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Efficient Synthesis of Sulfinate Esters and Sulfinamides via Activated Esters of *p*-Toluenesulfinic Acid

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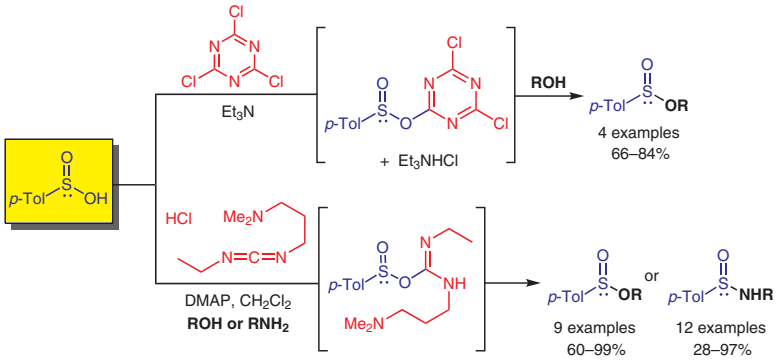

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Abstract Sulfinate esters were prepared by the process of activating *p*-toluenesulfinic acid with either cyanuric chloride, methanesulfonyl chloride, or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC-HCl). Activation of *p*-toluenesulfinic acid with cyanuric chloride led to the formation of sulfinate esters that were accompanied by the formation of the corresponding sulfones. The use of methanesulfonyl chloride for activation via methanesulfonic *p*-toluenesulfinic anhydride afforded mixtures of sulfinate esters and methanesulfonates. The use of the carbodiimide EDC proved to yield the best results with the highly selective formation of the target sulfinate esters. The use of trimethylacetic *p*-toluenesulfinic anhydride or cyanuric chloride to achieve the synthesis of sulfinamides proved to be ineffective due to poor chemoselectivity of the nucleophilic attack on the activated *p*-toluenesulfinic acid anhydride. Ultimately, the use of EDC-HCl to form the sulfinamides proved to be the best pathway for synthesis.

Key words sulfinate ester, sulfinic acid, sulfinamide, cyanuric chloride, EDC, activated ester

The development of synthetic methods for the preparation of sulfinate esters has been of interest due to their utility in the synthesis of synthetic intermediates[1] and their application in biochemical studies as chemical probes for live cell imaging.[2,3] This utility has been the stimulus for much method development with sulfinate esters. Since the pioneering efforts of Douglass in the preparation of sulfinate esters from sulfinyl chlorides,[4] a variety of methods have been developed. These preparative pathways may originate from sulfinyl chlorides **2**,[5] sodium sulfinates **3**,[6] sulfinic acids **4**,[7] sulfonyl chlorides **5**,[8] sulfonyl hydrazides **6**,[9] and *p*-toluenesulfonylmethyl isocyanides **7**[10] (Figure 1). Basak and co-workers have recently published on the synthesis of sulfinate esters through the Wittig ylide-mediated decomposition of *N*-sulfonylhydrazones **8**.[11] Our work in this field focused on the expedient synthesis of sulfinate esters through the use of the putative mixed anhydride *p*-toluenesulfinic trimethylacetic anhydride derived the reaction of sodium *p*-toluenesulfinate with trimethylacetyl chloride.[12] In this regard, there was an interest in developing a more efficient synthetic pathway that would possess beneficial aspects of low cost, expediency, and purification of the sulfinate ester products.

Furukawa and co-workers[7b,c] had demonstrated that 2-chloro-1-methylpyridiniium iodide (Mukaiyama's salt) could be used to effect the synthesis of sulfinate esters in yields ranging from 23–76% (Scheme 1). This method was attractive for the ease of activating the sulfinic acid, but was lacking in terms of the yield, which was most likely involved the necessary removal of the *N*-methylpyridone by-product as mentioned by the authors.[7] With this limitation taken into consideration, an alternate activating agent was sought. Blotny[13] had demonstrated that cyanuric chloride (**13**), a versatile chlorinating agent,[14] could be employed in the preparation of sulfonyl chlorides **15**. The successful use of cyanuric chloride by Blotny served as the inspiration for its application in this work.

Cyanuric chloride (**13**) was considered as a potential alternate activating agent that might offer a degree of improvement over the 2-chloro-1-methylpyridinium iodide as the by-product of the use of cyanuric chloride hydrolyzes in water. Thus, the investigation began with the treatment of *p*-toluenesulfinic acid (**4**, R = *p*-MeC_6H_4) with cyanuric chloride to form the putative activated sulfinate ester **17** (R = *p*-MeC_6H_4). It was not determined if the activated ester **17** formed the corresponding sulfinyl chloride **2**. Nonetheless, the reaction mixture was stirred for 30 minutes and an alcohol substrate was added. *p*-Nitrobenzyl alcohol was used as the initial test substrate. The initial reaction design (Table 1, entry 1) involved the use of 0.55 equivalent of cyanuric chloride and dichloromethane as the solvent. These conditions resulted in a 61% conversion (as determined by 500 ^{1}H

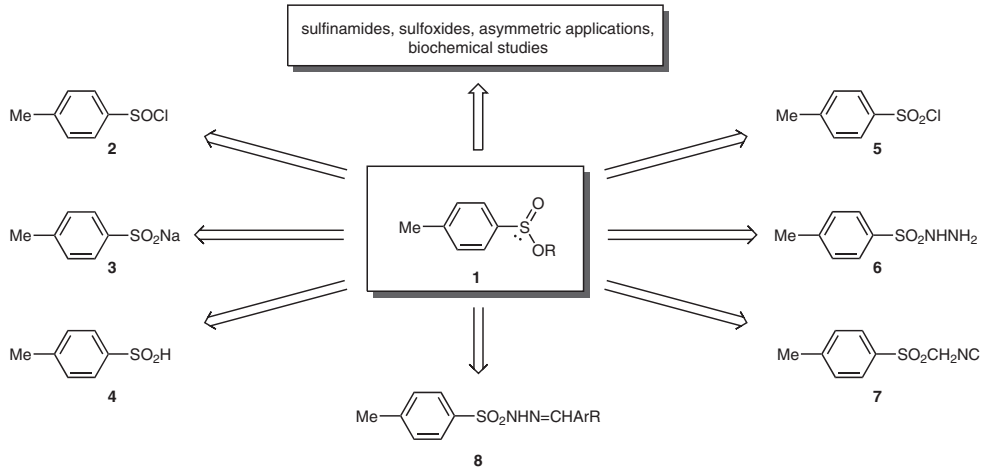
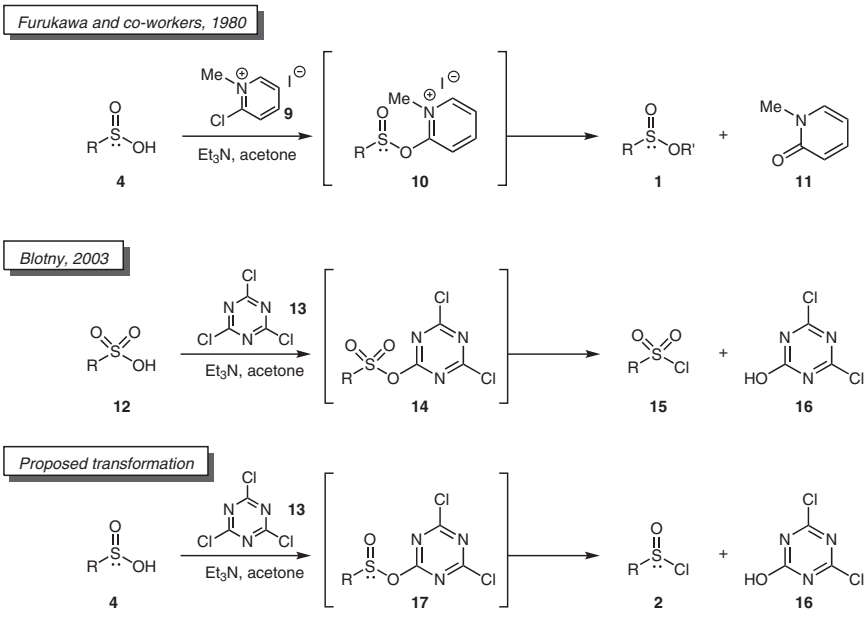


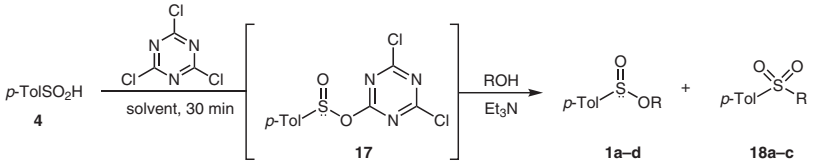
Figure 1 Methods for the synthesis of sulfinate esters



Scheme 1 Proposed cyanuric chloride pathway

NMR spectroscopic analysis) of the starting alcohol to the target sulfinate ester **1a** with concomitant formation of the corresponding sulfone **18a** in a ratio of 90:10. The number of equivalents of cyanuric chloride was increased by a factor of two (1.10 equiv) in an attempt to increase the percent conversion. In this way, a 95% conversion was achieved with a nearly doubling of the formation of the unwanted sulfone **18a**. The sulfone by-product is proposed to originate from activation of the *p*-nitrobenzyl alcohol by cyanuric chloride, and subsequent nucleophilic substitution by the *p*-toluenesulfinic acid (Scheme 2). When the solvent was changed to THF, the amount of the sulfone **18a** formed was significantly decreased. Presumably, the use of THF favored formation and reaction of the activated ester **17** over the presumed intermediate **20** illustrated in Scheme 2. Further experimentation was conducted with *p*-chloro- and *p*-bromobenzyl alcohol leading to comparable results. Interestingly, the use of L-menthol led to a complete conversion to the corresponding sulfinate ester with no observed formation of the L-menthyl *p*-tolyl sulfone. The absence of the corresponding sulfone was attributed to the steric environment of the secondary alcohol of L-menthol as compared to the more reactive primary benzylic alcohols.

Table 1 Cyanuric Chloride as an Activating Agent

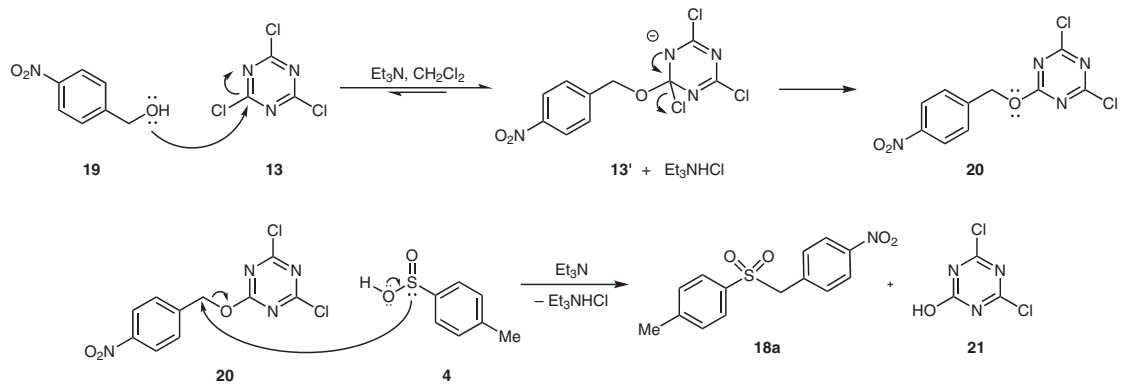


Entry	Alcohol, R	Solvent	Sulfinate ester	$C_3N_3Cl_3$ (equiv)	Sulfone[a] Yield (%)	Conv. (%)	Yield (%)[b]
1	*p*-$O_2NC_6H_4CH_2$	CH_2Cl_2	**1a**	0.55	**18a**, 10	61	nd
2	*p*-$O_2NC_6H_4CH_2$	CH_2Cl_2	**1a**	1.10	**18a**, 17	95	nd
3	*p*-$O_2NC_6H_4CH_2$	THF	**1a**	0.55	**18a**, 1.0	70	69
4	*p*-$O_2NC_6H_4CH_2$	THF	**1a**	1.10	**18a**, 7.0	88	77
5	*p*-$ClC_6H_4CH_2$	THF	**1b**	0.55	**18b**, 0.5	87	70
6	*p*-$ClC_6H_4CH_2$	THF	**1b**	1.10	**18b**, 10	90	66
7	*p*-$BrC_6H_4CH_2$	THF	**1c**	0.55	**18c**, 1.5	94	71
8	*p*-$BrC_6H_4CH_2$	THF	**1c**	1.10	**18c**, 5.0	85	79
9	L-menthol	THF	**1d**	1.10	**18d**, 0	100[c]	84

[a] Percentage of sulfone in the crude reaction mixture as determined by 500 MHz ^{1}H NMR spectroscopy.
[b] Isolated chemical yield after flash chromatography. nd: Not detected.

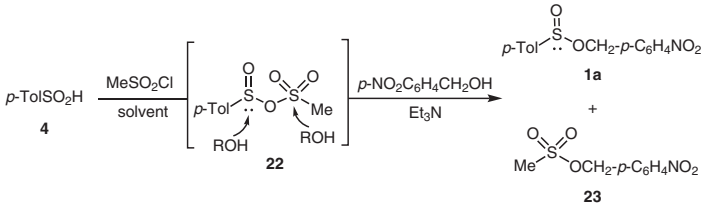
While the formation of the sulfinate esters **1a–d** through the cyanuric chloride activation method was successful, there was an ongoing concern of the concomitant formation of the sulfone by-product. The development of a synthetically useful pathway via an activated ester approach was still considered an obtainable goal. To this end, the use of methanesulfonyl chloride as an activating agent was explored in place of cyanuric acid. *p*-Toluenesulfinic acid was reacted with methanesulfonyl chloride for a period of 30 minutes followed by the addition of the *p*-nitrobenzyl alcohol and the scavenger base triethylamine, and the reaction was stirred for 12 hours (Table 2). Analysis of the crude product by 500 MHz ^{1}H NMR spectroscopy revealed that the sulfinate ester **1a** had formed in addition to the methanesulfonate ester **23** in a ratio of 70:30, respectively.

There was a concern that not enough time had been given for the formation of the presumed methanesulfonic *p*-toluenesulfinic anhydride (**22**). If this were the case, then the methanesulfonate **23** was forming due to the presence of unreacted methanesulfonyl chloride. To address this concern, the reaction time for formation of **22** was extended to two hours. In addition to the change in the induction time for the formation of the mixed anhydride, the solvents dichloromethane and THF were used in competing reactions. It was determined that the amount of the methanesulfonate increased when the induction time was increased to two hours and the solvent employed was dichloromethane.



Scheme 2 Proposed pathway of sulfone formation

Table 2 Synthesis and Application of the Methanesulfonic *p*-Toluenesulfinic Anhydride



Entry	Solvent	Induction time	Conversion (%)	**1a**/**23**
1	CH_2Cl_2	30 min	100	70:30
2	CH_2Cl_2	2 h	100	60:40
3	THF	2 h	96	87:13

When THF was used as the solvent, the formation of the sulfinate ester **1a** over the sulfonate **23** improved significantly. However, the ratio was still not considered ideal as the products **1a** and **23** could not be easily separated by chromatography due to the similarities in polarity. The formation of these two products is proposed to originate from the formation of the activated ester **22** upon which nucleophilic attack is not chemoselective enough to warrant synthetic utility. Consequently, this activation method was abandoned as there was no straightforward method to suppress formation of the methanesulfonate ester to levels that would be synthetically useful.

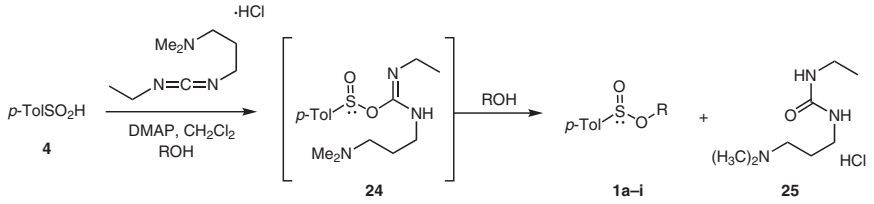
The last option that was considered was based on the work of Kobayashi and co-workers[7d] who had demonstrated the utility of *N*,*N*′-dicyclohexylcarbodiimide (DCC) as an activating agent for the formation of sulfinate esters. Furukawa and co-workers[7b,c] also employed DCC, and more recently, Hajipour and co-workers[7a] also used DCC in the synthesis of sulfinate esters, but under solvent-free conditions. The limitation from these combined works were focused on the chromatographic separation of residual DCC starting material from the reaction mixture, the chromatographic removal of the dicyclohexylurea by-product, and to a lesser degree the formation and removal of the commonly encountered by-product of sulfinate ester formation, namely thiosulfonates originating from coupling reactions between sulfinic acids and their activated counterparts.[12]

Despite these limitations, the carbodiimide approach was still considered to be attractive for its ease of operation. To exploit the carbodiimide approach in a manner that would address these limitations fully, or in part, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC-HCl), was selected. This carbodiimide reagent is known to generate a water-soluble urea by-product thereby facilitating isolation of the desired organic product without concomitant contamination and necessitated chromatographic removal of the urea. With this taken into consideration, EDC-HCl was employed in a series of reactions focused on the synthesis of sulfinate esters through a carbodiimide-based approach. Freshly prepared *p*-toluenesulfinic acid was combined with an alcohol substrate, and 4-(dimethylamino)pyridine (DMAP) in dichloromethane. This reaction mixture was then treated with EDC-HCl and stirred for 12–15 hours (Table 3). The reactions were easily extracted and the water-soluble urea by-product was not observed. The isolated chemical yields ranged from 67 to 99% after chromatographic isolation. Attempts to influence the diastereoselectivity of sulfinate ester formation with L-menthol by altering the temperature (Table 3, entries 4, 5, 6) were not successful as the diastereomeric ratio only varied from 48:52 to 40:60 as determined by 500 MHz ^{1}H NMR spectroscopy.

Interestingly, the alcohol substrate *trans*-1,3-diphenyl-2-propen-1-ol afforded the corresponding sulfone rather than the sulfinate ester. Alcohols that are benzylic *and* allylic have been shown to form the corresponding sulfone under conditions designed for sulfinate ester formation.[15] Nonetheless, the utility of the activation approach for the formation of sulfinate esters had been demonstrated with activating agents such as cyanuric chloride and EDC-HCl.

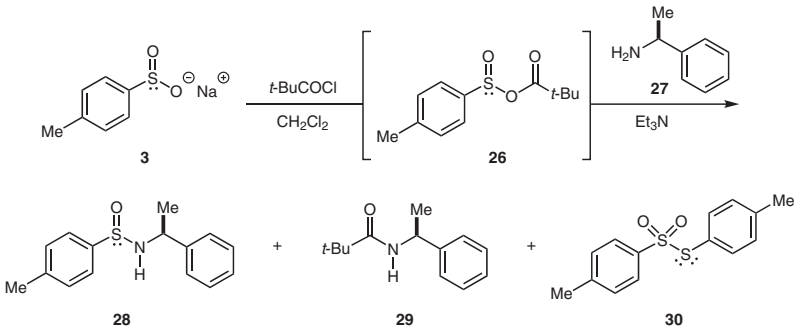
Based on the success of these approaches in the synthesis of sulfinate esters, there was also an interest in the preparation of the related sulfinamides[16] through a common pathway. Before exploring usage of the cyanuric chloride and EDC-HCl activation methodologies, the previously developed mixed anhydride methodology was investigated. To this end, the trimethylacetic *p*-toluenesulfinic anhydride was prepared and reacted with (*S*)-(−)-1-phenylethylamine (**27**) (Scheme 3). This reaction generated a mixture of products that included the expected sulfinamide **28** (46% isolated yield) and the corresponding pivalamide **29** in a nearly 1:1 ratio as determined by 500 MHz ^{1}H NMR spectroscopy, and a thiosulfonate by-product **30**.

Table 3 Synthesis of Sulfinate Esters by EDC Activation of *p*-Toluenesulfinic Acid



Entry	Alcohol	Sulfinate ester	Yield (%)[a]
1	*p*-nitrobenzyl alcohol	**1a**	69
2	*p*-chlorobenzyl alcohol	**1b**	70
3	*p*-bromobenzyl alcohol	**1c**	69
4	L-menthol (reaction ran at 25 °C)	**1d**	99 (48:52)
5	L-menthol (reaction ran at –15 °C)	**1d**	97 (40:60)
6	L-menthol (reaction ran at –78 °C)	**1d**	95 (40:60)
7	2-phenylethanol	**1e**	96
8	*sec*-butyl alcohol	**1f**	85
9	*trans*-1,3-diphenyl-2-propen-1-ol	**1g**	60[b]
10	(*S*)-(+)-3-hydroxytetrahydrofuran	**1h**	67 (48:52)
11	(1*S*,2*S*,3*S*,5*R*)-(+)-isopinocampheol	**1i**	85 (45:55)

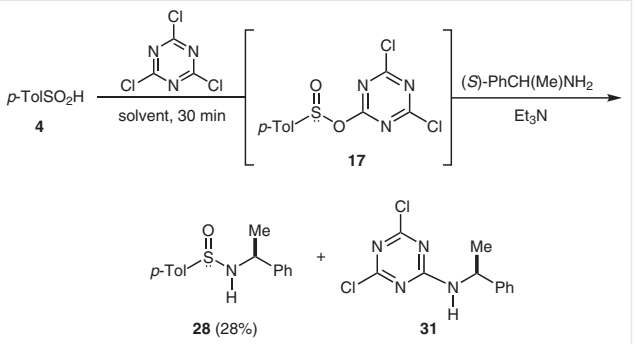
[a] Isolated chemical yield after flash chromatography. Ratio of the sulfinate diastereomers determined by 500 MHz ^{1}H NMR spectroscopy is given in parentheses.
[b] The product was isolated as the sulfone.



Scheme 3 Sulfinamide synthesis via the mixed anhydride approach

The failure of the mixed anhydride pathway to yield a practical methodology for the preparation of sulfinamides led to the pursuit of the cyanuric chloride methodology. To this end, freshly prepared *p*-toluenesulfinic acid (**4**) was treated with cyanuric chloride and stirred for 30 minutes followed by addition of (*S*)-1-phenylethylamine and triethylamine (Scheme 4). The sulfinamide product **28** was obtained in 28% yield after isolation by flash column chromatography. The low yield was attributed to the higher nucleophilicity of the amine substrate towards the cyanuric chloride leading to formation of the putative aminated by-product **31**.[17] The low yield of the product suggested that the neither of these methodologies would be suitable for a practical synthesis of sulfinamides. The use of EDC as the activating agent was pursued as it had been successful in its application in the synthesis of sulfinate esters.

A variety of conditions were explored for the optimized preparation of sulfinamides through the EDC route. It was determined that when the order of addition involved the reaction of the *p*-toluenesulfinic acid with the carbodiimide over a 30-minute period, the yield of the target sulfinamide was compromised (25–62%) and there was significant formation of the thiosulfonate by-product (Scheme 5). When the reagents were combined and the carbodiimide was added last, the thiosulfonate by-product was minimized and the sulfinamide product could be isolated more



Scheme 4 Sulfinamide synthesis using cyanuric chloride as the activating agent

readily. The examples included primary amines, sterically congested primary amines, cyclic secondary amines, a carbazate, and a hydrazide (Table 4). The isolated chemical yields ranged from 28 to 97%. The low yield of 28% for the synthesis of the benzhydrazide-based sulfinamide was attributed to the low solubility of the benzhydrazide starting material in the reaction solvent dichloromethane. Nonetheless, the isolated yields were mostly good to excellent for the preparation of the target sulfinamides.

With the methodology for sulfinamide synthesis in hand, the preparation of amino ester based sulfinamides was pursued (Table 5). To this end freshly prepared *p*-toluenesulfinic acid was reacted with the commercially available enantiomerically pure amino esters in triethylamine followed by the addition of EDC to induce the coupling to afford the sulfinamides in good to excellent yields. The ratio of the diastereomers formed was determined by the integration of the methyl ester signal in the 500 MHz ^{1}H NMR spectra.

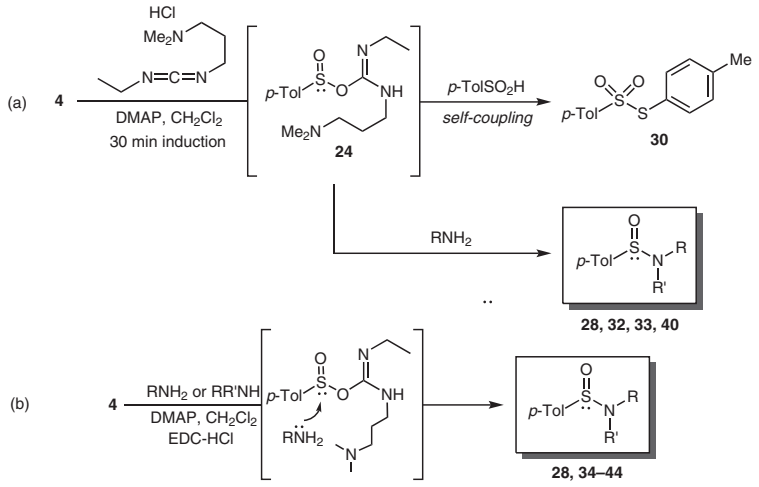
In the case of the L-phenylglycine methyl ester **46b**, a diastereomeric mixture of sulfinamides was obtained in

Table 4 Synthesis of Sulfinamides by EDC-HCl Activation of *p*-Toluenesulfinic Acid[a]

Entry	Amine	Sulfinamide	Yield (%)[b] Method a	Method b
1	*sec*-butylamine	**34**	36	68
2	benzylamine	**35**	25	92
3	phenethylamine	**36**	–	58
4	3,4-dimethoxyphenethylamine	**37**	–	90
5	(*R*)-(+)-1-phenylethylamine	**28**	62	74
6	(*S*)-(–)-1-(1-naphthyl)ethylamine	**38**	–	67
7	*tert*-butylamine	**39**	–	44
8	pyrrolidine	**40**	18	33
9	piperidine	**41**	–	78
10	morpholine	**42**	–	61
11	*tert*-butyl carbazate	**43**	–	97
12	benzhydrazide	**44**	–	28

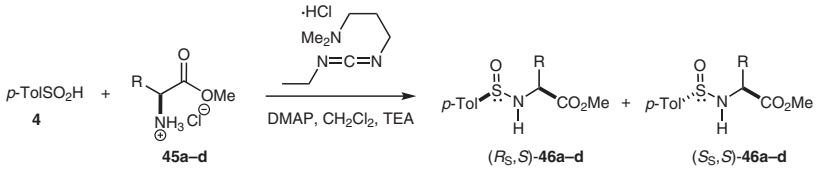
[a] See Scheme 5 for methods.
[b] All yields are derived from product isolation through chromatographic purification.

78% yield. Since the diastereomers (epimeric at the stereogenic sulfur) had marginally different retention factors on silica gel, a careful separation of the diastereomers by column chromatography was carried out. Although complete separation was not possible, the early fractions from the column contained a diastereomer that readily recrystallized. The latter fractions contained a mixture of the diastereomers that proved to be more difficult to recrystallize due to the viscous, oil like nature of the fractions. The absolute configuration of the pure white crystalline compound was determined to be (S_s,*S*) by X-ray crystallography (Figure 2). This corresponded to the diastereomeric configuration of (S_S,*S*)-**46b**, which in turn corresponded to the 500 MHz



Scheme 5 EDC-based synthesis of sulfinamides

Table 5 Synthesis of Amino Acid-Based Sulfinamides by EDC Activation of Sulfinic Acid



Entry	R	Compound	Yield (%)	δ (CO_2CH_3) (S_S,S)	δ (CO_2CH_3) (R_S,S)	Ratio
1	Bn	**46a**	54	3.64	3.74	56:44
2	Ph	**46b**	78	3.66	3.74	57:43
3	*i*-Pr	**46c**	64	3.70	3.79	62:38
4	*t*-Bu	**46d**	94	3.68	3.78	60:40

^{1}H NMR spectral signal for the methyl ester peak at 3.66 ppm. There is a likelihood that the other *N*-*p*-tolylsulfinyl-α-amino esters **45a**,**c**,**d** adopt a similar conformation in the solution state of the NMR sample ($CDCl_3$), and consequently, there is a likelihood that the methyl ester peak resonating at the lower ppm value (see Table 5) represents the (S_S,*S*)-diastereomer in those cases as well.

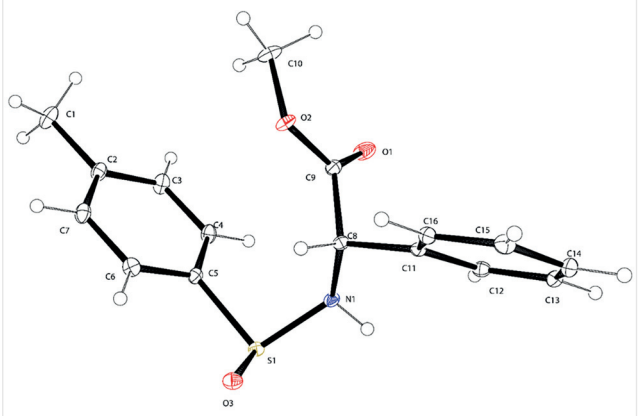


Figure 2 ORTEP diagram of (S_S,*S*)-**46b**

In conclusion, a unified one-pot activation method employing the carbodiimide EDC has been developed for the preparation of both sulfinate esters and sulfinamides. The EDC activation approach proved to be superior to the use of cyanuric chloride as an activating agent. Cyanuric chloride formed sulfinate esters, but with concomitant formation of the corresponding sulfone. The EDC methodology did not form significant amounts of the sulfone product, but did cleanly form the target compounds. The method proved to be successful in the synthesis of a series of *N*-*p*-tolylsulfinyl-α-amino esters. While the diastereoselectivities were not optimal, it was possible to isolate a single diastereomer from the L-phenylglycine series.

Chemical reagents were used as purchased. CH_2Cl_2 was purchased as an anhydrous reagent. All reactions were conducted in flame-dried or oven dried glassware under a 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 $CDCl_3$ or DMSO-d_6 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 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 were collected using a ThermoScientific Q-Exactive ESI mass spectrometer.

Sulfinate Esters 1; 4-Bromobenzyl *p*-Toluenesulfinate (1c), Typical Procedure

To a 250 mL flame-dried N_2 purged round-bottomed flask was added *p*-toluenesulfinic acid (0.525 g, 3.36 mmol), 4-bromobenzyl alcohol (0.598 g, 3.20 mmol), and DMAP (0.078 g, 0.64 mmol) sequentially and dissolved in anhyd CH_2Cl_2 (14 mL). To the solution was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (0.644 g, 3.36 mmol) in one portion and stirred for 16 h at r.t. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with aq 1 M HCl (30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and solvents removed under reduced pressure. The crude product was purified by flash column chromatography (hexanes/EtOAc, 95:5; R_f = 0.14) to yield 0.719 g (69%) of the title compound as a transparent yellow oil.

IR (neat): 3048, 1912, 1595, 1133, 1014, 804 cm^{-1}.

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.37 (s, 3 H), 4.42 (d, *J* = 11.7 Hz, 1 H), 4.88 (d, *J* = 11.7 Hz, 1 H), 7.05–7.07 (m, 2 H), 7.27–7.28 (m, 2 H), 7.37–7.39 (m, 2 H), 7.54–7.56 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 64.6, 122.5, 125.3, 129.9, 130.2, 131.7, 134.8, 141.5, 143.0.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{13}BrO_2SNa$ (M + Na^+): 346.9712; found: 346.9714.

4-Nitrobenzyl *p*-Toluenesulfinate (1a)

The crude product was purified by flash column chromatography (hexanes/EtOAc, 95:5; R_f = 0.14) to yield 0.719 g (69%) of the title compound as a yellow oil.

IR (neat): 3054, 1607, 1347, 1134, 1081, 852, 814 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ = 2.37 (s, 3 H), 4.53 (d, *J* = 12.6 Hz, 1 H), 5.01 (d, *J* = 12.6 Hz, 1 H), 7.29–7.30 (m, 2 H), 7.34–7.38 (m, 2 H), 7.56–7.58 (m, 2 H), 8.09–8.13 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 63.4, 123.7, 125.3, 128.7, 129.9, 141.1, 143.1, 143.4, 147.5.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{13}NO_4SNa$ (M + Na^+): 314.0457; found: 314.0460.

4-Chlorobenzyl *p*-Toluenesulfinate (1b)

The crude product was purified by flash column chromatography (hexanes/EtOAc, 95:5; R_f = 0.14) to yield 0.634 g (70%) of the title compound as a transparent oil.

IR (neat): 1598, 1134, 1017, 954, 922, 808 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ = 2.37 (s, 3 H), 4.44 (d, *J* = 11.7 Hz, 1 H), 4.90 (d, *J* = 11.7 Hz, 1 H), 7.12–7.14 (m, 2 H), 7.21–7.24 (m, 2 H), 7.27–7.28 (m, 2 H), 7.54–7.56 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 64.5, 125.3, 128.7, 129.8, 129.9, 134.3, 141.5, 143.0.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{13}ClO_2SNa$ (M + Na^+): 303.0217; found: 303.0219.

(1*R*,2*S*,5*R*)-(–)-Menthyl *p*-Toluenesulfinate (1d)

The crude product was purified by flash column chromatography (hexanes/EtOAc, 98:2; R_f = 0.14) to yield 1.02 g (99%) of the title compound as a wax.

IR (neat): 1596, 1133, 1080, 956, 916 cm^{-1}.

^1H NMR (500 MHz $CDCl_3$): δ (mixture of diastereomers) = 0.74 (d, *J* = 6.9 Hz, 3 H), 0.85–0.91 (m, 8 H), 0.92 (d, *J* = 1.5 Hz, 3 H), 0.93 (d, *J* = 2.0 Hz, 3 H), 1.02–1.11 (m, 2 H), 1.21–1.31 (m, 2 H), 1.35–1.44 (m, 2 H), 1.45–1.55 (m, 2 H), 1.66–1.74 (m, 4 H), 2.08–2.19 (m, 3 H), 2.28–2.33 (m, 1 H), 2.44 (s, 6 H), 4.14 (ddd, *J* = 10.8, 10.8, 4.5 Hz, 1 H), 4.22 (ddd, *J* = 10.8, 10.8, 4.5 Hz, 1 H) 7.33–7.35 (m, 4 H), 7.61–7.64 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (mixture of diastereomers) = 15.5, 15.6, 20.9, 20.9, 21.5, 21.5, 23.1, 23.2, 25.2, 25.5, 31.7, 31.9, 33.9, 34.0, 43.0, 43.6, 47.9, 48.2, 80.0, 81.9, 124.5, 124.9, 129.6, 129.60, 142.3, 142.5, 143.3, 143.3.

ESI-HRMS: *m*/*z* calcd for $C_{17}H_{26}O_2SNa$ (M + Na^+): 317.1546; found: 317.1552.

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

The crude product was purified by flash column chromatography (hexanes/EtOAc, 95:5; R_f = 0.14) to yield 0.803 g (96%) of the title compound as a transparent yellow oil.

IR (neat): 3030, 1597, 1133, 1081, 967, 865, 814 cm^{-1}.

^1H NMR (500 MHz $CDCl_3$): δ = 2.44 (s, 3 H), 2.95 (m, 2 H) 3.84 (dt, *J* = 10.1, 6.9 Hz, 1 H), 4.25 (ddd, *J* = 10.1, 7.4, 6.9 Hz, 1 H), 7.15–7.18 (m, 2 H), 7.23–7.26 (m, 1 H), 7.29–7.32 (m, 4 H), 7.51–7.53 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 36.3, 64.7, 125.3, 126.7, 128.5, 129.1, 129.7, 137.4, 141.7, 142.7.

ESI-HRMS: *m*/*z* calcd for $C_{15}H_{16}O_2SNa$ (M + Na^+): 283.0763: found: 283.0764.

***s*-Butyl *p*-Toluenesulfinate (1f)**

The crude product was purified by flash column chromatography (hexanes/EtOAc, 95:5; R_f = 0.17) to yield 1.00 g (85%) of the title compound as a transparent oil.

IR (neat): 1597, 1137, 1026, 993, 964, 890 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ (mixture of diastereomers) = 0.90 (t, *J* = 7.4 Hz, 3 H), 0.98 (t, *J* = 7.5 Hz, 3 H), 1.25 (d, *J* = 6.3 Hz, 3 H), 1.40 (d, *J* = 6.3 Hz, 3 H), 1.51–1.79 (m, 4 H), 2.44 (s, 6 H), 4.35–4.47 (m, 2 H), 7.33–7.35 (m, 4 H), 7.61–7.65 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of diastereomers) = 9.5, 9.6, 21.31, 21.4, 30.1, 30.4, 77.4, 77.6, 124.8, 124.9, 129.5, 124.8, 124.9, 129.5, 142.3, 142.9, 143.0.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{16}O_2SNa$ (M + Na^+): 235.0763; found: 235.0765.

***trans*-1,3-Diphenyl-2-propenyl *p*-Tolyl Sulfone (1g)**

The crude product was purified by flash column chromatography (hexanes/EtOAc, 90:10; R_f = 0.17) to yield 0.337 g (60%) of the title compound as a transparent oil.

IR (Nujol): 1756, 1377, 1142, 978, 811, 750, 713 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ = 2.42 (s, 3 H), 4.84 (d, *J* = 7.76 Hz, 2 H), 6.53–6.63 (m, 2 H), 7.22–7.24 (m, 2 H), 7.29–7.39 (m, 10 H), 7.55–7.57 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 75.4, 120.3, 126.8, 128.5, 128.65, 128.69, 128.9, 129.3, 129.7, 132.6, 134.5, 136.0, 138.0, 144.6.

ESI-HRMS: *m*/*z* calcd for $C_{22}H_{20}O_2SNa$ (M + Na^+): 371.1076; found: 371.1082.

(*S*)-(+)-3-Hydroxytetrahydrofuryl *p*-Toluenesulfinate (1h)

The crude product was purified by flash column chromatography (hexanes/EtOAc, 85:15; R_f = 0.17) to yield 0.615 g (67%) of the title compound as a transparent oil.

IR (neat): 1136, 1079, 959, 907, 862, 814 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ (mixture of diastereomers) = 1.96–2.02 (m, 2 H), 2.17–2.23 (m, 2 H), 2.46 (s, 6 H), 3.64–3.71 (m, 2 H), 3.78–3.88 (m, 4 H), 3.90–3.99 (m, 2 H), 4.93–4.98 (m, 2 H), 7.36–7.38 (m, 4 H), 7.61–7.63 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of diastereomers) = 21.4, 33.7, 34.2, 66.7, 73.2, 73.7, 76.2, 76.5, 125.0, 125.1, 129.70, 129.7, 142.0, 142.8, 142.9.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{14}O_3SNa$ (M + Na^+): 249.0556; found: 249.0558.

(1*S*,2*S*,3*S*,5*R*)-(+)-Isopinocampheyl *p*-Toluenesulfinate (1i)

The crude product was purified by flash column chromatography (hexanes/EtOAc, 98:2; R_f = 0.14) to yield 0.867 g (85%) of the title compound as a clear oil.

IR (neat): 15.97, 1134, 1081, 970, 911, 15.97, 1134, 1081, 970, 911, 836 cm^{-1}.

^1H NMR (500 MHz $CDCl_3$): δ (mixture of diastereomers) = 0.91 (s, 3 H), 0.92 (s, 3 H), 0.96 (d, *J* = 7.4 Hz, 3 H), 1.09 (dd, *J* = 16.3, 9.9 Hz, 2 H), 1.20 (d, *J* = 7.4 Hz, 3 H), 1.22 (s, 3 H), 1.24 (s, 3 H), 1.81–1.91 (m, 4 H), 1.96–1.99 (m, 1 H), 2.05–2.09 (m, 1 H), 2.13–2.26 (m, 3 H), 2.34–2.40

(m, 2 H), 2.45 (s, 6 H), 2.61–2.69 (m, 1 H), 4.59 (ddd, *J* = 9.6, 5.2, 4.5 Hz, 1 H), 4.68 (ddd, *J* = 9.8, 5.3, 4.7 Hz, 1 H), 7.34–7.37 (m, 4 H), 7.63–7.65 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (mixture of diastereomers) = 19.4, 19.7, 21.4, 23.8, 23.8, 27.4, 33.7, 33.8, 37.0, 37.6, 38.2, 41.4, 44.7, 45.2, 47.5, 47.6, 78.0, 79.1, 125.0, 125.1, 129.5, 129.5, 142.3, 143.0.

ESI-HRMS: *m*/*z* calcd for $C_{17}H_{24}O_2SNa$ (M + Na^+): 315.1389; found: 315.1393.

Sulfinamides; General Procedure

To a flame-dried, N_2 purged 100 mL round-bottomed flask was added *p*-toluenesulfinic acid (0.30 g, 1.9 mmol), DMAP (0.039 g, 0.32 mmol) and dissolved in CH_2Cl_2 (8 mL). To the solution was added the desired amine (1.6 mmol) followed by EDC-HCl (0.36 g, 1.9 mmol) and stirred for 18 h. Afterwards, the reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with aq 1 M HCl (20 mL) and brine (20 mL) sequentially. The organic layer was dried ($MgSO_4$), filtered, and solvents removed under reduced pressure to give the crude reaction product, which was then purified by flash chromatography.

rac-*N*-(*p*-Tolylsulfinyl)-*s*-butylamine (34)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.23 g (68%) of the title compound as clear oil.

IR (Nujol): 3205, 1597, 1088, 1063 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (both diastereomers) = 0.78 (t, *J* = 7.4 Hz, 3 H), 0.90 (t, *J* = 7.4 Hz, 3 H), 1.10 (d, *J* = 6.5 Hz, 2 H), 1.21 (d, *J* = 6.5 Hz, 2 H), 1.28–1.60 (m, 6 H), 2.34 (s, 3 H), 3.24–3.369 (m, 4 H), 3.63 (d, *J* = 6.7 Hz, 1 H), 3.75 (d, *J* = 5.7 Hz, 1 H), 7.19–7.24 (m, 4 H), 7.52 (d, *J* = 3.1 Hz, 2 H), 7.53 (d, *J* = 3.1 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (both diastereomers) = 10.0, 10.2, 21.2, 22.0, 22.4, 31.0, 31.1, 51.1, 52.2, 125.6, 125.8, 129.3, 129.3, 140.9, 140.9, 142.3, 142.7.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{17}NOS$ (M + H^+): 212.1104; found: 212.1105.

N-(*p*-Tolylsulfinyl)benzylamine (35)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.23 g (92%) of the title compound as a white solid; mp 69–72 °C.

IR (Nujol): 3215, 1596, 1087, 1055 cm^{-1}.

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.42 (s, 3 H), 3.91 (dd, *J* = 14.7, 8.4 Hz, 1 H), 4.18–4.32 (m, 2 H), 7.26–7.34 (m, 7 H), 7.62–7.70 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 44.6, 126.0, 127.6, 128.3, 128.6, 129.6, 137.9, 141.0, 141.3.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{15}NOS$ (M + H^+): 246.0947; found: 246.0947.

N-Tolylsulfinylphenethylamine (36)

The crude product was purified via flash chromatography (70:30, hexanes/EtOAc) to yield 0.24 g (58%) of the product as a white solid; mp 51–54 °C.

IR (Nujol): 3206, 1598, 1089, 1061 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 2.82 (t, *J* = 7.1 Hz, 2 H), 3.06–3.14 (m, 1 H), 3.33–3.42 (m, 1 H), 4.36 (brs, 1 H), 7.16 (d, *J* = 7.4 Hz, 2 H), 7.20–7.31 (m, 5 H), 7.55 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 36.9, 42.1, 126.1, 126.4, 128.5, 128.9, 129.5, 138.8, 141.0, 141.2.

ESI-HRMS: *m*/*z* calcd for $C_{15}H_{17}NOSNa$ (M + Na^+): 282.0923; found: 282.0925.

N-(*p*-Tolylsulfinyl)-3,4-dimethylphenethylamine (37)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.46 g (90%) of the title compound as a clear oil.

IR (neat): 3298, 1593, 1516, 1261, 1156, 1088, 1030, 812, 754 cm^{-1}.

^{1}H NMR (400 MHz $CDCl_3$): δ = 2.41 (s, 3 H), 2.76 (t, *J* = 6.9 Hz, 2 H), 3.02–3.12 (m, 1 H), 3.31–3.41 (m, 1 H), 3.84 (s, 3 H), 3.86 (s, 3 H), 3.98–4.06 (m, 1 H), 6.64–6.72 (m, 2 H), 6.79 (d, *J* = 8.1 Hz, 1 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 7.53 (d, *J* = 8.1 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 36.5, 42.3, 42.3, 55.8, 56.0, 111.4, 112.1, 120.8, 125.9, 129.5, 131.0, 141.1, 141.2, 147.7, 149.0.

ESI-HRMS: *m*/*z* calcd for $C_{17}H_{21}NO_3S$ (M + H^+): 320.1315; found: 320.1315.

N-Toluenesulfinyl-(*R*)-(+)-1-phenylethylamine (28)

The crude product was purified via flash chromatography (70:30, hexanes/EtOAc) to yield 0.307 g (74%) of the product as a white solid; mp 68–70 °C; $[\alpha]_D$ +21.19 (*c* = 1.00, $CHCl_3$).

IR (Nujol): 3206, 1595, 1084, 1053 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (both diastereomers) = 1.49 (d, *J* = 6.8 Hz, 3 H), 1.65 (d, *J* = 6.8 Hz, 3 H), 2.40 (s, 3 H), 2.44 (s, 3 H), 4.13 (d, *J* = 16.8 Hz, 1 H), 4.25 (d, *J* = 16.8 Hz, 1 H), 4.57–4.62 (m, 1 H), 4.68–4.73 (m, 1 H), 7.2–7.3 (m, 10 H), 7.39–7.46 (m, 4 H), 7.59 (d, *J* = 8.1 Hz, 2 H), 7.63 (d, *J* = 8.1 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (both diastereomers) = 21.3, 24.1, 24.6, 52.1, 53.5, 125.6, 125.9, 126.4, 127.0, 127.3, 127.5, 128.5, 128.6, 129.3, 129.5, 141.0, 141.1, 141.5, 142.6, 143.5, 144.0.

ESI-HRMS: *m*/*z* calcd for $C_{15}H_{17}NOS$ (M + H^+): 260.1104; found: 260.1107.

N-Tolylsulfinyl-(*S*)-(–)-α-(1-naphthyl)ethylamine (38)

The crude product was purified via flash chromatography (70:30, hexanes/EtOAc) to yield 0.331 g (67%) of the product as a white solid; mp 110–113 °C; $[\alpha]_D$ +97.3 (*c* = 1.00, $CHCl_3$).

IR (Nujol): 3187, 1594, 1054 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (both diastereomers) = 1.70 (d, *J* = 6.7 Hz, 3 H), 1.81 (d, *J* = 6.7 Hz, 3 H), 2.31 (s, 3 H), 2.40 (s, 3 H), 4.44 (s, 1 H), 4.60 (s, 1 H), 5.39–5.44 (m, 1 H), 5.51–5.56 (m, 1 H), 7.12 (d, *J* = 8.12 Hz, 2 H), 7.28 (d, *J* = 7.8 Hz, 2 H), 7.40–7.56 (m, 8 H), 7.59–7.64 (m, 3 H), 7.68 (d, *J* = 7.2 Hz, 1 H), 7.74 (d, *J* = 8.1 Hz, 1 H), 7.83 (d, *J* = 8.6 Hz, 2 H), 7.92 (d, *J* = 7.9 Hz, 1 H), 8.00 (d, *J* = 5.3 Hz, 1 H), 8.31 (d, *J* = 8.6 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (both diastereomers) = 21.2, 21.3, 23.4, 24.2, 47.9, 50.6, 123.0, 123.4, 123.7, 123.9, 125.4, 125.5, 125.6, 125.7, 125.8, 126.1, 126.3, 128.0, 128.3, 128.9, 129.1, 129.3, 129.5, 130.2, 130.8, 133.8, 134.1, 139.0, 139.4, 141.1, 141.3, 141.4, 142.7.

ESI-HRMS: *m*/*z* calcd for $C_{19}H_{19}NOS$ (M + H^+): 310.1260; found: 310.1264.

N-Tolylsulfinyl-*tert*-butylamine (39)

The crude product was purified via flash chromatography (70:30, hexanes/EtOAc) to yield 0.149 g (44%) of the product as a white solid; mp 79–81 °C.

IR (Nujol): 1596, 1087, 1042, 818 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (s, 3 H), 2.40 (s, 3 H), 3.79 (s, 1 H), 7.28 (d, *J* = 8.3 Hz, 2 H), 7.58 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.2, 31.1, 54.1, 125.6, 129.3, 140.8, 143.6.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{17}NOS$ (M + H^+): 212.1104; found: 212.1103.

N-(*p*-Tolylsulfinyl)pyrrolidine (40)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.11 g (33%) of the title compound as a transparent oil.

IR (neat): 3026, 1597, 1088, 1067 cm^{-1}.

^{1}H NMR (MHz $CDCl_3$): δ = 1.80–1.89 (m, 4 H), 2.40 (s, 3 H), 2.96–3.05 (m, 2 H), 3.29–3.39 (m, 2 H), 7.27–7.30 (m, 2 H), 7.54–7.58 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 26.0, 46.0, 125.8, 129.5, 140.8, 141.6.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{15}NOS$ (M + H^+): 210.0947; found: 210.0947.

N-(*p*-Tolylsulfinyl)piperidine (41)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.28 g (78%) of the title compound as a transparent oil that slowly solidified to a white solid; mp 62–64 °C.

IR (neat): 1651, 1597, 1452, 1212, 1088, 1038, 912, 813 cm^{-1}.

^{1}H NMR (400 MHz $CDCl_3$): δ = 1.48–1.68 (m, 6 H), 2.41 (s, 3 H), 2.90–3.00 (m, 2 H), 3.05–3.15 (m, 2 H), 7.30 (d, *J* = 7.9 Hz, 2 H), 7.53 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 24.0, 26.2, 46.9, 126.2, 129.5, 140.4, 141.0.

ESI-HRMS: *m*/*z* calcd for $C_{12}H_{17}NOS$ (M + H^+): 224.1104; found: 224.1103.

N-Tolylsulfinylmorpholine (42)

The crude product was purified via flash chromatography (70:30, hexanes/EtOAc) to yield 0.22 g (61%) of the product as a white solid; mp 120–121 °C.

IR (Nujol): 1594, 1108, 1066, 819 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 2.93–3.00 (m, 2 H), 3.12–3.19 (m, 2 H), 3.66–3.76 (m, 4 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.55 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 45.7, 66.9, 126.1, 129.6, 139.2, 141.5.

ESI-HRMS: *m*/*z* calcd for $C_{11}H_{15}NO_2S$ (M^+): 225.0824; found: 225.1962.

*N*2-(*p*-Tolylsulfinyl)-*tert*-butyl Carbazate (43)

The product was purified by flash chromatography (60:40, hexanes/EtOAc) to yield 0.42 g (97%) of the title compound as a yellow oil.

IR (Nujol): 3154, 1597, 1017 cm^{-1}.

^{1}H NMR (400 MHz $CDCl_3$): δ = 1.36 (s, 9 H), 2.41 (s, 3 H), 6.08 (br, 1 H), 6.58 (br, 1 H), 7.32 (d, *J* = 7.9 Hz, 2 H) 7.67 (d, *J* = 7.9 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 28.1, 81.3, 126.1, 129.5, 138.2, 142.2, 155.6.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{14}N_2O_2S$ (M + H^+): 271.1111; found: 271.1110.

*N*2-(*p*-Tolylsulfinyl)benzhydrazide (44)

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.12 g (28%) of the title compound as a white solid; mp 129–132 °C.

IR (neat): 3436, 3187, 1662, 1295, 1216, 1090, 1065, 940 cm^{-1}.

^{1}H NMR (MHz $CDCl_3$): δ = 2.42 (s, 3 H), 6.89 (br d, *J* = 4.2 Hz, 1 H), 7.35(d, *J* = 8.2 Hz, 2 H), 7.39–7.45 (m, 2 H), 7.51–7.54 (m, 1 H), 7.69 (d, *J* = 7.4 Hz, 2 H), 7.74 (d, *J* = 8.0 Hz, 2 H), 8.00 (br d, *J* = 4.6 Hz, 1 H).

^{13}C NMR (MHz, $CDCl_3$): δ = 20.8, 125.5, 127.1, 128.2, 129.3, 131.6, 131.9, 137.8, 142.4, 168.1.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{14}N_2O_2S$ (M + H^+): 275.0849; found: 275.0848.

N-*p*-Tolylsulfinamido-L-phenylalanine Methyl Ester [(R_S,*S*)- and (S_S,*S*)-46a]

The product was purified via flash column chromatography ($CHCl_3$/MeOH, 99:1) and was obtained as a translucent oil (0.29 g, 57%).

IR (neat): 3291, 1493, 1211, 1172, 1069 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 2.41 (s, 3 H), 2.43 (s, 3 H), 2.77–2.85 (m, 2 H), 3.07 (dd, *J* = 13.8, 6.82 Hz, 1 H), 3.20 (dd, *J* = 13.8, 6.82 Hz, 1 H), 3.64 (s, 3 H), 3.74 (s, 3 H), 3.93–3.97 (m, 1 H), 4.25–4.29 (m, 1 H), 4.64 (d, *J* = 8.6 Hz, 1 H), 4.92 (d, *J* = 9.7 Hz, 1 H), 6.97–6.99 (m, 4 H), 7.19–7.35 (m, 6 H), 7.40 (d, *J* = 8.3 Hz, 4 H), 7.49 (d, *J* = 8.3 Hz, 4 H).

^{13}C NMR (125 MHz $CDCl_3$): δ = 21.3, 39.9, 40.6, 52.3, 52.5, 53.7, 56.9, 125.7, 126.0, 126.9, 127.1, 128.4, 128.6, 129.4, 129.5, 129.5, 129.6, 135.8, 136.0, 140.3, 141.2, 141.3, 141.5, 172.5, 173.3.

ESI-HRMS: *m*/*z* calcd for $C_{17}H_{20}NO_3S$ (M + H^+): 318.1158; found: 318.1155

N-*p*-Tolylsulfinamido-L-phenylglycine Methyl Ester [(R_S,*S*)- and (S_S,*S*)-46b]

The product was purified via flash column chromatography ($CHCl_3$/MeOH, 99:1) and was obtained as a clear wax (0.33 g, 69%).

IR (neat): 3236, 1738, 1204, 1166, 1092 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 2.37 (s, 3 H), 2.45 (s, 3 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 4.88 (d, *J* = 7.5 Hz, 1 H), 5.07 (d, *J* = 5.8 Hz, 1 H), 5.17 (d, *J* = 5.8 Hz, 1 H), 5.56 (d, *J* = 7.5 Hz, 1 H), 7.00–7.03 (m, 2 H), 7.16–7.22 (m, 2 H), 7.33–7.45 (m, 6 H), 7.50 (d, *J* = 8.2 Hz, 4 H), 7.64 (d, *J* = 8.2 Hz, 4 H).

^{13}C NMR (125 MHz $CDCl_3$): δ = 21.3, 21.4, 52.8, 53.0, 55.0, 58.7, 125.6, 126.3, 127.2, 128.0, 128.5, 128.7, 129.0, 129.3, 129.6, 136.9, 137.1, 140.0, 141.4, 141.7, 171.5, 172.3.

ESI-HRMS: *m*/*z* calcd for $C_{17}H_{19}NO_3S$ (M + H^+): 304.1002; found: 304.1012.

Chromatographic purification allowed for the partial isolation of the faster eluting diastereomer **(S_S,*S*)-46b**.

N-*p*-Tolylsulfinamido-L-phenylglycine Methyl Ester [(S_S,*S*)-46b]

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 2.34 g (78%) of the title compound as a mixture of diastereomers (only the major isolated diastereomer is reported); mp 72–75 °C.

^{1}H NMR (500 MHz $CDCl_3$): δ = 2.42 (s, 3 H), 3.63 (s, 3 H), 5.07 (d, *J* = 5.8 Hz, 1 H), 5.17 (d, *J* = 5.8 Hz, 1 H), 7.30–7.44 (m, 7 H), 7.60–7.64 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 52.9, 58.8, 125.7, 127.8, 128.8, 129.1, 129.8, 137.0, 141.5, 141.9, 171.7.

ESI-HRMS: *m*/*z* calcd for $C_{16}H_{17}NO_3S$ (M + H^+): 304.1002; found: 304.1003.

N-*p*-Tolylsulfinamido-L-valine Methyl Ester [(*R*$_S$,*S*)- and (*S*$_S$,*S*)-46c]

The product was purified via flash column chromatography ($CHCl_3$/MeOH, 99:1) and was obtained as a clear oil (0.35 g, 81%).

IR (neat): 3243, 1740, 1202, 1179 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 0.70 (d, *J* = 6.7 Hz, 3 H), 0.79 (d, *J* = 6.9 Hz, 3 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 1.05 (d, *J* = 6.7 Hz, 3 H), 1.79–1.89 (m, 1 H), 2.07–2.16 (m, 1 H), 2.44 (s, 6 H), 3.43 (dd, *J* = 10.4, 5.5 Hz, 1 H), 3.70 (s, 3 H), 3.79 (s, 3 H) 3.83 (dd, *J* = 8.5, 5.5 Hz, 1 H), 7.28–7.34 (m, 4 H), 7.57–7.64 (m, 4 H).

^{13}C NMR (125 MHz $CDCl_3$): δ = 17.7, 18.0, 18.8, 19.2, 21.4, 31.4, 32.2, 52.2, 52.3, 57.5, 61.7, 125.5, 126.2, 129.4, 129.6, 140.6, 141.4, 141.6, 141.9, 173.1, 173.9.

ESI-HRMS: *m*/*z* calcd for $C_{13}H_{20}NO_3S$ (M + H^+): 270.1158; found: 270.1154.

Chromatographic purification allowed for the partial isolation of the faster eluting diastereomer **(*S*$_S$,*S*)-46c**.

N-*p*-Tolylsulfinamido-L-valine Methyl Ester [(*S*$_S$,*S*)-46c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.8 Hz, 3 H), 1.02 (d, *J* = 6.8 Hz, 3 H), 2.04–2.14 (m, 1 H) 2.41 (s, 3 H), 3.68 (s, 3 H), 3.81 (dd, *J* = 8.8, 5.2 Hz, 1 H), 4.60 (d, *J* = 8.8 Hz, 1 H), 7.28–7.34 (m, 2 H), 7.57–7.64 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 19.3, 21.4, 32.3, 52.3, 61.8, 125.6, 129.6, 141.7, 142.0, 173.2.

ESI-HRMS: *m*/*z* calcd for $C_{13}H_{19}NO_3S$ (M + H^+): 270.1158; found: 270.1157.

N-*p*-Tolylsulfinamido-L-*tert*-leucine Methyl Ester [(*R*$_S$,*S*)- and (*S*$_S$,*S*)-46d]

The product was purified by flash chromatography (70:30, hexanes/EtOAc) to yield 0.42 g (94%) of the title compound as a clear oil.

IR (neat): 3293, 1739, 1217, 1160, 814 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of diastereomers) = 0.78 (s, 9 H), 1.02 (s, 9 H), 2.44 (s, 6 H), 3.21 (d, *J* = 11.2 Hz, 1 H), 3.68 (s, 3 H), 3.69 (d, *J* = 9.8 Hz, 1 H), 3.78 (s, 3 H), 4.63 (d, *J* = 9.8 Hz, 1 H), 5.00 (d, *J* = 11.2 Hz, 1 H), 7.33 (d, *J* = 7.9 Hz, 4 H), 7.58 (d, *J* = 8.2 Hz, 2 H), 7.62 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (125 MHz $CDCl_3$): δ = 21.3, 26.5, 33.6, 34.8, 51.8, 52.0, 60.0, 64.9, 125.4, 126.2, 129.3, 129.5, 140.0, 141.4, 141.5, 142.0, 172.8, 173.6.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{22}NO_3S$ (M + H^+): 284.1315; found: 284.1323.

Chromatographic purification allowed for the partial isolation of the faster eluting diastereomer (*S*$_S$,*S*)-**46d**.

N-*p*-Tolylsulfinamido-L-*tert*-leucine Methyl Ester [(*S*$_S$,*S*)-46d]

^{1}H NMR (400 MHz $CDCl_3$): δ = 1.00 (s, 9 H), 2.42 (s, 3 H), 3.66 (s, 3 H), 3.67 (d, *J* = 9.8 Hz, 1 H), 4.62 (d, *J* = 9.8 Hz, 1 H), 7.28–7.34 (m, 2 H), 7.56–7.63 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 26.5, 33.7, 52.1, 60.1, 126.3, 129.4, 140.1, 141.5, 173.7.

ESI-HRMS: *m*/*z* calcd for $C_{14}H_{21}NO_3S$ (M + H^+): 284.1315; found: 284.1313.

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Supporting Information

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