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An efficient method for aromatic Friedel–Crafts alkylation, acylation, benzoylation, and sulfonylation reactions

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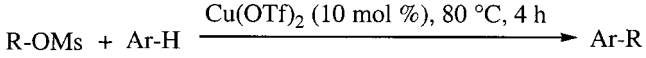
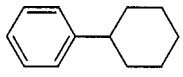
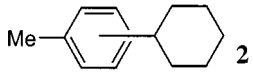
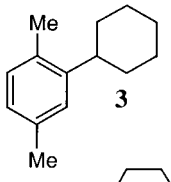
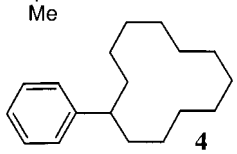
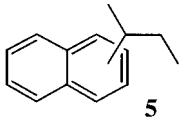
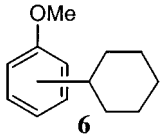
Abstract—Aromatic electrophilic substitution reactions such as alkylation, acylation, benzoylation, and sulfonylation were studied in the presence of a catalytic amount of $Cu(OTf)_2$ and $Sn(OTf)_2$. $Cu(OTf)_2$ was very efficient for alkylation, acylation, and benzoylation reactions. However, in case of sulfonylation reactions, $Sn(OTf)_2$ gave better results.

Aromatic Friedel–Crafts reactions are very well established in organic synthesis.[1] Typically, the reaction is performed using alkyl halide (for alkylation), acid anhydride or acid chloride (for acylation), and sulfonyl chloride (for sulfonylation) in the presence of Lewis acids such as $AlCl_3$ or BF_3. Although the alkylation reaction proceeds in the presence of a catalytic amount of a Lewis acid, the acylation, benzoylation, and sulfonylation reactions require more than stoichiometric amounts of the traditional Lewis acids. Because of the importance of the Friedel–Crafts reactions in industry, a variety of new and efficient catalysts have been reported in the literature. Catalysts such as $Hf(OTf)_4$,[2a] $Bi(OTf)_3$,[2b] $LiClO_4$–$MeNO_2$,[2c] $Ln(OTf)_3$–$LiClO_4$,[2d] and $Ga(OSO_2C_8F_{17})_3$[2e] have been reported for acylation reactions. Recently, $Sc(OTf)_3$,[3] was reported for alkylation reactions. A variety of catalysts such as metal halides,[4] Bronsted acids,[5] zeolites,[6] clays,[7] etc. have been reported to catalyze the sulfonylation of arenes. Recently, $Bi(OTf)_3$[8] and doped $BiCl_3$[9] have been used for the same purpose. While working on asymmetric synthesis using chiral copper complexes, we discovered that copper(II)trifluoromethanesulfonate [$Cu(OTf)_2$] is an efficient catalyst for TMSCN addition to ketones,[10] thioacetalization of ketones,[11] and acylation of alcohols, phenols, thiols, amines, and aldehydes.[12,13] Recently, we also reported that epoxides[14] and aziridines[15] can be cleaved with aromatic amines in an efficient manner in the presence of a catalytic amount of $Cu(OTf)_2$ or $Sn(OTf)_2$. In this paper we report application of these catalysts in aromatic Friedel–Crafts alkylation, acylation, benzoylation, and sulfonylation reactions.

Table 1. $Cu(OTf)_2$ catalyzed Friedel–Crafts alkylation of aromatic compounds with alkyl mesylate (for low boiling substrates, the reaction was carried out by using them as solvent whereas for solids and high boiling substrates, the reaction was carried out in dichloroethane)



Entry	Ar–R	Yield (%)
1	 **1**	81
2	 **2**	98[a]
3	 **3**	50
4	 **4**	97
5	 **5**	97[b]
6	 **6**	98[c]

[a] *ortho*/*para* Ratio 42:58 (by ^1H NMR).
[b] α/β Ratio 75:25 (by ^1H NMR).
[c] *ortho*/*para* Ratio 47:53 (by ^1H NMR).

Keywords: aromatic Friedel–Crafts alkylation, acylation, benzoylation, and sulfonylation reactions; copper(II)tri-fluoromethanesulfonate; tin(II)tri-fluoromethanesulfonate.

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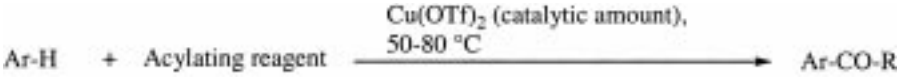
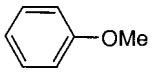
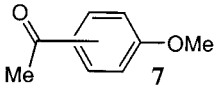
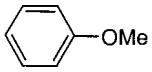
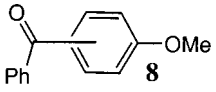
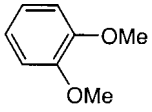
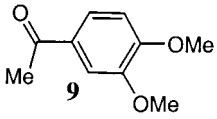
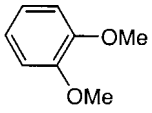
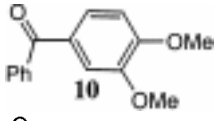
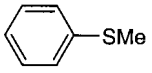
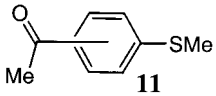
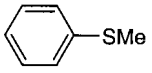
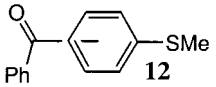
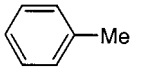
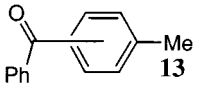
Table 2. $Cu(OTf)_2$ Catalyzed Friedel–Crafts acylation and benzoylation of aromatic compounds (the reaction was done by taking an excess of Ac_2O for acylation and excess of aromatic compounds for benzoylation reactions)



Entry	Ar–H	Acylating reagent	Reaction condition	Product	Yield (%)
1		Ac_2O	50°C, 3 h	 **7**	99[a]
2		PhCOCl	80°C, 8 h	 **8**	83[b]
3		Ac_2O	50°C, 3 h	 **9**	79
4		PhCOCl	80°C, 12 h	 **10**	96
5		Ac_2O	50°C, 6 h	 **11**	78[c]
6		PhCOCl	80°C, 12 h	 **12**	71[d]
7		PhCOCl	80°C, 12 h	 **13**	63[e]

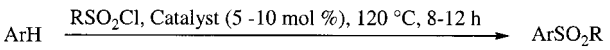
[a] *ortho*/*para* Ratio 9.7:90.3 (by HPLC).
[b] *ortho*/*para* Ratio 10.3:89.7 (by HPLC).
[c] *ortho*/*para* Ratio 12:88 (by HPLC).
[d] *ortho*/*para* Ratio 17.4:82.6 (by HPLC).
[e] *ortho*/*para* Ratio 36:64 (by HPLC).

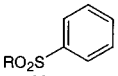
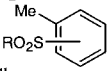
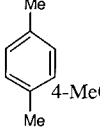
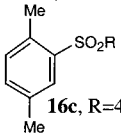
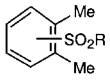
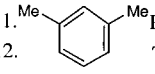
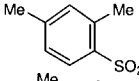
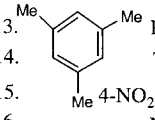
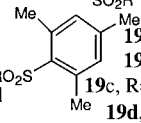
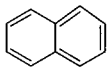
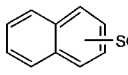
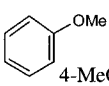
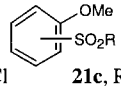
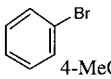
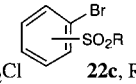
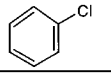
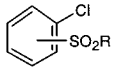
For alkylation reaction, a secondary mesylate and an aromatic compound were treated with 10 mol% of $Cu(OTf)_2$ at reflux temperature for 4 h to provide an alkylated product in high yield (Table 1). In most of the cases a large excess of the aromatic compound was used, however, in the case of solid or high boiling aromatics, the reaction was carried out by taking stoichiometric amount of the compound in dichloroethane as a solvent. The reaction was not clean when $Sn(OTf)_2$ was used as a catalyst. For example, benzene in the presence of $Sn(OTf)_2$ gave alkylated product in 28% yield compared with 81% yield using $Cu(OTf)_2$ (Table 1, entry 1). The reaction was carried out on a variety of aromatic compounds. It was observed that electron donating groups such as alkyl and OMe groups gave satisfactory yields of the product, however, there was no regioselectivity in the reaction as a 1:1 mixture of *ortho*- and *para* compounds was obtained (Table 1, entry 6). The other electron donating groups such as hydroxyl, amino, and dialkylamino gave very poor yields (~10%) of the alkylated product. The reaction did not proceed at all with electron withdrawing substitutents on the aromatic rings. The alkylation reaction proceeded only with secondary mesylates. Primary mesylates failed to give alkylated product. Alkyl tosylates did not react at all in the above alkylation reaction.

The use of $Cu(OTf)_2$ was extended to acylation reactions of aromatic compounds. Anisole (1 equiv.) was treated with Ac_2O (as a solvent) in the presence of 5 mol% of $Cu(OTf)_2$ at 50°C for 3 h. Usual work-up and purification over silica gel gave acylated product in quantitative yield. The benzoylation reaction was carried out in the same manner except that excess of aromatic compound and 1 equiv. of benzoyl chloride in the presence of 10 mol% of $Cu(OTf)_2$ were taken and the reaction required a little higher temperature (80°C for 8 h). The reaction was extended to a variety of aromatic compounds and results are summarized in Table 2. It was observed that only electron donating groups on aromatic compounds gave good results. The acylation and benzoylation reactions gave a mixture of *ortho* and *para* regioisomers and the ratios were determined by ^1H NMR and HPLC. The reaction was also attempted in the presence of other catalysts such as $CuCl_2$, $SnCl_2$, $AgCO_3$–TfOH, and $Sn(OTf)_2$, but it was not satisfactory as only a 25–50% yield of the acylated product was obtained. Use of solvents such as CH_2Cl_2, MeCN, $MeNO_2$, and AcOH gave poor results (30–50% yield).

For Sulfonylation reactions, an excess of aromatic hydrocarbon was treated with sulfonyl chloride in the presence of

Table 3. Catalytic electrophilic sulphonylation of aromatic compounds (with $Cu(OTf)_2$, 10 mol% of the catalyst was used and the reaction was done for 12 h. With $Sn(OTf)_2$, 5 mol% of the catalyst was used and the reaction was done for 8 h)



Entry	Ar-H	RSO_2Cl	$ArSO_2R$	% Yield (*o*:*m*:*p*) $Cu(OTf)_2$	% Yield (*o*:*m*:*p*) $Sn(OTf)_2$
1.		$PhSO_2Cl$	 **14a**, R=Ph	37	89
2.		TsCl	**14b**, R=Tol.	63	90
3.		$PhSO_2Cl$	 **15a**, R=Ph	71(36:4:60)	98 (37:4:59)
4.		TsCl	**15b**, R=Tol.	89 (12:8:80)	99 (14:10:76)
5.		$4\text{-MeO-}C_6H_4SO_2Cl$	**15c**, R=4-MeO-C_6H_4-	78 (14:8:78)	73 (13:4:83)
6.		$PhSO_2Cl$	 **16a**, R=Ph	98[a]	99[a]
7.		TsCl	**16b**, R=Tol.	76[a]	96[a]
8.		$4\text{-MeO-}C_6H_4SO_2Cl$	**16c**, R=4-MeO-C_6H_4-	75[a]	60[a]
9.		$PhSO_2Cl$	 **17a**, R=Ph	70[b]	98[b]
10.		TsCl	**17b**, R=Tol.	71[b]	99[b]
11.		$PhSO_2Cl$	 **18a**, R=Ph	55[c]	97[c]
12.		TsCl	**18b**, R=Tol.	66[c]	98[c]
13.		$PhSO_2Cl$	 **19a**, R=Ph	90[a]	98[a]
14.		TsCl	**19b**, R=Tol.	89[a]	97[a]
15.		$4\text{-NO}_2\text{-}C_6H_4SO_2Cl$	**19c**, R=4-NO_2-C_6H_4-	39[a]	40[a]
16.		MsCl	**19d**, R=Me	37[a]	40[a]
17.		$PhSO_2Cl$	 **20a**, R=Ph	73[b]	98[b]
18.		TsCl	**20b**, R=Tol.	95 (24:76)[d]	99 (27:73)[d]
19.		$PhSO_2Cl$	 **21a**, R=Ph	41 (35:0:65)	81 (38:0:62)
20.		TsCl	**21b**, R=Tol.	60 (16:0:84)	91 (17:0:83)
21.		$4\text{-MeO-}C_6H_4SO_2Cl$	**21c**, R=4-MeO-C_6H_4-	85 (12:0:88)	77 (10:0:90)
22.		$PhSO_2Cl$	 **22a**, R=Ph	10 (4:0:96)	66 (5:0:95)
23.		TsCl	**22b**, R=Tol.	10 (6:0:94)	95 (4:0:96)
24.		$4\text{-MeO-}C_6H_4SO_2Cl$	**22c**, R=4-MeO-C_6H_4-	no reaction	30 (34:0:64)
25.		$PhSO_2Cl$	 **23a**, R=Ph	07 (5:0:95)	66 (6:0:94)
26.		TsCl	**23b**, R=Tol.	08[e]	88[e]

[a] Only *ortho* to Me.
[b] Ratio not determined.
[c] Only *para* to Me.
[d] α,β ratio.
[e] Only *para* compound.

a catalytic amount of either $Cu(OTf)_2$ or $Sn(OTf)_2$ at 120°C for 8–12 h and the results are summarized in Table 3. The reaction with benzene was carried out only at 80°C. In most of the cases, a very high yield of the sulfonylated product was obtained. It was observed that results from $Sn(OTf)_2$ were better than those with $Cu(OTf)_2$. Aromatic sulfonating reagents gave better yields than aliphatic ones. This observation was used in selective sulfonylation of mesitylene with benzenesulfonyl chloride. When mesitylene was treated with a 1:1 mixture of benzenesulfonyl chloride and methanesulfonyl chloride, a ratio of 72:28 of the respective sulfonated product was obtained.

In conclusion, we have studied the aromatic Friedel–Crafts reactions using a catalytic amount of Cu- and $Sn(OTf)_2$.

1. Experimental

^1H NMR spectra were recorded on Jeol and Brucker NMR machines, as mentioned in the Experimental, using TMS as internal standard. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. IR spectra were recorded on Perkin–Elmer 580 and 1320 spectrometers. HPLC was done on a Perkin–Elmer machine.

Routine monitoring of reactions was performed using silica gel-G obtained from Acme. All the chromatographic separations were carried out using silica gel (Acme's, 60–120 mesh). Petroleum ether used was of boiling range 60–80°C. Reactions, which needed anhydrous conditions, were run under an atmosphere of dry nitrogen or argon using

flame-dried glasswares. The organic layer was washed with brine and stored over *anhydrous* Na_2SO_4 for 30 min before use. Evaporation of solvents was performed at reduced pressure, using a Büchi rotary evaporator.

1.1. General procedure for aromatic alkylation reactions

To a stirred suspension of $Cu(OTf)_2$ (0.1 mmol; 10 mol%) in dry dichloroethane (5 mL) alkyl mesylate (1 mmol) and an aromatic compound (1 mmol) were added and then heated at 80°C for 4 h. The reaction mixture was concentrated in vacuo and purified over silica gel column chromatography using petroleum ether as solvent to provide pure product (Table 1).

1.1.1. Cyclohexylbenzene (1).[3] Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.32 (m, 5H), 1.74 (m, 5H), 2.47 (m, 1H), 7.19 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.2, 27.0, 34.5, 44.6, 125.7, 126.61, 128.2, 148.0.

1.1.2. 2-Cyclohexyltoluene and 4-cyclohexyltoluene (2).[3] Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29 (m, 5H), 1.74 (m, 5H), 2.3 (d, J=2.4 Hz, 1.8H), 2.31 (d, J=2.4 Hz, 1.2H), 2.45 (m, 0.6H), 2.69 (m, 0.4H), 7.05 (m, 4H).

1.1.3. 2-Cyclohexyl-*p*-xylene (3).[3] Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.27 (m, 5H), 1.74 (m, 5H), 2.27 (s, 3H), 2.29 (s, 3H), 2.66 (m, 1H), 6.88 (dd, J=7.5, 1.2 Hz, 1H), 7.0 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.9, 21.2, 26.4, 27.2, 33.7, 40.1, 126.14, 126.18, 130.1, 131.9, 135.3, 145.68.

1.1.4. Dodecylbenzene (4). White solid; mp 41–42°C; IR (KBr): 910, 2890–3000 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.34 (m, 20H), 1.75 (m, 2H) 2.75 (pent, J=6.5 Hz, 1H), 7.16 (m, 3H), 7.26 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.7, 23.2, 23.5, 23.9, 24.0, 31.6, 39.7, 125.6, 127.6, 128.1, 147.6. Anal. Calcd for $C_{18}H_{28}$: C, 88.52, H, 11.47; Found: C, 88.56, H, 11.40.

1.1.5. 2-Butyl-1-naphthalene and 2-butyl-2-naphthalene (5). White solid; mp 48–49°C; IR (KBr): 910, 2900–3000 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (t, J=7.3 Hz, 0.75H), 1.0 (t, J=7.3 Hz, 2.25H), 1.40 (d, J=7.0 Hz, 0.75H), 1.45 (d, J=7 Hz, 2.25H), 1.77 (m, 1H), 1.91 (m, 1H), 2.83 (m, 0.25H), 3.58 (m, 0.75H), 7.37–8.26 (m, 7H). Anal. Calcd for $C_{14}H_{16}$: C, 91.30, H, 8.69; Found: C, 91.46, H, 8.80.

1.1.6. 2-Cyclohexylanisole and 4-cyclohexylanisole (6).[3] Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.34 (m, 5H), 1.82 (m, 5H), 2.42 (m, 0.47H), 2.94 (m, 0.53H), 3.71 (s, 1.5H), 3.75 (s, 1.5H), 6.7–7.2 (aromatics, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.2, 26.5, 27.0, 27.2, 33.2, 34.8, 36.8, 43.7, 55.1, 55.2, 110.3, 113.6, 120.6, 126.4, 126.5, 127.6, 136.2, 140.3, 156.7, 157.7. Anal. Calcd for $C_{13}H_{18}O$: C, 82.10, H, 9.4; Found: C, 82.36, H, 9.52.

1.2. General procedure for aromatic acylation reactions

A solution of $Cu(OTf)_2$ (0.05 mmol; 5 mol%), Ac_2O (2 mL), and an aromatic compound (1 mmol) was heated at 50°C till the reaction was complete (see Table 2). The reaction mixture was diluted with CH_2Cl_2, washed with water, aq sodium bicarbonate solution, and brine. The organic layer was dried and concentrated in vacuo. The crude product was purified over silica gel column chromatography to provide pure product (Table 2).

1.3. General procedure for aromatic benzoylation reactions

A solution of $Cu(OTf)_2$ (0.1 mmol; 10 mol%), benzoyl chloride (1 mmol), and an aromatic compound (in excess) was heated at 80°C till the reaction was complete (see Table 2). The reaction mixture was diluted with CH_2Cl_2, washed with water, aq sodium bicarbonate solution, and brine. The organic layer was dried and concentrated in vacuo. The crude product was purified over silica gel column chromatography to provide pure product (Table 2).

1.3.1. 2-Methoxyacetophenone and 4-methoxyacetophenone (7).[16] Colorless liquid; R_f 0.5 (10% EtOAc in petroleum ether); IR (neat) 1720, 1230, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.51 (s, 2.7H), 2.57 (s, 0.3H), 3.82 (s, 2.7H), 3.86 (s, 0.3H), 6.89 (d, J=8.8 Hz, 2H), 7.89 (d, J=8.8 Hz, 2H). HPLC analysis (MeOH/water 1:1): t_R=7.19 min (90.3%), t_R=7.93 (9.7%).

1.3.2. 2-Methoxybenzophenone and 4-methoxybenzophenone (8).[17] Colorless liquid; R_f 0.6 (10% EtOAc in petroleum ether); IR (neat) 1670, 1240, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.79 (s, 3H), 6.83 (d, J=8.7 Hz, 2H), 7.17 (d, J=8.7 Hz, 2H), 7.28 (m, 5H). HPLC analysis (MeOH/water 1:1): t_R=24.86 min (10.3%), t_R=36.89 (89.7%). Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.24, H, 5.66; Found: C, 79.56, H, 5.70.

1.3.3. 3,4-Dimethoxyacetophenone (9).[18] Colorless liquid; R_f 0.5 (10% EtOAc in petroleum ether); IR (neat) 1715, 1260, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.57 (s, 3H), 3.94 (s, 3H), 3.95 (s, 3H) 6.89 (d, J=8.3 Hz, 1H), 7.53 (d, J=2.0 Hz, 1H), 7.58 (dd, J=8.3, 2.0 Hz, 1H). HPLC analysis (MeOH/water 1:1): t_R=3.95 min. Calcd for $C_{10}H_{12}O_3$: C, 66.66H, 6.66; Found: C, 66.86, H, 6.74.

1.3.4. 3,4-Dimethoxybenzophenone (10).[19] White solid; mp 86–90°C, R_f 0.8 (10% EtOAc in petroleum ether); IR (KBr) 1660, 1250, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.94 (s, 3H), 3.96 (s, 3H), 6.89 (d, J=8.3 Hz, 1H), 7.38 (dd, J=8.3, 1.7 Hz, 1H), 7.48 (m, 3H), 7.57 (m, 1H), 7.76 (m, 2H). HPLC analysis (MeOH/water 1:1): t_R=14.09 min.

1.3.5. 2-Thiomethylacetophenone and 4-thiomethylacetophenone (11).[20] White solid; mp 49–53°C, R_f 0.6 (1% EtOAc in petroleum ether); IR (KBr) 1620, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.48 (s, 3H), 2.52 (s, 3H), 7.22 (d, J=8.4 Hz, 2H), 7.83 (d, J=8.4 Hz, 2H). HPLC analysis

(MeOH/water 1:1): t_R=7.19 min (12.12%), t_R=11.53 (87.88%).

1.3.6. 2-Thiomethylbenzophenone and 4-thiomethylbenzophenone (12).[21] White solid; mp 60–64°C; R_f 0.6 (1% EtOAc in petroleum ether): IR (KBr) 1630; 770 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.42 (s, 0.3H), 2.53 (s, 2.7H), 7.25–8.2 (aromatics, 9H). HPLC analysis (MeOH/water 1:1): t_R=9.32 min (82.5%), t_R=15.71 (17.5%). Anal. Calcd for $C_{14}H_{12}OS$: C, 73.68, H, 5.26, S 14.03; Found: C, 73.96, H, 5.20.

1.3.7. 2- and 4-Methylbenzophenone (13).[22] Colorless oil; R_f 0.7 (10% EtOAc) in petroleum ether); IR (neat) 1710, 780 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.33 (s, 2.1H), 2.43 (s, 0.9H), 7.2–7.82 (aromatics, 9H). HPLC analysis (MeOH/water 1:1): t_R=7.62 min (36.5%), t_R=13.7 (63.5%).

1.4. General procedure for aromatic sulfonylation

To a stirred suspension of $Sn(OTf)_2$ (23 mg, 5 mol%) in aromatic hydrocarbon (3 mmol) was added sulfonylating reagent (1 mmol) at rt. The reaction mixture was heated up to 120°C till the reaction was complete (12 h). It was diluted with CH_2Cl_2 (10 mL) was washed successively with 1N HCl, water, and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography to provide the pure materials (Table 3).

1.4.1. Diphenylsulphone (14a). White solid; mp 117–118°C (lit.[23] 123–124°C); IR (KBr) 3000, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39–7.51 (m, 6H), 7.88 (m, 4H).

1.4.2. Phenyltolylsulphone (14b). White solid; mp 126–127°C (lit.[24] mp 125–126°C); R_f 0.50 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.33 (s, 3H), 7.22 (d, J=8.0 Hz, 2H), 7.45 (m, 3H), 7.76 (d, J=8.0 Hz, 2H), 7.86 (d, J=7 Hz, 2H).

1.4.3. Tolylphenylsulphone (15a).[24] White solid; mp 78–79°C; IR (KBr) 3000, 720 cm^{-1}; R_f 0.35 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.27 (s, 1.77H, *p*-**15a**), 2.29 (s, 0.12H, *m*-**15a**), 2.33 (s, 1.1H, *o*-**15a**), 7.19 (d, J=8.5 Hz, 2H), 7.36–7.48 (m, 4H), 7.73 (m, 2H), 7.83 (m, 1H).

1.4.4. Ditolylsulfone (15b).[25] White solid; mp 146–149°C; R_f 0.30 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.32 (s, 4.56H, *p*-**15b**), 2.35 (s, 0.6H, *m*-**15b**), 2.40 (s, 0.84H, *o*-**15b**), 7.23 (d, J=8.0 Hz, 4H), 7.76 (d, J=8.0 Hz, 4H).

1.4.5. (Tolyl)-4-methoxyphenylsulphone (15c).[26] White solid; mp 85–86°C; IR (KBr) 3000, 710 cm^{-1}; R_f 0.25 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.43 (s, 3H), 3.81 (s, 2.49H, –*OMe*, *p*-**15c**), 3.82 (s, 0.12H, *m*-**15c**), 3.83 (s, 0.39H, –*OMe*, *o*-**15c**), 6.91 (d, J= 7.8 Hz, 2H), 7.25 (d, J=9.8 Hz, 2H), 7.77 (d, J=8.3 Hz, 2H), 7.83 (d, J=8 Hz, 2H).

1.4.6. (2,5-Dimethylphenyl)phenylsulfone (16a).[27] White solid; mp 101–103°C; R_f 0.40 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.34 (s, 3H), 2.38 (s, 3H), 7.07 (d, J=7.8 Hz, 1H), 7.25 (d, J=7.8 Hz, 1H), 7.46–7.55 (m, 3H), 7.82 (d, J=8 Hz, 2H), 8.01 (s, 1H).

1.4.7. (2,5-Dimethylphenyl)tolylsulfone (16b).[28] White solid; mp 105–107°C; R_f 0.50 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.34 (s, 3H), 2.37 (s, 6H), 7.05 (m, 1H), 7.24 (m, 3H), 7.71 (d, J=8 Hz, 2H), 7.99 (s, 1H).

1.4.8. (2,5-Dimethylphenyl)-4-methoxyphenylsulfone (16c). White solid; mp 104–106°C; IR (KBr) 3000, 1280, 720 cm^{-1}; R_f 0.35 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.36 (s, 3H), 2.37 (s, 3H), 3.83 (s, 3H), 6.93 (d, J=8.3 Hz, 2H), 7.07 (d, J=8.0 Hz, 1H), 7.24 (d, J=7.6 Hz, 1H), 7.76 (d, J=8 Hz, 2H), 7.98 (s, 1H).

1.4.9. (Xylyl)phenylsulfone (17a). White solid; mp 86–88°C; IR (KBr) 2990, 1270, 740 cm^{-1}; R_f 0.35 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.27 (s, 6H), 7.23–7.28 (m, 1H), 7.44–7.67 (m, 5H), 7.83–7.92 (m, 2H).

1.4.10. (Xylyl)tolylsulfone (17b).[29] White solid; mp 113–115°C; R_f 0.50 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.23 (s, 6H), 2.32 (s, 3H), 7.17–7.24 (m, 3H), 7.61–7.89 (m, 4H).

1.4.11. (2,4-Dimethylphenyl)phenylsulfone (18a).[29] Mp 92–94°C; R_f 0.38 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.39 (s, 3H), 2.42 (s, 3H), 7.07 (s, 1H), 7.23 (d, J=8.0 Hz, 1H), 7.52 (m, 2H), 7.58 (m, 1H), 7.86 (d, J=8.5 Hz, 2H), 8.14 (d, J=8.3 Hz, 1H).

1.4.12. (2,4-Dimethylphenyl)tolylsulfone (18b).[30] White solid; mp 51–52°C; R_f 0.50 (10:90, EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.30 (s, 3H), 2.35 (s, 6H), 6.98 (s, 1H), 7.12 (d, J=8.5 Hz, 1H), 7.22 (d, J=8.2 Hz, 2H), 7.68 (d, J=8.5 Hz, 2H) 8.04 (d, J=8.3 Hz, 1H).

1.4.13. (2,4,6-Trimethylphenyl)phenylsulfone (19a).[31] White solid; mp 79–81°C; R_f 0.56 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.27 (s, 3H), 2.56 (s, 6H), 6.92 (s, 2H), 7.43–7.53 (m, 3H), 7.59 (d, J= 8.5 Hz, 2H).

1.4.14. (2,4,6-Trimethylphenyl)tolylsulfone (19b).[32] White solid; mp 115–117°C (lit.[36] 119°C); R_f 0.50 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H) 2.35 (s, 3H), 2.56 (s, 6H), 6.91 (s, 2H), 7.23 (d, J=8.2 Hz, 2H), 7.72 (d, J=7.9 Hz, 2H).

1.4.15. (2,4,6-Trimethylphenyl)-4-nitrophenylsulfone (19c). White flake solid; mp 144–146°C; R_f 0.22 (10:90 EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.30 (s, 3H) 2.55 (s, 6H), 6.96 (s, 2H), 7.94 (d, J=8.2 Hz, 2H), 8.31 (d, J=8.2 Hz, 2H).

1.4.16. (2,4,6-Trimethylphenyl)methylsulfone (19d).[33] Solid; mp 122–124°C; R_f 0.35 (10:90 EtOAc/petroleum

ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.30 (s, 3H) 2.66 (s, 6H), 3.03 (s, 3H), 6.96 (s, 2H).

1.4.17. Napthylphenylsulfone (20a).[34] Solid; mp 69–71°C; R_f 0.45 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39–7.57 (m, 6H), 7.79–8.03 (m, 4H), 8.50 (d, J=8.5 Hz, 1H), 8.63 (d, J=7.9 Hz, 1H).

1.4.18. Napthyltolylsulfone (20b).[35] Solid; mp 102–104°C; R_f 0.35 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.24 (s, 2.19H, *–Me*, β-**20b**), 2.28 (s, 0.81H, α-**20b**), 7.21 (m, 2H), 7.45–7.59 (m, 2H), 7.76–8.06 (m, 5H), 8.49 (d, J=8.9 Hz, 1H), 8.67 (d, J=8.5 Hz, 1H).

1.4.19. Anisylphenylsulfone (21a). White solid; mp 79–80°C; IR (KBr) 3010, 1280, 720 cm^{-1}; R_f 0.28 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.74 (s, 1.14H, *–OMe*, *o*-**21a**), 3.82 (s, 1.86H, *–OMe*, *p*-**21a**), 6.92 (m, 2H), 7.51 (m, 4H), 7.90 (m, 3H).

1.4.20. Anisyltolylsulfone (21b).[35] White solid; mp 80–82°C; R_f 0.35 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.33 (s, 2.49H, *p*-**21b**), 2.35 (s, 0.51H, *o*-**21b**), 3.78 (s, 3H, *–OMe*), 6.90 (d, J=7.9 Hz, 2H), 7.23 (d, J=8.3 Hz, 2H), 7.73 (d, J=8.5 Hz, 2H), 7.81 (d, J= 8.0 Hz, 2H).

1.4.21. Dianisylsulfone (21c). Solid, mp 104–106°C; IR (KBr) 3000, 1250, 710 cm^{-1}; R_f 0.20 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.80 (s, 6H), 6.91 (d, J=8.9 Hz, 4H), 7.81 (d, J=8.3 Hz, 4H).

1.4.22. (Bromophenyl)phenylsulfone (22b).[36] White solid; mp 92–94°C; R_f 0.50 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42–7.86 (m, 9H).

1.4.23. (Bromophenyl)tolylsulfone (22b).[37] White solid; mp 132–134°C; R_f 0.35 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3H), 7.30 (d, J=8.3 Hz, 2H), 7.62 (d, J=8.3 Hz, 2H), 7.80 (m, 4H).

1.4.24. (Bromophenyl)-4-methoxyphenylsulfone (22c). White solid; mp 95–96°C; IR (KBr) 2990, 1280, 730 cm^{-1}; R_f 0.28 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.83 and 3.84 (2s, 3H, *o*-, *p*-**22c**), 6.93–6.98 (m, 2H), 7.62 (d, J=7.8 Hz, 2H), 7.79 (d, J=7.9 Hz, 2H), 7.86 (m, 2H).

1.4.25. (Chlorophenyl)phenylsulfone (23a).[38] White solid; mp 77–78°C; R_f 0.50 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46–7.60 (m, 5H), 7.86–7.96 (m, 4H).

1.4.26. (Chlorophenyl)tolylsulfone (23b).[25] White solid; mp 115–117°C; R_f 0.40 (10:90 EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3H), 7.30 (d, J=8.2 Hz, 2H), 7.46 (d, J=7.9 Hz, 2H), 7.80 (d, J=7.9 Hz, 2H), 7.86 (d, J=8.0 Hz, 2H).

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