1360, 1599, 2910, 3300 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 6.95 (d, 2 H, J = 8.3 Hz, Ar-H), 7.31 (d, 2 H, J = 7.4 Hz, Ar-H), 7.85 (d, 2 H, J = 8.3 Hz, Ar-H), 7.90 (d, 2 H, J = 7.4 Hz, Ar-H).

(14) Olah, G. A.; Kobayashi, S.; Nishimura, J. *J. Am. Chem. Soc.* **1973**, *95*, 564.

(15) Hofle, G.; Steglich, W.; Vorbruggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

(16) Green, T. W.; Wutts, P. G. M. In *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, **1991**.

(17) Brown, L.; Koreeda, M. *J. Org. Chem.* **1984**, *49*, 3875.

(18) (a) Holey, A.; Soucek, M. *Tetrahedron Lett.* **1971**, 185.
(b) Stawinski, J.; Hozumi, T.; Narang, S. A. *J. Chem. Soc., Chem. Commun.* **1976**, 243. (c) Szeja, W. *Synthesis* **1979**, 821. (d) Schlessiner, R. H.; Lopes, A. *J. Org. Chem.* **1981**, *46*, 5252. (e) Hanessian, S.; Roy, R. *Can. J. Chem.* **1985**, *63*, 163. (f) Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1986**, *51*, 1006. (g) Pautrad, A. M.; Evans, S. A. Jr. *J. Org. Chem.* **1988**, *53*, 2300. (h) Smith, A. B. III; Hale, H. I. *Tetrahedron Lett.* **1989**, *30*, 1037.

(19) Sano, T.; Ohashi, K.; Oriyama, T. *Synthesis* **1999**, *7*, 1141.

(20) **Typical Procedure for Benzoylation**: A mixture of benzyl alcohol (5 mmol), benzoyl chloride (5 mmol) and $LiClO_4$ (1 mmol) was stirred for 7 h at 25 °C (Table 3, entry 3). After completion of the reaction (TLC), the solvent was removed under reduced pressure and the product was purified by column chromatography on silica gel. Yield = 80%; IR(neat): 712, 1065, 1107, 1272, 1450, 1716 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 4.4 (s, 2 H), 7.3–7.4 (m, 5 H), 8.1–8.15 (m, 5 H); ^{13}C NMR: δ = 70.2, 125.8, 127.77, 128.42, 128.61, 129.74, 130.55, 133.02, 141.78, 145.81, 175.9.