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Remarkably Mild and Simple Preparation of Sulfenate Anions from β-Sulfinylesters: A New Route to Enantioenriched Sulfoxides

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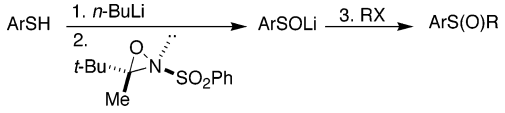
A general, efficient, and experimentally simple method for the generation of sulfenate salts has been developed using β-sulfinylesters as substrates. The process is based on a retro-Michael reaction, initiated by deprotonation at low temperature. Upon treatment with alkyl halides, the liberated sulfenates are subsequently converted into sulfoxides in good to excellent yield. Extension of the methodology to an unprecedented access to nonracemic sulfoxides by introduction of an enantiopure ligand, (−)-sparteine, is also described.

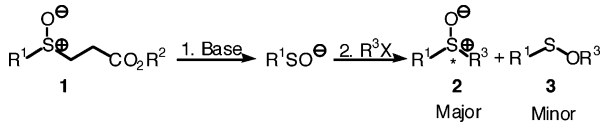
Sulfenate salts RSO^- are not common sulfur nucleophiles for the organic chemist, the major contributing factor being a lack of efficient methods for their generation.[1] However, these anions are very attractive as precursors of sulfenic acids, sulfoxides, sulfenate esters, sulfenamides, and thiols. Furthermore, interest in sulfenates has recently been heightened by their identification as key intermediates in some bioorganic transformations.[1]

As part of our research[2] into the oxidation of thiolates with *N*-sulfonyloxaziridines, we have previously reported an original and efficient approach to arenesulfenate anions[2a,b] and introduced an unusual *N*-sulfonyloxaziridine derived from pinacolone as the ideal reagent (Scheme 1). Subsequent S-alkylation with aliphatic halides led to sulfoxides in good to excellent yield. The mild conditions we developed (−78 °C) allowed the reaction to be quite general with high chemoselectivity and compatibility with a wide range of thiophenols. However, application of the methodology to the preparation of alkanesulfenates was unsuccessful. Under similar conditions, instead of the desired monooxidation product, the sulfinate salt (RSO_2Li) was isolated as a consequence of an unwanted double-oxidation reaction.[3]

SCHEME 1. Arenesulfenates by Thiolate Oxidation



SCHEME 2. Sulfenates from β-Sulfinylesters



Other reported approaches[1] to sulfenate anions involve transformations of sulfenate esters, sulfines, or sulfoxides, but very few are efficient with a broad spectrum of applicability.[4] As a consequence, new methods for the generation of sulfenates are needed, the ideal strategy being one that proceeds efficiently in both the aryl and alkyl series. We reasoned that β-sulfinylesters **1** could be suitable precursors[5] through a base-promoted retro-Michael reaction (Scheme 2). On the basis of pK_a values,[6] proton abstraction should occur regioselectively α to the carbonyl group; the enolate thus formed should then be susceptible to fragmentation with concomitant liberation of the sulfenate salt and an acrylate byproduct.[7−9] In this

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(1) For a recent review including chemical and biological aspects of sulfenates: O'Donnell, J. S.; Schwan, A. L. *J. Sulfur Chem.* **2004**, *25*, 183-211.

(2) (a) Sandrinelli, F.; Perrio, S.; Beslin, P. *J. Org. Chem.* **1997**, *62*, 8626−8627. (b) Sandrinelli, F.; Perrio, S.; Averbuch-Pouchot, M.-T. *Org. Lett.* **2002**, *4*, 3619−3622. (c) Sandrinelli, F.; Fontaine, G.; Perrio, S.; Beslin, P. *J. Org. Chem.* **2004**, *69*, 6916−6919. (d) Sandrinelli, F.; Perrio, S.; Beslin, P. *Org. Lett.* **1999**, *1*, 1177−1180.

(3) Despite having screened a range of oxaziridines with varying structural characteristics, we have thus far been unable to identify a suitable reagent for this reaction.

(4) For the most relevant contributions: Schwan introduced methyl β-sulfinylacrylate esters as a convenient source of sulfenate anions with an addition/elimination methodology. (a) O'Donnell, J. S.; Schwan, A. L. *Tetrahedron Lett.* **2003**, *44*, 6293−6296. Tanaka reported the formation of zinc sulfenates by oxidative addition of 1-alkynyl sulfoxides with a Pd(0) catalyst followed by transmetalation with Et_2Zn. (b) Maezaki, N.; Yagi, S.; Ohsawa, S.; Ohishi, H.; Tanaka, T. *Tetrahedron* **2003**, *59*, 9895−9906. (c) Maezaki, N.; Yagi, S.; Maeda, J.; Yoshigami, R.; Tanaka, T. *Heterocycles* **2004**, *62*, 263−277. (d) Maezaki, N.; Yagi, S.; Yoshigami, R.; Maeda, J.; Suzuki, T.; Ohsawa, S.; Tsukamoto, K.; Tanaka, T. *J. Org. Chem.* **2003**, *68*, 5550−5558.

(5) According to literature precedents, the synthesis of **1** can be achieved in only two steps from the appropriate thiol. See for example: (a) Ranu, B. C.; Dey, S. S.; Hajra, A. *Tetrahedron* **2003**, *59*, 2417−2421. (b) Greenhalgh, R. P. *Synlett* **1992**, 235−236.

(6) The pK_a value (in DMSO) of a proton α to a sulfoxide group is 33−36, compared with around 30 for a proton α to an ester carbonyl.

(7) Concomitant liberation of an alkene and a sulfenate salt was recently reported with a secondary α-lithiosulfinyl carbanion through a tandem zinc homologation−β-elimination reaction, but the authors focused only on the olefin product. Abramovitch, A.; Varghese, J. P.; Marek, I. *Org. Lett.* **2004**, *6*, 621−623.

(8) Reaction with analogous compounds incorporating sulfide or sulfone functionalities has already been examined by other groups and provided an elegant and highly efficient access to thiolate and sulfinate anions, respectively: (a) Becht, J.-M.; Wagner, A.; Mioskowski, C. *J. Org. Chem.* **2003**, *68*, 5758−5761. (b) Becht, J.-M.; Wagner, A.; Mioskowski, C. *Tetrahedron Lett.* **2004**, *45*, 7031−7033. (c) Baskin, J. M.; Wang, Z. *Tetrahedron Lett.* **2002**, *43*, 8479−8483.

(9) Substrates **1** have been reported to undergo a facile thermolysis to the corresponding sulfenic acid, which was efficiently trapped in situ with an activated alkene or alkyne: (a) Bilokin, Y. V.; Melman, A.; Niddam, V.; Benhamú, B.; Bachi, M. D. *Tetrahedron* **2000**, *56*, 2425−2437. (b) Melwig, J. Y.; Jullien, Y.; Curci, M.; Mieloszynski, J.

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SCHEME 3. Preparation of β-Sulfinylesters

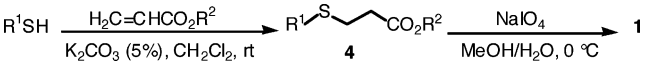


TABLE 1. Influence of the Base and Solvent with 1a (R^1 = 4-MeC_6H_4 and R^2 = Et) According to Scheme 2

entry	base	solvent	R^3X	sulfoxide	isolated yield[a] (%)
1	NaHMDS[b]	THF	BnBr	**2a$_1$**	91
2	NaH	THF	BnBr	**2a$_1$**	77
3	KHMDS[c]	THF	BnBr	**2a$_1$**	82
4	KHMDS[c]	toluene	BnBr	**2a$_1$**	79
5	LDA[d]	THF	BnBr	**2a$_1$**	83
6	BuLi	THF	BnBr	**2a$_1$**	65
7	*t*-BuOK[e]	THF	BnBr	**2a$_1$**	77
8	*t*-BuOK[e]	THF	MeI	**2a$_2$**	83 (15)
9	*t*-BuOK[e]	THF	EtI	**2a$_3$**	88 (5)

[a] Isolated yields of sulfenate esters **3** (if produced) are shown in parentheses. [b] 2 M solution in THF. [c] 0.5 M in toluene . [d] Freshly prepared by reaction of BuLi with *i*-Pr_2NH. [e] 1 M solution in THF.

Note, we present the results obtained with this approach, and the generated sulfenates were all converted into sulfoxides **2** by treatment with alkyl halides. We also describe an asymmetric variant on this theme in which enantioselective alkylation of the prochiral sulfenates affords enantioenriched sulfoxides.

We began by investigating 3-*p*-tolylsulfinylpropionic acid ethyl ester **1a** (R^1 = 4-MeC_6H_4 and R^2 = Et, Scheme 3) as the substrate. Reaction of 4-methylthiophenol with ethyl acrylate in the presence of a catalytic amount of K_2CO_3 gave thioether **4a** in 92% yield. Subsequent oxidation with $NaIO_4$ in a methanol/water solution afforded the desired sulfoxide in 75% yield.[10] Conveniently, the intermediate sulfide **4a** was used in its crude form and the final sulfoxide **1a** purified by a rapid filtration on silica gel. The synthesis was routinely performed on a 20 g scale without loss of efficiency.

The validity of our concept was then examined using our prototype compound **1a** and a variety of bases and solvents. The sulfoxide **1a** was treated at low temperature (−78 °C) with stoichiometric amounts of bases, including NaHMDS, NaH, KHMDS, LDA, BuLi, and *t*-BuOK.[11] After 20 min, benzyl bromide was added to trap the eventual sulfenate anion formed. The results obtained are listed in Table 1. In all cases, the anticipated benzyl sulfoxide **2a$_1$** was produced and isolated in a good to excellent yield (65−91%, entries 1−7). Examination of the crude product revealed the absence of sulfenic ester, which might arise through a competing O-alkylation of the ambident sulfenate.[12] Variation of the solvent employed is also possible, sulfoxide **2a$_1$** being formed with the same efficiency in THF and toluene (compare entries 3 and 4). Use of methyl and ethyl iodides as alternative electrophiles with the *t*-BuOK/THF conditions likewise led to the corresponding sulfoxides **2a$_2$** and **2a$_3$** in yields of ≥83% (entries 8 and 9). Contamination with sulfenate esters **3a$_2$** and **3a$_3$** was observed this time, but only to a small degree (<15%).[13] Both S-and O-alkylation products were readily separated by purification on a silica gel column. The overall yield for the alkylation was 98 and 93%, respectively, again demonstrating the efficiency of the intermediate sulfenate formation.

TABLE 2. Sulfoxides 2 via Sulfenates According to Scheme 2

entry	substrate	R^1	R^2	R^3X	product	isolated yield[a] (%)
1	**1b**	2-$MeOC_6H_4$	Et	MeI	**2b**	80 (13)
2	**1c**	2,6-$Me_2C_6H_3$	Et	BnBr	**2c**	68
3	**1d**	Me	Me	BnBr	**2d**	68
4	**1e**	*n*-Bu	Et	BnBr	**2e**	95
5	**1f**	Bn	Et	BnBr	**2f**	57[b]
6	**1g**	cyclo-C_6H_{11}	Et	BnBr	**2g**	76
7	**1h**	*t*-Bu	Et	BnBr	**2h**	79

[a] Isolated yield of sulfenate ester **3b** is shown in parentheses. [b] Yield was 56% with NaHMDS in THF.

To investigate the scope of the reaction, a range of sulfinyl esters **1** with various aromatic and aliphatic R^1 substituents were then examined using *t*-BuOK as a base and THF as the solvent.[14] In all cases, the corresponding arene- and alkanesulfenates were formed, with alkylation affording the corresponding sulfoxides **2** in good to excellent yield (Table 2). Furthermore, there appears to be no restrictions on structure in the aliphatic series, as primary (entries 3−5), secondary (entry 6), and tertiary (entry 7) sulfenates were efficiently generated. As already reported above, sulfenic ester **3b** was obtained as a side product when methyl iodide was used as the electrophile (entry 1).

Having developed a general and efficient access to sulfenate anions with wide experimental tolerances, we felt it had the potential for further development, its use in asymmetric synthesis being of particular interest. Sulfenates being prochiral, a stereogenic sulfur center is produced upon alkylation. Any control over the resulting stereochemistry arises through a discrimination between the two sulfur lone pairs of the sulfenate. However, use of these sulfur nucleophiles in this area has received scant attention. Diastereoselective approaches with lithium sulfenates already possessing a chiral center have been reported,[2b,4a,15] and high asymmetric inductions, with diastereomeric ratios of up to 98:2, were accomplished upon reaction with alkyl halides. In addition, an asymmetric sulfinylzincation of alkynoates has been investigated by Tanaka et al, whose best diastereoselectivity (92:8) was obtained using an isoborneol

L.; Paquer, D. *Phosphorus Sulfur* **1996**, *118*, 105−111. (c) Tsukurimichi, E.; Yoshimura, T.; Yoshizawa, M.; Itakura, H.; Shimasaki, C. *Phosphorus Sulfur* **1989**, *46*, 113−120. (d) Crich, D.; Lim L. B. L. *J. Chem. Res., Synop.* **1987**, 353. (e) Bachi, M. D.; Gross, A. *J. Org. Chem.* **1982**, *47*, 897−898. (f) Shelton, J. R.; Davis, K. E. *Int. J. Sulfur Chem.* **1973**, *8*, 205−216.

(10) If the temperature is rigorously controlled (<0 °C), no sulfone is detected.

(11) Sulfinylester **1a** survived base workup with saturated Na_2CO_3 or K_2CO_3 and 1 N NaOH solutions.

(12) (a) Hogg, D. R.; Robertson, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1125−1128. (b) Kobayashi, M.; Toriyabe, K. *Sulfur Lett.* **1985**, *3*, 117−122.

(13) Alkylation with the soft alkyl halide still takes place predominantly at the soft sulfur center of the sulfenates. Use of NaHMDS as a base in THF and methyl iodide as the electrophile led to sulfenate ester **2a$_2$** in 9% yield. In contrast, only a 3.5% yield of **2a$_2$** was obtained with *n*-BuLi.

(14) Commercial 1 M *t*-BuOK solution in THF was preferred over the other bases previously on account of its ease of handling, liberation of the water-soluble *tert*-butyl alcohol, and isolation of cleaner crude products according to their ^1H NMR spectra.

(15) (a) Blake, A. J.; Westaway, S. M.; Simpkins, N. S. *Synlett* **1997**, 919−920. (b) Blake, A. J.; Cooke, P. A.; Kendall, J. D.; Simpkins, N. S.; Westaway, S. M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 153−163.

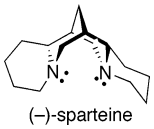
TABLE 3. Solvent Effect in the (−)-Sparteine-Mediated Alkylation of a Sulfenate Generated from 1a (R^1 = 4-MeC_6H_4 and R^2 = Et) at −40 °C According to Scheme 2

entry	R^3X	sulfoxide	solvent	yield (%)[a]	ee (%)	configuration
1	MeI	**2a$_2$**	THF	42	0	
2	MeI	**2a$_2$**	Et_2O	47	0	
3	MeI	**2a$_2$**	cumene	59	0	
4	MeI	**2a$_2$**	pentane	4	0	
5	MeI	**2a$_2$**	TMTHF	44	5	*S*
6	MeI	**2a$_2$**	toluene	54	23	*S*
7	BnBr	**2a$_1$**	toluene	59	17	*S*

[a] Alkylation time was set at 4 h.

derivative.[4b] With regard to enantioselective approaches, Kobayashi achieved a modest transfer of chirality (23% ee) in the alkylation of anthraquinone-1-sulfenate with an enantiopure sulfonium salt.[16]

We envisaged an alternative and conceptually different approach based on an external ligand-controlled enantioselective alkylation. By introduction of an enantiopure coordinating ligand, both lone pairs on sulfur become diastereotopic, and we can expect that one will react preferentially to give an enantioenriched sulfoxide.[17] This could provide an original and convergent route to nonracemic sulfoxides, the traditional strategies being asymmetric oxidations of prochiral sulfides or Andersen-type reactions.[18] As a preliminary study, we chose for our purposes (−)-sparteine, a tetracyclic lupine alkaloid with broad applications in asymmetric synthesis, when associated to a lithium cation.[19] The influence of solvent and temperature was examined using the *p*-tolyl-substituted sulfinyl ester **1a**.



The chiral lithium base was prepared at room temperature by reaction of equimolar amounts of *n*-BuLi and (−)-sparteine and then added to a cooled solution (−40 °C) of *β*-sulfinylester **1a** in one of the six solvents listed in Table 3. Methyl iodide (1 equiv) is then added, with the alkylation time arbitrarily set at 4 h. After hydrolysis and purification by column chromatography,[20] the enantiomeric excesses were determined by enantioselective stationary phase HPLC (OB−H column). Use of THF, diethyl ether, and cumene led to the formation of the anticipated sulfoxide **2a$_2$** in 42−59% yield, but in racemic form[21] (entries 1−3). Even though these results were

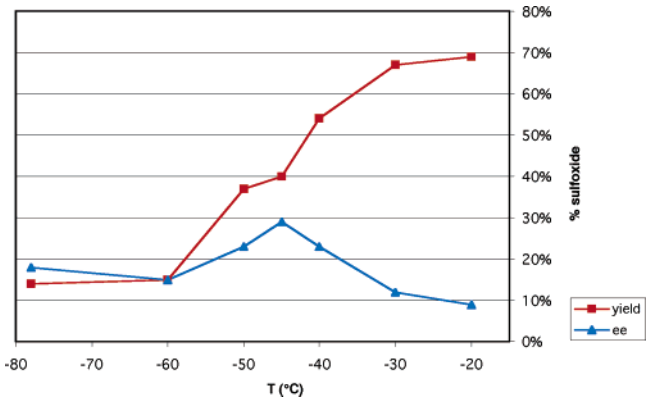


FIGURE 1. Effect of temperature on the (−)-sparteine-mediated alkylation of the sulfenate anion of **1a** (R^1 = 4-MeC_6H_4) with methyl iodide (R^3X = MeI, 1 equiv) in toluene for 4 h according to Scheme 2.

disappointing in terms of enantioselectivity, they indicated clearly that the presence of the chiral bidentate ligand does not adversely affect sulfenate formation and the subsequent alkylation. A lack of enantioselectivity was also observed in pentane in which the yield was a mere 4% due to the poor solubility of the reactants (entry 4). A slight enantiomeric excess of 5% in favor of the (*S*)-enantiomer was observed in 2,2,5,5-tetramethyltetrahydrofuran as a solvent (entry 5). Gratifyingly, a significant improvement with a 23% ee for the (*S*)-configuration product and a 54% yield was obtained in toluene (entry 6).[22] Use of benzyl bromide (1 equiv) as an alternative electrophile under similar conditions led to sulfoxide **2a$_1$** in 17% ee (AD-H column), likewise with the (*S*)-stereochemistry and 59% yield.[22]

With toluene having been identified as the best solvent, the influence of the temperature over a range from −78 to −20 °C was next examined. This parameter was found to play a crucial role in both the conversion and the enantioselectivity, as can be seen from Figure 1. The isolated yield of sulfoxide **2a$_2$** increases almost linearly with the temperature. Whereas a poor yield of 14% was obtained at −78 °C, an increase to 69% was observed at −20 °C, though with an enantioselectivity of only 9%. A nonclassical temperature effect, explained by the principle of isoinversion[23] introduced by Scharf et al., was observed for the enantioselectivity, the highest enantiomeric excess (29%) being obtained at −45 °C for the (*S*)-enantiomer.

In summary, we have developed a practical and highly efficient route to versatile sulfenate salts through a base-promoted retro-Michael reaction of *β*-sulfinylesters. Subsequent alkylation at the sulfur center with alkyl halides led to sulfoxides in good to excellent yield. Use of a 1:1

(16) Kobayashi, M.; Manabe, K.; Umemura, K.; Matsuyama, H. *Sulfur Lett.* **1987**, *6*, 19−24.

(17) Asymmetric dehydration of sulfenic acid *t*-BuSOH in the presence of enantiopure amines led to thiosulfinate *t*-BuS(O)S*t*-Bu with an optimal ee of 26%. Drabowicz, J.; Lyzwa, P.; Mikolajczyk, M. *Phosphorus Sulfur* **1983**, *16*, 267−270.

(18) Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651−3705.

(19) (a) *Organolithiums in Enantioselective Synthesis, Topics in Organometallic Chemistry*, Hodgson, D. M., Ed.; Springer: Berlin, 2003; Vol. 5. (b) Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282−2316. (c) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Baldwin, J. E., Williams, R. M., Eds; Pergamon Press: Oxford, 2002; Vol. 23.

(20) No sulfenic ester was detected this time.

(21) THF and Et_2O probably compete with the (−)-sparteine as a lithium ligand.

(22) Stereochemistry assignment can be found in Supporting Information.

(23) (a) Buschmann, H.; Scharf, H.-D.; Hoffmann, N.; Esser, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 477−515. (b) Gypser, A.; Norrby, P.-O. *J. Chem Soc., Perkin Trans. 2* **1997**, 939−943. (c) Cainelli, G.; Giacomini, D.; Galletti, P. *J. Chem. Soc., Chem. Commun.* **1999**, 567−572. (d) Nowaczyk, S.; Alayrac, C.; Metzner, P.; Averbuch-Pouchot, M.-T. *J. Org. Chem.* **2002**, *67*, 6852−6855. (e) Hénin, F.; Létinois, S.; Muzart, J. *Tetrahedron: Asymmetry* **2000**, *11*, 2037−2044. (f) Enders, D.; Ullrich, E. C. *Tetrahedron: Asymmetry* **2000**, *11*, 3861−3865. (g) Pardigon, O.; Tenaglia, A.; Buono, G. *J. Mol. Catal. A: Chem.* **2003**, *196*, 157−164.

n-BuLi/(−)-sparteine combination allowed an asymmetric extension of the methodology, with *p*-tolyl methyl and *p*-tolyl benzyl sulfoxides produced in 29 and 17% ee, respectively. Though this novel route to enantiomerically enriched sulfoxides is not as yet competitive with the classical repertoire, our preliminary results described herein demonstrate unambiguously the synthetic utility of this concept. An additional feature of this approach is the formation of the sulfoxide by asymmetric creation of the carbon−sulfur bond, in contrast to the sulfur−oxygen one by the more conventional oxidation reaction. Our immediate goal is to improve the enantioselectivity through optimization of the external ligand and investigation of other substrates. Current work is also focused on rationalization of the asymmetric induction, and a model will be reported in due course.[24]

Experimental Section

Typical Procedure for the Preparation of Racemic Sulfoxides 2 with *t*-BuOK as a Base. A solution of β-sulfinylester **1** (1.0 mmol, 1 equiv) in dry THF (5 mL) was cooled to −78 °C, and *t*-BuOK (1.1 mL of a 1 M solution in THF, 1.1 mmol, 1.1 equiv) was added. After the mixture was stirred at −78 °C for 20 min, the alkyl halide (1.2 mmol, 1.2 equiv) was added. The reaction mixture was stirred at −78 °C for 1 h 30 and then allowed to warm to room temperature for 18 h. After concentration in a vacuum, EtOAc (15 mL) was added and the organic layer was washed with water (15 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL). The organic layers were combined, washed with saturated aqueous NaCl (50 mL), dried over $MgSO_4$, filtered, and evaporated to dryness. The resulting crude product was then purified by column chromatography to afford anticipated racemic sulfoxide **2**. Use methyl or ethyl iodides as the electrophile also produced sulfenate ester **3** (O-alkylation product), which was readily separated from the major sulfoxide (S-alkylation product).

1-Benzylsulfinyl-4-methylbenzene 2a$_1$.[25a] Obtained from β-sulfinylester **1a** (R^1 = 4-MeC_6H_4, R^2 = Et, 240 mg, 1.00 mmol) with benzyl bromide as the electrophile. Yield 77% (176 mg, 0.77 mmol). White solid. Mp 139−140 °C (lit.[25a] 140−141 °C). TLC (CH_2Cl_2/AcOEt, 80:20) R_f = 0.43. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.39 (s, 3H), 3.97 and 4.09 (AB, J = 12.5, 2H), 6.97−7.01 (m, 2H), 7.20−7.89 (m, 7H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.4, 63.7, 124.5, 128.2, 128.4, 129.4, 129.6, 130.4, 139.7, 141.6. IR (KBr, cm^{-1}): ν 3058, 3032, 2960, 2910, 1033. MS (CI, isobutane) *m/z* 271 [(M + $C_3H_5^+$), 2], 269 [(M + $C_3H_3^+$), 2], 231 (MH^+, 100), 215 (6).

1-Methylsulfinyl-4-methylbenzene 2a$_2$.[25b] Obtained as the major alkylation product from β-sulfinylester **1a** (R^1 = 4-MeC_6H_4, R^2 = Et, 245 mg, 1.02 mmol) and methyl iodide as the electrophile. Yield 83% (131 mg, 0.85 mmol). White solid. Mp 43−44 °C, cyclohexane (lit.[25a] 42−43 °C). TLC (heptane/AcOEt, 50:50) R_f = 0.08. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.42 (s, 3H), 2.70 (s, 3H), 7.26−7.31 (m, 2H), 7.52−7.56 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.8, 44.4, 123.9, 130.4, 141.9, 142.9. IR (KBr, cm^{-1}): ν 2928, 1592, 1490, 1046. MS (EI) *m/z* 154 (M^+, 99), 139 (100), 138 (42), 91 (29), 77 (46), 65 (27), 63 (19). The corresponding sulfenic ester **3a$_2$** resulting from the competing O-alkylation of the intermediate sulfenate was also produced.

4-Methylbenzenesulfenic Acid Methyl Ester 3a$_2$.[25c] Yield 15% (23 mg, 0,15 mmol). Colorless oil. TLC (CH_2Cl_2) R_f = 0.32. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.03 (s, 3H), 7.35 (d_{app}, J = 8.0 Hz, 2H), 7.80−7.83 (m, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.8, 44.7, 127.5, 130.1, 137.9, 144.8. IR (NaCl, cm^{-1}): ν 3010, 2959, 2926, 2854, 1320, 1299, 1287, 1144, 1090. MS (EI) *m/z* 155 (MH^+, 86), 154 (M^+, 33), 139 (11), 107 (75), 91 (100), 77 (4), 65 (28).

Typical Procedure for Enantioenrichied Sulfoxides 2 with *n*-BuLi/(−)-Sparteine as a Base: Alkylation of the Intermediate Sulfenate at −45 °C. *n*-BuLi (770 μL of a 1.43 M solution in hexanes, 1.1 mmol, 1.1 equiv) was added at room temperature to a solution of (−)-sparteine (234 mg, 1 mmol, 1 equiv) in toluene (2 mL). After being stirred for 15 min, the resulting complex was added dropwise to a solution of β-sulfinylester **1a** (240 mg, 1 mmol, 1 equiv) in toluene (5 mL) previously cooled at −45 °C. The reaction mixture was stirred at −45 °C for 30 min, treated with methyl iodide (65 μL, 1 mmol, 1 equiv), stirred at this temperature for 4 h, and quenched with a saturated aqueous NH_4Cl solution (20 mL). The resulting mixture was extracted with ethyl acetate (3 × 25 mL). The combined organic layers were successively washed with a saturated aqueous NH_4Cl solution (20 mL) and a saturated aqueous NaCl solution (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting solid was then purified on silica gel eluting with diethyl ether to afford enantioenriched sulfoxide **2a$_2$** as a white solid (62 mg, 40%, 29% ee).

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Supporting Information Available: General methods of the Experimental Section, stereochemistry assignment for (*S*)-**2a$_1$** and (*S*)-**2a$_2$**, and full spectroscopic data for **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(24) There is a lack of literature information on lithium sulfenates in solution. As a consequence, the proposition of an unambiguous transition state model is not straightforward.

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