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Sulfenate Substitution as a Complement and Alternative to Sulfoxidation in the Diastereoselective Preparation of Chiral β-Substituted β-Amino Sulfoxides

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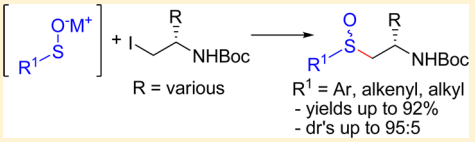
Supporting Information

ABSTRACT: Building from a previous communication, the reaction of sulfenate anions with chiral *N*-Boc-protected β-substituted β-amino iodides was evaluated as a conceptually different synthetic approach to chiral β-substituted β-amino sulfoxides. Using arenesulfenates, yields typically ranged from 71% to 92%, and dr's were often near 9:1. Alkanesulfenates proved less reactive, delivering lower yields and dr's. 1-Alkenesulfenates demonstrated high reactivity, returning chemical yields of 60−86% and dr's often close to 9:1 and as high as 95:5. (*S*)-β-Amino iodide electrophiles yielded (R_S,S_C)-β-amino sulfoxides, whereas (*R*)-amino iodides afford (S_S,R_C)-β-amino sulfoxides. The absolute configuration of the products makes the sulfenate protocol complementary to other existing preparations, including the commonly employed sulfoxidation of β-amino sulfides. The reactivity of *N*-Boc-protected 2-benzyl-2-aminoethyl iodide was found to be superior to the less sterically encumbered *n*-butyl iodide. A transition state model is proposed to account for the stereochemistry of the products and also for the high reactivity of the electrophile. Overall, the chemistry represents a new means of introducing sulfur stereogenicity in a molecule.



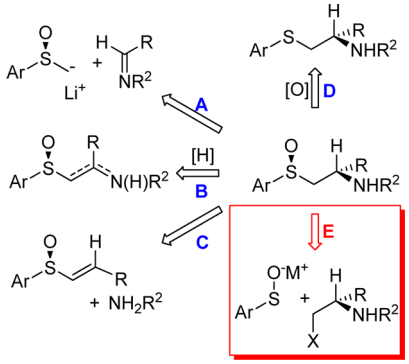
INTRODUCTION

The sulfoxide functionality has remained a staple for developing new synthetic methodology.[1−4] The stability of homochiral sulfoxides and their ability to induce chirality elsewhere in the molecule have proved useful on a vast number of fronts. The evolution of modern synthetic methodology has, more recently, led to the use of sulfoxide-containing compounds as chiral ligands[5−17] and organocatalysts[18−22] for inducing chirality in *other* molecules.

Homochiral β-amino sulfoxides and derivatives of them represent a set of sulfoxides that have been used in organocatalysis,[23−25] as ligands in organometallic chemistry,[26−33] and as valuable precursors of larger synthetic targets.[34−40] Furthermore, the β-amino sulfoxide unit has been recognized and assembled as a constituent of many biologically and/or medicinally important compounds.[39−53]

Scheme 1 demonstrates the main synthetic protocols that have been used to prepare representative β-amino sulfoxides or their derivatives. Deprotonated homochiral sulfoxides can add diastereoselectively to imines for the rapid construction of *N*-functionalized β-amino sulfoxides (**A**).[35,39,40,54−57] Using this method, chemical yields and diastereoselection are maximized when the system carries stereogenicity in both the sulfoxide and R^2 substituent of the imino nitrogen.[35,39,40,45−47,54−56,58] A useful and effective alternative involves the asymmetric reduction of homochiral β-imino sulfoxides under Lewis acid catalysis[34,59−61] or reduction of the corresponding β-aminovinyl sulfoxide tautomer[48,62](**B**). The conjugate addition of amine to chiral vinyl sulfoxide (**C**) has been evaluated, but the reaction requires the application of heat and de's have not proved to be synthetically useful.[49,63−66]

Scheme 1. Retrosynthetic Accesses to β-Amino Sulfoxides



The oxidation of homochiral β-amino sulfides has been employed the most extensively, presumably since the protocol gives the most rapid access to sulfoxide by way of a readily accessible amino sulfide (**D**).[26,28,36−38,42,50−53,66−79] Surprisingly, despite the presence of the stereogenic carbon, the diastereoselection of oxidation protocols has only rarely exceeded dr values of 90%.[77,80,81] In most cases, ratios range from 1:1 to 3:2,[26,28,36,37,42,51,67−71,79] and on many occasions, diastereoselectivities are not even reported or acknowledged.[38,52,53,66,72−76] In the few instances when an asymmetric oxidizing agent was employed to complement the stereogenic carbon in the substrate, selected de values reach 95% but only for particular substrates and conditions.[78,82−84]

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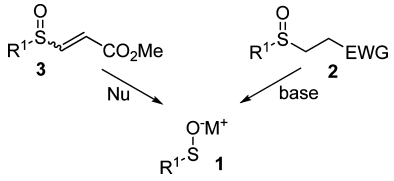
In this paper, we expand upon a previously introduced[85] and conceptually different synthetic access to *N*-Boc-protected *β*-substituted *β*-amino sulfoxides, utilizing a sulfenate nucleophile as a tool to simultaneously deliver the sulfur *and oxygen* into a substrate (Scheme 1, **E**). Sulfenic acid anions, or sulfenates (**1**, Scheme 2), are an emerging functionality that can effect S−C

Scheme 2. Common Preparations of Sulfenate Anions



bond formation while carrying a single oxygen on the sulfur during the process.[86−88] The additional atom on the sulfur renders the sulfenate prochiral, in contrast to oxygen-free thiolates.

There are a growing number of reports of the enantioselective,[89−92] diastereoselective[93−98] or regioselective[99] preparations of sulfoxides by way of sulfenate chemistry. In many of those reports,[95,97,99] the sulfenate oxygen and, perhaps more importantly, its accompanying counterion are alleged to play a role in setting the chirality during C−S bond formation. It was thought here that some of the principles proposed by others for counterion-to-heteroatom complexation could also be active in an intermolecular sense. Although a variety of electrophiles have been documented for sulfenate alkylations,[86,100] most have not possessed heteroatoms proximal to the alkylation site.

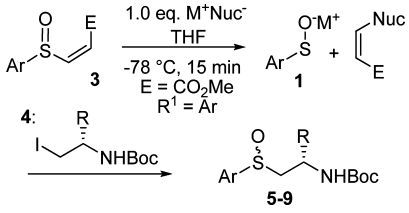
RESULTS

Arenesulfenates. Over the past decade, two principle methods have emerged for the generation of arene- and alkanesulfenates (**1**) as indicated in Scheme 2.[92,101] The Perrio/Metzner method involves the deprotonation and retro-Michael fragmentation of sulfoxides (**2**) bearing a strong EWG on a *β*-carbon.[92] A method developed in our lab invokes addition/elimination chemistry in *β*-sulfinyl acrylate esters (**3**). Both protocols have the benefit of facile preparation of starting materials. The Perrio/Metzner method can accommodate reaction temperatures up to 70 °C.[89,90] To begin this investigation, it was decided to go with the "home-grown" method because of our familiarity with the protocols and since the chemistry has been shown to be suitable with base sensitive substrates.[97]

For preliminary work, *p*-toluenesulfenate was selected as a trial sulfenate and methyl (*Z*)-2-(*p*-tolylsulfinyl)acrylate was prepared as the starting substrate. (*S*)-*N*-Boc-2-Amino-3-phenylpropyl iodide ((*S*)-**4a** (R = Bn)) was selected as a representative electrophile. The protocol requires the addition of a nucleophile to a *β*-sulfinyl acrylate, and several options are available.[101] A number of reactions were performed, with variation of the nucleophile and other parameters, and the outcome of these key experiments has been summarized previously.[85,102]

The working conditions evolving from that study suggest the use of *n*BuLi as the base, with addition of it to methyl (*Z*)-2-(*p*-tolylsulfinyl)acrylate at −78 °C in THF. After 15 min at −78 °C, 2 equiv of the iodide was added, and stirring was continued at −78 °C for 3 h, before the solution was permitted to slowly warm to rt (Scheme 3). Under these conditions, an 87% yield

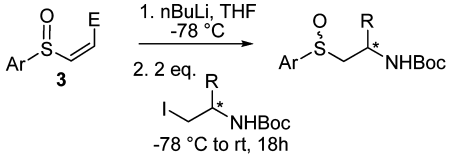
Scheme 3. General Mode of Release and Capture of Arenesulfenates



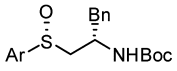
of **5a** was obtained and the ratio of diastereomers obtained was 91:9. Other nucleophiles provided lower yields and/or dr's. Similarly, the lithium counterion proved superior to sodium or potassium. It should be noted that the sulfenate-generating reaction conditions limit a comprehensive evaluation of solvent effects.

These conditions were then employed for the chemistry of other arenesulfenates with electrophiles (*S*)-**4a** and (*R*)-**4a**, and the results are indicated in Chart 1 (*a* and *b*). The diastereomeric ratios were usually determined by HPLC on a Daicel OJ-H column. Additional examples were prepared under the optimized conditions by changing substituents on the electrophile; variation of the R groups was performed, using

Chart 1. Products from the Alkylation of Aryl Sulfenates with Chiral Electrophiles 4[a]

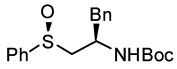


a: -reacting various ArSO⁻Li⁺ and (*S*)-**4a**



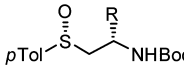
5a: Ar = *p*Tol, 87% (91:9)
6: Ar = Ph, 71% (91:9)
7: Ar = 2-naph, 91% (88:12)
8: Ar = 2-BrC_4H_6, 71% (83:17)
9: Ar = 2-pyridyl, 82% (63:37)

b: -reacting PhSO⁻Li⁺ and (*R*)-**4a**

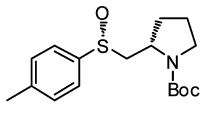


***ent*-6**: 73% (93:7)

c: -reacting *p*TolSO⁻Li⁺ and iodides (*S*)-**4b**, **c**, **d**, **e**, **f**

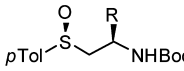


5b: R = Me, 81% (87:13)
5c: R = *i*Pr, 71% (90:10)
5d: R = *i*Bu, 92% (91:9)
5e: R = $CH_2OTBDPS$, 84% (87:13)



5f: 61% (95:5)

d: -reacting *p*TolSO⁻Li⁺ and iodides (*R*)-**4a**, **f**, **g**



***ent*-5a**: R = Bn, 84% (92:8)
5g: R = Ph, 79% (73:27)
5h: R = Et, 81% (94:6)

[a]dr's were determined by HPLC on a Daicel OJ-H column except for **5e** and **9**, which were established by ^{1}H NMR.

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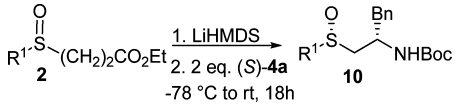
both configurations of the electrophile. The electrophiles employed were (*S*)-*N*-Boc-2-aminopropyl iodide ((*S*)-**4b**), (*S*)-*N*-Boc-2-amino-3-methylbutyl iodide ((*S*)-**4c**), (*S*)-*N*-Boc-2-amino-4-methylpentyl iodide ((*S*)-**4d**), (*S*)-*N*-Boc-2-amino-3-(*tert*-butyldiphenylsilyloxy)propyl iodide ((*S*)-**4e**), (*S*)-*N*-Boc-2-(iodomethyl)pyrrolidine ((*S*)-**4f**), (*R*)-*N*-Boc-2-aminobutyl iodide ((*R*)-**4g**), (*R*)-*N*-Boc-2-amino-2-phenylethyl iodide ((*R*)-**4h**), and (*R*)-*N*-Boc-2-amino-3-phenylpropyl iodide ((*R*)-**4a**). The examples are compiled in Chart 1 (*c* and *d*).

Confirmation of the absolute configuration of **5f** was established through X-ray crystal structure analysis.[85] Thereafter the stereochemistry of the other products was established through comparative optical rotations, consistency of elution sequence in the HPLC, and matching with literature data for **6**, ***ent*-6**, and a deprotected form of **6**.[81] A noteworthy observation from the whole chart is that the configuration of the sulfinyl group of the major diastereomer changes with the stereogenicity of the electrophilic iodide.

Alkanesulfenates. Attention was turned to the substitution chemistry of alkanesulfenates. Continuing with the fact that a lithium counterion is preferred, lithium α-toluenesulfenate (benzyl sulfenate) was generated by the standard method (Scheme 3). However, this compound could not be alkylated with iodide (*S*)-**4a** (Table 1, entry 1) even with after raising the temperature to rt. Similarly, lithium hexanesulfenate proved unreactive with (*S*)-**4a** (Table 1, entry 2). It has previously been established that the alkylated sulfenates generated by the addition/elimination protocol decompose if not alkylated near 0 °C.[103] So, in order to probe alkylation chemistry at higher temperatures, the alkanesulfenates had to be generated by a different protocol. Given that the Perrio/Metzner method can withstand temperatures at least up to 70 °C, that protocol was adopted.[92] Four 3-(alkylsulfinyl)propionates (**2**) were prepared as described in the literature; the chemistry of ethyl 3-(phenylmethylsulfinyl)propionate was initially reacted to generate lithium benzyl sulfenate, which in turn was probed for its alkylation chemistry with iodide (*S*)-**4a**. Entries 3–5 of Table 1 demonstrated that the onset of some alkylation chemistry occurred only after the mixture reached 50 °C. A maximum yield of sulfoxide was obtained only after refluxing the mixture in THF (2–3 h) (entry 6).

Table 1. Alkylations of Selected Alkyl Sulfenates with (*S*)-4a



no.	method[a]	temp	R^1	product (yield %/dr)[b,c]
1	1	−78 °C to rt	Bn	**10a** (0/−)
2	1	−78 °C to rt	nC_6H_{13}	**10b** (0/−)
3	2	−78 °C	Bn	**10a** (0/−)
4	2	−78 to 0 °C	Bn	**10a** (0/−)
5	2	−78 to 50 °C	Bn	**10a** (tr/−)
6	2	−78 °C to reflux	Bn	**10a** (54/85:15)
7	2	−78 °C to reflux	nC_6H_{13}	**10b** (42/82:18)
8	2	−78 °C to reflux	*t*Bu	**10c** (63/78:22)
9	2	−78 °C to reflux	cC_6H_{11}	**10d** (78/91:9)

[a]Method 1 = sulfenate release as shown in Chart 1. Method 2 = sulfenate release as per the reaction shown in the table. [b]dr's were determined by HPLC on a Daicel OJ-H column for **10a–c** and by ^{1}H NMR for **10d**. [c]The configuration of the major diastereomer is shown in the equation above and was assigned to be (R_S,S_C) for **10a**, **10c**, and **10d** and (S_S,S_C) for **10b** (due to a change in atomic priority) through comparison of optical rotation trends set by the aromatic congeners (Chart 1).

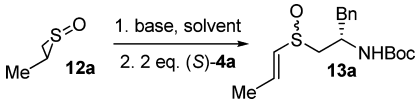
Entries 7–9 of Table 1 depict the outcome when three other alkyl sulfenates were treated with iodide (*S*)-**4a** under the same conditions. Compared to the standards established in Chart 1 for arenesulfenates, the yields and dr's are a little lower except for lithium cyclohexanesulfenate, which gave suitable results, providing sulfoxide **10d** in 78% yield with 91:9 dr. Lithium *tert*-butanesulfenate provided sulfoxide **10c** in 63% and a dr of 78:22. This outcome was particularly disappointing, as *tert*-butyl sulfoxides possess value as ligands[6,13–17] and as a source of sulfenic acids.[104–106] Given that these alkanesulfenates collectively failed to provide useful results, this aspect of the investigation was no longer pursued.

Alkenesulfenates. Several years ago, a facile procedure for the stereoselective generation of exclusively (*E*)-1-alkenesulfenates (**11**) by way of deprotonation and rearrangement of *anti*-alkyl thiirane *S*-oxides (**12**, eq 1) was reported.[107,108] Although

a small variation of electrophiles was demonstrated to react with the alkenesulfenates, there was no experimentation with the iodides utilized in the current study. Given the success with the arenesulfenates noted above, this chemistry was pursued, beginning with 1-propenesulfenate (**11a**), which can be generated from *anti*-methyl thiirane *S*-oxide. Some reaction optimization was done, and moreover, the methodology permitted some variation solvent polarity on the reaction yield and the corresponding dr.

As above with arenesulfenates, the lithium counterion provided superior dr's compared to sodium or potassium and the highest yield (Table 2, entries 1–3). Other trials provided results close to entry 1. However, varying the solvent brought about change. Although the electrophile was presented as a THF solution, sulfenate **11a** could be generated in other solvents. The use of 1,4-dioxane lowered the yield of alkylation but with a dr of 9:1 (entry 6), whereas DMSO did not permit alkylation. Changing to a less polar solvent maintained the dr

Table 2. Optimization of Diastereoselective Alkylations of 1-Propenesulfenate



no.	base[a]	solvent	temp	yield % (dr)[b]
1	LiHMDS	THF	−78 °C to rt	68 (84:16)
2	NaHMDS	THF	−78 °C to rt	62 (76:24)
3	KHMDS	THF	−78 °C to rt	31 (73:27)
4	MeLiLiBr[c]	THF	−78 °C to rt	70 (87:13)
5	LiHMDS	THF	−40 °C to rt	77 (86:14)
6	LiHMDS	1,4-dioxane/THF (25:1)	rt	54 (90:10)
7	LiHMDS	DMSO/THF (12:1)	rt	tr (−)
8	LiHMDS	pentane/THF (6:1)	−78 °C to rt	70 (89:11)
9	LiHMDS	Et_2O/THF (4.5:1)	−78 °C to rt	81 (90:10)

[a]In THF unless otherwise indicated. [b]dr established by chiral HPLC. [c]In ether.

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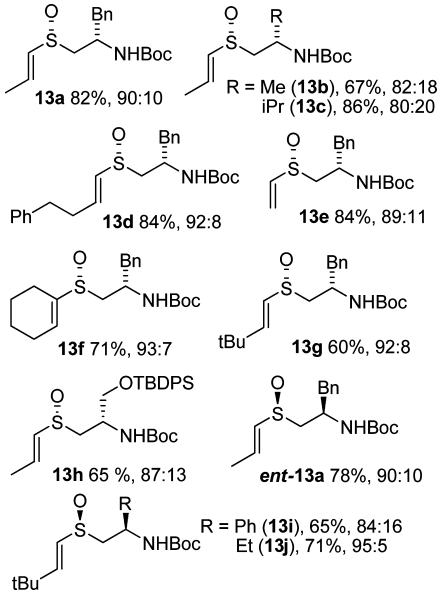
near 9:1 (entries 8 and 9), and ether as a cosolvent provided the highest yield.

Given the optimized conditions, other lithium (*E*)-1-alkenesulfenates were alkylated with some of the electrophiles employed above, and the products obtained comprise Chart 2.

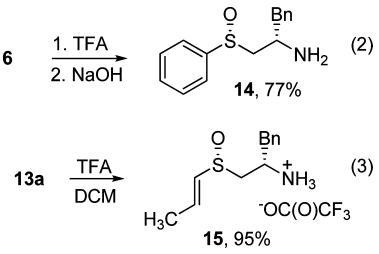
Chart 2. Products of the Diastereoselective Alkylations of 1-Alkenesulfenates[a]



[a]dr's were established by ^{1}H NMR analysis except for **13a** and ***ent*-13a** (chiral HPLC).

Many entries exhibit dr's near or exceeding 9:1, and all dr's are ≥8:2. Also noteworthy are some of the chemical yields that exceed 80%, a level of alkylation efficiency that had never previously been achieved with alkenesulfenates.[107−109] The stereochemical outcome of this reaction was firmly established by X-ray diffraction analysis of compound **13a**.[110] Thereafter, optical rotations were telling of the configurations of the other vinylic aminosulfoxides. The configurations obtained match the trends established for the aromatic sulfenate alkylations of Chart 1.

Nitrogen Deprotection. The release of amines from Boc protection in the presence of an enriched sulfoxide is well established.[41,111−113] This reaction was executed on aromatic derivative **6** to reiterate the ease of deprotection, creating **14** and also to obtain a substrate to confirm the absolute configuration of **6** (*vide supra*), eq 2. The deprotection of vinylic sulfoxide **13a** was also executed, and the ammonium form **15** was isolated in high yield as its trifluoroacetate salt, eq 3.



Alkylation Competition Experiments. Rarely if ever has the nature of the electrophile been a significant factor in the simple alkylation of sulfenate anions. Past chemistry has focused on methods for the generation of sulfenates, some of which possessed chirality. Sulfenate alkylations were then carried out with reactive electrophiles such as benzyl bromides, methyl iodide, or primary halides, often employing more than a single molar equivalent.[114−119]

The alkylation chemistry of this paper not only unveils the value of chiral electrophiles but also indicates that iodides possessing β-substitution and heteroatoms are suitable, even when only 2 equiv are used.[120] This was viewed as a surprising mode of reactivity and as such, some sulfenate competition reactions were performed to establish the relative reactivity of (*S*)-**4a** in relation to other common or representative electrophiles (Table 3). Both lithium *p*-toluenesulfenate and lithium (*E*)-1-propenesulfenate reacted with (*S*)-**4a** at a faster rate than with *n*BuI (entries 1 and 2). On the other hand pyrrolidine-based iodide (*S*)-**4f** is slower to react than *n*BuI (entry 4). A competition of (*S*)-**4a** and BnBr demonstrated the latter to be substantially more reactive; no amino sulfoxide was observed in the mixture (entry 3). In a competition of two sulfenates, lithium *p*-toluenesulfenate proved substantially more reactive than lithium 2-pyridinesulfenate (entries 5 and 6).

DISCUSSION

The configurations of the products displayed in Charts 1 and 2 and Table 1 arise from substitutions that consistently afford the same relative relationship between the sulfoxide and that of the carbon chirality of the electrophile.[121] In this regard, the substitution occurs in a stereospecific manner. Figure 1 offers possible transition states that can account for the high stereoselectivity of the substitution using a generic *Sc* electrophile and a sulfenate. A key element to the proposed structures is a precoordination of the lithium of the sulfenate to the nitrogen lone pair of the electrophile. Such an interaction has been invoked previously in an intramolecular sense[95,97] and would explain the surprising reactivity of the electrophiles used in this paper. The outcomes of the competition experiments of Table 3 (entries 1 and 2) clearly support some sort of reaction-accelerating feature, and nitrogen precoordination can serve as a suitable one, despite the higher steric demands of the chiral electrophiles.

Accepting the role of Li−N precoordination, the two reactive atoms can then assume a reactive orientation forming a six-membered transition state. Two possibilities are presented in Figure 1. Structure **I** has three groups of the electrophile positioned in an equatorial or pseudoequatorial arrangement, with the key destabilizing feature being the eclipsing iodide and the R group. This arrangement also requires that the sulfenate R^1 group assume an axial position to deliver the R_S stereocenter.

Structure **II** represents a chair ring flip of **I** such that the electrophile R group adopts an axial position. This structure would appear to be advantageous since the departing iodide would only eclipse a C−H bond. To provide the major stereoisomer, the sulfenate R^1 group fills the equatorial space ensuring no unfavorable 1,3-diaxial interaction between R and R^1 groups. The minor isomer may arise from the other sulfur lone pair participating in either **I** or **II** or through breakdown of these models.

The dr's are among the lowest for R = phenyl of the electrophile using an aryl and an alkenyl sulfenate. The phenyl

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Table 3. Competitive Sulfenate Alkylation Reactions[a]

	sulfenate (equiv)	E-I (equiv)	alk-X (equiv)	ratio[b]	k_{rel}[c]
1	*p*TolSOLi (1)	(*S*)-**4a** (2)	*n*BuI (10)	1:1.2	~4
2	**11** (R^2 = Me) (1)	(*S*)-**4a** (2)	*n*BuI (10)	1.4:1	~7
3	*p*TolSOLi (1)	(*S*)-**4a** (5)	BnBr (5)	*p*TolS(O)Bn	
4	*p*TolSOLi (1)	(*S*)-**4f** (2)	*n*BuI (10)	*p*TolS(O)*n*Bu	
5	*p*TolSOLi (5) and 2-PySOLi (5)		BnBr (2.5)	*p*TolS(O)Bn	
6	*p*TolSOLi (5) and 2-PySOLi (5)	(*S*)-**4a** (1)		**5a**	

[a]See Experimental Section for a description of these experiments. [b]Ratio of products with E-containing sulfoxide is initially listed. The entry of a single compound means only that product was obtained. [c]Obtained by adjusting the ratio for relative equivalents of competitive reactant. No entry suggests a reactivity difference of ≥50 times.

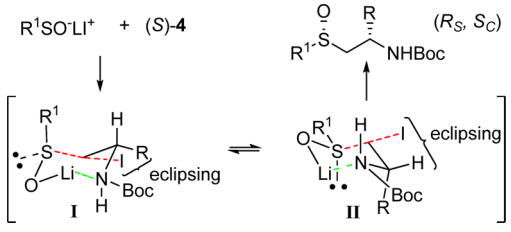

Figure 1. Possible transition states for alkylations with electrophiles (*S*)-**4**.

group is well recognized for its larger steric demands compared to benzyl, isopropyl, etc.,[122] and presumably the size of the phenyl hinders the rigorous alignment required by transition state **II**. There is probably no significant involvement of the hydrogen on the nitrogen of the electrophile in determining the stereochemistry of the product, since compound **5f** forms with high diastereoselection. Of note, however, is that (*S*)-**4f** alkylates rather slowly (Table 3, entry 4). Although this could be due to increased steric encumbrance for this particular electrophile, one cannot rule out a possible rate-accelerating role for the carbamate hydrogen of other electrophiles during alkylation chemistry.

As presented in our previous communication[85] and again encountered with the vinylic sulfenates, the counterion of the sulfenate has a clear dependence on the yield and diastereoselectivity of the alkylation, with lithium clearly exhibiting the superior dr values. When the solvent system was composed of a solvent with cation coordination propensity weaker than that of THF,[123−125] the experiments yielded dr's slightly improved compared to those with the use of THF alone. Presumably, the weaker solvent coordination facilitates formation of a transition state such as **II**. Weaker coordination may also minimize the separation of lithium and sulfenate ions.[124] The chemical yields were highest when using a high percentage of ethyl ether.

Lithium 2-pyridinesulfenate was alkylated in good yield, but with an attenuated dr (**9**, Chart 1). Table 3 (entries 5 and 6) indicates this sulfenate is slow to alkylate compared to α-toluenesulfenate, whether using BnBr or (*S*)-**4a**. Lithium 2-pyridinesulfenate likely adopts an internal nitrogen-to-lithium complex mirroring the behavior of alkoxides derived from 2-pyridyl carbinols.[126] Such an arrangement would be expected to hinder the precomplexation with (*S*)-**4a**, retarding the rate of alkylation but also presumably obstructing clean formation of a transition state such as **II**.

The protocol presented herein is for the synthesis of (R_S,S_C) and (S_S,R_C) β-substituted β-amino sulfoxides. When the sulfoxide substituent (R^1) is aryl or 1-alkenyl, the dr's are generally near 9:1. The yields and dr's of the alkylated sulfoxides are less compelling and that family of compounds has less applicability going forward and as such, will not be part of the remaining discussion.

The most efficient methods for the preparation enriched β-aminoalkyl aryl sulfoxides appears to be two from the Garcia Ruano group.[54,60] One key contribution involves the Lewis acid mediated DIBAL reduction of *N*-benzyl protected (*R*)-*p*-tolyl 2-iminoalkyl sulfoxides (path **B**, Scheme 1).[60] That reduction delivers exclusively the (R_S,R_C)-amino sulfoxides, generally in good yields. Our contribution is the complement of that work, as the products possess a similar backbone, but with the (R_S,S_C) stereochemistry.

Product **5g** is formed with one of the lowest dr's in the current work. For amino sulfoxide substrates with aryl groups on the sulfoxide (R^1 = Ar) *and* also α to the amino group (R = Ph), an alternative protocol by Garcia Ruano should be considered.[54] The reaction of (*S*)-benzylidine-*p*-toluenesulfinamide with (*R*)- or (*S*)-methyl *p*-tolyl sulfoxide (path **A**, Scheme 1) delivers the corresponding (R_S,R_C) or (R_S,S_C) versions of **5g**, respectively, albeit bearing *p*-toluenesulfinyl rather than Boc nitrogen protection. Although that protocol employs two chiral influences, it is the preferred one, particular for the "matched" pair of reactants, which provide the (R_S,R_C) isomer in 99% yield with >99:1 dr.[54]

The Garcia Ruano methods begin with a chiral sulfoxide and deliver good yields and dr's for selected β-amino sulfoxides of certain configurations.[54,60] The chemistry shown herein clearly fulfills a function for synthetic access selected target β-amino sulfoxides of complementary configurations. However, a closer comparison of our chemistry is sulfoxidation. As outlined in the introduction section, this protocol has been used extensively and in essence, instinctively by chemists targeting β-amino sulfoxides. In many cases, dr's fail to exceed 60:40. However, there are two general papers that perform simple oxidation creating sulfoxides similar to the ones presented herein.[77,81] In a communication, the Skarzewski group outlines the diastereoselctive oxidation of simple chiral amino sulfides using NaOCl/KBr/cat. TEMPO.[77] In a follow-up full paper, the authors outline additional noteworthy oxidations, offer thorough characterization of the sulfoxides, and mention the low diastereoselectivity of $NaIO_4$ and MCPBA oxidations.[81]

In the Skarzewski papers, the authors prepare β-amino sulfoxides in good yields, with high dr's such as 85:15, 94:6,[77] 98:2, and 92:8.[81] Some of the lower dr ratios were found at 53:47 or 64:36.[81] Most importantly, the major isomers were the (R_S,R_C) or (S_S,S_C) diastereomers in every case. Among the other rare examples of oxidation reactions delivering high diastereoselectivity, the MCPBA oxidation of protected *S*-alkylated cysteine gave high yields of the corresponding (R_S,R_C) amino sulfoxides.[80] Similarly an enzyme-catalyzed oxidation

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protocol also brings about the (R_S,R_C) isomer.[83] Again the complementarity of the sulfenate protocol is underscored upon comparison. It should be mentioned that many of the high dr's reported in the literature are isolated examples. The arenesulfenate substitution reactions exhibit significantly more uniformity of results across all the examples studied. As a methodology, the arenesulfenate substitution appears to hold more generality than oxidation protocols, at least based on the family of electrophiles studied.

Sulfoxides **13** are all new compounds, and the synthesis of close analogues of **13** by way of sulfide oxidation has not been explored; no comparison of methodologies is possible. There is one example of 1-propenethiolate reaction with serinyl chloride hydrochloride,[52] but the ratio of sulfinyl isomers obtained by way of subsequent oxidation was not reported. Other examples of oxidations of (*S*)-1-alkenyl cysteine derivatives are also known, but either the existence of two sulfinyl isomers was not recognized,[127,128] or low dr's were obtained.[97,129] Indeed, in one case, the authors suggest the use of an alternative (asymmetric oxidation) protocol if one is seeking superior diastereoselectivity.[129]

In the current work, the overall transformation of thiirane *S*-oxide to (*E*)-1-alkenyl *β*-aminoalkyl sulfoxides is an example of a one-pot double diastereoselection. The thiirane *S*-oxide ring-opening gives exclusively the (*E*)-1-alkenesulfenate, while the ensuing sulfenate substitution delivers products **13**, with at least 4:1 dr and many products exhibiting a dr close to 9:1. Given the insignificant dr's of the oxidation reactions the *S*-1-alkenyl cysteine derivatives, it is unlikely that oxidation of sulfide precursors of oxides **13** will demonstrate significant diastereoselection. Furthermore, 1-alkenesulfenates are actually easier to prepare than 1-alkenethiolates, as then do not require reducing metal conditions.[52,130−133] The sulfenate methodology provides compounds **13** with good dr's and should be viewed as a preferred methodology on its own merits and because of the few alternatives available. Exploration the diastereoselection of intramolecular aza-Michael addition chemistry of these compounds is underway.

CONCLUSIONS

Sulfenate substitution represents a viable protocol for the preparation of diastereomerically enriched *β*-substituted *β*-amino sulfoxide, particularly when the other sulfoxide group is aryl or 1-alkenyl. The identity of the counterion to the sulfenate was found to be vital and should be lithium. The configurations of the possible products, which can be (R_S,S_C) or (S_S,R_C), are complementary to other protocols including oxidation. Indeed, sulfenate substitution presents a new alternative to the paradigm of sulfoxidation, which actually does not typically deliver useful dr's. Vinylic sulfoxides **13** represent a new family of *β*-amino sulfoxides.

A model is proposed to account for the observed diastereoselection during the substitution reactions. Precoordination of the sulfenate lithium to the nitrogen of the electrophile is believed to be essential for both the stereoselection and as a rate accelerating feature of the overall substitution. The transition state model suggests that electrophilic centers with appropriately positioned proximal heteroatoms such as oxygen, halogen,[134] or nitrogen in other forms can react with various sulfenates at an accelerated pace and may do so stereoselectively. We plan to evaluate some of the amino sulfoxides and/or their derivatives as ligands in organocatalytic transformations.

EXPERIMENTAL SECTION

Many general experimental methods have recently been reported.[135] All dry and pure solvents were obtained from a solvent purification system. All chemicals were obtained from commercial sources unless otherwise noted. All air- and water-sensitive reagents were transferred *via* oven-dried nitrogen-purged syringes into flame-dried flasks. HPLC experiments were performed using a Chiralcel OJ-H or OD-H (0.46 cm × 25 cm) column with *i*-PrOH/hexane as the eluant. The synthesis of *β*-arylsulfinyl acrylate esters **3** has been reported previously.[85,136] Homochiral amino iodides were prepared as previously described.[85,137] Thiirane *S*-oxides prepared in this paper were prepared and purified as previously described.[138−141] The experimental procedures for the alkanesulfenate substitution chemistry can be found in the Supporting Information section.

General Procedure for Preparation of Aryl *β*-Amino Sulfoxides 5−9. 2-Carbomethoxyethenyl aryl sulfoxide (1.0 equiv) was dissolved in THF (1 mL/0.1 mmol) under nitrogen and stirred at −78 °C. To the sulfoxide was added *n*-BuLi (1.6 M/hexanes, 1.0 equiv) via syringe. Following 5−10 min of stirring, a solution of the chiral iodide (2.0 equiv) in THF (4 mL/mmol) at −78 °C was added via syringe to the sulfenate. The mixture was stirred at −78 °C for 3−4 h and then allowed to slowly warm to rt overnight. Solvent was removed under reduced pressure, and diastereomers were isolated by flash chromatography using EtOAc/hexanes as the eluent. Diastereomeric ratios were determined by HPLC using ^{i}PrOH/hexanes as the eluent. The major diastereomer was purified by recrystallization from EtOAc/hexanes. *β*-Amino sulfoxide yields were derived from 2-carbomethoxyethenyl sulfoxides. Experimental details and characterization data for **5a**−**5d**, **5f**, **6**−**8**, and ***ent*-6** have been listed elsewhere.[85] The absolute stereochemistry of the *major* product is listed as part of the compounds name.

(R_S,2*S*)-*N*-Boc-1-Phenyl-3-(2-pyridylsulfinyl)propan-2-amine (9). A mixture of 2-carbomethoxyethenyl 2-pyridyl sulfoxide (0.100 g, 0.473 mmol) in THF (3 mL), *n*-BuLi (0.295 mL), and electrophile (*S*)-**4a** (0.341 g, 0.947 mmol) in THF (3 mL) afforded a diastereomeric mixture of *β*-amino sulfoxides **9** (82%, 0.140 g, dr = 63:37 by NMR integration) following flash chromatography (30% EtOAc/hexanes). Recrystallization attempts failed to improve optical purity: mp 100−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.60−8.57 (m, 2H), 8.01−7.89 (m, 4H), 7.38−7.18 (m, 12 H), 5.51 (br s, 1H, minor isomer), 4.85 (br s, 1H, major isomer), 4.40−4.31 (m, 2H), 3.43−2.93 (m, 8H), 1.43 (s, 9H, minor isomer), 1.38 (s, 9H, major isomer); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* major isomer 164.6, 154.8, 149.7, 138.0, 137.1, 129.46, 128.54, 126.7, 124.5, 120.1, 79.5, 58.0, 48.2, 40.4, 28.3; minor isomer 164.6, 155.1, 149.7, 138.1, 137.2, 129.5, 128.6, 127.3, 124.6, 119.9, 79.5, 58.2, 49.2, 41.6, 28.4; IR (neat) cm^{-1} 3288, 3084, 3052, 3028, 2976, 2929, 1707, 1562, 1522, 1452, 1422, 1391, 1365, 1251, 1169, 1084, 1036, 771; $[\alpha]_D^{25}$ −14.80 (*c* 1.25, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{24}N_2O_3S$ [M] + H 361.1586, found 361.1573.

(R_S,2*S*)-*N*-Boc-*O*-TBDPS-1-Hydroxy-3-(*p*-tolylsulfinyl)propan-2-amine (5e). A mixture of 2-carbomethoxyethenyl *p*-tolyl sulfoxide (0.100 g, 0.446 mmol) in THF (3 mL), *n*-BuLi (0.281 mL), (*S*)-**4e** (0.481 g, 0.892 mmol) in THF (3 mL) afforded a diastereomeric mixture of *β*-amino sulfoxides **5e** (84%, 0.206 g, dr = 87:13 by NMR integration) following flash chromatography (30% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.67−7.65 (m, 4H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.45−7.36 (m, 6H), 7.31 (d, *J* = 8.2 Hz, 2H), 5.63 (br d, *J* = 6.8 Hz, 1H), 4.24 (br m, 1H), 3.90 (m, 2H); 3.13−3.11 (m, 1H), 3.00−2.97 (m, 1H), 2.41 (s, 3H), 1.44 (s, 9H), 1.08 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* 155.2, 141.7, 140.9, 135.6, 132.9, 130.1, 129.9, 128.0, 123.9, 79.6, 64.7, 59.1, 49.4, 28.4, 27.0, 21.5, 19.3; IR (neat) cm^{-1} 3276, 3071, 3049, 2999, 2961, 2930, 2892, 2858, 1709, 1525, 1494, 1427, 1391, 1364, 1276, 1248, 1171, 1111, 1087, 1027, 910, 809; $[\alpha]_D^{25}$ +96.80 (*c* 5.40, $CHCl_3$). Anal. Calcd for $C_{31}H_{41}NO_4SSi$: C, 67.47; H, 7.49. Found: C, 67.30; H, 7.60. Minor isomer, partial characterization: ^{1}H NMR (400 MHz) *δ* 4.96 (br s, 1H), 2.39 (s, 3 H), 1.40 (s, 9H), 1.04 (s, 9H); ^{13}C

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NMR (100.6 MHz) δ 155.1, 140.9, 139.9, 135.5, 132.7, 130.0, 129.9, 128.0, 125.0, 79.6, 64.7, 59.0, 49.3, 28.4, 26.7, 21.4, 19.3.

Generation and Alkylation of Alkanesulfenates. Use of Methyl 2-(Alkylsulfinyl) Acrylates for Alkylation Chemistry with (*S*)-4a. Methyl 2-(benzylsulfinyl) acrylate and methyl 2-(*n*-hexylsulfinyl) acrylate have been prepared previously.[101] These compounds were evaluated for their release of alkanesulfenates according to the procedure above (Preparation of Aryl β-Amino Sulfoxides **5**−**9**). Capture with (*S*)-**4a** as outlined above did not result in an alkyl β-amino sulfoxide.

General Preparation of 2-(Carboethoxy)ethyl Alkyl Sulfoxides (2). Ethyl acrylate (1 equiv) was added dropwise to a suspension of potassium carbonate (0.05 equiv) and thiol (1 equiv) in DCM (1 mL/mmol of thiol). The resulting mixture was stirred at room temperature for 12 h. Next, the reaction mixture was washed successively with aqueous 1 M NaOH solution, water, and then brine and dried over $MgSO_4$. Filtration and solvent evaporation under reduced pressure provided 2-(carboethoxy)ethyl alkyl sulfide, which was used in the next step without further purification. A solution of the 2-(carboethoxy)ethyl alkyl sulfide (1 equiv) in MeOH (2 mL/mmol sulfide) was cooled to 0 °C, and a solution of $NaIO_4$ (1.05 equiv) in water (1 mL/mmol sulfide) was added dropwise. The reaction mixture was stirred for 18 h at room temperature. Sodium iodate was filtered, methanol was removed under vacuum, and the residue extracted with EtOAc. The combined organic layers were washed with brine solution, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was then purified by column chromatography on silica gel to afford pure 2-(carboethoxy)ethyl alkyl sulfoxide **2**. The data for 2-(carboethoxy)ethyl benzyl sulfoxide (**2a**) and 2-(carboethoxy)ethyl *tert*-butyl sulfoxide (**2c**) matched that from the literature.[92]

2-(Carboethoxy)ethyl *n*-Hexyl Sulfoxide (2b). Application of the general procedure above to *n*-hexyl mercaptan (5.97 mL, 42.3 mmol) provided crude 2-(carboethoxy)ethyl *n*-hexyl sulfide. Yield 81% (7.45 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (q, J = 7.2 Hz, 2H), 2.78 (t, J = 7.2 Hz, 2H), 2.59 (t, J = 7.6 Hz, 2H), 2.53 (t, J = 7.2 Hz, 2H), 1.62- 1.54 (m, 2H), 1.41- 1.25 (m, 9H), 0.89 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 172.0, 60.6, 35.0, 32.1, 31.4, 29.5, 28.5, 27.0, 22.5, 14.2, 14.0. Application of the general oxidation procedure above to the crude sulfide (1.00 g, 4.58 mmol) afforded sulfoxide **2b**. Yield 87% (994 mg). White solid. Mp: 28−29 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.18 (q, J = 4.8 Hz, 2H), 3.05−3.01 (m, 1H), 2.90−2.74 (m, 4H), 2.70−2.68 (m, 1H), 1.78 (m, 2H), 1.46 (m, 2H), 1.34−1.31 (m, 4H), 1.28 (t, 4.8 Hz, 3H), 0.90 (t, J = 4.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.4, 61.2, 52.8, 46.8, 31.4, 28.5, 27.2, 22.6, 22.4, 14.2, 14.0; IR (neat) cm^{-1} 2978, 2953, 2924, 2857, 1740, 1467, 1421, 1374, 1242, 1179, 1019, 980. Anal. Calcd for $C_{11}H_{22}O_3S$: C, 56.37; H, 9.46. Found: C, 56.51; H, 9.44.

2-(Carboethoxy)ethyl *c*-Hexyl Sulfoxide (2d). Application of the general procedure above to *c*-hexyl mercaptan (4.22 mL, 34.4 mmol). Yield 81% (6.01 g). Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.16 (q, J = 7.2 Hz, 2H), 2.82 (m, 2H), 2.58 (t, J = 7.4 Hz, 3H), 2.00−1.95 (m, 2H), 1.79−1.76 (m, 2H), 1.63−1.51 (m, 1H), 1.38−1.24 (m, 8H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 172.0, 60.5, 43.2, 35.3, 33.6, 26.0, 25.8, 25.0, 14.3. Application of the general oxidation procedure above to the crude sulfide (6.01 g, 20.2 mmol) afforded sulfoxide **2d**. Yield 84% (3.50 g). Yellow oil.^{1}H NMR (600 MHz, $CDCl_3$) δ 4.18 (q, J = 7.2 Hz, 2H), 3.06−2.99 (m, 1H), 2.89−2.81 (m, 3H), 2.59 (m, 1H), 2.15−2.12 (m, 1H), 1.96−1.88 (m, 3H), 1.72 (m, 1H), 1.51−1.27 (m, 5H), 1.28 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.6, 61.2, 59.4, 43.7, 27.4, 26.2, 25.5, 25.4, 25.1, 25.0, 14.2; IR (neat) cm^{-1} 2981, 2932, 2856, 1735, 1450, 1393, 1373, 1348, 1235, 1184, 1039, 851. Anal. Calcd for $C_{11}H_{20}O_3S$: C, 56.86; H, 8.68. Found: C, 56.69; H, 8.52.

General Procedure: Synthesis of Alkyl β-Amino Sulfoxides. Sulfoxide **2** (1.0 equiv) was dissolved in THF (1 mL/0.1 mmol) under nitrogen and stirred at −78 °C. To the sulfoxide was added LiHMDS (1.0 M/hexanes, 1.00−1.2 equiv) via syringe. Following 15−20 min of stirring, a solution of the chiral iodide (∼2.0 equiv) in THF (4 mL/mmol) at −78 °C was added via syringe to the sulfenate. Immediately after addition of electrophile the reaction mixture was refluxed for 2−3 h. Solvent was removed under reduced pressure, and diastereomers were isolated by flash chromatography using EtOAc/hexanes as the eluent. Diastereomeric ratios were determined by HPLC using ^{i}PrOH/hexanes as the eluent or by ^{1}H NMR peak integration. β-Amino sulfoxide yields were derived from starting sulfoxides. The absolute stereochemistry of the *major* product is listed as part of the compounds name.

(R_S,2*S*)-*N*-Boc-1-Phenyl-3-(benzylsulfinyl)propan-2-amine (10a). 2-(Carboethoxy)ethyl benzyl sulfoxide (**2a**) (0.100 g, 0.416 mmol) in THF (3 mL) was treated dropwise with LiHMDS (0.437 mL). Next, electrophile **4a** (0.360 g, 0.832 mmol) in THF (3 mL) was added to sulfenate via syringe. A diastereomeric mixture of β-amino sulfoxides **10a** (54%, 0.084 g, dr = 85:15 HPLC integration) was isolated following flash chromatography (30% EtOAc/hexanes). HPLC (5% *i*-PrOH/hexanes, 0.4 mL/min flow rate, OD-H column): 39.47 min (minor), 60.03 min (major). The diastereomeric mixture was recrystallized from EtOAc/hexanes to give improved optical purity of 97:3: mp 203−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 3H), 7.26−7.21 (m, 5H), 7.10 (d, J = 6.8 Hz, 2H), 5.47 (br d, J = 6.4 Hz, 1H), 4.20 (m, 1H), 4.00 (ABq, $\Delta\delta_{AB}$ = 0.09, J_{AB} = 4.4 Hz, 2H), 3.18−3.15 (m, 1H), 2.91 (dd, J = 12.8, 8 Hz, 1H), 2.83−2.78 (m, 1H), 2.72−2.69 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.4, 130.1, 129.4, 129.3, 129.0, 128.6, 128.5, 126.7, 79.6, 58.9, 53.3, 49.5, 39.9, 28.4; IR (neat) cm^{-1} 3354, 3028, 2962, 2932, 1688, 1523, 1266, 1251, 1170, 1045, 1013; $[\alpha]_D^{25}$ +70.00 (c 0.1, $CHCl_3$). Anal. Calcd for $C_{21}H_{27}NO_3S$: C, 67.53; H, 7.29. Found: C, 67.42; H, 7.50. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (br s, J = 7.2 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.3, 136.8, 136.8, 130.3, 129.3, 128.8, 128.6, 128.3, 126.9, 79.8, 57.5, 53.4, 49.4, 39.9, 28.4.

(R_S,2*S*)-*N*-Boc-1-Phenyl-3-(*n*-hexylsulfinyl)propan-2-amine (10b). 2-(Carboethoxy)ethyl *n*-hexyl sulfoxide (**2a**) (0.100 g, 0.426 mmol) in THF (3 mL) was treated dropwise with LiHMDS (0.447 mL). Next, electrophile **4a** (0.307 g, 0.892 mmol) in THF (3 mL) was added to sulfenate via syringe. A diastereomeric mixture of β-amino sulfoxides **10b** (42%, 0.065 g, dr = 82:18 HPLC integration) was isolated following flash chromatography (30% EtOAc/hexanes). HPLC (8% *i*-PrOH/hexanes, 0.4 mL/min flow rate, OD-H column): 18.89 min (minor), 20.15 min (major). The diastereomeric mixture was recrystallized from EtOAc/hexanes to give improved optical purity of 93:7: mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.22 (m, 5H), 5.56 (br d, J = 8.0 Hz, 1H), 4.24 (m, 1H), 3.22 (dd, J = 13.6, 6.8 Hz, 1H), 3.00 (dd, J = 13.6, 8.4 Hz, 1H), 2.89−2.70 (m, 3H), 2.66−2.58 (m, 1H), 1.82−1.68 (m, 2H), 1.49−1.38 (m, 2H), 1.42 (s, 9H), 1.32−1.28 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.6, 129.3, 128.6, 126.7, 79.5, 54.6, 53.1, 49.6, 39.9, 31.3, 28.4, 28.4, 22.5, 22.4, 14.0.; IR (neat) cm^{-1} 3362, 3244, 3062, 3028, 3005, 2957, 2926, 2857, 1689, 1523, 1454, 1366, 1268, 1251, 1171, 1043, 1016; $[\alpha]_D^{25}$ +28.66 (c 0.15, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{20}H_{33}NO_3S$ [M + Na] 390.2079, found 390.2079. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 (br s,1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.0, 129.5, 128.6, 126.9, 56.5, 53.0, 48.8, 40.8, 31.3, 28.5, 28.3, 22.4, 14.

(R_S,2*S*)-*N*-Boc-1-Phenyl-3-(*tert*-butylsulfinyl)propan-2-amine (10c). 2-(Carboethoxy)ethyl *tert*-butyl sulfoxide (**2c**) material (0.100 g, 0.485 mmol) in THF (3 mL) was treated dropwise with LiHMDS (0.509 mL). Next, electrophile **4a** (0.350 g, 0.970 mmol) in THF (3 mL) was added to sulfenate via syringe. A diastereomeric mixture of β-amino sulfoxides **10c** (63%, 0.104 g, dr = 78:22 HPLC integration) was isolated following flash chromatography (30% EtOAc/hexanes). HPLC (5% *i*-PrOH/hexanes, 1.0 mL/min flow rate, OD-H column): 9.59 min (minor), 10.51 min (major). The diastereomeric mixture was recrystallized from EtOAc/hexanes to give improved optical purity of 84:16: mp 130−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.20 (m, 5H), 5.78 (br d, J = 8.0 Hz, 1H), 4.24 (m, 1H), 3.28 (dd, J = 13.6, 6.8 Hz, 1H), 3.02 (dd, J = 13.6, 8.8 Hz, 1H), 2.74 (dd, J = 12.8, 6.4 Hz, 1H), 6.60 (dd, J = 13.2, 4.0 Hz, 1H), 1.42 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.9, 129.4, 128.6, 126.7, 79.4,

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53.2, 50.1, 46.8, 39.7, 28.4, 22.7; IR (neat) cm^{-1} 3266, 3028, 2976, 2930, 2869, 1708, 1525, 1455, 1391, 1365, 1271, 1252, 1172, 1043, 1011, 733, 699; $[\alpha]_D^{25}$ +32.66 (*c* 0.75, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{18}H_{29}NO_3S$ [M + Na] 362.1766, found 362.1748. Minor isomer, partial characterization: ^1H NMR (400 MHz, $CDCl_3$) δ 5.05 (br s,1H); 2.48 (dd, *J* = 13.2, 5.6 Hz, 1H) ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.4, 129.6, 128.5, 126.6, 79.6, 53.4, 49.8, 47.0, 41.3, 28.3, 22.7.

(*R*$_S$,2*S*)-*N*-Boc-1-Phenyl-3-(*c*-hexylsulfinyl)propan-2-amine (10d). 2-(Carboethoxy)ethyl *c*-hexyl sulfoxide (**2d**) (0.100 g, 0.431 mmol) in THF (3 mL) was treated dropwise with LiHMDS (0.431 mL). Next, electrophile **4a** (0.374 g, 1.034 mmol) in THF (3 mL) was added to sulfenate via syringe. A diastereomeric mixture of β-amino sulfoxides **10d** (78%, 0.122 g, dr = 91:9 by NMR integration) was isolated following flash chromatography (30% EtOAc/hexanes). The product was isolated as a 91:9 diastereomeric mixture: mp 152−154 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.312−7.23 (m, 5H), 5.72 (br d, *J* = 6.8 Hz, 1H), 4.26 (m, 1H), 3.24 (dd, *J* = 13.2, 6.4 Hz, 1H), 3.01 (dd, *J* = 12.8, 8.4 Hz, 1H), 2.88−2.83 (m, 1H), 2.76 (dd, J = 12.8, 3.2 Hz, 1H), 2.57 (m, 1H), 2.12−2.09 (m, 1H), 1.93- 1.71 (m, 4H), 1.69- 1.27 (m, 5 H), 1.42 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.3, 137.8, 129.4, 128.6, 126.7, 79.4, 59.9, 50.9, 50.0, 39.8, 28.4, 26.2, 25.5, 25.3, 25.1, 25.0; IR (neat) cm^{-1} 3365, 3260, 3062, 3028, 2976, 2929, 2853, 1690, 1519, 1450, 1391, 1365, 1298, 1268, 1250, 1169, 1042, 1016, 742, 699; $[\alpha]_D^{25}$ +24.42 (*c* 0.95, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{20}H_{31}NO_3S$ [M + Na] 388.1922, found 388.1927. Minor isomer, partial characterization: ^1H NMR (400 MHz, $CDCl_3$) δ 4.97 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.3, 137.8, 129.6, 128.9, 126.8, 79.4, 58.9, 52.7, 49.2, 40.4, 28.3, 26.5, 25.5, 25.3, 25.1, 25.0.

General Procedure: Synthesis of 1-Alkenyl β-Amino Sulfoxides. All sulfenate reactions were performed under anhydrous conditions under an inert N_2(g) atmosphere. To a solution of LiHMDS (1.0 M in THF, 1.1 equiv) in Et_2O (10 mL/mmol LiHMDS) at −78 °C was added dropwise a solution of the thiirane *S*-oxide (1.0 equiv) in Et_2O (~5.4 mL/mmol thiirane *S*-oxide) at −78 °C. The mixture was allowed to stir for ca. 15 min, at which time a precooled (−78 °C) solution of the amino iodide (**4**, 1.1 equiv) in THF (~2.5 mL/mmol iodide) was added dropwise via syringe. After 2−3 h of stirring at −78 °C the reaction vessel was removed form the cold bath and allowed to warm to rt. Reactions were stirred until completion as monitored by TLC (usually 1 h at rt). Following completion the solvent was removed under reduced pressure, and the residue was dissolved in DCM. The organic layer was washed with satd ammonium chloride solution, water, and brine and then dried over $MgSO_4$. The organic layer was then filtered, and solvent was removed under reduced pressure. The crude reaction mixture was subjected to flash chromatography using mixtures of ethyl acetate/hexanes as the eluent, which yielded the β-amino sulfoxides **13** as a mixture of diastereomers. The diastereomeric ratios were determined by comparison of relative ^1H NMR peak integrations and/or relative integrations of peaks from an HPLC separation on a chiral column (Daicel chiralpak OJ-H or OD-H column). In most cases the diastereomeric mixture could be recrystallized from mixtures of ethyl acetate and hexanes to provide the major diastereomer. The absolute stereochemistry of the *major* product is listed as part of the compounds name.

(*R*$_S$,2*S*)-*N*-Boc-1-Phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (13a). A solution of LiHMDS (1.22 mL), propylene thiirane *S*-oxide (0.100 g, 1.11 mmol), and (*S*)-**4a** (0.441 g, 1.22 mmol) (3 mL) afforded a diastereomeric mixture of β-amino sulfoxide **13a** (82%, 0.292 g, dr = 90:10) following flash chromatography (60% EtOAc/hexanes); HPLC (1% *i*-PrOH/hexanes, 1.0 mL/min flow rate): 21.23 min (major), 28.52 min (minor). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 145−147 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.21 (m, 5H), 6.47 (sextet, *J* = 6.7 Hz, 1H), 6.23 (d, *J* = 15.1 Hz, 1H), 5.50 (br d, *J* = 6.3 Hz, 1H), 4.21 (m, 1H), 3.18 (dd, *J* = 13.0, 6.5 Hz, 1H), 2.99 (dd, *J* = 12.8, 7.7 Hz, 1H), 2.91−2.87 (m, 1H), 2.82 (dd, *J* = 13.2, 3.9 Hz, 1H), 1.91 (d, *J* = 6.7 Hz, 3H), 1.42 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 137.5, 137.0, 133.3, 129.4, 128.6, 126.7, 79.5, 56.6, 49.4, 39.9, 28.4, 17.8; IR (neat) cm^{-1} 3358, 3267, 3086, 3062, 2978, 2915, 1691, 1522, 1366, 1268, 1251, 1171, 1047, 1022, 959; $[\alpha]_D^{25}$ +16.58 (*c* 1.2, $CHCl_3$); HRMS (HRMS (TOF, ESI) calcd for $C_{17}H_{25}NO_3S$ [M]+: 323.1555; found: 323.1547. Minor isomer, partial characterization: ^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (br s, 1H), 1.42 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.1, 137.02, 136.99, 133.3, 129.5, 128.6, 126.8, 79.4, 58.3, 48.2, 40.8, 28.4, 17.8.

(*S*$_S$, 2*R*)-*N*-Boc-1-Phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (*ent*-13a). A solution of LiHMDS (1.22 mL), propylene thiirane *S*-oxide (0.100 g, 1.11 mmol), and (*R*)-**4a** (0.441 g, 1.22 mmol) afforded a diastereomeric mixture of β-amino sulfoxide ***ent*-13a** (78%, 0.289 g, dr = 90:10) following flash chromatography (60% EtOAc/hexanes); HPLC (1% *i*-PrOH/hexanes, 1.0 mL/min flow rate): 25.37 min (major), 37.31 min (minor). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 145−147 °C. See enantiomer above for spectral data $[\alpha]_D^{25}$ −16.69 (*c* 1.6, $CHCl_3$). Anal. Calcd for $C_{17}H_{25}NO_3S$: C, 63.13; H, 7.79. Found: C, 62.90; H, 7.50 .

(*R*$_S$,2*S*)-*N*-Boc-3-Methyl-1-((*E*)-1-propenylsulfinyl)butan-2-amine (13b). A solution of LiHMDS (1.22 mL), propylene thiirane *S*-oxide (0.100 g, 1.11 mmol), and **4c** (0.381 g, 1.22 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13b** (70%, 0.215 g, dr = 80:20 by ^1H NMR integration of mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 149−150 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 6.89 (br d, *J* = 8.9 Hz, 1H), 6.51 (dd, *J* = 15.0, 1.4 Hz, 1H), 6.30 (dq, *J* = 15.0, 6.7 Hz, 1H), 3.68 (m, 1H), 2.78−2.68 (m, 1H), 2.59 (dd, *J* = 13, 2.5 Hz, 1H), 1.85 (dd, *J* = 6.8, 1.3 Hz, 3H), 1.74 (m, 1H), 1.37 (s, 9H), 0.80 (dd, *J* = 6.8, 2.0 Hz, 6H); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 155.2, 134.8, 134.1, 77.6, 56.6, 50.1, 32.2, 28.2, 18.4, 18.0, 17.3; IR (neat) cm^{-1} 3230, 3034, 2969, 2915, 2872, 1700, 1542, 1449, 1367, 1297, 1252, 1174, 1038, 1018, 957 $[\alpha]_D^{25}$ +23.88 (*c* 0.90, $CHCl_3$). Anal. Calcd for $C_{13}H_{25}NO_3S$: C, 56.69; H, 9.15. Found: C, 56.52; H, 9.30. Minor isomer, partial characterization: ^1H NMR (400 MHz, $CDCl_3$) δ 6.95 (br d, *J* = 9.2 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.1, 135.4, 134.3, 77.7, 56.2, 49.9, 32.0, 28.0, 18.7, 17.8, 17.4.

(*R*$_S$,2*S*)-*N*-Boc-((*E*)-1-pPropenylsulfinyl)propan-2-amine (13c). A solution of LiHMDS (1.11 mL), propylene thiirane *S*-oxide (0.100 g, 1.11 mmol), and (*S*)-**4b** (0.443 g, 1.55 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13c** (67%, 0.187 g, dr = 82:18 by ^1H NMR integration of mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 107−108 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 6.51 (dq, *J* = 15.2, 6.8 Hz, 1H), 6.29 (dd, *J* = 15.2, 1.6 Hz, 1H), 5.31 (br s, 1H), 4.14 (m, 1H), 2.90−2.89 (m, 1H), 2.83 (dd, *J* = 12.8, 4.8 Hz, 1H), 1.94 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.438 (s, 9H) 1.41 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.0, 137.1, 133.4, 79.5, 59.7, 43.8, 28.4, 20.4, 17.9; IR (neat) cm^{-1} 3232, 3040, 2973, 2930, 2872, 1698, 1539, 1449, 1364, 1272, 1252, 1174, 1093, 1028; $[\alpha]_D^{25}$ +19.33 (*c* 0.15, $CHCl_3$). Anal. Calcd for $C_{11}H_{21}NO_3S$: C, 53.41; H, 8.56. Found: C, 53.49; H, 8.51. Minor isomer, partial characterization: ^1H NMR (400 MHz, $CDCl_3$) δ 6.40 (d, *J* = 15.4 Hz, 1H), 5.63 (br d, *J* = 7.9 Hz, 1H), 4.01 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.0, 136.3, 133.2, 79.0, 60.9, 42.8, 28.3, 20.9, 17.7.

(*R*$_S$,2*S*)-*N*-Boc-1-Phenyl-3-((*E*)-4-phenyl-1-butenylsulfinyl)-propan-2-amine (13d). A solution of LiHMDS (0.61 mL), 4-phenylbut-1-ene thiirane *S*-oxide (0.100 g, 0.555 mmol), and (*S*)-**4a** (0.221 g, 0.610 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13d** (84%, 0.192 g, dr = 92:8 by ^1H NMR integration of mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 154−155 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.12 (m, 10H), 6.49 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.16 (d, *J* = 15.1 Hz, 1H), 5.42 (br d, *J* = 7.2 Hz, 1H), 4.20 (m, 1H), 3.17 (dd, *J* = 13.5, 6.4 Hz, 1H), 2.97 (dd, *J* = 13.4, 7.9 Hz, 1H), 2.84−2.72 (m, 4H), 2.55 (q, *J* = 7.6 Hz, 2H), 1.42 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.4, 139.9, 137.5, 132.8, 129.4, 128.7, 128.5, 128.4, 126.8, 126.3, 79.6, 56.7, 49.4, 39.9, 34.4, 33.7, 28.4; IR (neat)

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cm^{-1} 3362, 3269, 3061, 3025, 2977, 2924, 2857, 1690, 1522, 1267, 1252, 1170, 1102, 1046, 1020, 894; $[\alpha]_D^{25}$ +16.59 (*c* 1.2, $CHCl_3$). Anal. Calcd for $C_{24}H_{31}NO_3S$: C, 69.70; H, 7.56. Found: C, 70.05; H, 7.12. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.23 (d, *J* = 15.2 Hz, 1H), 4.95 (br d, *J* = 7.9 Hz, 1H), 4.09 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.6, 140.0, 137.0, 132.7, 129.5, 129.0, 129.0, 128.66, 126.9, 126.3, 79.6, 58.4, 48.3, 40.8, 34.4, 33.7, 28.4.

(*R*$_S$,2*S*)-*N*-Boc-1-Phenyl-3-(vinylsulfinyl)propan-2-amine (13e). A solution of LiHMDS (1.45 mL), ethylene thiirane *S*-oxide (0.100 g, 1.314 mmol), and iodide (*S*)-**4a** (0.569 g, 1.58 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13e** (84%, 0.341 g, dr = 89:11 by ^{1}H NMR integration of mixture) following column chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 137−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.21 (m, 5H), 6.60 (dd, *J* = 16.4, 9.8 Hz, 1H), 6.12 (d, *J* = 16.5 Hz, 1H), 5.96 (d, *J* = 9.8 Hz, 1H), 5.41 (br d, *J* = 6.2 Hz, 1H), 4.23 (m, 1H), 3.20 (dd, *J* = 12.3, 7.0 Hz, 1H), 3.00 (dd, *J* = 13.5, 7.6 Hz, 2H), 2.78 (dd, *J* = 13.2, 3.9 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.5, 137.3, 129.4, 128.7, 126.8, 122.0, 79.7, 56.5, 49.4, 39.9, 28.4; IR (neat) cm^{-1} 3455, 3359, 3033, 2980, 2920, 1690, 1522, 1267, 1250, 1170, 1052,1022; $[\alpha]_D^{25}$ +41.86 (*c* 0.80, $CHCl_3$). Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; Found; C, 61.96; 7.48. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (dd, *J* = 16.8, 9.8 Hz, 1H), 5.97 (d, *J* = 9.8 Hz, 1H), 4.84 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.5, 136.8, 128.6, 128.4, 126.9, 122.1, 79.7, 57.9, 49.0, 40.7, 28.3.

(*R*$_S$,2*S*)-*N*-Boc-1-(Cyclohexenylsulfinyl)-3-phenylpropan-2-amine (13f). A solution of LiHMDS (0.92 mL) in THF (6 mL), cyclohexene thiirane *S*-oxide (0.100 g, 0.767 mmol) in THF (3 mL), and (*S*)-**4a** (0.332 g, 0.920 mmol) in THF (3 mL) afforded two β-amino sulfoxide diastereomers (**13f**), which were isolated from one another by flash column chromatography (40% EtOAc/hexanes) (71%, 0.197 g, dr = 93:7 (based on peak integration of diastereomeric mixture)). Major isomer: mp 131−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.21 (m, 5H), 6.44 (s, 1H), 5.60 (br d, 5.7 Hz, 1H), 4.16 (m, 1H), 3.22 (dd, *J* = 13.4, 6.0 Hz, 1H). 3.00 (dd, *J* = 13.5, 8.1 Hz, 1H), 2.87−2.77 (m, 2H), 2.22−2.15 (m, 3H), 2.04−2.01 (m, 1H), 1.67 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.8, 137.7, 132.3, 129.4, 128.6, 126.7, 79.4, 53.6, 49.8, 39.9, 28.4, 25.5, 22.2, 21.9, 20.7; IR (neat) cm^{-1} 3263, 3027, 2975, 2932, 2860, 1709, 1525, 1364, 1269, 1252, 1171, 1043, 1007, 699; $[\alpha]_D^{25}$ +81.1 (*c* 0.45, $CHCl_3$). Anal. Calcd for $C_{20}H_{29}NO_3S$: C, 66.08; H, 8.04. Found: C, 66.04; H, 7.87. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (br d, *J* = 8.0 Hz, 1H), 4.01 (br m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 140.5, 137.2, 134.1, 129.5, 129.0, 126.8, 79.4, 54.4, 49.7, 40.9, 28.4, 25.6, 22.1, 21.9, 19.6.

(*R*$_S$,2*S*)-*N*-Boc-1-((*E*)-3,3-Dimethyl-1-butenylsulfinyl)-3-phenylpropan-2-amine (13g). A solution of LiHMDS (0.83 mL), propylene thiirane *S*-oxide (0.100 g, 0.757 mmol), and iodide (*S*)-**4a** (0.300 g, 0.832 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13g** (60%, 0.166 g, dr = 92:8 by NMR integration of diastereomeric mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.22 (m, 5H), 6.46 (d, *J* = 15.4 Hz, 1H), 6.09 (d, *J* = 15.4 Hz, 1H), 5.50 (br d, *J* = 6.9 Hz, 1H), 4.21 (m, 1H), 3.21 (dd, *J* = 13.3, 6.8 Hz, 1H), 3.00 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.89 (m, 1H), 2.81 (dd, *J* = 13.2, 3.9 Hz, 1H), 1.43 (s, 9H), 1.09 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 151.1, 137.6, 129.4, 128.7, 128.0, 126.7, 79.5, 56.7, 49.6, 39.9, 34.2, 28.8, 28.4; IR (neat) cm^{-1} 3361, 3251, 3039, 2963, 2906, 2867, 1706, 1525, 1365, 1270, 1253, 1173, 1046, 1020; $[\alpha]_D^{25}$ +14.20 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{20}H_{31}NO_3S$: C, 65.72; H, 8.55. Found: C, 65.44; H, 8.68. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (br d, *J* = 8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.2, 151.3, 137.0, 129.5, 129.0, 128.0, 126.8, 79.5, 58.3, 48.4, 40.7, 34.2, 28.8, 28.4.

(*R*$_S$,2*S*)-*N*-Boc-*O*-TBDPS-1-Hydroxy-3-((*E*)-1-propenylsulfinyl)propan-2-amine (13h). A solution of LiHMDS (0.59 mL), propylene thiirane *S*-oxide (0.050 g, 0.554 mmol), and **4e** (0.538 g, 0.997 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13h** (65%, 0.181 g, dr = 87:13 by ^{1}H NMR integration of mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 167−169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.63 (m, 4H), 7.46−7.37 (m, 6H), 6.47 (dq, *J* = 15.2, 6.8 Hz, 1H), 6.26 (dd, *J* = 15.2, 1.6 Hz, 1H), 5.40 (br d, *J* = 8.0 Hz, 1H), 4.19 (m, 1H), 3.87−3.83 (m, 2H), 3.03 (dd, *J* = 12.8, 6.8 Hz, 1H), 2.92 (m, 1H), 1.92 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.43 (s, 9H), 1.07 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.1, 137.1, 135.6, 133. 7, 132.9, 129.9, 127.9, 79.6, 64.8, 55.5, 48.9, 28.4, 26.9, 19.3, 17.9; IR (neat) cm^{-1} 3234, 3071, 3050, 3027, 2971, 2957, 2933, 2908, 2859, 1705, 1543, 1443, 1427, 1315, 1280, 1249, 1175, 1106, 1012, 961, 828 706 $[\alpha]_D^{25}$ +297.33 (*c* 0.75, $CHCl_3$). Anal. Calcd for $C_{27}H_{41}NO_4SSi$: C, 64.37; H, 8.20. Found: C, 64.63; H, 7.87. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (dd, *J* = 13.2, 6.8 Hz, 1H), 4.99 (br d, *J* = 8.4 Hz, 1H), 4.01 (m, 1H), 1.44 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.1, 137.2, 135.5, 133.3, 133.0, 129.9, 127.9, 79.6, 65.4, 57.3, 48.2, 28.4, 26.9, 19.3, 17.9.

(*S*$_S$,1*R*)-*N*-Boc-2-((*E*)-3,3-Dimethyl-1-butenylsulfinyl)-1-phenylethanamine (13i). A solution of LiHMDS (0.83 mL), propylene thiirane *S*-oxide (0.100 g, 0.757 mmol), and **4h** (0.315 g, 0.908 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13i** (65%, 0.172 g, dr = 84:16 by NMR integration of diastereomeric mixture) was isolated following flash column chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 180−182 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.33 (m, 4H), 7.32−7.28 (m, 1H), 6.44 (d, *J* = 15.4 Hz, 1H), 6.24 (br s, 1H), 6.11 (d, *J* = 15.4 Hz, 1H), 5.24 (br s, 1H), 3.12−3.10 (m, 2H), 1.41 (s, 9H), 1.08 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.1, 151.7, 140.3, 128.8, 127.8, 127.8, 126.3, 79.8, 59.8, 51.9, 34.3, 28.8, 28.4; IR (neat) cm^{-1} 3264, 3033, 2963, 2868, 1707, 1528, 1365, 1251, 1170, 1045, 1019; $[\alpha]_D^{25}$ −32.00 (*c* 0.75, $CHCl_3$). Anal. Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32. Found: C, 64.70; H, 8.12. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (d, *J* = 15.2 Hz, 1H), 6.13 (d, *J* = 15.2 Hz, 1H), 5.07 (br m,1H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 154.9, 151.6, 140.4, 128.8, 128.1, 127.8, 126.3, 79.7, 61.0, 51.7, 34.2, 28.7, 28.3.

(*S*$_S$,2*R*)-*N*-Boc-1-((*E*)-3,3-Dimethyl-1-butenylsulfinyl)butan-2-amine (13j). A solution of LiHMDS (0.83 mL), propylene thiirane *S*-oxide (0.100 g, 0.757 mmol), and **4g** (0.248 g, 0.832 mmol) afforded a diastereomeric mixture of β-amino sulfoxide **13j** (71%, 0.163 g, dr = 95:5 by ^{1}H NMR integration of mixture) following flash chromatography (60% EtOAc/hexanes). The major diastereomer was isolated via recrystallization from EtOAc/hexanes. Major isomer: mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (d, *J* = 15.4 Hz, 1H), 6.16 (d, *J* = 15.4 Hz, 1H), 5.31 (br d, *J* = 7.5 Hz, 1H), 3.92 (sextet, *J* = 7.7 Hz, 1H), 2.95 (dd, *J* = 13.0, 7.2 Hz, 1H), 2.85 (dd, *J* = 13.1, 3.4 Hz, 1H), 1.78 (m, 2H), 1.44 (s, 9H), 1.10, (s, 9H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.3, 151.1, 128.3, 79.4, 58.3, 49.3, 34.2, 28.8, 28.4, 27.3, 10.7; IR (neat) cm^{-1} 3220, 3039, 2966, 1698, 1545, 1363, 1289, 1249, 1174, 1053, 1028, 979; $[\alpha]_D^{25}$ −5.71 (*c* 0.18, $CHCl_3$). Anal. Calcd for $C_{15}H_{29}NO_3S$: C, 59.37; H, 9.63. Found: C, 59.26; H, 9.42. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.86 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.3, 151.1, 128.3, 79.4, 58.3, 49.3, 34.2, 28.8, 28.4, 28.0, 10.7.

Deprotection of β-Amino Sulfoxides. (*R*$_S$,2*S*)-1-Phenyl-3-(phenylsulfinyl)propan-2-amine (14). To a 1:1 solution of TFA/DCM (20 mL) at 0 °C was added a solution of protected β-amino sulfoxide **6** (0.250 g, 0.70 mmol) in DCM (3 mL). The reaction mixture was stirred for 1 h at 0 °C to reach completion. A 2 M aqueous solution of NaOH was added until a basic pH was achieved. The aqueous layer was extracted with DCM (3 × 10 mL). Organic layers were then combined, washed with water, followed by brine, and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Known sulfoxide **14**[81] (0.138 g, 77% yield) was isolated following workup as a clear oil. $[\alpha]_D^{25}$ −223.9 (*c* 0.2, $CHCl_3$) [lit.[81] −225.0 (*c* 0.2, $CHCl_3$).

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(R_S,2*S*)-1-Phenyl-3-((*E*)-1-propenylsulfinyl)propan-2-ammonium Trifluoroacetate (15). To a 1:1 solution of TFA/DCM (20 mL) at 0 °C was added a solution of protected *β*-amino sulfoxide (0.673 g, 2.08 mmol) in DCM (3 mL). The reaction mixture was stirred for 1 h at 0 °C at which time TLC exhibited reaction completion. Solvent was removed under reduced pressure, and then 20 mL of hexanes was added to the residue and removed under reduced pressure. This process was repeated three times in order to ensure removal of trifluoroacetic acid. Crude product was purified by flash chromatography using MeOH/DCM (9:1) as the eluent to give the pure product as a clear colorless oil (95%, 0.668 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (br s, 3H), 7.34−7.16 (m, 5H), 6.51 (dq, J = 14.8, 6.8 Hz, 1H), 5.87 (dd, J = 14.8, 1.6 Hz, 1H), 4.06 (m, 1H), 3.41 (dd, J = 14.8, 9.6 Hz, 1H), 3.34 (dd, J = 13.6, 4.8 Hz, 1H), 2.98 (dd, J = 13.6, 10.8 Hz, 1H), 2.53 (dd, J = 14.8, 1.6 Hz, 1H), 1.94 (dd, J = 6.8, 1.6 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 140.5, 134.2, 129.2, 129.1, 128.6, 127.9, 49.4, 48.3, 38.6, 17.8; IR (neat) cm^{-1} 3420, 3032, 2977, 2923, 1680, 1497, 1436, 1203, 1135, 1009, 952, 837, 801, 747; $[\alpha]_D^{25}$ −56.8 (*c* 2.0, $CHCl_3$). Anal. Calcd for $C_{14}H_{18}F_3NO_3S$: C, 49.84; H, 5.38. Found: C, 49.83; H, 5.31.

Sulfenate Alkylation Competition Experiments (see Table 3). *Experiment 1.* 2-Carbomethoxyethenyl ar(alk)yl sulfoxide (0.100 g, 0.446 mmol) was dissolved in THF (3 mL) under nitrogen and stirred at −78 °C. To the sulfoxide was added *n*-BuLi (0.279 mL,1.6 M in hexanes) via syringe. Following 5−10 min of stirring, a solution of the chiral iodide (*S*)-**4a** (0.805 g, 2.23 mmol) and benzyl bromide (0.237 mL, 2.23 mmol) in THF (3 mL) at −78 °C was added via syringe to the sulfenate. The mixture was stirred at −78 °C for 3−4 h and then allowed to slowly warm to rt overnight. Solvent was removed under reduced pressure. Column chromatography using an EtOAc/hexanes (30:70) mixture as the eluent provided *p*-tolyl benzyl sulfoxide as a white solid and the sole product (96%, 0.101 g). Mp: 138−140 °C [lit.[92] 139−140 °C].

Experiment 2. 2-Carbomethoxyethenyl ar(alk)yl sulfoxide (0.100 g, 0.446 mmol) was dissolved in THF (3 mL) under nitrogen and stirred at −78 °C. To the sulfoxide was added *n*-BuLi (0.279 mL,1.6 M in hexanes) via syringe. Following 5−10 min of stirring, a solution of the chiral iodide (*S*)-**4a** (0.322 g, 0.892 mmol) and butyl iodide (0.508 mL, 4.46 mmol) in THF (3 mL) at −78 °C was added via syringe to the sulfenate. The mixture was stirred at −78 °C for 3−4 h and then allowed to slowly warm to rt overnight. Solvent was removed under reduced pressure. Column chromatography using an EtOAc/hexanes (30:70) mixture as the eluent provided *p*-tolyl butyl sulfoxide[142] (33%, 0.029 g) as an orange oil and a 91:9 diastereomeric mixture of **5a** as a solid (27%, 0.043 g).

Experiment 3. 2-Carbomethoxyethenyl ar(alk)yl sulfoxide (0.100 g, 0.446 mmol) was dissolved in THF (3 mL) under nitrogen and stirred at −78 °C. To the sulfoxide was added *n*-BuLi (0.279 mL,1.6 M in hexanes) via syringe. Following 5−10 min of stirring, a solution of the chiral iodide (*S*)-**4a** (0.277 g, 0.892 mmol) and butyl iodide (0.508 mL, 4.46 mmol) in THF (3 mL) at −78 °C was added via syringe to the sulfenate. The mixture was stirred at −78 °C for 3−4 h and then allowed to slowly warm to rt overnight. Solvent was remove under reduced pressure. Column chromatography using an EtOAc/hexanes (30:70) mixture as the eluent provided *p*-tolyl butyl sulfoxide[142] as the sole product as an orange oil (92%, 0.081 g).

Experiment 4. A solution of LiHMDS (1.22 mL) in diethyl ether (12 mL) at −78 °C was treated dropwise with precooled (−78 °C) propylene thiirane *S*-oxide (0.100 g, 1.11 mmol) in diethyl ether (6 mL). Next a −78 °C solution of (*S*)-**4a** (0.801 g, 2.22 mmol) and butyl iodide (1.26 mL, 11.1 mmol) in THF (3 mL) was added to the sulfenate via syringe. The reaction was stirred for 3 h at −78 °C then allowed to warm to rt overnight. Solvent was removed under reduced pressure. The product ratio of 1-propenyl butyl sulfoxide:**13a** was found to be 1:1.4 as determined by analysis of ^{1}H NMR peak integration. Data for 1-propenyl butyl sulfoxide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (dq, J = 15.2, 6.8 Hz, 1H), 6.24 (dq, J = 15.2, 1.6 Hz, 1H), 2.71 (t, J = 8.0 Hz, 2H), 1.93 (dd, J = 6.4, 1.6 Hz, 3H), 1.76−1.64 (m, 2H), 1.50 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 136.70, 133.56, 53.63, 24.10, 21.95, 17.81, 13.69; IR (neat) cm^{-1} 3008, 2959, 2933, 2873, 1636, 1465, 1458, 1405, 1090, 1035, 956.

Experiment 5. A 1:1 molar solution of 2-(carbomethoxy)ethenyl 2-pyridyl sulfoxide (0.094 g, 0.446 mmol) and 2-(carbomethoxy)ethenyl tolyl sulfoxide (0.100 g, 0.446 mmol) in THF (3 mL) at −78 °C was treated dropwise with 1.6 M *n*-BuLi (0.558 mL, 0.892 mmol). The solution was stirred for ∼10 min at −78 °C to ensure sulfenate generation. Next a −78 °C solution of benzyl bromide (0.026 mL, 0.223 mmol) in THF (3 mL) was added to sulfenate pot via syringe. The reaction was stirred for 3 h at −78 °C and then allowed to warm to rt overnight. Following standard workup the crude ^{1}H NMR revealed the sole formation of the *p*-tolyl benzyl sulfoxide,[92] which was isolated via column chromatography using EtOAc/hexanes (40:60) as the eluent.

Experiment 6. A 1:1 molar solution of 2-(carbomethoxy)ethenyl 2-pyridyl sulfoxide (0.094 g, 0.446 mmol) and 2-(carbomethoxy)ethenyl tolyl sulfoxide (0.100 g, 0.446 mmol) in THF (3 mL) at −78 °C was treated dropwise with 1.6 M *n*-BuLi (0.558 mL, 0.892 mmol). The solution was stirred for ∼10 min at −78 °C to ensure sulfenate generation. Next a −78 °C solution of (*S*)-**4a** (0.032 g, 0.089 mmol) in THF (3 mL) was added to sulfenate pot via syringe. The reaction was stirred for 3 h at −78 °C and then allowed to warm to rt overnight. Following standard workup the crude NMR revealed the sole formation of the **5a** (78%, 0.025 g), which was isolated via column chromatography using EtOAc/hexanes (40:60) as the eluent.

■ ASSOCIATED CONTENT

Supporting Information

Data relating to X-ray crystallographic identification of **13a**; ^{1}H NMR and ^{13}C NMR spectra of new starting materials and new amino sulfoxides. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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