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N-*p*-Toluenesulfinylimidazole: A New in situ Reagent for the Mild and Efficient Synthesis of *p*-Toluenesulfinate Alkyl Esters and Aryl Esters

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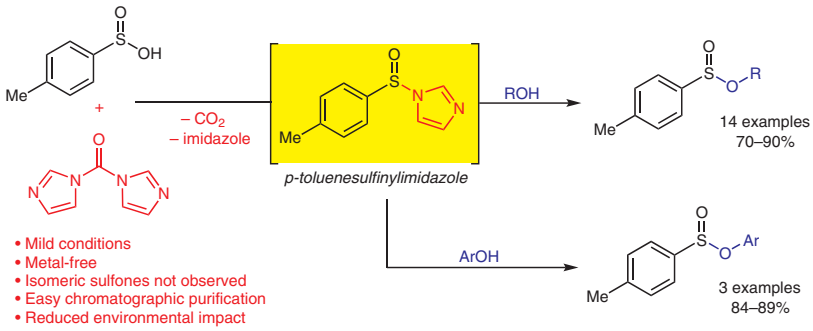

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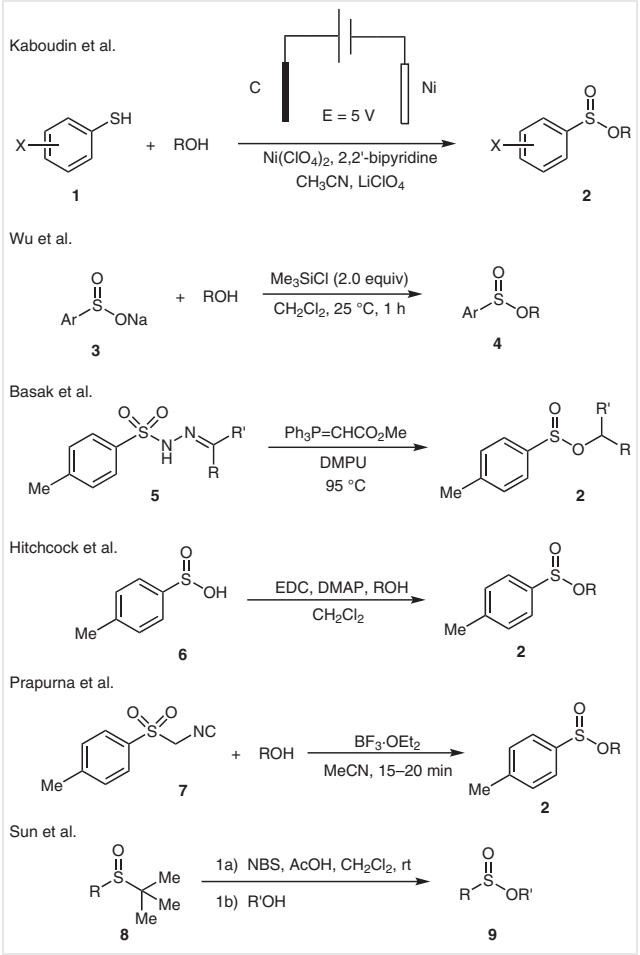
Abstract A new synthetic methodology has been developed for the synthesis of sulfinate alkyl and aryl esters. The methodology involves the combination of *p*-toluenesulfinic acid and 1,1′-carbonyldiimidazole (CDI) to create the putative reagent sulfinylimidazole. The process spontaneously releases carbon dioxide upon the addition of the CDI to the acid suggesting the rapid formation of the proposed reagent. Reaction of this reagent with a series of alcohols (primary, secondary, and tertiary) afforded the corresponding sulfinate alkyl esters in good to excellent yields by the addition of alcohols. It was also possible to form the related sulfinate aryl esters by treating the proposed sulfinylimidazole with selected phenols (phenol, *p*-*tert*-butylphenol, and thymol). The aryl esters were formed in excellent conversion based on analysis of the 500 MHz ^{1}H NMR spectra of the crude reaction mixtures.

Keywords sulfinate ester, sulfinate aryl ester, *p*-toluenesulfinic acid, 1,1′-carbonyldiimidazole, sulfinylimidazole

Sulfinate alkyl esters are versatile tools in the synthesis of an array of synthetically useful sulfur compounds and can serve as key intermediates in the preparation of chiral sulfoxides and sulfinamides, materials that can be employed in catalytic asymmetric syntheses. The stereoselective synthesis of sulfinamides and sulfoxides has been recently reviewed by Wojaczyńska and Wojaczyński.[1] Sulfinate esters are valuable starting materials for the preparation of a variety of sulfinyl compounds. In this context, Kaboudin[2a] and Wei[2b] independently developed the use of electrochemistry to synthesize sulfinates (Scheme 1). Wu and co-workers developed an improved procedure for the synthesis of sulfinate esters using trimethylsilyl chloride in the absence of a metal catalyst.[3a–c] Basak and



Scheme 1 Methods for the preparation of sulfinate esters

co-workers disclosed a Wittig ylide-mediated degradation of *N*-sulfonylhydazones as a means of preparing sulfinate alkyl esters.[4] Our research group developed a carbodiimide approach employing 1-ethyl-(3-dimethylaminopropyl)carbodiimide (EDC) and 4-(dimethylamino)pyridine (DMAP).[5,6] Prapurna et al. prepared sulfinate alkyl esters via the $BF_3{\cdot}OEt_2$-catalyzed conversion of *p*-toluenesulfonylmethyl isocyanides.[7] Sun and co-workers developed an NBS promoted activation of *tert*-butyl sulfoxides as an entry point into sulfinate alkyl esters and other sulfinyl derivatives.[8] There are various other synthetic methods beyond the examples that are mentioned here.[9–11]

In the search for an improved methodology (ease of preparation and purification, commercially available reagents, and reduced environmentally impact) for the synthesis of sulfinate esters, a new method of sulfinyl group activation was considered. Conceptually, the preparation of sulfinate esters from sulfinic acids would require the formation of a suitable leaving group for the sulfinyl group. The introduction of suitable leaving groups had been previously demonstrated in our group by reaction of *p*-toluenesulfinic acid with a variety of activating agents including pivaloyl chloride,[11] cyanuric chloride,[5] and EDC and DMAP[5] (Figure 1).

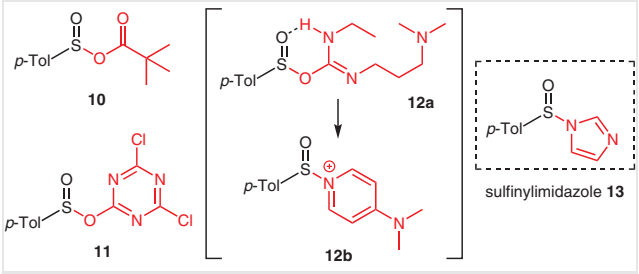
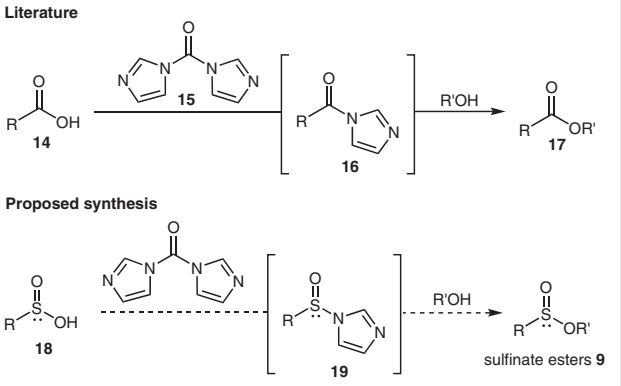


Figure 1 Activated sulfinyl groups

Each method was successfully employed in the synthesis of sulfinyl derivatives, but each methodology had limitations. The use of pivaloyl chloride to create a mixed sulfinic anhydride **10** leads to sulfinate esters but is limited in the preparation of the related sulfinamides.[11] The use of cyanuric chloride to create the labile *O*-sulfinyl 3,5-dichlorocyanurate **11** was limited in that it yielded sulfone by-products that can be troublesome to remove from the targeted sulfinate esters by chromatography.[5] The use of the EDC/DMAP reagent combination to create an *O*-sulfinylisourea **12** has long reaction times accompanied by the formation of the by-product common to sulfinate ester synthesis, namely *S*-*p*-tolyl *p*-toluenethiosulfonate.[5] These early examples of sulfinyl group activation served as the motivation for the pursuit of an alternate strategy that would allow for the effective formation of sulfinate esters.

In considering a new means of activation, the use of 1,1′-carbonyldiimidazole (CDI) became an attractive option to achieve the stated goal of an improved pathway of sulfinyl activation (Scheme 2). The use of CDI in the formation of esters from carboxylic acids has been well documented in the chemical literature.[12–17] It is proposed that CDI might serve as an activating agent that would act on sulfinic acids **18** to create reactive sulfinylimidazoles **19** in the same fashion as CDI reacts with carboxylic acids to create acyl imidazoles **16**. This pathway would be attractive in terms of the ease of formation of the sulfinylimidazole and would then presumably react to displace the labile imidazole group. Herein, we describe our efforts to exploit CDI as a reagent for the efficient synthesis of sulfinate esters.

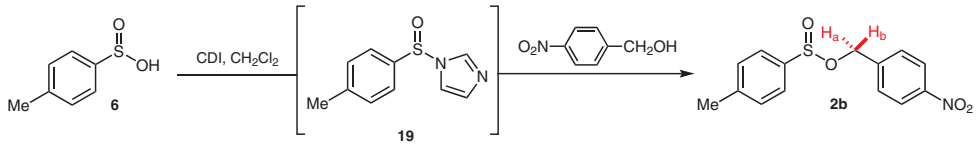


Scheme 2 1,1′-Carbonyldiimidazole as an activating agent

The study was initiated by reacting anhydrous *p*-toluenesulfinic acid with 1,1′-carbonyldiimidazole in dichloromethane (Table 1). These reagents were combined and reacted together for an induction time before the addition of the test alcohol, *p*-nitrobenzyl alcohol. The progress of the reaction was determined via 500 MHz ^{1}H NMR spectroscopy by comparison of the methylene protons of the unreacted alcohol versus the diastereotopic protons of the nearly formed *p*-nitrobenzyl sulfinate ester **2**. When the *p*-toluenesulfinic acid and CDI were combined, the reactions were noticed to undergo bubbling, presumably representing the loss of carbon dioxide via a mechanistic pathway similar to that described in the case of the reaction between carboxylic acids and CDI.[12–17] It was determined that the longer induction time was deleterious to the overall success of the reaction. When the induction time was 90 minutes (Table 1, entry 1), the ratio of product to starting material was 86:14 as determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture. In contrast, the transformation reached a level of 98:2 favoring the formation of the product when there was no induction time (entry 6, all reagents added in succession). It is proposed that the putative sulfinylimidazole intermediate **19** has a limited life-time before some mechanism of decomposition becomes prevalent.

There was a concern that the reaction was completed more quickly than the 18 hour window. Thus, another trial was carried out wherein there was no induction time. In

Table 1 Initial Trial Studies on the CDI-Mediated Sulfinylation

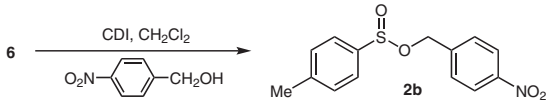


Entry[a]	Induction time	Reaction time	Ratio product/starting material[b]
1	90	18 h	84:16
2	60	18 h	90:10
3	30	18 h	92:8
4	15	18 h	94:6
5	15	60 min	95:5
6	**0**	**18 h**	**98:2**
7	0	60 min	91:9

[a] All reactions were conducted with a stoichiometric ratio 1.1:1.1:1.0 of sulfinic acid/CDI/alcohol.
[b] The ratio of the product to starting material was determined by analysis of the 500 MHz ^{1}H NMR spectra.

this set of the experiments, the amount of the *p*-toluenesulfinic acid and CDI were increased to a ratio of 1.5 equivalents relative to the alcohol to ensure the completion of the reaction (Table 2). It was determined that 75 minutes was a sufficient time to allow completion of the transformation. Interestingly, there was no observable formation of the isomeric sulfone product, and there was little formation of *S*-*p*-tolyl *p*-toluenethiosulfonate, a common by-product in the synthesis of sulfinate esters or alternatively obtained in the course of the preparation of sulfinate esters.[5]

Table 2 CDI-Mediated Sulfinylation with No Induction Time



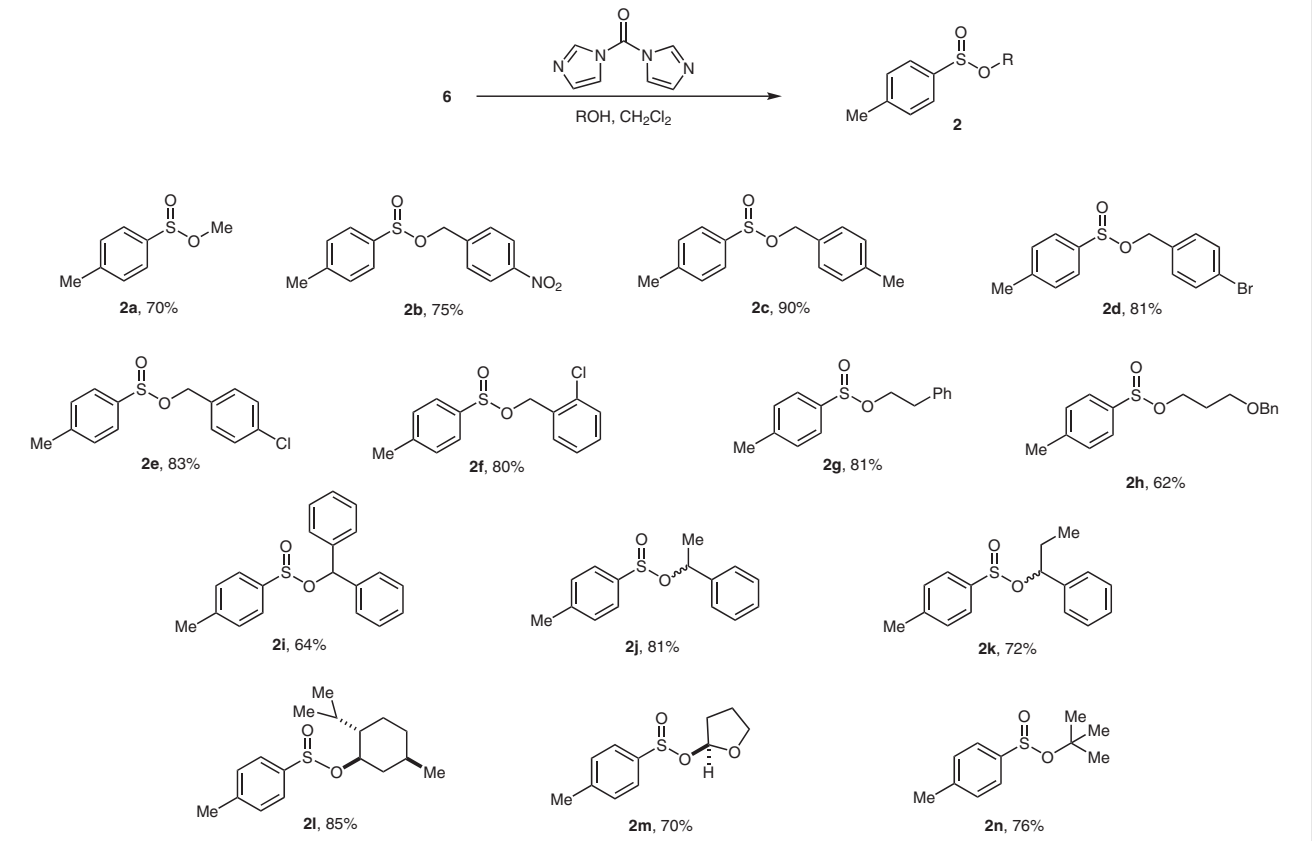
Entry[a]	Reaction time	Ratio product/starting material[b]
1	75 min	100:0
2	60 min	99:1
3	30 min	88:17
4	15 min	85:15

[a] All reactions were conducted with a stoichiometric ratio 1.5:1.5:1.0 of sulfinic acid/CDI/alcohol.
[b] The ratio of the product to starting material was determined by analysis of the 500 MHz ^{1}H NMR spectroscopy.

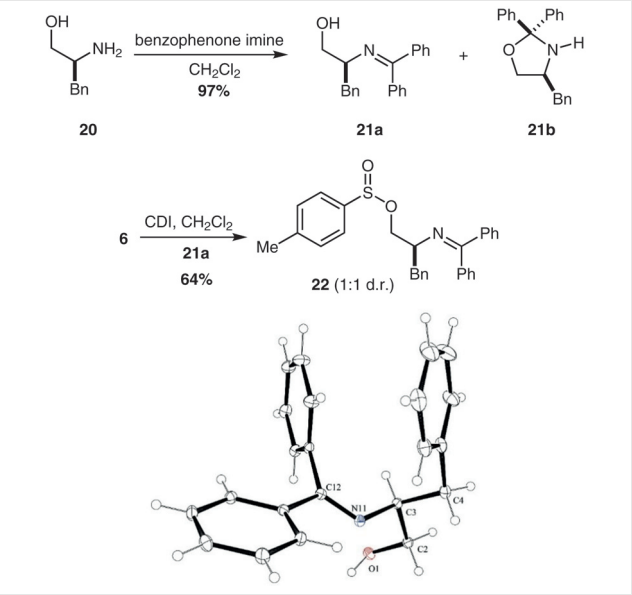
With a methodology established, a series of sulfinate esters were prepared using primary and secondary alcohols (Scheme 3). These examples included the sterically demanding diphenylmethanol, which yielded the corresponding sulfinate ester **2i** in 64% yield. Chiral alcohols such as, *rac*-1-phenyl-1-ethanol, and *rac*-1-phenyl-1-propanol, L-menthol, and (*S*)-3-hydroxytetrahydrofuran proved to be viable starting materials with good yields. There was no significant diastereoselection with these examples with the diastereomeric ratios occurring in a nearly 1:1 ratio in all cases as determined by 500 MHz ^{1}H NMR spectroscopy.

There was an interest in exploring the utility of this method in the context of an acid sensitive substrate. There are existing methodologies for the preparation of sulfinate esters that employ conditions that occur in the presence of catalytic sulfuric acid[10] or Lewis acids (e.g., $BF_3{\cdot}OEt_2$).[3c,17] and these conditions would not be compatible with such substrates. To demonstrate the utility of this new method, the diphenylimine of L-phenylalaninol was prepared by reaction of L-phenylalaninol with commercially available benzophenone imine (Scheme 4).[18,19] The structure of the imine **21a** was confirmed by X-ray crystallography (Supporting Information) as there was a concern over the identity of the crystals that had been collected from the reaction via recrystallization from ethyl acetate and hexanes. The β-iminoalcohol was then reacted under the *p*-toluenesulfinic acid/CDI reaction conditions to afford a 1:1 diastereomeric mixture of *p*-toluenesulfinate esters in 64% isolated yield.

There was also an interest in pursuing the synthesis of sulfinate aryl esters **25**, a class of sulfinate esters that are not commonly described in the chemical literature concerning sulfinate ester preparative methods.[20] Menezes, Oliveira, and co-workers explored the synthetic preparation of sulfinate aryl esters using an acid-catalyzed sulfinate esterification process[10] but were not able to isolate any sulfinate aryl ester products (Scheme 5). It is proposed here that the sulfinate esters may have formed as unstable products that may degraded to the starting materials under the reaction conditions. This served as the inspiration for the application of the *p*-toluenesulfinic acid/CDI methodology to the problem of the synthesis of these substrates.

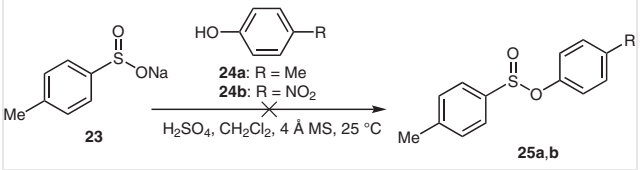


Scheme 3 Substrate scope of reactions with the *p*-toluenesulfinic acid/CDI reagent combination. *Reagents and conditions*: The sulfinic acid (1.5 equiv) and 1,1′-carbonyldiimidazole (1.5 equiv) were reacted with the substrate (1.0 equiv) in dichloromethane. Isolated yields are shown. For **2n**: the reaction was conducted with an excess of the alcohol. For **2j–m**: diastereomeric ratio was determined by ^{1}H NMR spectroscopy.



Scheme 4 *p*-Toluenesulfinylation of an acid-sensitive alcohol substrate

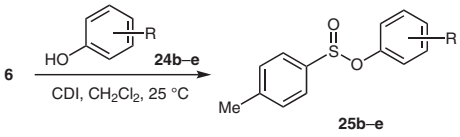
The *p*-toluenesulfinic acid/CDI reagent combination was prepared in dichloromethane at room temperature as before (Table 3). Directly after these reagents were combined, the respective phenolic substrate [*p*-nitrophenol (**24b**); *p*-*tert*-butylphenol (**24c**); *p*-methoxyphenol (**24d**); and 2-isopropyl-5-methylphenol (thymol) (**24e**)] was added. This process afforded sulfinate aryl esters **25c–e** in very good chemical yields. The formation of the sulfinate aryl ester based on *p*-nitrophenol (**24b**) proved to be problematic as the collected product was revealed to be a complex mixture as determined by ^{1}H NMR spectroscopy. It was noted that compounds **25c–e** became impure with prolonged storage at room temperature and proved to be difficult to purify by flash chromatography. Analysis of the 500 MHz ^{1}H NMR



Scheme 5 Attempted synthesis of phenoxysulfinate esters by Menezes, Oliveira, and co-workers

spectra suggested that the sulfinate aryl esters were hydrolyzing to release the phenol and *p*-toluenesulfinic acid starting materials. Based on this assessment, the sulfinate aryl esters were directly characterized without purification. Ultimately, the quality of the 500 MHz ^{1}H NMR spectroscopic data of these compounds suggested that the compounds could be recovered in 95% purity (see Supporting Information). Overall, this approach of employing the *p*-toluenesulfinic acid with CDI proved to be successful in the synthesis of these compounds that have not received significant attention.

Table 3 *p*-Toluenesulfinate/CDI Approach to the Synthesis of *p*-Toluenesulfinate Aryl Esters

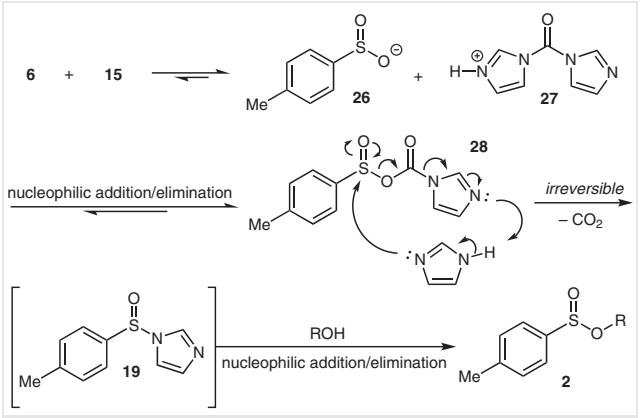


Entry[a]	Phenol	Product	Yield (%)[b]
1	*p*-nitrophenol (**24b**)	**25b**	n/a[c]
2	*p*-*tert*-butylphenol (**24c**)	**25c**	87
3	*p*-methoxyphenol (**24d**)	**25d**	89
4	thymol (**24e**)	**25e**	84

[a] All reactions were conducted with a stoichiometric ratio 1.5:1.5:1.0 of sulfinic acid/CDI/alcohol/additive.
[b] The yield that is reported is based on the product obtained after extraction.
[c] The product was not isolated. n/a: Not available.

Based on the experiments conducted, it is proposed that the reaction mechanism proceeds by an initial proton exchange between the *p*-toluenesulfinic acid (**6**) and CDI (**15**) (Scheme 6). In this context, the reaction is significantly compromised when the sodium salt of *p*-toluenesulfinic acid is employed. Nucleophilic addition–elimination of **26** to activated CDI **27** is presumed to lead to the formation of *p*-toluenesulfinyl *O*-acylimidazole **28**.[21] There is an observable evolution of gas at the beginning of the reaction suggesting that this intermediate irreversibly releases carbon dioxide and imidazole to yield the presumptive intermediate *p*-toluenesulfinylimidazole (**19**). This intermediate then undergoes a final nucleophilic addition/elimination with the alcohol substrate. Interestingly, there is no observed formation of carbonates [$(RO)_2C{=}O$)] in any significant means suggesting that the reaction between the sulfinic acid and the CDI occurs more rapidly than the reaction between the alcohol and the CDI.

In conclusion, the utility of the combination of *p*-toluenesulfinic acid and 1,1′-carbonyldiimidazole has been demonstrated in the synthesis of a series of sulfinate alkyl esters. The methodology does not require the preparation of synthetic precursors and does not require metal catalysts. The formation of the isomeric sulfone products was not observed and the common thiosulfonate by-product was only observed as a minor product. The method proved to be applicable in the case of an acid-sensitive substrate as well. In this context, the reagent combination was also successfully employed in the synthetic preparation of a series of sulfinate aryl esters.



Scheme 6 Proposed mechanism for the formation of sulfinate esters

Chemical reagents were used as purchased. All reactions were conducted in flame-dried glassware under a dry N_2 atmosphere. Crude reaction mixtures were purified by flash chromatography using an automated flash chromatograph. The stationary phase was 40 g normal phase silica gel cartridges. The collected fractions were analyzed by TLC with TLC plates coated with fluorescent indicator F_{254} and visualized with UV light. All ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using a Bruker Ultrashield Avance III NMR spectrometer operating at 500 MHz (or 400 MHz) for ^{1}H NMR spectra and operating at 125 MHz (or 100 MHz), respectively. Chemical shifts were reported in parts per million (δ scale) and coupling constant (*J* values) are listed in hertz (Hz). TMS was used as internal standard (δ = 0). IR spectra were recorded using NaCl plates. IR spectral values were reported in reciprocal centimeters (cm^{-1}) and were measured as a neat liquid, Nujol mull, or as a neat liquid film from an evaporated $CDCl_3$ solution. For electrospray ionization high resolution mass spectrometry (ESI-HRMS), samples were prepared in concentrations of 5–25 ppm in HPLC grade MeOH/H_2O/formic acid (1:1:0.01). Analytical data was collected using a ThermoScientific Q-Exactive ESI mass spectrometer.

Anhydrous *p*-Toluenesulfinic Acid (6)

To a 500 mL Erlenmeyer flask was added *p*-toluenesulfinic acid sodium salt hydrate (5.00 g, 28.1 mmol), Et_2O (60 mL), and aq 1 M HCl (60 mL). The reaction mixture was stirred at rt for 45 min. The mixture was placed into a separatory funnel and the layers were separated. The Et_2O layer was washed with brine (2 × 20 mL), dried ($MgSO_4$), and the solvents were removed by rotary evaporation under high vacuum for 2 h. The temperature of the water bath should be no greater than 25 °C as the *p*-toluenesulfinic acid decomposes at temperatures of 35 °C and higher. The process yielded an average value of 3.28 g of the corresponding anhyd *p*-toluenesulfinic acid. Once isolated, this material was used directly in the following reactions.

Sulfinate Esters; General Procedure

In a flame-dried, N_2-purged 100 mL round-bottomed flask equipped with a stir bar was placed freshly prepared *p*-toluenesulfinic acid (**6**; 703 mg, 4.50 mmol) and CH_2Cl_2 (15 mL). A magnetic stir bar was added to provide moderate stirring throughout. To the solution was added 1,1-carbonyldiimidazole (730 mg, 4.50 mmol) in one portion, after which significant bubbling was immediately observed. This addition was followed by the respective alcohol/phenol (3.05 mmol) to give a light yellow-orange solution. The reaction was allowed to sit and stir for 75 min. After this, the reaction mixture was diluted with CH_2Cl_2 (80 mL) and transferred to a separatory funnel for extraction. The reaction mixture was extracted with aq 1 M NaOH (2 × 20 mL), and the bottom organic layer was collected. Minimal exposure of the organic layer to the aqueous environment was sought. The organic layer was then washed with aq 1 M HCl (20 mL), brine (20 mL), dried ($MgSO_4$), and gravity filtered. Solvents were removed via rotary evaporation followed by high vacuum to afford the desired product.

Methyl *p*-Toluenesulfinate (2a)

The *p*-toluenesulfinic acid (**6**; 586 mg, 3.75 mmol) served as the limiting reactant with the use of excess MeOH (5 equiv). The product was recovered and characterized without purification; yield: 0.447 g (70%). Crude was isolated to give a clear colorless oil (>95% yield as determined by analytical data).

IR (neat): 2985, 1596, 1130, 1081, 812 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.2 Hz, 2 H), 7.35 (d, *J* = 7.9 Hz, 2 H), 3.49 (s, 3 H), 2.45 (s, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 142.8, 140.9, 129.7, 125.3, 49.4, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_8H_{10}O_2SNa$: 193.0293; found: 193.0296.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[6]

4-Nitrobenzyl *p*-Toluenesulfinate (2b)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a white waxy solid; yield: 0.6588 g (75%).

IR (neat): 1134, 817, 746 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.2 Hz, 2 H), 7.63 (d, *J* = 8.2 Hz, 2 H), 7.42–7.44 (m, 2 H), 7.35–7.37 (m, 2 H), 5.07 (d, *J* = 11.6 Hz, 2 H), 4.59 (d, *J* = 11.6 Hz, 2 H), 2.44 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 147.7, 143.4, 143.1, 141.1, 128.9, 128.6, 125.3,123.7, 63.4, 21.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_4SNa$: 314.0457; found: 314.0453.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

4-Methylbenzyl *p*-Toluenesulfinate (2c)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a clear yellow liquid; yield: 0.472 g (90%).

IR (neat): 1127, 805, 724 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.2 Hz, 2 H), 7.32 (d, *J* = 8.2 Hz, 2 H), 7.12–717 (m, 4 H), 4.97 (d, *J* = 11.2 Hz, 1 H), 4.51 (d, *J* = 11.2 Hz, 1 H), 2.42 (s, 3 H), 2.33 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 142.6, 141.6, 138.2, 132.4, 129.6, 129.1, 128.6, 125.2, 65.6, 21.4, 21.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{16}O_2SNa$: 283.0763; found: 283.0756.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

4-Bromobenzyl *p*-Toluenesulfinate (2d)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a white waxy solid; yield: 0.7931 g (81%).

IR (neat): 1129, 738, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.2 Hz, 2 H), 7.43 (d, *J* = 8.2 Hz, 2 H), 7.33–7.35 (m, 2 H), 7.12–7.14 (m, 2 H), 4.94 (d, *J* = 11.7 Hz, 1 H), 4.48 (d, *J* = 11.7 Hz, 1 H), 2.43 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 142.9, 141.3, 134.6, 131.6, 130.0, 129.7, 125.2, 122.4, 64.4, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}BrO_2SNa$: 346.9712; found: 346.9705.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

4-Chlorobenzyl *p*-Toluenesulfinate (2e)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a clear colorless oil; yield: 0.703 g (83%).

IR (neat): 1129, 915, 744 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.2 Hz, 2 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 7.28–7.30 (m, 2 H), 7.18–7.20 (m, 2 H), 4.96 (d, *J* = 11.6 Hz, 1 H), 4.49 (d, *J* = 11.6 Hz, 1 H), 2.43 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 142.9, 141.4, 134.2, 134.0, 129.8, 129.7, 128.6, 125.2, 64.4, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}ClO_2SNa$: 303.0217; found: 303.0211.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

2-Chlorobenzyl *p*-Toluenesulfinate (2f)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a clear colorless oil; yield: 0.676 g (80%).

IR (neat): 1130, 815, 745 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.2 Hz, 2 H), 7.33–7.35 (m, 4 H), 7.23–7.25 (m, 2 H), 5.12 (d, *J* = 12.1 Hz, 1 H), 4.71 (d, *J* = 12.1 Hz, 1 H), 2.42 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 142.9, 141.4, 133.6, 133.4, 130.3, 129.7, 129.6, 129.4, 126.8, 125.2, 63.0, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}ClO_2SNa$: 303.0217; found: 303.0210.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

2-Phenylethyl *p*-Toluenesulfinate (2g)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a clear yellow oil; yield: 0.630 g (81%).

IR (neat): 1129, 809, 724 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.2 Hz, 2 H), 7.21–7.29 (m, 5 H), 7.13–7.15 (m, 2 H), 4.22 (dt, *J* = 7.0, 10.0 Hz, 1 H), 3.81 (dt, *J* = 7.0, 10.0 Hz, 1 H), 2.92 (td, *J* = 0.93, 6.9 Hz, 2 H), 2.41 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 142.6, 141.6, 137.3, 129.6, 128.9, 128.5, 126.6, 125.2, 64.7, 36.3, 21.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{16}O_3SNa$: 283.0763; found: 283.0758.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

3-Benzyloxy-1-propyl *p*-Toluenesulfinate (2h)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a clear colorless oil; yield: 0.4755 g (62%).

IR (neat): 2858, 1452, 1130, 1103, 968, 810, 695 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.2 Hz, 2 H), 7.30–7.35 (m, 7 H), 4.49 (s, 2 H), 4.17 (dt, *J* = 6.2, 10 Hz, 1 H), 3.79 (dt, *J* = 6.2, 10 Hz, 1 H), 3.55 (td, *J* = 0.8, 6.2 Hz, 2 H), 2.43 (s, 3 H), 1.92 (q, *J* = 6.2 Hz, 2 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 142.6, 141.9, 138.4, 129.7, 128.3, 127.6, 127.5, 125.2, 72.9, 66.3, 61.7, 30.2, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{20}O_3SNa$: 327.1025; found: 327.1022.

Diphenylmethyl *p*-Toluenesulfinate (2i)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a white solid; yield: 0.5125 g (64%); mp >60 °C (dec.).

IR (neat): 3059, 3029, 1134, 1180, 1079, 811, 738, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.2 Hz, 2 H), 7.24–7.29 (m, 6 H), 7.14–7.16 (m, 4 H), 7.08–7.09 (m, 2 H), 6.26 (s, 1 H), 2.31 (s, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 142.7, 142.2, 140.3, 140.1, 129.9, 129.4, 128.5, 128.2, 127.8, 127.7, 127.3, 125.1, 80.1, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{18}O_2SNa$: 345.0919; found: 345.0918.

1-Phenylethyl *p*-Toluenesulfinate (2j)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to yield a 1:1 diastereomeric mixture as a clear colorless oil; yield: 0.5297 g (81%).

IR (neat): 3030 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 7.55 (d, *J* = 8.2 Hz, 2 H), 7.50 (d, *J* = 8.2 Hz, 2 H), 7.35–7.37 (m, 2 H), 7.29–7.31 (m, 2 H), 7.20–7.23 (m, 5 H), 7.12–7.14 (m, 2 H), 5.45 (q, *J* = 6.6 Hz, 1 H), 5.35 (q, *J* = 6.5 Hz, 1 H), 2.41 (s, 3 H), 2.37 (s, 3 H), 1.65 (d, *J* = 6.6 Hz, 3 H), 1.56 (d, *J* = 6.6 Hz, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (mixture of diastereomers) = 142.8, 142.6, 142.5, 142.1, 141.8, 141.5, 129.6, 129.4, 128.6, 128.3, 128.2, 127.8, 126.4, 126.2, 125.3, 124.9, 75.4, 24.2, 24.0, 21.5, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{16}O_2SNa$: 283.0763; found: 283.0761.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

1-Phenyl-1-propyl *p*-Toluenesulfinate (2k)

The product was purified by flash chromatography on silica gel using 95:5 hexanes/EtOAc as the eluent to yield a diastereomeric mixture as a clear colorless oil; yield: 0.4948 g (72%).

IR (neat): 3031, 2971, 1596, 1137, 1037, 753, 699 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 7.44 (d, *J* = 8.1 Hz, 2 H), 7.38 (d, *J* = 8.1 Hz, 2 H), 7.26–7.31 (m, 6 H), 7.21 (d, *J* = 8.1 Hz, 2 H), 7.11–7.12 (m, 3 H), 7.07 (d, *J* = 8.2 Hz, 2 H), 6.90–7.00 (m, 2 H), 5.08–5.10 (t, *J* = 6.8 Hz, 1 H), 5.00–5.03 (t, *J* = 6.8 Hz, 1 H), 2.33 (s, 3 H), 2.28 (s, 3 H), 1.85–1.95 (m, 2 H), 1.73–1.85 (m, 2 H), 0.79 (t, *J* = 7.41 Hz, 6 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (mixture of diastereomers) = 143.0, 142.5, 142.4, 142.1, 140.6, 140.4, 129.5, 129.2, 128.5, 128.3, 128.0, 127.6, 126.9, 126.6, 125.2, 124.8, 82.8, 80.4, 31.0, 30.8, 21.5, 21.4, 9.96, 9.92.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{18}O_2SNa$: 297.0919; found: 297.0918.

L-Menthyl *p*-Toluenesulfinate (2l)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to give a white solid; yield: 0.505 g (85%); mp 99–105 °C.

IR (neat): 2947, 2919, 1130 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 7.60 (d, *J* = 8.2 Hz, 2 H), 7.32 (d, *J* = 8.2 Hz, 2 H), 7.26 (s, 1 H), 4.12 (td, *J* = 10.8, 10.8 Hz, 1 H), 2.25–2.31 (m, 1 H), 2.41 (s, 3 H), 2.05–2.17 (m, 1 H), 1.63–1.71 (m, 2 H), 1.43–1.53 (m, 1 H), 1.31–1.43 (m, 1 H), 1.21–1.30 (m, 2 H), 0.98–1.12 (m, 1 H), 0.96 (d, *J* = 6.6 Hz, 3 H), 0.86 (d, *J* = 7.2 Hz, 3 H), 0.72 (d, *J* = 6.9 Hz, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz $CDCl_3$,): δ (mixture of diastereomers) = 143.3, 143.2, 142.4, 142.3, 129.5, 124. 9, 124.4, 81.9, 80.0, 71.4, 50.1, 48.2, 47.8, 45.0, 43.5, 42.9, 34.5, 34.0, 33.9, 31.8, 31.7, 31.6, 25.8, 23.1, 23.0, 22.1, 22.0, 21.8, 21.5, 21.4, 20.9, 15.4, 15.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_2O_2SNa$: 317.1546; found: 317.1538.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[5]

3-Oxacyclopentyl *p*-Toluenesulfinate (2m)

The product was purified by flash chromatography on silica gel using 95:5 hexanes/EtOAc as the eluent to give a clear colorless oil; yield: 0.3941 g (70%).

IR (neat): 1595, 1135, 1078, 813 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 8.5 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 4.90–4.95 (m, 1 H), 3.85–3.95 (m, 2 H), 3.75–3.84 (m, 1 H), 3.64–3.66 (m, 1 H), 2.43 (s, 3 H), 2.16–2.19 (m, 1 H), 1.94–1.98 (m, 1 H).

^{13}C $\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 143.0, 142.9, 142.0, 129.8, 129.7, 125.1, 125.0, 76.6, 76.1, 73.8, 73.2, 66.8, 34.2, 33.7, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{11}H_{14}O_3SNa$: 249.0555; found: 249.0556.

The collected spectroscopic data were consistent with the spectroscopic data reported in the chemical literature.[11]

tert-Butyl p-Toluenesulfinate (2n)

The *p*-toluenesulfinic acid (3.75 mmol) served as the limiting reactant with the use of excess *tert*-butyl alcohol (5 equiv). The product was purified by flash chromatography on silica gel using 95:5 hexanes/EtOAc as the eluent to give a clear colorless oil; yield: 0.606 g (76%).

IR (neat): 1596, 1125, 852, 782, 718 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 7.9 Hz, 2 H), 7.18 (d, *J* = 7.9 Hz, 2 H), 2.33, (s, 3 H), 1.47 (s, 9 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 143.8, 141.7, 129.4, 124.7, 82.1, 29.7, 21.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{11}H_{16}O_2SNa$: 235.0763; found: 235.0763.

Benzophenone Imine of L-Phenylalaninol (21a)

To a 1000 mL flame dried, N_2 purged round-bottomed flask were added anhyd CH_2Cl_2 (250 mL), benzophenone imine (11.7 mL, 69.4 mmol), and L-phenylalaninol (10.0 g, 66.1 mmol), and the reaction mixture was stirred for 24 h at rt. The organic layer was washed with brine (20 mL), dried ($MgSO_4$), filtered under gravity, and the solvent was removed by rotary evaporation. The target compound was isolated as a yellow solid, which was recrystallized from EtOAc (30 mL) and hexane (2 mL). The yellow crystals were recovered by vacuum filtration and hexane-wash and air-dried at rt. First and second seeds were obtained, which yielded a total amount of 20.1 g (97%) of the title compound as cream-colored crystals; mp 121–124 °C.

IR ($CHCl_3$ film): 3232, 1620, 1294, 732, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.62 (m, 2 H), 7.26–7.39 (m, 6 H), 7.12–7.20 (m, 3 H), 6.94–6.96 (m, 2 H), 6.64 (d, *J* = 7.1 Hz, 2 H), 3.77–3.91 (m, 1 H), 3.66–3.71 (m, 2 H), 2.84 (dq, *J* = 5.4, 7.8 Hz, 2 H), 2.13 (s, 1 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 169.8, 144.6, 139.7, 138.9, 138.6, 136.7, 130.1, 129.8, 128.9, 128.6, 128.3, 128.2, 128.1, 127.8, 127.6, 127.4, 126.5, 126.3, 126.0, 125.8, 100.0, 70.5, 66.2, 65.5, 59.6, 39.8, 39.1.

ESI-HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{28}N_2O_3Na$: 338.1515; found: 338.1505.

2-Diphenylimino-3-phenylpropyl p-Toluenesulfinate (22)

The product was purified by flash chromatography on silica gel using 90:10 hexanes/EtOAc as the eluent to afford a clear colorless oil; yield: 0.8531 g (64%).

IR (neat): 2921, 1624, 1445, 949, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 6.8 Hz, 2 H), 7.47 (d, *J* = 8.1 Hz, 2 H), 7.37–7.38 (m, 1 H), 7.32–7.34 (m, 2 H), 7.29–7.31 (m, 1 H), 7.15–7.22 (br m, 7 H), 6.92–6.94 (m, 2 H), 6.41 (d, *J* = 7.1 Hz, 2 H), 4.21–4.25 (m, 1 H), 3.88 (dd, *J* = 4.5, 5.3 Hz, 1 H), 3.70–3.76 (m, 1 H), 2.80 (dd, *J* = 2.4, 5.6 Hz, 2 H), 2.38 (s, 3 H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 169.5, 142.5, 142.0, 139.7, 138.1, 136.5, 130.0, 129.7, 129.5, 128.5, 128.1, 128.0, 127.9, 127.6, 126.1, 125.1, 68.9, 63.5, 39.3, 21.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{27}NO_2SNa$: 476.1655; found: 476.1642.

p-tert-Butylphenoxy p-Toluenesulfinate (25c)

The crude product was directly isolated as a clear colorless oil; yield: 0.753 g (87%).

IR (neat): 1505, 1364, 1203, 824 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 9 H), 2.44 (s, 3 H), 7.04 (m, 2 H), 7.34 (m, 4 H), 7.68 (d, *J* = 8.2 Hz, 2 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 21.5, 31.4, 34.4, 120.8, 125.0, 126.2, 126.5, 129.7, 142.4, 143.3, 148.6, 150.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{20}O_2SNa$: 311.1076; found: 311.1075;

p-Methoxyphenoxy p-Toluenesulfinate (25d)

Crude product was isolated to give a yellow wax; yield: 0.72 g (89% as determined by analytical data).

IR (neat): 1511, 1235, 831 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.3 Hz, 2 H), 7.35 (d, *J* = 8.3 Hz, 2 H), 7.00 (d, *J* = 9.2 Hz, 2 H), 6.81 (d, *J* = 9.2 Hz, 2 H), 3.78 (s, 3 H), 2.34 (s, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 157.5, 145.6, 143.4, 142.1, 126.7, 125.0, 123.1, 114.5, 55.6, 21.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{14}O_3SNa$: 285.0555; found: 285.0557.

2-Isopropyl-5-methylphenoxy p-Toluenesulfinate (25e)

The crude product was directly isolated as a clear colorless oil; yield: 0.739 g (84% as determined by analytical data).

IR (neat): 2963, 1503, 1237, 939, 812 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.2 Hz, 2 H), 7.39 (d, *J* = 8.2 Hz, 2 H), 7.17 (d, *J* = 7.9 Hz, 1 H), 7.11 (s, 1 H), 7.00 (d, *J* = 7.9 Hz, 1 H), 3.17–3.25 (m, 1 H), 2.45 (s, 3 H), 2.33 (s, 3 H), 1.17 (d, *J* = 7.1 Hz, 3 H), 1.14 (d, *J* = 7.1 Hz, 3 H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 150.8, 143.4, 143.0, 137.7, 136.9, 129.8, 126.5, 124.8, 121.8, 26.6, 23.4, 22.9, 21.6, 20.9.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{20}O_2SNa$: 311.1076; found: 311.1076.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1472-7578. ^1H and ^{13}C NMR spectroscopic data, and X-ray crystallographic data for **21a**, are included.

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