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A simple method for the synthesis of sulfonic esters

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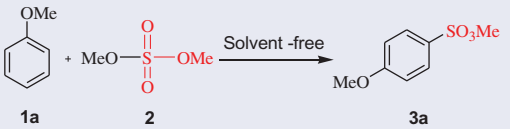
ABSTRACT

An efficient and simple approach for the direct synthesis of aryl and heteroaryl sulfonic esters was developed using DMS and DES as alkoxysulfonylation reagents. The reaction is operationally simple and scalable. This protocol does not require solvent, expensive catalysts, base, ligand additives or other reagents. A wide range of sulfonic esters were synthesized in moderate to good chemical yields. This method has the advantage of low cost, facile and tolerated a wide range of substrates.

GRAPHICAL ABSTRACT



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KEYWORDS
Dimethyl sulfate; diethyl sulfate; sulfonic esters; solvent-free synthesis; catalyst-free synthesis

Introduction

Aromatic sulfonic esters are valuable intermediates in organic synthesis, and various sulfonic esters have important pharmacological properties.[1–5] Sulfonic ester is a common fragment in many pharmaceuticals, materials, dyes, pesticides and other bioactive compounds.[6–12] Sulfonates are also one of the most important classes in surfactant industry as detergents and surface active agents.[13] In addition, sulfonic esters are also play a unique role in coupling reactions.[14,15]

Studies indicate that sulfonic esters exhibit a wide range of bioactivities including antitumor, antimalarial, antiproliferative and MAO inhibitory activities (Fig. 1).[12a,16–21]

Generally, the sulfonic esters are accessible by several steps through tedious procedures.[22] However; these processes suffer from some limitations with respect to functional group tolerance, stability and harsh reaction conditions. Traditionally sulfonic esters are synthesized by the reaction of the appropriate alcohol or phenol with sulfonyl chlorides in the presence of bases[21–25] (Scheme 1a), which required the preparation of highly sensitive and unstable sulfonyl chlorides.

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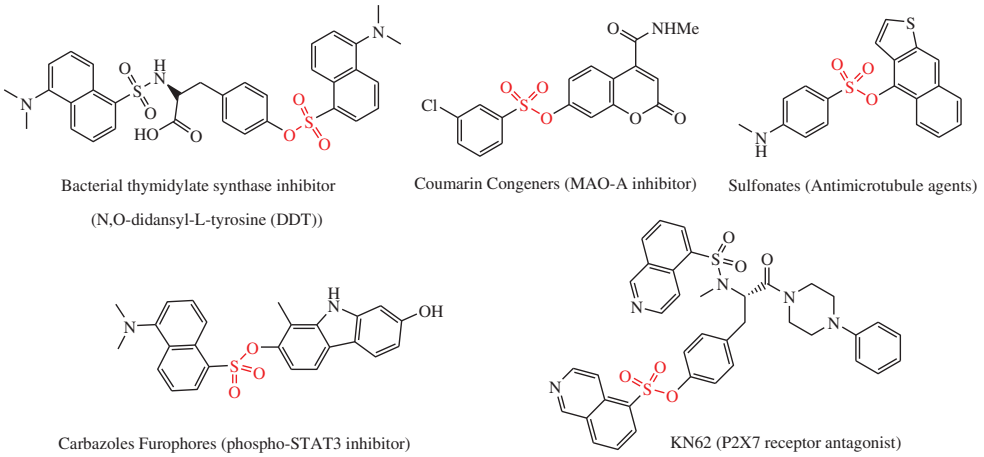


Figure 1. Bioactive compounds containing sulfonic esters.

To overcome these issues, various synthetic strategies have been developed, which includes the reaction of aryl diazonium salts with alcohols[26] (Scheme 1b), sulfonic acids with trimethyl and triethylorthoformates[27] (Scheme 1c), sulfonation using sulfur trioxide amine complexes,[28] phenols with thiols using H_2O_2–$POCl_3$ system[29] (Scheme 1d), aromatic compounds with copper sulfate as the sulfonation reagent,[30] sulfonyl fluorides with phenols,[31] thiophenols with alcohols using 9-mesityl-10-methyl acridinium ion (Acr^+−Mes) as a photocatalyst[32] (Scheme 1e), sulfonic acids using polymer-bound triazenes,[33] sodium sulfinates with phenol[34] (Scheme 1f), phenols with sulfonyl chlorides using cupric oxide as catalyst[35] and other routes have been also reported.[36–38]

However, these protocols have some limitations, such as long reaction times, harsh reaction conditions, use of ligand additives, bases, expensive catalysts or reagents, number of side reactions, or multistep synthesis. Therefore, it is still need to develop a straightforward and general protocol.

Though the dimethyl and diethyl sulfates are mainly used as alkylating agents in organic synthesis and these are preferred by the industry because of its low cost and high reactivity, we found that these sulfates are also useful to generate aromatic or heterocyclic aromatic sulfonic esters in one step (Tables 2–10).

Fortunately, not much literature has reported describing the utilization of alkylating reagents such as DMS, DES or other sulfates as alkoxysulfonylation reagents. Despite the importance of sulfonic esters, there currently exists no procedure for achieving the transformation of aromatic or heterocyclic aromatic compounds directly to a sulfonic ester in one synthetic step.

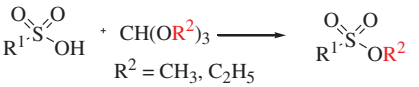
Thus, direct alkoxysulfonylation using the DMS or DES will be remarkably different from traditional or recently developed methods, which do not involve solvent, catalyst, base, ligand additives or other expensive reagents. Herein, we report alkoxysulfonylation process employing DMS and DES as the sulfonation reagents to afford various arene and heteroarene sulfonic esters in moderate to good yields (Tables 2–10). The significance of the given chemistry is the direct one-step transformation of low-cost DMS or DES to sulfonic esters.

Previous works:

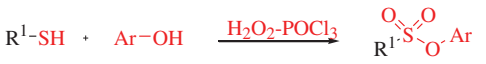
a) Traditional approaches

b) Copper catalyzed synthesis of sulfonic esters from alcohols and DABSO

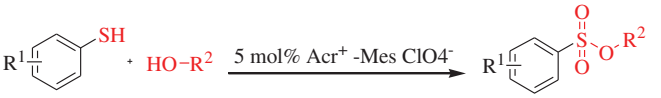
c) Esterification of sulfonic acid with trimethyl and triethyl orthoformates



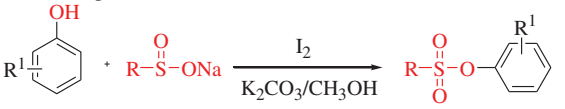
d) Phenols with thiols using H_2O_2 - $POCl_3$ system



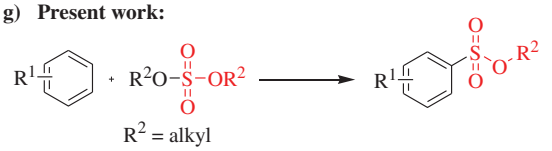
e) Thiophenols to sulfonic esters under photopromoted oxidative reaction conditions



f) Iodine-induced synthesis of sulfonate esters *via* cross-coupling reactions of sodium sulfinates with phenols



g) **Present work:**



Direct one-step synthesis of sulfonic esters from aromatic and heterocyclic aromatic compounds

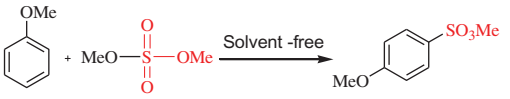
Scheme 1. Synthesis of sulfonic esters

Results and discussion

Initial stages of our work, we selected anisole and dimethyl sulfate as model substrates for the alkoxysulfonylation. After a series of screening studies on the reaction conditions with DMS as sulfonation reagent (for details, see Table 1), we found that the use of 3 mol of DMS with anisole (1.0 mol) delivered the maximum yield (62%) of corresponding ester **3a** (see Table 1, entry 3). The yield was lower when the amount of DMS was reduced to 1.0 equiv. (Table 1, entry 1). A similar result was obtained when 2.0 equiv. of DMS was utilized (Table 1, entry 2), increasing the amount of DMS to 4 or 6 equiv. did not show any obvious improvement on the chemical yield (Table 1, entries 4 and 5).

Generally, temperature is an important factor for various reactions. We then studied the temperature effect on the reaction and found that, the temperature have significant

Table 1. Optimization of the reaction conditions for the formation of sulfonic ester **3a**[a].



1a **2** **3a**

Entry	DMS (equiv)	Temp. (0 °C)	Reaction time (h)	Yield (%)[b]
1	1.0	95	4	30
2	2.0	95	4	48
3	3.0	95	4	62
4	4.0	95	4	62
5	6.0	95	4	63
6	3.0	rt	20	0
7	3.0	50	15	0
8	3.0	150	4	37
9	3.0	180	4	7

[a]Reaction conditions: anisole (10 mmol), under N_2 atmosphere.
[b]Isolated yield

effect on the reaction (Table 1, entries 6–9). Initially, the reaction of anisole with DMS was examined at room temperature and 50 °C, no desired product was observed (Table 1, entries 6 and 7). To our delight, the sulfonic ester was isolated in 62% yield when the reaction temperature was increased to 95 °C (Table 1, entry 3). We further explored the reaction at higher temperatures. It was found that no better yields were obtained at elevated temperatures (Table 1, entries 8 and 9), and 95–100 °C was demonstrated as the best choice. The results are presented in Table 1.

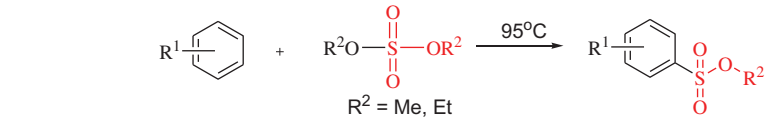
With the optimized reaction conditions in hand, to demonstrate the generality of this method, we then started to explore the substrate scope of this reaction and the results are shown in Tables 2–10. Substrate generality studies showed that this process provided a facile access toward diversely substituted sulfonic esters with good efficiency.

According to results, a series of functional groups on the aromatic ring, including alkyl, alkoxy, aryl, aryloxy, amine, ester, halide and hydroxy functional groups all are well tolerated in this transformation. A variety of sulfonic esters could be produced under the reaction conditions (Tables 2–10). Halogenated aromatic moieties survived the reaction conditions well, allowing for subsequent structural elaboration of the sulfonic esters.

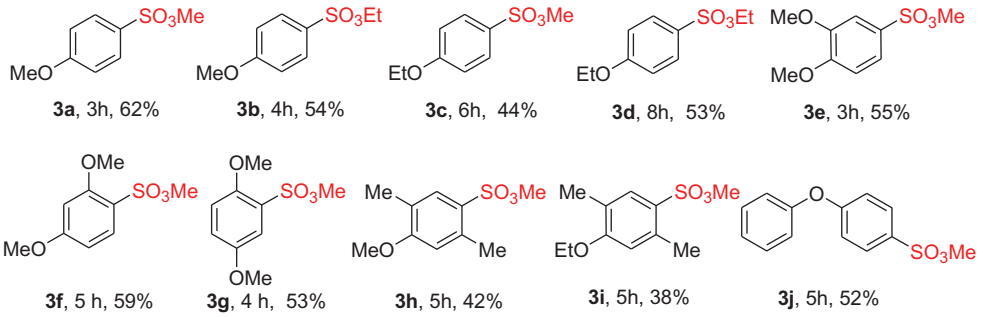
To evaluate the scope of the sulfonating groups, two reagents DMS and DES were tested with anisole under the standard conditions. As shown in Table 2 (**3a** and **3b**), both of the reagents participating in the coupling and gave the corresponding sulfonic esters in good yields.

It was found that the reaction was efficient with electron-donating groups such as methyl, ethyl, isopropyl, tert-butyl, phenyl, methoxy, ethoxy, phenoxy, amine and hydroxy groups are present on the aromatic ring. On the other hand, the presence of electron withdrawing groups such as halogens and nitro groups on the aromatic ring drastically influenced the reactivity, low yields or no sulfonic ester formation was observed (Table 6).

Table 2. Substrate scope for alkoxysulfonylation of aryl ethers[a,b].

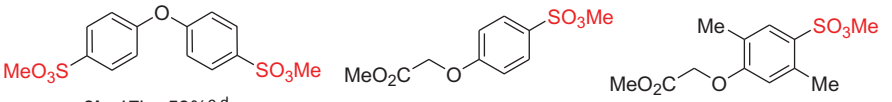


1 2 3



3a, 3h, 62% **3b**, 4h, 54% **3c**, 6h, 44% **3d**, 8h, 53% **3e**, 3h, 55%

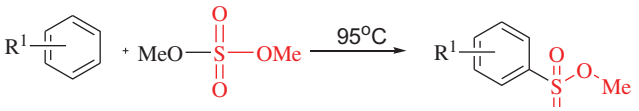
3f, 5 h, 59% **3g**, 4 h, 53% **3h**, 5h, 42% **3i**, 5h, 38% **3j**, 5h, 52%



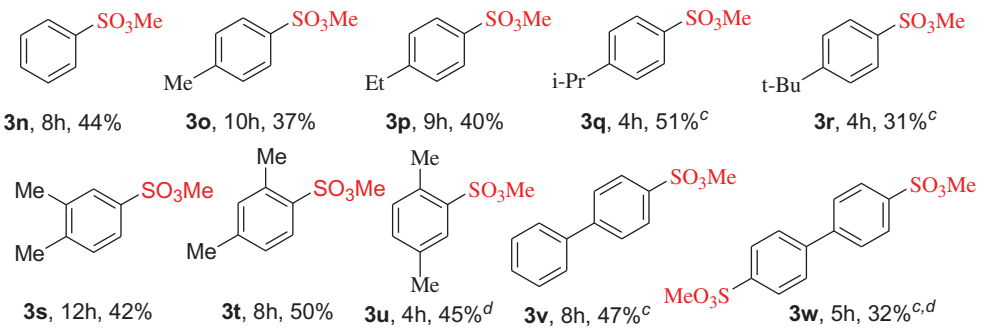
3k, 17h, 58%[c,d] **3l**, 6h, 64% **3m**, 4h, 55%

[a]Reaction conditions: **1** (10 mmol), DMS or DES (30 mmol) under N_2 atm.
[b]Isolated yield.
[c]Temp.110 °C.
[d]DMS (60 mmol).

Table 3. Substrate scope for alkoxysulfonylation of benzene and its alkyl and aryl derivatives[a,b].



1 2 3

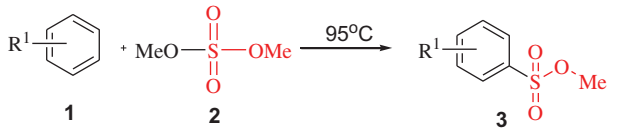


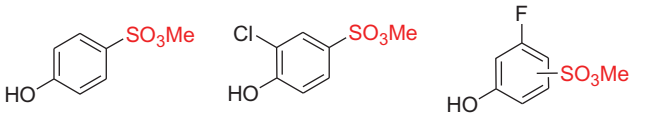
3n, 8h, 44% **3o**, 10h, 37% **3p**, 9h, 40% **3q**, 4h, 51%[c] **3r**, 4h, 31%[c]

3s, 12h, 42% **3t**, 8h, 50% **3u**, 4h, 45%[d] **3v**, 8h, 47%[c] **3w**, 5h, 32%[c,d]

[a]Reaction conditions: **1** (10 mmol), DMS (30 mmol) under N_2 atm.
[b]Isolated yield.
[c]Temp. 150 °C.
[d]DMS (50 mmol).

Table 4. Substrate scope for alkoxysulfonylation of phenol and its derivatives[a,b].

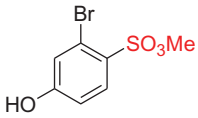




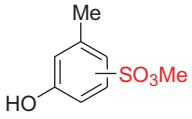
3x, 3h, 60%

3y, 5h, 50%

3z, 2-F, 4-OH, 4h, 36%
3aa, 2-OH, 4-F, 4h, 12%



3ab, 6h, 39%

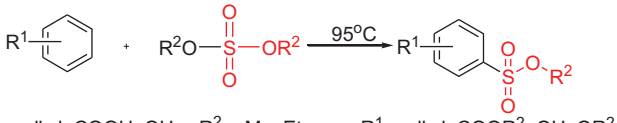


3ac, 2-Me, 4-OH, 3h, 33%
3ad, 2-OH, 4-Me, 3h, 20%

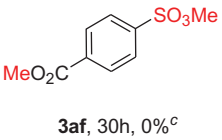
3ae, 10h, 45%

[a]Reaction conditions: **1** (10 mmol), DMS (30 mmol) under N_2 atm.
[b]Isolated yield.

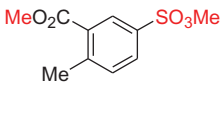
Table 5. Substrate scope for alkoxysulfonylation of aromatic acids[a,b].



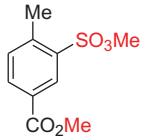
R^1 = alkyl, COOH, OH **1** R^2 = Me, Et **2** R^1 = alkyl, $COOR^2$, OH, OR^2 **3**



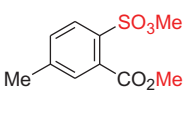
3af, 30h, 0%[c]



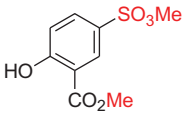
3ag, 5h, 33%[c]



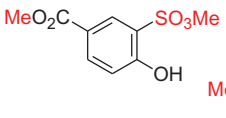
3ah, 10h, 51%[c]



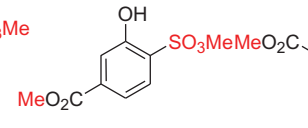
3ai, 25h, 0%



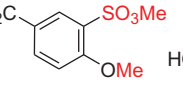
3aj, 8h, 47%



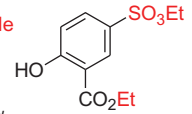
3ak, 7h, 65%



3al, 10h, 43%



3am, 8h, 15%[c,d]

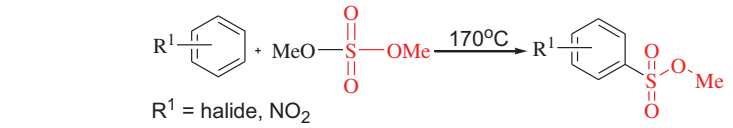


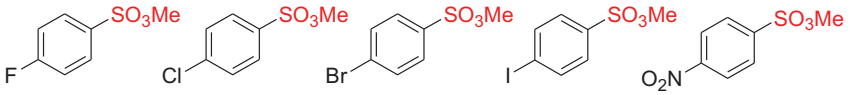
3an, 5h, 42%

[a]Reaction conditions: **1** (10 mmol), DMS or DES (40 mmol) under N_2 atm.
[b]Isolated yield.
[c]Temp. 140 °C.
[d]DMS (50 mmol).

First, alkoxysulfonylation of aryl ethers was explored (Table 2, entries **3a**–**3k**) with DMS/DES. As expected, all the reactions proceeded efficiently to provide the corresponding products in good yields. In addition, alkoxysulfonylation of phenoxyacetic acid methyl ester and (2,5-dimethylphenoxy)acetic acid methyl ester using DMS was accomplished, and the corresponding **3l** and **3m** were obtained in 64% and 55% yields, respectively (Table 2). The successful application of the alkoxysulfonylation protocol

Table 6. Substrate scope for alkoxysulfonylation of aryl halides and nitro benzene[a,b].

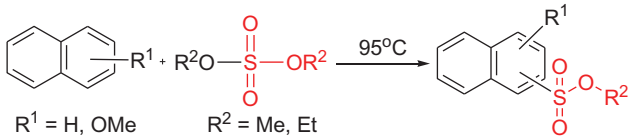


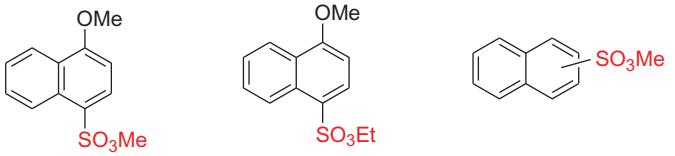


3ao, 25h, 0% **3ap**, 25h, 0% **3aq**, 25h, 8% **3ar**, 24h, 6% **3as**, 25h, 0%

[a]Reaction conditions: **1** (10 mmol), DMS (30 mmol) under N_2 atm.
[b]Isolated yield.

Table 7. Substrate scope for alkoxysulfonylation of polycyclic aromatic compounds[a,b].

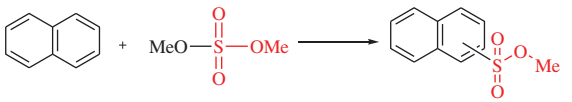




5a, 3h, 47% **5b**, 6h, 41% **5c & 5d**, 57% (C1 : C2 = 70 : 30)[c]

[a]Reaction conditions: **1** (10 mmol), DMS or DES (30 mmol) under N_2 atm.
[b]Isolated yield.
[c]Isomers, the ratio of **5c** and **5d** was determined by ^{1}H NMR spectroscopy analysis.

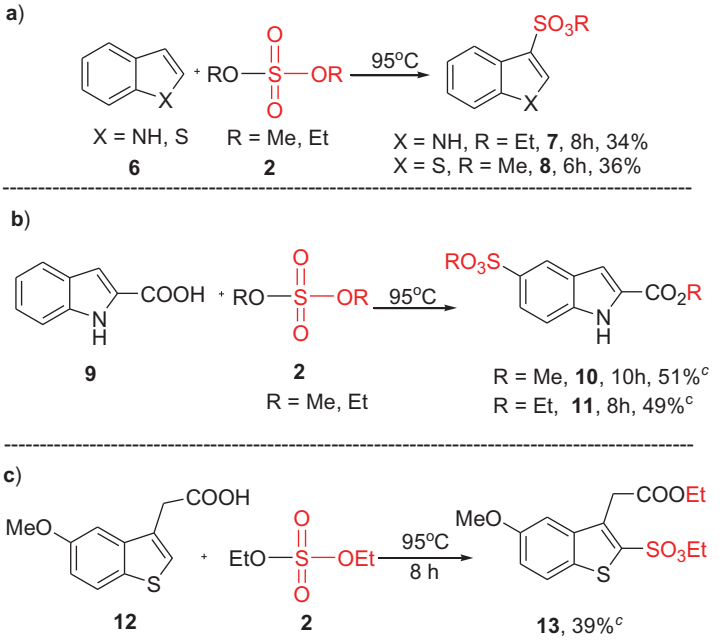
Table 8. Isomer distribution in the sulfonic ester of naphthalene **5c** and **5d**[a].



Entry	Temp. (0 °C)	Reaction time (h)	Yield (%)[b]	Ratio[c] of **5c** and **5d**
1	95	7	57	70:30
2	95	25	54	55:45
3	95	40	53	45:55
4	120	6	56	63:37
5	170	4	50	42:58
6	170	20	23	0:100

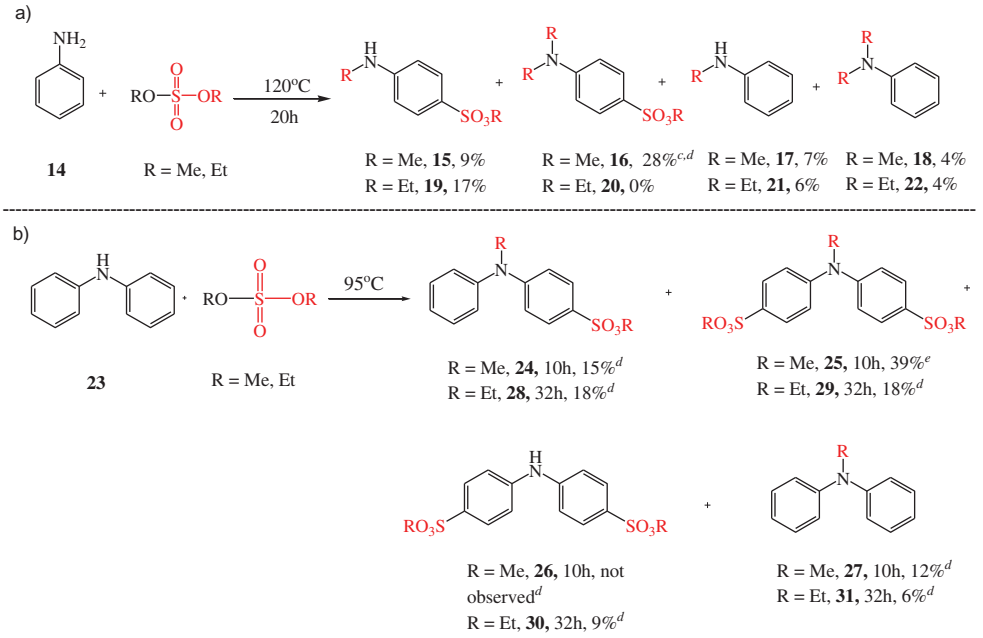
[a]Reaction conditions: Naphthalene (10 mmol), DMS (30 mmol), under N_2 atmosphere.
[b]Isolated yield.
[c]The ratio of **5c** and **5d** was determined by ^{1}H NMR spectroscopy analysis

Table 9. Substrate scope for alkoxysulfonylation of heterocyclic aromatic compounds[a,b].



[a]Reaction conditions: **1** (10 mmol), DMS or DES (30 mmol) under N_2 atm.
[b]Isolated yield. [c]DMS or DES (40 mmol)

Table 10. Substrate scope for alkoxysulfonylation of aromatic amines[a,b].



[a]Reaction conditions: **1** (10 mmol), DMS or DES (30 mmol) under N_2 atm.
[b]Isolated yield.
[c]Temp.150 °C.
[d]DMS (50 mmol).
[e]DMS (70 mmol).

with aryl ethers to obtain **3a–3m** encouraged our further efforts toward the preparation of other aromatic/heterocyclic aromatic sulfonic esters (results shown in Tables 3–10).

The reaction of benzene gave the desired product **3n** in 44% yield. Next, the effects of moderate electron donating groups (alkyl) on the aromatic ring such as methyl, ethyl, isopropyl and tert-butyl were investigated. Alkyl derivatives of benzene such as toluene, ethyl benzene, cumene and tert-butylbenzene under these conditions proceeded smoothly to give the desired products (Table 3, **3o–3r**) in good yields. In addition, the dialkyl derivatives of benzene such as *o*, *m* and *p*-xylene's were also transformed into the desired products (Table 3, **3s–3u**) in 42%, 50% and 45% yields, respectively.

Alkoxysulfonylation of biphenyl afforded 47% of mono (**3v**) and 8.0% of di-substituted (**3w**) sulfonic esters with DMS 3.0 equiv. and increasing the amount of DMS to 5 equiv. gave mono (**3v**) and diesters (**3w**) in 24% and 32% yields, respectively (Table 3). Next, Phenol was examined in this system under the standard reaction conditions and the desired sulfonic ester was obtained in 60% yield (Table 4, **3x**) along with 6% methoxy-sulfonic ester (Table 2, **3a**). Halo and alkyl substituted phenols, such as *o*-chloro, *m*-bromo and *p*-cresol all proceeded smoothly to afford the corresponding products (Table 4, **3y, 3ab** and **3ae**) in good yields. Whereas, *m*-fluorophenol under standard conditions gave two isomers such as 2-fluoro-4-hydroxy benzenesulfonic acid methyl ester and 4-fluoro-2-hydroxybenzenesulfonic acid methyl ester in 36% and 12% yields, respectively (Table 4, **3z** and **3aa**). *m*-cresol also gave two isomers **3ac** and **3ad** in 33% and 20% yields, respectively (Table 4).

We next studied the reaction with aromatic carboxylic acids such as benzoic acid and *o*, *p* and *m*-toluic acids. Results show that, non-substituted benzoic acid failed to produce sulfonic ester under the reaction conditions (Table 5, **3af**), only carboxylic ester was formed, which may be due to the electronic effects, whereas *o* and *p*-toluic acids undergo carboxylic acid esterification and ring alkoxysulfonylation reactions simultaneously (Table 5, **3ag** and **3ah**). In the case of *m*-toluic acid, the reaction with DMS gave only methyl ester, tried at different temperatures (95 °C, 120 °C, 150° and 175 °C), no sulfonic ester formation was observed, (Table 5, **3ai**). The reason for this fact may be arisen from the steric effect and low activity of *m*-toluic acid. The position of the substituted groups on the ring also showed an effect on the reaction. When the two substituent's on the ring are not the same, results become more complex, in the above compound both are different directing groups (*ortho* and *meta*), methyl is a week electron donor, whereas carboxylic group is strong withdrawing, reduced electron density at *o*-and *p* positions to methyl group in *m*-toluic acid could be influenced the reaction.

To examine whether the present protocol can useful to hydroxy-benzoic acids, we took different phenolic acids (Table 5) and subjected them to the reaction conditions. Interestingly, along with esterification of carboxylic group, sulfonic ester formation was noticed for *o*, *p* and *m*-hydroxy benzoic acids (see Table 5). Reaction with *p*-hydroxybenzoic acid was studied at elevated temperatures to check the possibility of *O*-methylation of hydroxy group, along with carboxylic acid esterification and sulfonic ester formation, methylation of the hydroxy group was noticed, however, a lower yield was obtained (see Table 5, **3am**).

The results listed in the Tables 2–5 showed that aromatic compounds with electron-donating groups attached on the phenyl ring underwent this process smoothly to give the corresponding products (**3a–3an**) in good to excellent yields.

Not surprisingly, the sulfonylation procedure was not effective for aryl halides, due to their deactivating nature toward electrophilic aromatic substitution because of the electronegative effect. Reaction of aryl halides such as fluoro and chloro under these conditions was unsuccessful and low yields were observed for bromo and iodo compounds. As expected the presence of strong electron-withdrawing nitro group on the aromatic ring failed to produce the sulfonic ester derivatives (see Table 6).

It should be noted that polycyclic aromatic compounds naphthalene and its derivatives were also suitable substrates for this transformation. We examined the reactions of naphthalene and 1-methoxynaphthalene under the optimized conditions. In the case of 1-methoxynaphthalene, the desired products (Table 7, **5a** and **5b**) were obtained in good yields with DMS and DES. However, in the case of naphthalene, two sites are available for substitution, C-1 and C-2, the alkoxysulfonylation of naphthalene with DMS under standard reaction conditions at 95 °C afforded two products as 7:3 ratio of inseparable regioisomers **5c** and **5d** (Table 7, 57% yield), identified by ^{1}H NMR (isolation by column chromatography was difficult). As expected, at 95 °C kinetically controlled product of C-1 isomer is obtained as major (**5c**). However, at higher temperatures and with time, the 1-ester rearranges to the thermodynamically more stable 2-ester (See Table 8, **5d**).

It is notable that the substrate scope could be further extended to heterocyclic aromatic compounds. Among heterocyclic aromatic compounds, indole, benzothiophene and their derivatives were chosen and tested. The reaction of indole and their derivatives was successful and the corresponding sulfonic esters were obtained in moderate to good yields (Table 9, 7, 10 and 11). Next, with benzothiophene and its derivatives, the corresponding reactions took place smoothly to give **8**, or **13** in 36%, or 39% yield, respectively.

To further extend the practicability of this process, we next explored the transformation of the aromatic amines to sulfonic esters. We found that both primary and secondary aromatic amines were capable for this alkoxysulfonylation, affording the desired products in low to moderate yields. Aromatic primary amine such as aniline gave a lower yield of 9% of **15** and 8% of **16** with DMS 3.0 equiv, and no desired products **15** and **16** were observed as well when 1.0 eq of DMS was added to the standard reaction. With 1.0 eq. of DMS, N-methyl aniline (**17**) and N,N-dimethyl aniline (**18**) could be isolated 34% and 20% yields, respectively. This result indicated that this alkoxysulfonylation experienced both N-methyl and N,N-dimethyl products as reaction intermediates. Because of the competitive reaction between both alkoxysulfonylation and methylation, increasing the amount of DMS 3–5 mol and temp. to 150 °C improved on the chemical yield of **16** to 28% (Table 10). However, surprisingly reaction of *tert*-aromatic amine, N,N-dimethylaniline with DMS was not given desired product. The reason was, although N,N-dimethylaniline is extremely reactive toward electrophilic aromatic substitution, possibility of formation of quaternary ammonium salt with DMS (N-alkylation) decreases the reactivity of N,N-dimethylaniline. The quaternary ammonium group is strong electron withdrawing, and electrophilic aromatic substitution is disfavored.

Finally, secondary aromatic amine, N,N-diphenylamine under standard conditions with DMS (5 equi.) gave mono and di sulfonic esters such as **24** and **25** in 15% and 33% yields, respectively, increasing the DMS to 7.0 equi. gave 39% disulfonic ester (**25**) as major product and only traces of mono ester was observed. Whereas, surprisingly reaction with DES (5 equi.) gave a mixture of three sulfonic esters along with N-ethyl N,N-diphenylamine (Table 10, **28**, **29** and **30**).

Conclusion

In summary, we have developed a simple, convenient and straightforward synthetic approach for the synthesis of sulfonic esters. Compared with literature procedures, the synthetic protocol developed herein showed advantages such as commercially available and inexpensive reagents, broad substrate scope with a wide range of functional group tolerance, and obviation of tedious step by step operations. Another advantage of this method over reported methods is that it does not require an expensive catalyst, base, ligand or other reagents. This methodology provides an easy access to the synthesis of sulfonic esters from aromatic and heterocyclic aromatic compounds under catalyst and solvent free conditions.

Experimental section

General description

Solvents and chemicals were purchased from commercial sources and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400-MHz instrument. Chemical shifts are (δ) reported in parts per million (ppm), and coupling constants (J) are reported in Hertz (Hz). Splitting patters are described as follows; br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Column chromatography was performed on silica gel (100–200 mesh). IR specta were recorded on a PerkinElmer Spectrum 100 FTIR spectrophotometer as KBr pellets or with the neat product. Mass spectra (MS) were recorded on an API 2000 LCMS/MS AB Sciex spectrometer. HRMS (ESI) were taken on an AB Sciex tripleTOF 5600+ and Bruker Daltonics MicrOTOF mass analyzers. Analytical thin-layer chromatography was carried out using E-Merck 60F254 aluminum-backed plates of silica gel (0.2 mm). Developed plates were visualized by using UV light or potassium permanganate solution.

General procedure a for the preparation of sulfonic esters

A mixture of arene/heteroarene (0.01 mol) and alkyl sulfate **2** (0.03 mol) was stirred at 95 °C under nitrogen atmosphere until the consumption of the starting material as monitored by TLC was complete. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (20 mL), and aq. ammonia solution (20 mL × 2). The organic layer was dried over anhydrous sodium sulfate, solvent was removed under reduced pressure, and then purified through silica gel column chromatography to give the corresponding sulfonic esters.

General procedure B for the preparation of sulfonic esters

A mixture of phenol (0.01 mol) and alkyl sulfate **2** (0.03 mol) was stirred at 95 °C under nitrogen atmosphere until TLC showed the disappearance of the starting material. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (20 mL). A solution of aqueous sodium hydroxide (10%, 10 mL) was added to the organic layer, and the resulting solution was stirred for 10 min. The layers were separated and the aqueous layer was acidified using aq.HCl (3.0 M), then extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure, and then purified through silica gel column chromatography to afford the corresponding sulfonic esters.

General procedure C for the preparation of sulfonic esters

A mixture of aromatic amine (0.01 mol) and alkyl sulfate **2** (0.03 mol) was stirred at 95 °C under nitrogen atmosphere until TLC showed the disappearance of the starting material. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (20 mL × 3). The organic layer was dried over anhydrous sodium sulfate, solvent was removed under reduced pressure, and then purified through silica gel column chromatography to afford the corresponding sulfonic esters.

4-Methoxybenzenesulfonic acid methyl ester (3a)

General procedure A was followed for the reaction of anisole (1.08 g, 10 mmol) and dimethyl sulfate (3.78 g, 30 mmol). The residue was purified by column chromatography on silica gel using ethyl acetate:hexane (10:90) as the eluent to afford product **3a**[26,32,39–43] (1.25 g, 62% yield) as a color less syrup; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 8.8$ Hz, 2H), 7.02 (d, $J = 8.8$ Hz, 2H), 3.88 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.87, 130.19, 126.37, 114.50, 56.10, 55.74; IR (Neat, cm^{-1}) ν_{max} 2953.44, 2843.64, 1579.04, 1597.88, 1499.03, 1358.11, 992.07, 564.03; MS: *m/z* 203.1 $(M + H)^+$.

^{1}H and ^{13}C NMR spectra, HRMS can be found via the "Supplementary Content" section of this article's Webpage.

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References

[1] (a) Yan, L.; Muller, C. E. Preparation, Properties, Reactions, and Adenosine Receptor Affinities of Sulfophenylxanthine Nitrophenyl Esters: Toward the Development of Sulfonic Acid Prodrugs with Peroral Bioavailability. *J. Med. Chem.* **2004**, *47*, 1031–1043. DOI: 10.1021/jm0310030. (b) Zuse, A.; Schmidt, P.; Baasner, S.; Bohm, K. J.; Muller, K.; Gerlach,

M.; Gunther, E. G.; Unger, E.; Prinz, H. Sulfonate Derivatives of Naphtho[2,3-b]Thiophen-4(9H)-One and 9(10H)-Anthracenone as Highly Active Antimicrotubule Agents. Synthesis, Antiproliferative Activity, and Inhibition of Tubulin Polymerization. *J. Med. Chem.* **2007**, *50*, 6059–6066. DOI: 10.1021/jm0708984.(c) Pisani, L.; Barletta, M.; Soto-Otero, R.; Nicolotti, O.; Mendez-Alvarez, E.; Catto, M.; Introcaso, A.; Stefanachi, A.; Cellamare, S.; Altomare, C.; Carotti, A. Discovery, Biological Evaluation, and Structure–Activity and – Selectivity Relationships of 6′-Substituted (E)-2-(Benzofuran-3(2H)-Ylidene)-N-Methylacetamides, a Novel Class of Potent and Selective Monoamine Oxidase Inhibitors. *J. Med. Chem.* **2013**, *56*, 2651–2664. DOI: 10.1021/jm4000769.

[2] (a) Hou, S.; Yi, Y. W.; Kang, H. J.; Zhang, L.; Kim, H. J.; Kong, Y.; Liu, Y.; Wang, K.; Kong, H.-S.; Grindrod, S.; et al. Novel Carbazole Inhibits Phospho-STAT3 Through Induction of Protein-Tyrosine Phosphatase PTPN6. *J. Med. Chem.* **2014**, *57*, 6342–6353. DOI: 10.1021/jm4018042. (b) Park, J.-H.; Lee, G.-E.; Lee, S.-D.; Hien, T. T.; Kim, S.; Yang, J. W.; Cho, J.-H.; Ko, H.; Lim, S.-C.; Kim, Y.-G.; et al. Discovery of Novel 2,5-Dioxoimidazolidine-Based P2X(7) Receptor Antagonists as Constrained Analogues of KN62. *J. Med. Chem.* **2015**, *58*, 2114–2134. DOI: 10.1021/jm500324g.

[3] Marquez, V. E.; Sharma, R.; Wang, S.; Lewin, N. E.; Blumberg, P. M.; Kim, I.; Lee, J. Conformationally Constrained Analogues of Diacylglycerol (DAG). 14. Dissection of the Roles of the sn-1 and sn-2 Carbonyls in DAG Mimetics by Isopharmacophore Replacement. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1757–1762. DOI: 10.1016/S0960-894X(98)00307-2.

[4] (a) Larock, R. C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; Wiley-VCH: Weinheim, 1997. (b) Horning, J. E. C. *In Synthetic Organic Chemistry*; Vol. 3; Wagner, R. B.; Zokk, H. D., Eds.; Wiley: New York, 1953.(c) Sandler, S. R.; Karo, W. *Organic Functional Group Preparations;* 2nd ed., Vol. 1; Academic Press: New York, 1983.

[5] (a) Kabalka, G. W.; Varma, M.; Varma, R. S.; Srivastava, P. C.; Knapp, F. F. The Tosylation of Alcohols. *J. Org. Chem.* **1986**, *51*, 2386–2388. DOI: 10.1021/jo00362a044. (b) Cragg, P. J. *A Practical Guide to Supramolecular Chemistry*; Wiley: Chichester, 2005.

[6] (a) Pauff, S. M.; Miller, S. C. Synthesis of near-IR Fluorescent Oxazine Dyes with Esterase-Labile Sulfonate Esters. *Org. Lett.* **2011**, *13*, 6196–6199. DOI: 10.1021/ol202619f. (b) Pauff, S. M.; Miller, S. C. A Trifluoroacetic Acid-Labile Sulfonate Protecting Group and Its Use in the Synthesis of a Near-IR Fluorophore. *J. Org. Chem.* **2013**, *78*, 711–716. DOI: 10.1021/jo302065u.

[7] Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. Analysis of the Reactions Used for the Preparation of Drug Candidate Molecules. *Org. Biomol. Chem.* **2006**, *4*, 2337–2347. DOI: 10.1039/b602413k.

[8] Dado, G. P.; Knaggs, E. A.; Nepras, M. J. *Kirk-Othmer Encyclopedia of Chemical Technology*; New York: John Wiley & Sons, Inc., 2000, DOI: 10.1002/0471238961.1921120611140107.a01.pub2.

[9] Roberts, D. W. Optimisation of the Linear Alkyl Benzene Sulfonation Process for Surfactant Manufacture. *Org. Process Res. Dev.* **2003**, *7*, 172–184. DOI: 10.1021/op020088w.

[10] (a) Zhang, M.; Moore, J. D.; Flynn, D. L.; Hanson, P. R. Development of High-Load, Soluble Oligomeric Sulfonate Esters via ROM Polymerization: application to the Benzylation of Amines. *Org. Lett.* **2004**, *6*, 2657–2660. DOI: 10.1021/ol049209y. (b) Mori, H.; Kudo, E.; Saito, Y.; Onuma, A.; Morishima, M. RAFT Polymerization of Vinyl Sulfonate Esters for the Controlled Synthesis of Poly(Lithium Vinyl Sulfonate) and Sulfonated Block Copolymers. *Macromolecules* **2010**, *43*, 7021–7028. DOI: 10.1021/ma100905w.

[11] (a) Li, F.; Liu, T.-X.; Wang, G.-W. Synthesis of [60]Fullerene-Fused Sultones via Sulfonic Acid Group-Directed C-H Bond Activation. *Org. Lett.* **2012**, *14*, 2176–2179. DOI: 10.1021/ol3007452. (b) DeBergh, J. R.; Niljianskul, N.; Buchwald, S. L. Synthesis of Aryl Sulfonamides via Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids. *J. Am.*

Chem. Soc. **2013**, *135*, 10638–10641. DOI: 10.1021/ja405949a.(c) Avitabile, B. G.; Smith, C. A.; Judd, D. B. Pentafluorophenyl Sulfonate Ester as a Protecting Group for the Preparation of Biaryl- and Heterobiaryl Sulfonate Esters. *Org. Lett.* **2005**, *7*, 843–846. DOI: 10.1021/ol047422o.(d) Elder, D.; Facchine, K. L.; Levy, J. N.; Parsons, R.; Ridge, D.; Semo, L.; Teasdale, A. An Approach to Control Strategies for Sulfonate Ester Formation in Pharmaceutical Manufacturing Based on Recent Scientific Understanding. *Org. Process Res. Dev.* **2012**, *16*, 1707–1710. DOI: 10.1021/op300216x.

[12] (a) Betts, L. M.; Tam, N. C.; Kabir, S. M. H.; Langler, R. F.; Crandall, I. Ether Aryl Sulfonic Acid Esters with Improved Antimalarial/Anticancer Activities. *Aust. J. Chem.* **2006**, *59*, 277–282. DOI: 10.1071/CH04299. (b) Maddaluno, J.; Durandetti, M. Dimerization of Aryl Sulfonates by in Situ Generated Nickel(0). *Synlett* **2015**, *26*, 2385–2388. – DOI: 10.1055/s-0035-1560712.

[13] (a) Suarez, L.; Diez, M. A.; Garcia, R.; Riera, F. A. Membrane Technology for the Recovery of Detergent Compounds: A Review. *J. Ind. Eng. Chem* **2012**, *18*, 1859–1873. DOI: 10.1016/j.jiec.2012.05.015. (b) Lu, J. R.; Thomas, R. K.; Penfold, J. Surfactant Layers at the Air/Water Interface: structure and Composition. *Adv. Colloid Interface Sci.* **2000**, *84*, 143–304. DOI: 10.1016/S0001-8686(99)00019-6.

[14] (a) Nguyen, H. N.; Huang, X.; Buchwald, S. L. The First General Palladium Catalyst for the Suzuki-Miyaura and Carbonyl Enolate Coupling of Aryl Arenesulfonates. *J. Am. Chem. Soc.* **2003**, *125*, 11818–11819. DOI: 10.1021/ja036947t. (b) Tang, Z.; Hu, Q. Room-Temperature Ni0-Catalyzed Cross-Coupling Reactions of Aryl Arenesulfonates with Arylboronic Acids. *J. Am. Chem. Soc.* **2004**, *126*, 3058–3059. DOI: 10.1021/ja038752r.(c) Yeung, P. Y.; So, C. M.; Lau, C. P.; Kwong, F. Y. A Mild and Efficient Palladium-Catalyzed Cyanation of Aryl Mesylates in Water or tBuOH/Water. *Angew. Chem* **2010**, *122*, 9102–9106. DOI: 10.1002/ange.201005121.(d) Gooßen, L. J.; Rodríguez, Nuria.; Lange, Paul P.; Linder, Christophe. Decarboxylative Cross-Coupling of Aryl Tosylates with Aromatic Carboxylate Salts. *Angew. Chem. Int. Ed. Engl.* **2010**, *49*, 1111–1114. DOI: 10.1002/anie.200905953.

[15] (a) Cho, C. H.; Yun, H. S.; Park, K. Nickel 0-Catalyzed Cross-Coupling of Alkyl Arenesulfonates with Aryl Grignard Reagents. *J. Org. Chem.* **2003**, *68*, 3017–3025. DOI: 10.1021/jo026449n. (b) Cai, C.; Rivera, N. R.; Balsells, J.; Sidler, R. R.; McWilliams, J. C.; Shultz, C. S.; Sun, Y. An Efficient Catalyst for Pd-Catalyzed Carbonylation of Aryl Arenesulfonates. *Org. Lett.* **2006**, *8*, 5161–5164. DOI: 10.1021/ol062208g.(c) Miller, S. C. Profiling Sulfonate Ester Stability: identification of Complementary Protecting Groups for Sulfonates. *J. Org. Chem.* **2010**, *75*, 4632–4635. DOI: 10.1021/jo1007338.

[16] Stang, P. J. Alkynyl Carboxylate, Phosphate, and Sulfonate Esters. *Acc. Chem. Res.* **1991**, *24*, 304–310. DOI: 10.1021/ar00010a004.

[17] Elder, D. P.; Delaney, E.; Teasdale, A.; Eyley, S.; Reif, V. D.; Jacq, K.; Facchine, K. L.; Oestrich, R. S.; Sandra, P.; David, F. The Utility of Sulfonate Salts in Drug Development. *J. Pharm. Sci.* **2010**, *99*, 2948–2961. DOI: 10.1002/jps.22058.

[18] (a) Wang, P.; Min, J.; Nwachukwu, J. C.; Cavett, V.; Carlson, K. E.; Guo, P.; Zhu, M.; Zheng, Y.; Dong, C.; Katzenellenbogen, J. A.; et al. Identification and Structure-Activity Relationships of a Novel Series of Estrogen Receptor Ligands Based on 7-Thiabicyclo[2.2.1]Hept-2-Ene-7-Oxide. *J. Med. Chem.* **2012**, *55*, 2324–2341. DOI: 10.1021/jm201556r. (b) Zhou, H.; Comninos, J. S.; Stossi, F.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. Synthesis and Evaluation of Estrogen Receptor Ligands with Bridged Oxabicyclic Cores Containing a Diarylethylene Motif: estrogen Antagonists of Unusual Structure. *J. Med. Chem.* **2005**, *48*, 7261–7274. DOI: 10.1021/jm0506773.

[19] Stang, P. J.; Treptow, W. L. Synthesis and Antitumor Activity of Simple Vinyl and Alpha-Methylene-Gamma-Butyrolactone Sulfonate Esters and Silyl Enol Ethers. *J. Med. Chem.* **1981**, *24*, 468–472. DOI: 10.1021/jm00136a019.

[20] Tondi, D.; Venturelli, A.; Ferrari, S.; Ghelli, S.; Costi, M. P. Improving Specificity vs Bacterial Thymidylate Synthases through N-Dansyl Modulation of Didansyltyrosine. *J. Med. Chem.* **2005**, *48*, 913–916. – DOI: 10.1021/jm0491445.

[21] Cyr, L.; Langler, R. F.; Crandall, I.; Lavigne, C. Antiproliferative Effects of a Series of Novel Synthetic Sulfonate Esters on Human Breast Cancer Cell Line MCF-7. *Anticancer Res* **2007**, *27*, 1437–1448.

[22] Hoyle, J. In *The Chemistry of Sulphonic Acids, Esters and Their Derivatives*; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester. 1991, pp 351–399

[23] Tamaddon, F.; Nasiri, A.; Farokhi, S. CsF–Celite as an Efficient Heterogeneous Catalyst for Sulfonylation and Desulfonylation of Heteroatoms. *Catal. Commun.* **2011**, *12*, 1477–1482. DOI: 10.1016/j.catcom.2011.04.005.

[24] (a) Huang, J.; Widlanski, T. S. Facile Synthesis of Sulfonyl Chlorides. *Tetrahedron Lett.* **1992**, *33*, 2657–2660. DOI: 10.1016/S0040-4039(00)79050-2. (b) Choe, Y. S.; Katzenellenbogen, J. A. Tetrabutylammonium Fluoride-Induced Conversion of Tresylates to Mesylates. *Tetrahedron Lett* **1993**, *34*, 1579–1580. DOI: 10.1016/0040-4039(93)85011-K. (c) Heiner, T.; Kozhushkov, S. I.; Noltemeyer, M.; Haumann, T.; Boese, R.; de Meijere, A. Intramolecular Diels-Alder Reactions of Furans with a Merely Strain-Activated Tetrasubstituted Alkene: Bicyclopropylidene. *Tetrahedron* **1996**, *52*, 12185–12196. DOI: 10.1016/0040-4020(96)00720-X.

[25] Dufresne, C.; Gallant, M.; Gareau, Y.; Ruel, R.; Trimble, L.; Labelle, M. Synthesis of Montelukast (MK-0476) Metabolic Oxidation Products. *J. Org. Chem.* **1996**, *61*, 8518–8525. DOI: 10.1021/jo9615817.

[26] Wang, Y.; Deng, L.; Deng, Y.; Han, J. Copper-Catalyzed Multicomponent Reaction of DABCO·(SO2)2, Alcohols, and Aryl Diazoniums for the Synthesis of Sulfonic Esters. *J. Org. Chem.* **2018**, *83*, 4674–4680. DOI: 10.1021/acs.joc.8b00447.

[27] Padmapriya, A. A.; Just, G.; Lewis, N. G. A New Method for the Esterification of Sulphonic Acids. *Synth. Commun.* **1985**, *15*, 1057–1062. DOI: 10.1080/00397918508076842.

[28] (a) Al-Horani, R. A.; Desai, U. R. Chemical Sulfation of Small Molecules – Advances and Challenges. *Tetrahedron* **2010**, *66*, 2907–2918. DOI: 10.1016/j.tet.2010.02.015. (b) Kelly, D. Sulfur Trioxide-Amine Adducts. *Synlett* **2003**, *14*, 2263–2264. DOI: 10.1055/s-2003-42110.

[29] Bahrami, K.; Khodaei, M. M.; Abbasi, J. Synthesis of Sulfonamides and Sulfonic Esters via Reaction of Amines and Phenols with Thiols Using H2O2–POCl3 System. *Tetrahedron* **2012**, *68*, 5095–5101. DOI: 10.1016/j.tet.2012.04.040.

[30] Hong, X.; Tan, Q.; Liu, B.; Xu, B. Isocyanide-Induced Activation of Copper Sulfate: Direct Access to Functionalized Heteroarene Sulfonic Esters. *Angew. Chem. Int. Ed. Engl.* **2017**, *56*, 3961–3965. DOI: 10.1002/anie.201612565.

[31] Tribby, A. L.; Rodríguez, I.; Shariffudin, S.; Ball, N. D. Pd-Catalyzed Conversion of Aryl Iodides to Sulfonyl Fluorides Using SO_2 Surrogate DABSO and Selectfluor. *J. Org. Chem.* **2017**, *82*, 2294–2299. DOI: 10.1021/acs.joc.7b00051.

[32] Singh, A. K.; Yi, H.; Zhang, G.; Bian, C.; Pei, P.; Lei, A. Photoinduced Oxidative Cross-Coupling for O–S Bond Formation: A Facile Synthesis of Alkyl Benzenesulfonates. *Synlett* **2017**, *28*, 1558–1563. DOI: 10.1055/s-0036-1588728.

[33] Vignola, N.; Dahmen, S.; Enders, D.; Brase, S. Efficient Synthesis of Sulfonic, Phosphoric, and Phosphinic Esters Employing Alkylating Polymer-Bound Reagents. *J. Comb. Chem.* **2003**, *5*, 138–144. DOI: 10.1021/cc0200787.

[34] Gao, J.; Pan, X.; Liu, J.; Lai, J.; Chang, L.; Yuan, G. Iodine-Induced Synthesis of Sulfonate Esters from Sodium Sulfinates and Phenols under Mild Conditions. *RSC Adv.* **2015**, *5*, 27439–27442. DOI: 10.1039/C5RA00724K.

[35] Meshram, G. A.; Patil, V. D. A Simple and Efficient Method for Sulfonylation of Amines, Alcohols and Phenols with Cupric Oxide under Mild Conditions. *Tetrahedron Lett.* **2009**, *50*, 1117–1121. DOI: 10.1016/j.tetlet.2008.12.085.

[36] (a) Martinelli, MichaelJ.; Vaidyanathan, Rajappa.; Pawlak, JosephM.; Nayyar, NareshK.; Dhokte, UlhasP.; Doecke, ChristopherW.; Zollars, LisaMH.; Moher, EricD.; Khau, VienVan.; Košmrlj, Berta. Catalytic Regioselective Sulfonylation of α-Chelatable Alcohols: Scope and Mechanistic Insight. *J. Am. Chem. Soc.* **2002**, *124*, 3578–3585. DOI: 10.1021/ja016031r. (b) Martinelli, M. J.; Nayyar, N. K.; Moher, E. D.; Dhokte, U. P.; Pawlak, J. M.;

Vaidyanathan, R. Dibutyltin Oxide Catalyzed Selective Sulfonylation of α-Chelatable Primary Alcohols. *Org. Lett.* **1999**, *1*, 447–450. DOI: 10.1021/ol990658l.(c) Yuasa, K.; Enomoto, K.; Maekawa, Y.; Kato, J.; Yamashita, T.; Yoshida, M. Electron-Beam-Induced Fries Rearrangement and Oxidation Reactions of Sulfonic Acid Esters in Crystalline State. *J. Photopol. Sci. Technol.* **2004**, *17*, 21–27. DOI: 10.2494/photopolymer.17.21.(d) Quan, Z.; Jing, F.; Zhang, Z.; Da, Y.; Wang, X. Cross-Coupling Reactions of Pyrimidin-2-yl Sulfonates with Phenols and Anilines: An Efficient Approach to C2-Functionalized Pyrimidines. *Chin. J. Chem.* **2013**, *31*, 1495–1502. DOI: 10.1002/cjoc.201300536.

[37] Song, G.; Cai, Y.; Peng, Y. Amino-Functionalized Ionic Liquid as a Nucleophilic Scavenger in Solution Phase Combinatorial Synthesis. *J. Comb. Chem.* **2005**, *7*, 561–566. DOI: 10.1021/cc049844v.

[38] (a) Oliverio, M.; Costanzo, P.; Paonessa, R.; Nardi, M.; Procopio, A. Catalyst-Free Tosylation of Lipophilic Alcohols in Water. *RSC Adv.* **2013**, *3*, 2548–2550. DOI: 10.1039/c2ra23067d. (b) Lakrout, Salah.; K'tir, Hacène.; Amira, Aïcha.; Berredjem, Malika.; Aouf, Nour-Eddine. A Simple and Eco-Sustainable Method for the Sulfonylation of Amines under Microwave-Assisted Solvent-Free Conditions. *RSC Adv.* **2014**, *4*, 16027–16032. DOI: 10.1039/C4RA01346H.(c) Zhao, N.; Li, Y.; Wang, Y.; Wang, J. A Facile and Efficient Synthesis of Aryl Toluenesulfonhydrazides and Aryl Toluenesulfonates under Solvent-Free Conditions. *J. Sulfur. Chem.* **2006**, *27*, 427–432. DOI: 10.1080/17415990600863752.(d) Xu, L.; Xia, C. Solvent-Free Synthesis of Aryl Tosylates under Microwave Activation. *Syn. Commun* **2004**, *34*, 1199–1205. DOI: 10.1081/SCC-120030306.

[39] Carr, M. H.; Brown, H. P. p-Alkoxybenzenesulfonic Acid Esters. *J. Am. Chem. Soc.* **1947**, *69*, 1170–1172. DOI: 10.1021/ja01197a052.

[40] Kametani, T.; Takahashi, K.; Ogasawara, K. A Novel Methylsulfonation of Hydroxy or Alkoxy Aromatics with Methyl Fluorosulfonate. *Synthesis* **1972**, *1972*, 473–474. DOI: 10.1055/s-1972-21901.

[41] Jackman, L. M.; Lange, B. C. Methylation of Lithioisobutyrophenone in Weakly Polar Aprotic Solvents. The Effect of Aggregation. *J. Am. Chem. Soc.* **1981**, *103*, 4494–4499. DOI: 10.1021/ja00405a034.

[42] Brinchi, L.; Profio, P. D.; Germani, R.; Savelli, G.; Spreti, N.; Bunton, C. A. The Hammett Equation and Micellar Effects on SN2 Reactions of Methyl Benzenesulfonates ?ms the Role of Micellar Polarity. *Eur. J. Org. Chem.* **2000**, *2000*, 3849–3854. DOI: 10.1002/1099-0690(200012)2000:23<3849::AID-EJOC3849>3.0.CO;2-P.

[43] Ninomiya, S. H. I. N. I. C. H. I.; Kohda, K. O. H. F. U. K. U.; Kawazoe, Y. U. T. A. K. A. Studies on Chemical Carcinogens and Mutagens. XXV. Chemoselectivity of Alkyl Sulfonates toward 4-(p-Nitrobenzyl)Pyridine (NBP) in Phosphate Buffer. *Chem. Pharm. Bull.* **1984**, *32*, 1326–1332. DOI: 10.1248/cpb.32.1326.