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A Versatile Reagent and Method for Direct Aliphatic Sulfonylation

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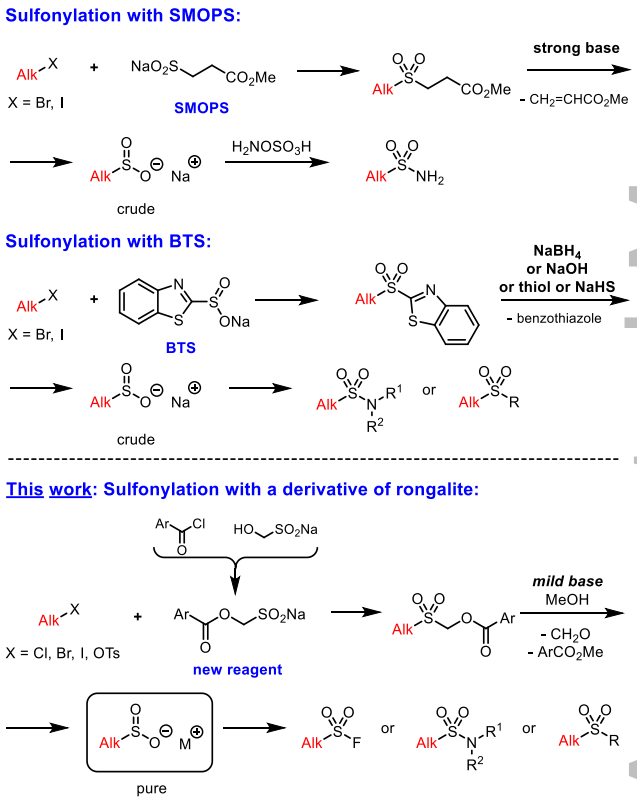
Abstract. An efficient methodology has been developed for the two-step synthesis of aliphatic sulfinate salts, sulfonamides, sulfonyl fluorides, and unsymmetrical sulfones on the basis of alkylation of a new versatile sulfonylating reagent. The new reagent is easily accessible; the developed protocols are conducted under mild conditions and have a broad substrate scope.

Keywords: alkyl halide; potassium sulfinate; zinc sulfinate; sulfone; sulfonamide; sulfonyl fluoride

Compounds bearing the sulfonyl structural motif have found numerous applications in the areas of pharmaceutical,[1a-c] agrochemical,[1d-e] and material sciences.[1f-g] For example, in the pharmaceutical field sulfones and sulfonamides have become established classes of compounds that exhibit various biological activities, desirable physico-chemical properties, and metabolic stability due to the intrinsic three-dimensional and electronic features of the sulfonyl moiety.[2] Furthermore, there has been substantial interest in sulfonyl fluorides as biological probes[3a,b] or as stable and more selective alternatives to sulfonyl chlorides in organic synthesis.[3c] Among recent applications of sulfinate salts,[4a] it is noteworthy to mention their use in carbon-carbon bond formation via desulfinative couplings based on Pd-catalyzed,[4b-d] oxidative,[4e-f] or photocatalytic processes,[4g-h] for biocompatible chemoselective ligation,[4i-j] and their emerging role as biological probes.[4k] Consequently, the development of efficient and versatile methodologies for the synthesis of sulfonyl-containing compounds continues to be of high interest to the scientific community.[5a]

Besides the classical synthetic approaches to this class of products, involving harsh oxidative and chlorination conditions[5b] and recent sulfinate syntheses via oxidation of heterocyclic sulfides,[5c-e] in the last decade significant efforts have been made to advance direct sulfonylation methodologies.[6a] In this approach, sulfur in higher oxidation states is incorporated by reactions with either the molecule of SO_2 or its surrogates,[6b] e.g. DABSO[6c-g] and $K_2S_2O_5$,[6h-j] or by using synthetic equivalents of SO_2^{2-} anion for *aliphatic* sulfonylation of alkyl halides (Scheme 1): sodium 3-methoxy-3-oxopropane-1-sulfinate (SMOPS),[7a] sodium salt of 2-sulfinyl benzothiazole (BTS),[8a] and rongalite (not shown).[9]

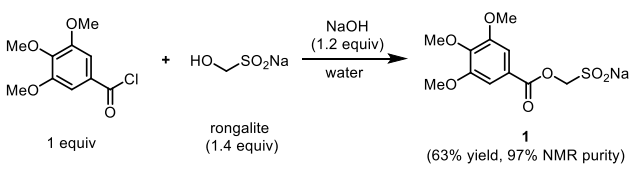


Scheme 1. Sulfonylating Methods Based on Synthetic Equivalents of SO_2^{2-} Anion.

Despite their convenience, the last three methods also carry substantial disadvantages. In particular, the substrate scope of the SMOPS-based method has been rather limited and its use has not been reported for sulfonylation of alkyl tosylates/mesylates and unactivated chlorides or secondary halides. Its utility

for the synthesis of aliphatic secondary and tertiary sulfonamides, sulfonyl fluorides, and dialkyl sulfones also has not been demonstrated. In addition, to promote release of the sulfinate salt, strongly basic anhydrous conditions are required, which can be detrimental for base-sensitive molecules. Other factors that may lead towards limited application of SMOPS could be its high cost[7b] and environmental/safety concerns for its preparation.[7c] The BTS-based method[8a] employs reductive or strongly basic/nucleophilic conditions for the intermediate cleavage and is not suitable for sensitive molecules; four-fold excess of BTS is applied, sulfonamides are obtained only in moderate yields, and sulfonyl fluoride synthesis has not been demonstrated. The reagent BTS also requires a two-step synthesis involving chromatography and has to be stored at -20 °C.[8b] In the method based on alkylation of rongalite,[9] the inherent instability of rongalite in the reaction medium (DMSO) and lability of the hydroxymethyl sulfone intermediate lead to a rather narrow substrate scope and moderate yields (and low yields for *activated* alkyl halides), due to a side-reaction forming undesirable symmetrical sulfones. Besides, the rongalite procedure requires high dilution in DMSO, which is not practical for scale-up syntheses. Importantly for all three described methods, isolation of pure, free from inorganic contaminants sulfinate salts has not been demonstrated. With all the above considerations in mind, a mild, convenient, high-yielding, and versatile method to generate sulfinate salts *in pure form* remains a desirable yet so far not readily attainable goal.

With the strategic objective of developing a more general, practical, readily accessible sulfonylating reagent and in the search for more effective SO_2^{2-} anion equivalents with improved stability and reactivity (Scheme 1), we discovered that the hydroxyl group of rongalite can be selectively protected by reacting with some electrophiles [see Supporting Information (SI) for the list of explored electrophiles]. Notably, the sulfinate group remains available for a subsequent derivatization. After optimizing the *O*-protecting group for rongalite, reagent **1** was selected for further methodology development based on the efficiency of its synthesis and yields of its *S*-alkylation (Scheme 2).[10a]

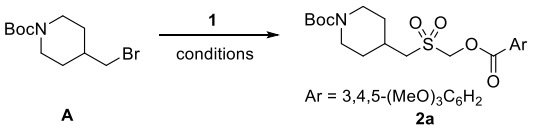


Scheme 2. Synthesis of Sulfonylation Reagent **1**.

Compound **1** was synthesized as shelf-stable,[10b] safe,[10c] non-hydroscopic, free-flowing solid in one simple step without chromatography on a 20 g scale from 3,4,5-trimethoxybenzoyl chloride in qNMR purity of 97%. As confirmation of molecular connectivity, its structure was validated by single crystal X-ray diffraction analysis (see SI).[10d] We envisioned that after alkylation of the sulfinate group of substance **1,** the obtained sulfone intermediate could be cleaved in *mild* basic conditions by nucleophilic attack at the carbonyl group with subsequent elimination of a benzoate byproduct and formaldehyde, to release the desired sulfinate salt (Scheme 1) for further transformations.

The optimization of the alkylation step began with the best conditions for alkylation of unprotected rongalite identified in our previous work.[9] Thus, alkyl bromide **A** was reacted with **1** in DMSO in the presence of catalytic TBAB and 1.2 equiv of DIPEA at 23 °C, which gave a mixture of the desired sulfone intermediate **2a** and the side-product of *O*-alkylation (sulfinate ester) in combined 27% NMR yield (Table 1, entry 1).

Table 1. Summary of Optimization for Alkylation of Reagent **1**[a]



A **2a**

entry	conditions	sulfone/sulfinate ester (%)[b]
1	DMSO, DIPEA, 23 °C, 44 h	24/3
2	DMSO, DIPEA, 50 °C	59/13
3	NMP, DIPEA, 50 °C	25/8
4	DMF, DIPEA, 50 °C	29/7
5	DMA, DIPEA, 50 °C	35/11
6	MeCN or MeOH, DIPEA, 50 °C	0/0
7	DMA, DIPEA, 80 °C,	55/20
8	DMA, 80 °C	40/0
9	DMA, **1** (1.5 equiv.), 80 °C	**68/0 (60/0)**[c]
10	DMA, **1** (1.8 equiv.), 80 °C	69/0

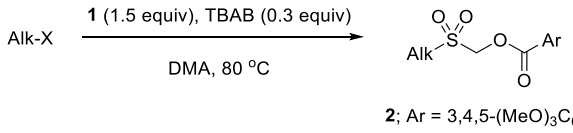
[a] Reaction conditions: alkyl bromide **A** (0.5 mmol), reagent **1** (1.2 equiv.), TBAB (0.3 equiv.), solvent (1.2 mL), 16 h.
[b] NMR yields.
[c] Isolated yield.

Conducting this reaction at 50 °C increased the yields of both products (entry 2). Using other solvents led to diminished yields (entries 3-6). Interestingly, for DMA, increasing the reaction temperature to 80 °C improved the sulfone yield from 35% to 55% (entry 7) and omitting DIPEA eliminated the sulfinate ester as a detectable product (entry 8), which was an important finding as this impurity was very difficult to separate by chromatography. Finally, increasing the amount of reagent **1** from 1.2 to 1.5 equiv. in the

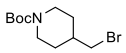
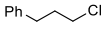
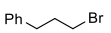
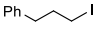
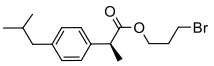
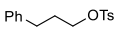
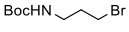
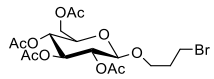
10.1002/adsc.201800071

absence of DIPEA resulted in 60% isolated yield without formation of the sulfinate ester side-product (entry 9) but no additional positive effect was achieved with a larger excess of **1** (entry 10).

Table 2. Representative Examples of Alkyl Electrophiles[a]



2; Ar = 3,4,5-$(MeO)_3C_6H_2$

entry	Alk-X	2	yield (%)[b]	entry	Alk-X	2	yield (%)[b]
1		**2a**	60	9		**2e**	87
2		**2b**	74	10		**2e**	93
3		**2b**	80	11		**2f**	75
4		**2b**	84	12			
5		**2b**	71	Sulfone product: **2g**; 67%			
6		**2c**	62	13			
7		**2d**	46	Sulfone product: **2h**; 77%			
8		**2d**	45				

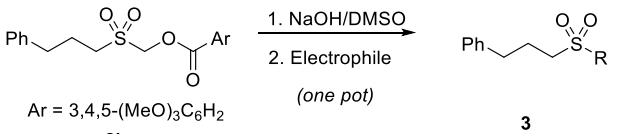
[a] Conditions: alkyl electrophile (0.35 mmol), **1** (1.5 equiv.), TBAB (0.3 equiv.), DMA (1.2 mL), 80 °C, 20 h.
[b] Isolated yield.

With the optimized conditions for alkylation of **1** identified, the scope of alkyl electrophiles was explored (Table 2). Both primary (entries 1-6, 9-10, 12-13) and secondary halides (entries 7, 8, 11) were competent substrates in this reaction. A broad range of activated and unactivated chlorides, bromides, iodides, tosylates gave good yields of the desired sulfone intermediates. Carbamate (entries 1, 6) and ester groups (entries 12, 13) were well tolerated. Importantly, no epimerization was observed at potentially epimerizable chiral centers (entries 12, 13). Products **2b** and **2e** were also scaled-up and isolated by crystallization (see SI).

Next, we developed a one-pot procedure[11] to cleave the sulfone intermediate **2b** with NaOH and capture the released sulfinate salt with various electrophiles (Table 3). Primary bromides (entries 1), primary and secondary iodides (entries 2, 4), tosylates (entry 3), and activated chlorides (entry 5) were found to be suitable for the second alkylation in the synthesis of unsymmetrical dialkylsulfones. Notably, electrophilic amination of the intermediate sulfinate with hydroxylamine-*O*-sulfonic acid led to the primary sulfonamide **3d** (entry 6).[7a, 9] It should be noted that a milder cleavage method with DIPEA/MeOH (*vide infra*) could also be used, in conjunction with solvent switch from MeOH to DMSO for reaction with the second electrophile.

With the aim of developing an expedient synthesis of aliphatic sulfonyl fluorides, the compatibility of the new sulfonylation with subsequent fluorination of the released sulfinate was investigated. In line with this goal, the sulfinic acid produced by NaOH-induced cleavage of the sulfone intermediate **2a**, readily reacted with *N*-fluorobenzenesulfonimide (NFSI), furnishing the desired sulfonyl fluoride in good yield (Table 4, entry 1). Other functionalized alkyl sulfonyl fluorides were synthesized in the same manner demonstrating generality of this protocol (Table 4).

Table 3. Representative Examples of One-Pot Synthesis of Dialkylsulfones[a]

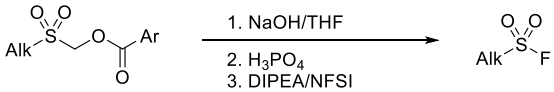


Ar = 3,4,5-$(MeO)_3C_6H_2$ **2b** **3**

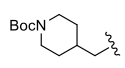
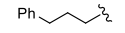
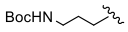
entry	electrophile	3	yield (%)[b]	entry	electrophile	3	yield (%)[b]
1		**3a**	81	4		**3b**	62
2		**3a**	88	5		**3c**	78[c]
3		**3a**	69	6	H_2NOSO_3H	**3d**	74[d]

[a] Reaction conditions: 1) **2b**, NaOH/DMSO/H_2O, 35 °C; 2) electrophile (2 equiv.), 50 °C, 18 h.
[b] Isolated yield.
[c] Step 2: electrophile (1.3 equiv.), 23 °C.
[d] Synthesis of primary sulfonamide. Step 2: H_2NOSO_3H (4 equiv.), AcONa (7 equiv.), 23 °C.

Table 4. Representative Examples of Expedient Synthesis of Sulfonyl Fluorides[a]



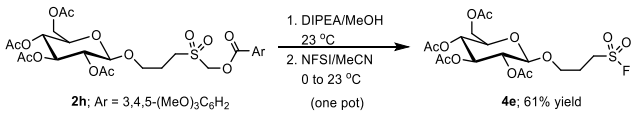
2; Ar = 3,4,5-$(MeO)_3C_6H_2$ **4**

entry	Alk	4	yield (%)[b]	entry	Alk	4	yield (%)[b]
1		**4a**	67	3		**4c**	64
2		**4b**	73	4		**4d**	81

[a] Reaction conditions: 1) **2** NaOH/THF/H_2O, 23 °C; 2) H_3PO_4 (2 equiv.); 3) DIPEA (2.0 equiv.), NFSI (2 equiv.), 0 to 23 °C, 1 h.
[b] Isolated yield.

For base-sensitive substrates a milder method for the cleavage of the sulfone intermediate was

developed. For example, by treating glycoside **2h** with a methanolic solution of DIPEA, the sulfinate protection was removed as a methyl benzoate ester to release the desired sulfinate salt. Next, a one-pot reaction with NFSI provided the target sulfonyl fluoride **4e** (Scheme 3). This sequence highlights the advantages of the new methodology, which allowed obtaining a labile product not accessible via previously available protocols.

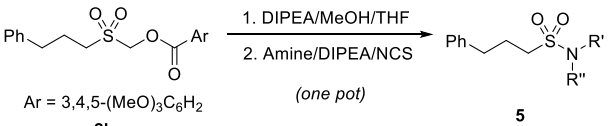


2h; Ar = 3,4,5-$(MeO)_3C_6H_2$ **4e**; 61% yield

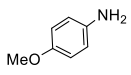
Scheme 3. One-Pot Synthesis of Sulfonyl Fluoride Derivative of a Base- and Acid-Sensitive Glycoside.

The same mild method of the intermediate cleavage was applied for the synthesis of aliphatic sulfonamides. Using the optimized conditions, the cleavage of **2b** was conducted in MeOH/THF at 50 °C, followed by solvent evaporation. The crude sulfinate was mixed with THF, the starting amine, and DIPEA. Subsequent addition of NCS produced desired sulfonamides in an efficient one-pot procedure (Table 5). Both primary and secondary amines furnished the desired sulfonamide products. Alkene, alkyne (entries 3-4), and hydroxyl functionalities (entry 5) were well tolerated providing possibilities for subsequent synthetic elaboration or bioorthogonal conjugation of the sulfonamide products. β-Aminoester (entry 6), hindered (entry 7), and aromatic amines (entry 8) similarly produced the target sulfonamides in useful yields.

Table 5. Representative Examples of One-Pot Synthesis of Sulfonamides[a]



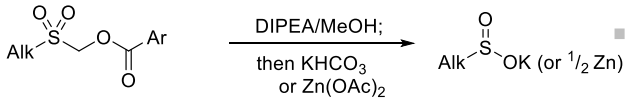
Ar = 3,4,5-$(MeO)_3C_6H_2$ **2b** **5**

entry	amine	5	yield (%)[b]	entry	amine	5	yield (%)[b]
1		**5a**	75	6		**5f**	50
2	$BnNH_2$	**5b**	79				
3		**5c**	84	7		**5g**	80
4		**5d**	69				
5		**5e**	64	8		**5h**	48

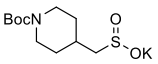
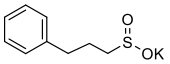
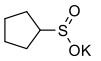
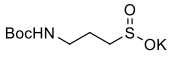
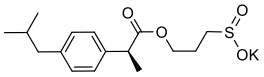
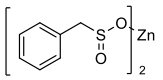
[a] Reaction conditions: 1) **2b** (0.25 mmol), DIPEA, MeOH, THF, 50 °C, 4 h; 2) amine (2 equiv.), NCS (1.0 equiv.), DIPEA (2.0 equiv.), THF, 0 to 23 °C, 1 h.
[b] Isolated yield.

Finally, due to their growing importance as alkyl radical sources[4e-h] and emerging role in biological applications,[4i-k] the synthesis of sulfinate salts *in pure form and under mild conditions* was highly desirable. As the result of our work towards this goal, DIPEA salts of alkylsulfinic acids were generated by cleavage of intermediates **2** in methanolic solutions followed by conversion to the corresponding potassium salts by quenching with aqueous $KHCO_3$ (Table 6). After concentration and trituration with MTBE, the target potassium sulfinates were isolated in pure form, free from the methyl benzoate byproduct.

Table 6. Synthesis of Alkylsulfinate Salts[a]



2; Ar = 3,4,5-$(MeO)_3C_6H_2$ **6**

entry	sulfinate **6**	ID	yield (%)[c]
1[a]		**6a**	78
2[a]		**6b**	70
3[a]		**6c**	84
4[a]		**6d**	73
5[a]		**6e**	70[d]
6[b]		**6f**	81

[a] Reaction conditions: **2**, DIPEA, MeOH at 50 °C; then aq. $KHCO_3$ at 23 °C.
[b] Reaction conditions: **2e**, DIPEA, $Zn(OAc)_2$, MeOH, THF, 50 °C.
[c] Isolated yield.
[d] qNMR purity: 96%; *er* > 99:1.

As depicted in Table 6, both acid- (entries 1, 4), and base-sensitive (entry 5) groups were tolerated, which would be difficult to achieve with the existing methods of sulfinate synthesis. Moreover, compound **6e** retained complete integrity of the chiral center (see SI), while ibuprofen esters are known to be readily racemized in basic media.[12] Its high qNMR purity of 96% and unaffected enantiomeric purity, relative to the starting ibuprofen, demonstrate the capacity of the developed method in the effective synthesis of alkyl sulfinates *in pure form.* In addition, because of the increasing use of zinc sulfinates as alkyl radical precursors,[4f, h] the efficacy of our methodology for accessing this class of reagents was demonstrated by

the synthesis of known zinc phenylmethanesulfinate **6f** from sulfone intermediate **2e** and zinc acetate (entry 6).

In summary, we have developed a versatile, stable, and low-cost sulfonylating reagent,[10a] as well as the corresponding methodology for the expedient preparation of aliphatic sulfinate salts, sulfones, sulfonamides, and sulfonyl fluorides starting from primary and secondary alkyl halides and tosylates. The developed protocols are performed under mild conditions, not sensitive to air and moisture, and exhibit high functional group tolerance. Compared to the existing methods, alkylsulfinate salts can be isolated in pure form after formation under very mild reaction conditions. We anticipate that the use of the new sulfonylating reagent will increase practical accessibility of diverse alkylsulfonyl products and expand their applications in various fields of science and technology.

Experimental Section

Synthesis of Sulfonylating Reagent 1

Sodium hydroxymethylsulfinate dihydrate (rongalite) (18.50 g, 120 mmol) was dissolved in a solution of NaOH (4.16 g, 104 mmol) in 104 mL of water and the clear solution was kept without stirring at room temperature for 90 min. A 40% solution of NaBr (50 mL) was added and the resulting solution was cooled to +3 °C under stirring. Solid 3,4,5-trimethoxybenzoyl chloride (20.0 g, 86.7 mmol) was added in one portion. The heavy slurry was warmed under stirring to room temperature in 1 h and stirred for 3 more hours (thin slurry formed). Solid NaBr (65 g) was added and the mixture was stirred for 1 h. The solid was filtered off and washed with 40% NaBr (2 x 80 mL) and ethyl acetate (2 x 80 mL), then dried on filter under vacuum suction and then in a vacuum oven at 45 °C for 18 h to obtain the target product as white solid (17.07 g, 63%).

General Procedure for the Alkylation of Reagent 1 - Synthesis of Sulfone Intermediates 2 (Table 2)

In a reaction flask were combined alkyl halide (or tosylate) (1 equiv.), reagent **1** (1.5 equiv.), tetrabutylammonium bromide (0.3 equiv.), and DMA (0.4 M). The solution was stirred at 80 °C for 20 h. The reaction was cooled to room temperature, quenched with half-saturated $NaHCO_3$ (5 mL) and extracted with ethyl acetate (3 x 3 mL). The combined organic extracts were dried over magnesium sulfate, concentrated and the residue was purified by chromatography on a silica gel column, eluting with a gradient of EtOAc in heptane or acetone in heptane.

General Procedure for One-Pot Preparation of Dialkyl Sulfones (Table 3)

To a mixture of **2b** (102 mg, 0.25 mmol) and TBAB (24 mg, 0.075 mmol) in DMSO (0.9 mL) was added aq. 10 M NaOH (0.063 mL, 0.63 mmol) was added followed by stirring at 35 °C for 2 h. Solid $NaHCO_3$ (63 mg, 0.75 mmol) was added and the suspension was stirred at 35 °C for 15 min. At this time, the starting electrophile (1.3-2.0 equiv.) was added and the mixture was stirred for 18 h at 23 °C (for activated electrophiles) or at 50 °C (for unactivated electrophiles). The reaction was partitioned between water (2 mL), brine (2 mL), and EtOAc (2 mL). The aqueous phase was re-extracted with additional EtOAc (2 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and loaded on silica gel. Chromatography on a silica gel column, eluting with a gradient from 0 to 50% of EtOAc in heptane gave the target sulfone product.

Preparation of Primary Sulfonamide 3d (Table 3)

To a mixture of **2b** (102 mg, 0.25 mmol) and THF (1.4 mL) was added 10 M aq. NaOH (0.055 mL, 0.55 mmol). The mixture was stirred at 35 °C for 2 h. The resulting clear solution was added dropwise to a stirred solution of hydroxylamine-*O*-sulfonic acid (85 mg, 0.75 mmol) and sodium acetate (92 mg, 1.12 mmol) in water (4 mL) at +5 °C. The mixture was warmed to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ (3 ml) was added and the mixture was stirred for 15 min, then diluted with brine (5 mL) and extracted with EtOAc (2 x 6 mL). The combined extracts were washed with brine, dried over MgSO4, and concentrated. Chromatography on a silica gel column, eluting with a gradient from 20 to 80% of EtOAc in heptane gave compound **3d** (59 mg, 74%) as white solid.

General Procedure for the Preparation of Alkylsulfonyl Fluorides (Table 4)

A mixture of sulfone intermediate **2** (0.25 mmol) in THF (0.8 mL) was treated with 10 M aq. NaOH (0.10 mL, 1.0 mmol), followed by stirring at 35 °C for 2 h (gradually went from a homogeneous solution to a heterogeneous suspension). At this time 2 M aq. H_3PO_4 (3 mL) and brine (1 mL) were added to the mixture followed by extraction with EtOAc (2 x 3 mL). The combined organic extracts were transferred to a 25 mL round-bottom flask. DIPEA (0.13 mL, 0.75 mmol) was added, the mixture was cooled to 0 °C under nitrogen, and a solution of *N*-fluorobenzenesulfonimide (79 mg, 0.25 mmol) in dry THF (1 mL) was added dropwise. Upon complete addition, the mixture was warmed to ambient temperature and the reaction was stirred for an additional 1 h. Without workup, silica gel (~1g) was added to the reaction mixture and all solvent was evaporated. The dried material was then purified on a silica gel column to give the expected sulfonyl fluoride product.

Preparation of Sulfonyl Fluoride 4e (Scheme 3)

To a solution of intermediate **2h** (90 mg, 0.13 mmol) in MeOH (1.6 mL) DIPEA (0.14 mL, 0.80 mmol) was added and the clear solution was kept at room temperature for 18 h. The starting material was consumed (TLC). The reaction

was concentrated in vacuo, then MeCN (5 mL) was added to the residue and the solution was concentrated (repeated 2 times). The residue was dissolved in dry MeCN (2 mL), the solution was cooled to 0 °C, and a solution of *N*-fluorobenzenesulfonimide (46 mg, 0.146 mmol) in dry THF (0.3 mL) was added dropwise. Upon complete addition, the mixture was warmed to room temperature and stirred for an additional 1 h. Without workup, silica gel (~1g) was added to the reaction mixture and all solvent was evaporated. The dried material was then purified on a silica gel column, eluting with a gradient from 10 to 70% of EtOAc in heptane, to give the target compound as colorless gum (38 mg, 61%).

General Procedure for One-Pot Preparation of Alkyl Sulfonamides (Table 5)

A mixture of sulfone intermediate **2b** (102 mg, 0.25 mmol), MeOH (1 mL), and THF (0.25 mL) was treated with DIPEA (0.180 mL, 1.0 mmol), followed by stirring at 50 °C for 4 h. At this time, the reaction was concentrated and the residue was azeotroped with toluene twice. The flask with the crude residue was flushed with nitrogen, followed by addition of THF (4.5 mL), DIPEA (0.090 mL, 0.50 mmol), and the amine (0.50 mmol). The reaction was cooled to 0 °C and under nitrogen solid *N*-chlorosuccinimide (33 mg, 0.25 mmol) was added in one portion. The mixture was warmed to room temperature and then stirred for 1 h. The byproduct ester was hydrolyzed in the same pot by addition of MeOH (2 mL) and 1 M aq. NaOH (1.5 mL) followed by stirring at ambient temperature for 18 h. The reaction was partitioned between water, brine, and MTBE. The organic phase was separated and the aqueous phase was re-extracted with MTBE. The combined organic extracts were dried over MgSO4, filtered, evaporated, and loaded on silica gel (~1g). Chromatography on a silica gel column, eluting with a gradient from 0 to 40% of EtOAc in heptane gave desired sulfonamide.

General Procedure for the Synthesis of Potassium Alkylsulfinates (Table 6)

The corresponding starting sulfone intermediate **2** (1 equiv.), MeOH (0.2 M), and DIPEA (3 equiv.) were combined in a reaction flask. The initial suspension was stirred at 50 °C for 0.5 to 2 h until starting material is consumed as monitored by TLC; the reaction mixture turned clear solution. The reaction was cooled to room temperature, treated with 1 M aq. $KHCO_3$ (1 equiv.), concentrated, and the residue was azetoroped with toluene to dryness. The crude residue was slurried repeatedly in portions of MTBE to extract methyl 3,4,5-trimethoxybenzoate byproduct. The final residue was dried in vacuo at 35 °C to yield the purified alkyl sulfinate as potassium salt.

Synthesis of Zinc Phenylmethanesulfinate 6f (Table 6)

A mixture of sulfone intermediate **2e** (180 mg, 0.47 mmol, 2 equiv.), zinc acetate (43 mg, 0.24 mmol, 1 equiv.), MeOH (4 mL), THF (1 mL), and DIPEA (0.25 mL, 1.42 mmol, 6 equiv.) was stirred at 50°C for 4 h. The reaction was cooled to room temperature and concentrated in vacuo to dryness. The crude residue was combined with DCM (1 mL) and then MTBE (5 mL) was slowly added under stirring. The suspension was stirred at room temperature for 2 h, then the solid was filtered off and dried in vacuo at 45°C to yield the pure title compound as white solid (72 mg, 81%). Known compound, analytical results are consistent with the literature data (see *Tetrahedron* **2006**, *62*, 4540).

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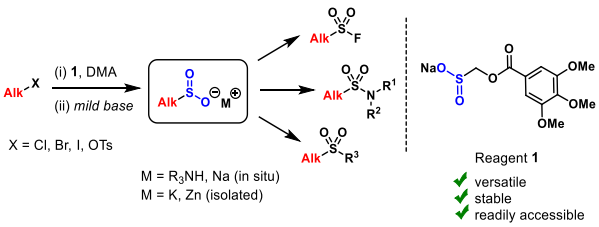
A Versatile Reagent and Method for Direct Aliphatic Sulfonylation



Adv. Synth. Catal. **2018**, *Volume*, Page – Page

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