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# Design, Synthesis, and Applications of Chiral *N*-2-Phenyl-2-propyl Sulfinyl Imines for Group-Assisted Purification (GAP) Asymmetric Synthesis

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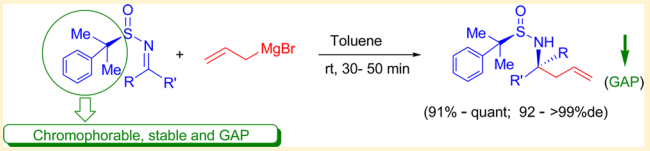
Supporting Information

**ABSTRACT:** A new chiral ($R_s$)-2-phenyl-2-propyl sulfinamide has been designed and synthesized; its derived aldimines and ketimines have been applied for asymmetric addition reaction with allylmagnesium bromide. The reaction was conveniently performed at room temperature to give a series of homoallylic amines in high yields (up to quant) and diastereoselectivity (up to >99% de). The pure products were obtained by relying on group-assisted purification (GAP) chemistry to avoid traditional purification methods of column chromatography or recrystallization. The conversion of disulfide to ($R_s$)-thiosulfinate which contains a newly generated polar group was also confirmed to be of the GAP chemistry in which washing crude product can generate pure enantiomer. The absolute stereochemistry has been determined by X-ray analysis.




## INTRODUCTION

Imine chemistry has been one of the most important topics in modern organic and medicinal chemistry.[1] The resulting chiral amino compounds are valuable synthetic building blocks and have been widely transformed into many natural products and medicinal targets.[2] Design of chiral N-protected imines and their applications to asymmetric reactions have dramatically advanced the asymmetric fields in the past several decades.[3] The search for greener chiral imines with high efficiencies for asymmetric synthesis still remains challenging. In the past several years, we have designed several chiral N-protected imines including *N*-phosphonyl,[4] *N*-phosphoryl,[5] and *N*-phosphinyl[6] auxiliaries. We successfully utilized them for many asymmetric transformations with good to excellent yields and diastereoselectivities without using traditional purification methods, which resulted in a new concept called group-assisted purification (GAP) chemistry.[6−8] By paying attention to this concept, the products can be purified by simply washing with the common solvents to save materials (silica gels, solvents, energy, and manpower) substantially. If products appear in the form of oil/liquid, washing can be performed via extractions in separation funnels. The GAP chemistry requires adequate control not only on the physical solubility but also on chemical reactivity and stereoselectivity of both reagents and resulting products. In the former, products must be soluble in some common solvents (e.g., THF and DCM) to enable further reactions, but they should not be dissolved well in some other solvents (petroleum ethers, hexane, and their cosolvents with EtOAc, etc.) to enable simple washing for purification. In the latter, the auxiliary-anchored reactants should have efficient reactivity toward various species and show efficient asymmetric induction to ensure the formation of excess amounts of desired isomeric products. In addition, the auxiliary group should be tolerable to many reaction conditions for further transformations, and preferably, they may be recovered for recycling.

Chiral *N*-phosphonyl and *N*-phosphinyl imine-based synthesis has been proven to meet the above requirements both physically and chemically.[4,6] For example, when chiral *N*-phosphonyl imines were subjected to the reaction with 2-lithio-1,3-dithianes via a special operation by slowly adding the solution of imines into that of lithium anions, the resulting umpolung products, $\alpha$-amino-1,3-dithianes, were obtained in up to 82% yields and >99:1 diastereoselectivities by following the GAP chemistry process.[7b] The pure chiral products can be easily generated by washing their crude products with hexane or the cosolvent of hexane−EtOAc to avoid the traditional purification of chromatography or recrystallization. Besides the use of chiral *N*-phosphonyl auxiliaries, we also applied their achiral *N*-phosphonyl counterpart to asymmetric catalysis of Strecker reaction. When achiral *N*-phosphonyl imines were utilized as the electrophiles to react with $Et_2AlCN$ in the presence of chiral catalysts such as primary free natural amino acids, amino alcohols, or BINOLs, the reaction was conducted to give excellent chemical yields and complete enantioselectivity.[7e,f] The achiral *N*-phosphonyl group also enabled the purification to be performed simply by the GAP process. In addition, achiral *N*-phosphonyl auxiliary can be readily cleaved under mild conditions with the quantitative recovery of *N*,*N*′-bis(naphthalen-1-ylmethyl)ethane-1,2-diamine via one-time extraction with *n*-butanol.

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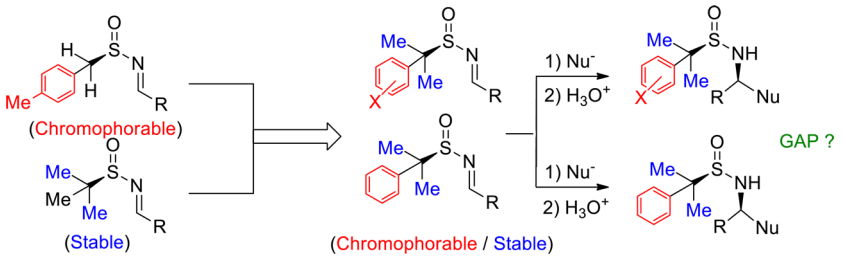
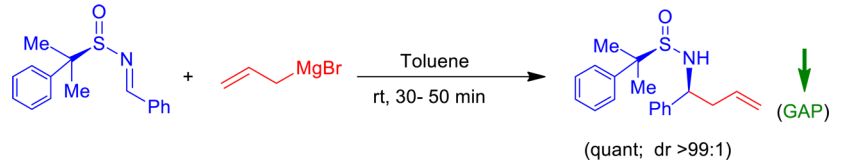
**Scheme 1**




**Scheme 2**




We believe that the unique polarity of the P═O bond in which negative and positive charges are heavily localized on oxygen and phosphorus atoms is responsible for the solid product formation to enable the GAP purification. In *N*-phosphonyl auxiliaries, *N*,*N*-diamino groups donate electron density to stabilize the positively charged phosphorus center, which can indirectly increase electron density on the terminal oxygen atom. In the solid state, the polarization effect between highly packed molecules is anticipated to further polarize the P═O bond, which would be closer to a single bond arrangement; this situation would be different in solution phase, particularly, when the P═O bond exists in *N*-phosphonyl imines. The above hypothesis can be proven by the observation in which *N*-phosphonyl imines usually cannot be synthesized via GAP chemistry operation. A similar situation exists in the "S═O" bond polarization in thio-oxime *S*-oxides, which describes the S═O bond as $S^{+}-O^{-}$.[7,9]

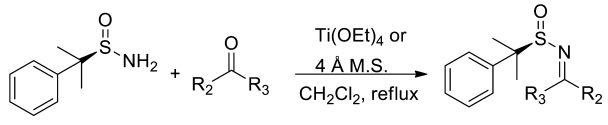
On the basis of the above analysis, we anticipated that the GAP chemistry phenomenon would exist in sulfinyl imine-based organic synthesis for making chiral amine compounds. Meanwhile, we would like to design new sulfinyl imines by taking advantage of *p*-toluenesulfimines (aromatic chromophore) and *t*-butanesulfinyl imines (chemical stability) to modify their solubility so that the GAP chemistry can be accomplished more efficiently (Scheme 1).

Considering the availability of starting materials, we first focused on the study of the new chiral *N*-2-phenyl-2-propyl sulfinamide, its derived imines, and their applications to the asymmetric reaction with allylmagnesium bromide. In this paper, we report our first results of this study as represented by Scheme 2 and the results summarized in Tables 1 and 2.

## RESULTS AND DISCUSSION

The synthesis of chiral ($R_s$)-2-phenyl-2-propyl sulfinamide was started from thiol **1** which is commercially available (Scheme 3). Thiol **1** was treated with 30% aqueous hydrogen peroxide in the presence of NaI to give the disulfide **2**. Asymmetric oxidation of disulfide **2** was accomplished with 30% aqueous $H_2O_2$ in the presence of vanadylacetoacetate and chiral ligand **3** to afford corresponding ($R_s$)-thiosulfinate **4** in 75% yield and 85% ee.[9] The enantiomeric excess was further improved to reach over 99% ee by washing this product with hexane twice as determined by chiral HPLC (AS-H column).[10] Interestingly,

**Table 1. Results of *N*-($R_s$)-2-Phenylpropyl-2-sulfinyl Imines**




**6** **7a- 7j** **8a-8j**

| entry | aldehyde or ketone | $R_2$ | $R_3$ | product | yield (%)[a] |
|---|---|---|---|---|---|
| 1 | **7a** | phenyl | H | **8a** | 98 |
| 2 | **7b** | 1-naphthyl | H | **8b** | 97 |
| 3 | **7c** | 2-Me-phenyl | H | **8c** | 89 |
| 4 | **7d** | 4-Me-phenyl | H | **8d** | 96 |
| 5 | **7e** | 4-F-phenyl | H | **8e** | 98 |
| 6 | **7f** | 2-furyl | H | **8f** | 92 |
| 7 | **7g** | isobutyl | H | **8g** | 87 |
| 8 | **7h** | cyclohexyl | H | **8h** | 88 |
| 9 | **7i** | *trans*-PhCH═CH | H | **8i** | 92 |
| 10 | **7j** | phenyl | Me | **8j** | 52 |
| 11 | **7k** | −COOEt | H | **8k** | 45[b] |
| 12 | **7l** | 4-$NO_2$-phenyl | H | **8l** | 80[c] |

[a]Isolated yields after column chromatography. [b]Instead of $Ti(OEt)_4$, 4 Å MS were used. [c]Reaction carried out at room temperature.

this preparation serves as another example of GAP chemistry in non-imine-based reactions. We believe this GAP phenomenon of enhancing % ee would have an extensive scope for other reactions and their resulting chiral products in asymmetric synthesis.

Surprisingly, the conversion of ($R_s$)-thiosulfinate **4** to sulfonamide **6** via the substitution reaction using Li/aq$NH_3$ failed to give the desired product, but this worked well in the preparation of *t*-butylsulfinamide. Treating thiosulfinate ester **4** with benzylamine in the presence of *n*-BuLi led to formation of benzyl-protected sulfinamide in a quantitative yield. Unfortunately, the next step of cleavage of the benzyl group via catalytic hydrogenation failed, for which the possible toxic effect on catalyst by the S═O group might be responsible.[11] The next attempt is to use LiHMDS as a stronger electrophile to react with thiosulfinate ester, but the extremely bulky $N(SiMe_3)_2$ group prevented the $S_N2$ reaction from occurring. However, this nucleophile works well with the *p*-tolenesulfinyl substrate of the Andersen reagent.[8,12] Then, the less bulky TBDMS-$NH_2$


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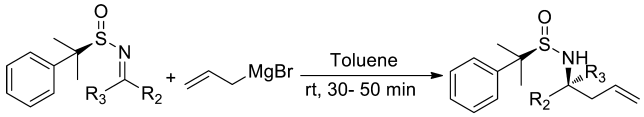
**Table 2. Results of the Allylmagnesium Grignard Addition Reaction to *N*-($R_s$)-2-Phenylpropyl-2-sulfinyl Imines**




8a-8j 9a-9j

| entry | imine | product | % yield[a,b] | % de[c] |
|---|---|---|---|---|
| 1 | **8a** | **9a** | quant | >99 |
| 2 | **8b** | **9b** | quant | >99 |
| 3 | **8c** | **9c** | 95 | >99 |
| 4 | **8d** | **9d** | 99 | 97 |
| 5 | **8e** | **9e** | 94 | 98 |
| 6 | **8f** | **9f** | 96 | 98 |
| 7 | **8g** | **9g** | quant | 98 |
| 8 | **8h** | **9h** | 99 | 97 |
| 9 | **8i** | **9i** | 94 | 92 |
| 10 | **8j** | **9j** | 91 | >99 |

[a]Isolated yields after washing with hexanes. [b]Combined yields of both the diastereomers. [c]Diastereoselectivity was determined by using $^1$H NMR of crude samples; >99% de means only one isomer was observed.

(1.0 N solution in THF), which was freshly prepared,[13] was then utilized as the nucleophile in the presence of *n*-BuLi. We were pleased that TBDMS-attached sulfinamide **5** was successfully obtained in a good yield of 93% without the observation of racemization. The subsequent mild deprotection of TBDMS using tetrabutylammonium fluoride (TBAF) gave ($R_s$)-2-phenyl-2-propyl sulfinamide **6** in 53% overall yield and excellent enantiomeric excess (Scheme 3).

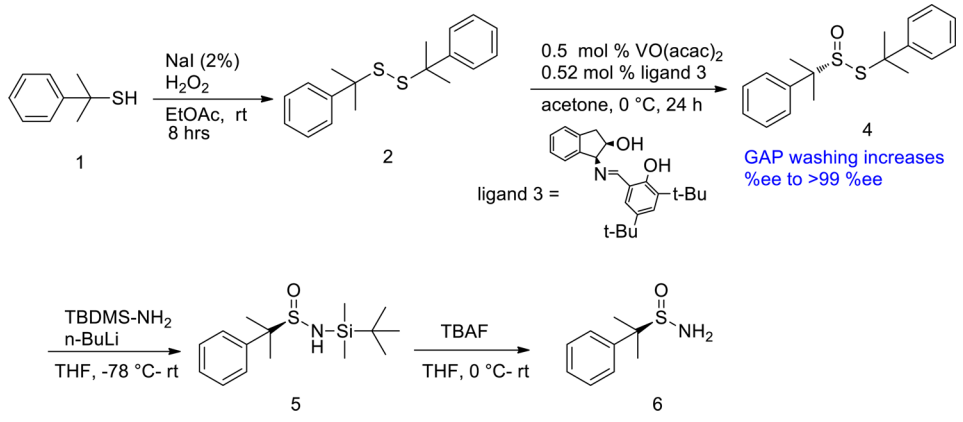
*N*-2-Phenyl-2-propylsulfinyl imines were readily synthesized by the condensation reaction of *N*-2-phenyl-2-propylsulfinyl amide with various aldehydes with the aid of $Ti(OEt)_4$.[14] As shown in Table 1, both aldehydes and ketones are suitable for forming sulfinyl imines with the new *N*-2-phenyl-2-propyl-sulfinyl amide. In general, good to excellent yields (80−98%) were achieved with both aromatic and aliphatic aldehydes (entries 1−9 and 12, Table 1). In two cases of acetophenone and glyoxymate, moderate yields of 52 and 45%, respectively, have been achieved under the conditions above (entries 10 and 11, Table 1).

The new chiral 2-phenyl-2-propyl sulfinyl imines are examined for their first application to the asymmetric addition reaction by allylmagnesium bromide. The resulting N-protected homoallyl amines from this reaction are very useful building blocks for a wide range of pharmaceuticals and biologically active substances[15] and have been transformed into nitrogen-containing heterocycles, such as enantiopure $C_2$-symmetrical *trans*-2,5-disubstituted pyrrolidines, to serve as organocatalysts, chiral catalytic ligands, and chiral auxiliaries.[16] Traditionally, allylation of imines through C−C bond formation by allylmetal reagents (such as allylindium, allylmagnesium, and allyzinc) is used to make homoallyl amines.[17] However, very few such syntheses were stereochemically efficient under room temperature conditions, or very low temperature is necessary.

Initially, we began our investigation with the addition of allylmagenisium bromide to *N*-sulfinyl imine **8a** in THF as solvent at −78 °C. Although the product was formed in a quantitative yield, no diastereoselectivity (∼1:1) was observed. However, when the reaction was performed at 0 °C, the diastereoselectivity was enhanced to 5:1, and at room temperature, it was further improved to 8:1. Increasing the temperature to 50 °C did not give any diastereoselectivity enhancement. With this observation, we then investigated the solvent effects. Several other solvents, such as toluene, benzene, dichloromethane, and ether were screened at room temperature. It was found that, among these solvents, toluene led to the best outcomes in terms of good yields (quant) and complete diastereoselectivity (>99% de) while others gave either poor yields or lower diastereoselectivity.

With the optimized conditions in hand, we examined the substrate scope of various imines under the conditions above. As revealed in Table 2, excellent diastereoselectivities were achieved for all cases that were studied. In general, the substituent on the aromatic rings of new 2-phenyl-2-propyl sulfinyl imines in regard to the nature and position does not have significant effects on asymmetric induction. For those imines tethered with reactive substituents, such as 4-nitro and $-CO_2Et$ (**8k** and **8l**, Table 1) failed to give clean desired products for this reaction. Importantly, the pure homoallylic amine products were obtained following the GAP chemistry purification without the use of traditional purification methods of column chromatography or recrystallization. The crude solid products were simply washed with minimum amounts of hexanes or heptanes to afford pure products and isomers. For homoallylic amino products formed in oils, washing combined organic phases containing the product with water in a separation funnel can also give >99% purity without the use

**Scheme 3**

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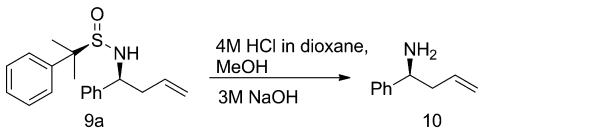
of column chromatography or recrystallization, which also belongs to the GAP chemistry as defined broadly.

The absolute stereochemistry of this reaction has been unambiguously determined by X-ray structural analysis of a sample of **9a**, which shows the sulfur center to be *R* and the resulting new chiral carbon center as *S* configuration (CCDC number 917467).

The deprotection of the sulfinyl group of **9a** was conducted by the treatment with hydrogen chloride in methanol solution to give the free homoallyl amine **10** after neutralization was performed by using sodium hydroxide (Scheme 4). The optical rotation of resulting free amino product was compared with that of an authentic sample,[18] which can further confirm the absolute stereochemistry of this reaction.

**Scheme 4**




$[\alpha]_D^{20}$ -48.4 (c=2, $CHCl_3$)
*S*-isomer literature $[\alpha]_D^{26}$ -44.2 (c=2, $CHCl_3$)

The resulting stereochemistry can be explained with a chair-like transition state shown in the Figure 1,[19] in which

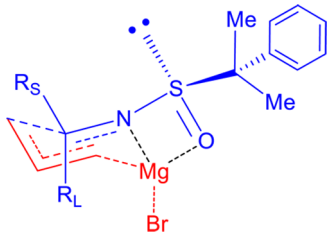



**Figure 1.** Transition state for allylmagnesium bromide addition.

magnesium metal coordinates with both nitrogen and oxygen atoms to anchor the attack of the nucleophile from the *Si* face of the imine electrophile, leading to the *S* stereochemical induction.

## CONCLUSIONS

In summary, the design and synthesis of new chiral *N*-($R_s$)-2-phenyl-2-propylsulfinyl amide and their derived imines have been successfully conducted, and the first application of chiral *N*-($R_s$)-2-phenyl-2-propylsulfinyl imines to the asymmetric addition reactions was performed by using allylamagnesium Grignard reagent to give good yields and excellent diastereoselectivities. The new auxiliary enables the purification of resulting homoallylic amine products to be performed via the economical and environmentally friendly GAP operation in which washing the crude product with minimum amounts of common solvents can lead to pure products. Further extension of the GAP chemistry to asymmetric synthesis using other sulfinyl imines is currently being explored in our laboratories.[21]

## EXPERIMENTAL SECTION

**General.** All chemicals and solvents were used as received without further purification unless otherwise stated. The NMR spectra were recorded on a 400 MHz spectrometer; chemical shifts ($\delta$) are expressed in parts per million; *J* values are given in hertz, and deuterated $CDCl_3$ was used as solvent. The reactions were monitored by thin layer chromatography (TLC) using silica gel. The melting points were uncorrected. High-resolution mass spectra for all new compounds were collected on a Q-TOF.

**Synthesis of Disulfide 2.**[20] To a stirred solution of thiol **1** (78.8 mmol) in 240 mL of ethyl acetate was added NaI (236 mg, 1.57 mmol), and to this reaction mixture was added slowly 30% aqueous $H_2O_2$ (8.9 mL, 78.8 mmol) at room temperature. Reaction mixture was stirred at room temperature for 18 h. At this stage, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with ethyl acetate. The resulting organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure. The crude mixture was purified by column chromatography with pure hexanes as eluent to give 9.29 g (78%) of disulfide **2**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.75 (s, 12 H), 7.42−7.44 (m, 2H), 7.49 −7.54 (m, 4H), 7.67−7.69 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 29.5, 52.2, 127.1, 127.4, 128.4, 128.5, 145.9; HRMS (TOF ES+) *m*/*z* calcd for $C_{18}H22S_2$ [$M^+$] 302.11630, found 302.11695.

**Synthesis of Thiosulfinate 4.**[9] A 100 mL Schlenk flask was loaded with ligand **3** (62.8 mg, 0.1719 mmol) and vanadylacetylacetanoate (44 mg, 0.165 mmol). Acetone (20 mL) was added and the resulting dark-green solution stirred at room temperature for 30 min while open to the air. To this solution was added disulfide **2** (10 g, 33.05 mmol). The resulting mixture was cooled to 0 °C, and 30% aqueous $H_2O_2$ was added slowly with a syringe pump over 20 h. The dark-brown solution was stirred for another 26 h at 0 °C. The reaction was quenched with saturated aqueous $Na_2S_2O_3$, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous $Na_2SO_4$. The organic layer was evaporated under reduced pressure to afford crude ($R_s$)-thiosulfinate **4** as white solid, which was washed with hexanes to provide 7.9 g (75%) of pure ($R_s$)-thiosulfinate **4** with 85% ee. The enantiomeric excess was further improved to 99% by washing with hexanes twice (10 mL of hexanes required for 1.0 g of thiosulfinate): HPLC Diacel Chiralpak AS-H column, 98:2 hexanes/$^i$PrOH; 1.0 mL/min, 230 nm, $t_R$ = 14.7 min; $t_S$ = 19.1 min; $[\alpha]_D^{25}$ +126.2 (*c* = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1. 63 (s, 3H), 1.77−1.82 (m, 9H), 7.24−7.41 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.8, 24.4, 31.0, 31.9, 53.3, 65.5, 126.6, 126.7, 127.4, 128.1, 128.3, 128.4, 139.8, 145.1; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{18}H_{23}OS_2$ [(M + H)$^+$] 319.1190, found 319.1187.

**Synthesis of TBDMS-Protected Sulfinamide 5.** TBDMS-$NH_2$ was prepared from TBDMS-Cl by known literature method.[13] Freshly synthesized 1 M solution of TBDMS-$NH_2$ (35.1 mL, 35.1 mmol) in THF was taken in a dry round-bottomed flask under argon. To this solution was added dropwise 1.6 M *n*-BuLi (22.0 mL, 35.16 mmol) at −78 °C, and the mixture was stirred at the same temperature. After 30 min, the predissolved solution of 94% ee thiosulfinate **4** (2.8 g, 8.79 mmol) in THF was added slowly at −78 °C. The reaction temperature increased to room temperature slowly and the mixture stirred until the starting material was consumed as monitored by TLC. At this stage, the reaction was quenched with 1 mL of aqueous $NH_4Cl$ solution and extracted with ethyl acetate. The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure to afford crude TBDMS-protected sulfinamide **5**. The crude product was purified by column chromatography to obtain 2.45 g (93%) of compound **5** as a white solid with 94% eeL HPLC, Diacel Chiralpak AS-H column, 93:7 hexanes/$^i$PrOH; 1.0 mL/min, 254 nm, $t_S$ = 4.8 min; $t_R$ = 7.2 min; $[\alpha]_D^{25}$ −31.8 (*c* = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 0.02 (d, *J* = 10.1 Hz, 6 H), 0.76 (s, 9 H), 1.52 (s, 3H), 1.65 (s, 3H), 2.48 (br, 1H), 7.28−7.34 (m, 1H), 7.35−7.40 (m, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = −4.7, −4.2, 17.5, 22.0, 22.4, 25.5, 62.8, 127.7, 127.8, 128.2, 136.7; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{15}H_{28}NOSSi$ [(M + H)$^+$] 298.1661, found 298.1669.

**Synthesis of Sulfinamide 6.** A dry round-bottomed flask was charged with TBDMS-protected sulfinamide **5** (1.32 g, 4.44 mmol) and THF (23 mL) under argon, and TBAF (5.33 mL, 5.33 mmol) was added at 0 °C. After 1 h, TLC indicated that all starting material was consumed. Then the reaction was quenched with 1 mL of water and extracted with ethyl acetate. The organic layer was dried over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anhydrous $Na_2SO_4$ and evaporated under reduced pressure to afford crude sulfinamide **6**. The crude product was purified by column chromatography with ethyl acetate as eluent to afford 0.8 g of pure sulfinamide **6** (98%) with 94% ee starting from 94% ee thiosulfinate **4**, and it was further improved to more than 99% ee by washing with hexane: HPLC, Diacel Chiralpak OD-H column, 93:7 hexanes/$^i$PrOH; 1.0 mL/min, 254 nm, $t_R$ = 21.0 min; $t_S$ = 24.9 min; $[\alpha]_D^{25}$ −100.2 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.52 (s, 3 H), 1.60 (s, 3 H), 3.69 (br, 2H) 7.24−7.27 (m, 1H), 7.31−7.39 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.7, 22.5, 61.0, 127.3, 127.5, 127.7, 136.5; HRMS (TOF ES$^+$) $m/z$ calcd for $C_9H_{14}NOS$ [(M + H)$^+$] 184.0796, found 184.0790.

**General Procedure for the Synthesis of ($R_s$)-2-Phenylpropyl-2-sulfinyl Imines.**[14] To a stirred solution of sulfinamide **6** (150 mg, 0.818 mmol) in freshly distilled dichloromethane (20 mL) were added aldehyde (1.636 mmol) and $Ti(OEt)_4$ (1.22 mL, 5.81 mmol) under argon. The flask was fitted with a condenser and the reaction refluxed for 12−16 h. Then the reaction was quenched with water (5 mL), and the precipitate was filtered through a Celite pad. The filter cake was washed with dichloromethane, and the filtrate was extracted with the same. The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure to afford crude sulfinyl imine. The crude product was purified by column chromatography, and hexanes/ethyl acetate mixture (4:1) was used as an eluent to obtain the corresponding sulfinyl imines. In the case of glyoxymate, for the synthesis of its imine, 4 Å molecular sieves was used instead of $Ti(OEt)_4$.

*Compound* ***8a:*** White crystalline solid; mp 119−121 °C; $[\alpha]_D^{25}$ +17.7 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.69 (s, 3 H), 1.75 (s, 3 H), 7.22−7.31 (m, 3H), 7.37−7.46 (m, 5H), 7.65−7.68 (m, 2H), 8.29 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.1, 21.8, 64.4, 127.3, 127.5, 127.8, 128.7, 129.1, 132.2, 133.8, 138.1, 162.6; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{16}H_{18}NOS$ [(M + H)$^+$], 272.1109; found, 272.1101.

*Compound* ***8b.*** Pale yellow solid; mp 98−103 °C; $[\alpha]_D^{25}$ +34.5 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.68 (s, 3 H), 1.82 (s, 3 H), 7.22−7.35(m, 3H), 7.45−7.53 (m, 5H), 7.82−7.86 (m, 2H), 7.96 (d, $J$ = 8.2 Hz, 1H), 8.70−8.73 (m, 1H), 8.82 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 19.9, 22.6, 64.4, 124.7, 125.0, 126.3, 127.3, 127.6, 127.8, 128.0, 128.6, 129.1, 130.9, 132.5, 133.3, 133.7, 138.6, 162.8; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{20}H_{20}NOS$ [(M + H)$^+$] 322.1266, found 322.1256.

*Compound* ***8c:*** Sticky liquid; $[\alpha]_D^{25}$ −53.9 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.68 (s, 3 H), 1.74 (s, 3 H), 2.37 (s, 3 H), 7.15−7.17 (m, 2H), 7.21−7.24 (m, 2H), 7.27−7.33 (m, 3H), 7.37−7.40 (m, 2H), 7.71−7.73 (m, 1H), 8.49 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 19.6, 21.2, 21.9, 64.3, 126.1, 127.4, 127.5, 127.8, 129.2, 131.1, 131.9, 161.6; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{17}H_{20}NOS$ [(M + H)$^+$] 286.1266, found 286.1255.

*Compound* ***8d:*** White solid; mp 93−95 °C; $[\alpha]_D^{25}$ + 58.3 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.73 (s, 3 H), 1.79 (s, 3 H), 2.43 (s, 3 H), 7.25−7.29 (m, 3H), 7.33−7.37 (m, 2H), 7.43−7.46 (m, 2H), 7.61−7.63 (m, 2H), 8.26 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.1, 21.6, 21.8, 64.3, 127.4, 127.5, 127.8, 129.2, 129.4, 131.4, 138.2, 143.0, 162.4; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{17}H_{20}NOS$ [(M + H)$^+$] 286.1266, found 286.1261.

*Compound* ***8e:*** White crystalline solid; mp 63−65 °C; $[\alpha]_D^{25}$ +20.1 ($c$ = 2.7, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.68 (s, 3 H), 1.74 (s, 3 H), 7.05−7.11 (m, 2H), 7.21−7.30 (m, 3H), 7.36−7.38 (m, 2H), 7.64−7.67 (m, 2H), 8.10 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.2, 21.9, 64.5, 115.9, 116.1, 127.3, 127.6, 127.8, 130 (d, $J$ = 2.8 MHz), 131.3 (d, $J$ = 8.5 MHz), 138.0, 161.2, 163.8, 166.3; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{16}H_{17}NOFS$ [(M + H)$^+$] 290.1015, found 290.1014.

*Compound* ***8f:*** Light yellow solid; mp 119−120 °C; $[\alpha]_D^{25}$ +105.8 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.70 (s, 6 H), 6.49−6.50 (m, 1 H), 6.83−6.84 (m, 1 H), 7.22−7.30 (m, 3H), 7.36−7.38 (m, 2H), 7.57−7.58 (m, 1H), 7.99 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.2, 21.9,64.7, 112.3, 118.6, 127.5, 127.6, 127.8, 137.7, 146.7, 149.6, 150.6; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{14}H_{16}NO_2S$ [(M + H)$^+$] 262.0902, found 262.0900.

*Compound* ***8g:*** Colorless liquid; $[\alpha]_D^{25}$ −230.5 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 0.88 (t, $J$ = 6.4 Hz, 6H), 1.73 (s, 3H), 1.74 (s, 3H), 1.81−1.91 (m, 1H), 2.16−2.21 (m, 2H), 7.31−7.33 (m, 1H), 7.35−7.41 (m, 4H), 7.72 (t, $J$ = 5.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.6, 21.8, 22.3, 22.5, 25.9, 44.6, 63.1, 127.3, 127.5, 127.8, 137.9, 169.5; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{14}H_{22}NOS$ [(M + H)$^+$] 252.1422, found 252.1419.

*Compound* ***8h:*** White solid; mp 38−40 °C; $[\alpha]_D^{25}$ −197.0 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.04−1.27 (m, 6H), 1.62−1.72 (m, 10H), 2.17−2.21 (m, 1H), 7.27−7.31 (m, 1H), 7.32−7.39 (m, 4H), 7.57 (d, $J$ = 4.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.5, 22.1, 25.2, 25.7, 28.7, 28.8, 43.8, 63.1, 127.4, 127.5, 127.7, 137.8, 172.6; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{16}H_{24}NOS$ [(M + H)$^+$] 278.1579, found 278.1570.

*Compound* ***8i:*** Light yellow solid; mp 98−100 °C; $[\alpha]_D^{25}$ −219.7 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.73 (s, 3 H), 1.78 (s, 3 H), 6.96−7.03 (m, 1 H), 7.09−7.13 (m, 1H), 7.31−7.37 (m, 1H), 7.40−7.54 (m, 9H), 8.11 (d, $J$ = 9.2 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 20.9, 21.8,64.2, 125.2, 127.2, 127.5, 127.7, 127.8, 128.7, 130.0, 134.7, 138.1, 146.2, 163.6; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{18}H_{20}NOS$ [(M + H)$^+$] 298.1266, found 298.1273.

*Compound* ***8j:*** Pale yellow liquid; $[\alpha]_D^{25}$ −223.6 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.76 (s, 3H), 1.78 (s, 3H), 2.16 (s, 3H), 7.21−7.37 (m, 5H), 7.41−7.43 (m, 3H), 7.69 (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 18.6, 19.4, 22.9, 64.5, 127.2, 127.6, 127.6, 128.1, 128.3, 131.5, 138.2, 139.2, 176.2; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{17}H_{20}NOS$ [(M + H)$^+$] 286.1266, found 286.1255.

*Compound* ***8k:*** Colorless liquid; $[\alpha]_D^{25}$ −127.0 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.29 (t, $J$ = 7.3 Hz, 3H), 1.72 (d, $J$ = 3.2 Hz, 6H), 4.25−4.28 (m, 2H), 7.25−7.32 (m, 5H), 7.51 (d, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 14.0, 21.4, 22.7, 62.2, 65.9, 127.4, 127.9, 128.1, 136.6, 155.1, 160.8; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{13}H_{18}NO_3S$ [(M + H)$^+$] 268.1007, found 268.1012.

*Compound* ***8l:*** Yellow solid; mp 131−133 °C; $[\alpha]_D^{25}$ +102.8 ($c$ = 1.85, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.72 (s, 3H), 1.79 (s, 3H), 7.19−7.29 (m, 3H), 7.34−7.36 (m, 2H), 7.79 (d, $J$ = 8.2 Hz, 2H), 8.24−8.26 (m, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.6, 22.0, 65.3, 124.0, 127.2, 127.8, 127.9, 129.7, 137.4, 138.6, 149.6, 160.3; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{16}H_{17}N_2O_3S$ [(M + H)$^+$] 317.0960, found 317.0969.

**General Procedure for the Addition of Allylmagnesium Bromide into ($R_s$)-2-Phenylpropyl-2-sulfinyl Imines.** A 25 mL flame-dried round-bottomed flask was charged under argon with *N*-sulfinyl imine (0.11 mmol) and freshly distilled toluene (10 mL). At room temperature, allylmagnesium bromide (0.22 mmol, 1.0 M solution in ether) was added slowly. Completion of the starting material was monitored by thin layer chromatography. At this stage, saturated ammonium chloride (1 mL) was added to the reaction mixture. Then, 3.0 mL of water was added to the reaction and extracted with 2 × 5 mL of ethyl acetate. The combined organic layers were washed with water (1 × 5 mL) and brine solution (1 × 5 mL) and dried over anhydrous $Na_2SO_4$. The solvent was evaporated, and the crude mixture was co-concentrated with hexanes. The products were dried under high vacuum. The solid products were washed with a minimum amount of hexanes or heptanes to afford pure product without column chromatography. The oil products obtained in this addition reaction were also more than 99% pure after washing with water, and co-concentration with hexanes was performed.

*Compound* ***9a:*** White solid; mp 109−110 °C; $[\alpha]_D^{25}$ −77.6 ($c$ = 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.56 (s, 3 H), 1.63 (s, 3 H), 2.14−2.22 (m, 1H), 2.33−2.38 (m, 1H), 3.05 (s, 1H), 4.24−4.27 (m, 1H), 4.76−4.84 (m, 2H), 5.36−5.41 (m, 1H), 7.13−7.15 (m, 2H), 7.23−7.29 (m, 3H), 7.35−7.42 (m, 3H), 7.45−7.47 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.4, 23.3, 43.3, 56.3, 61.7, 119.0, 127.3, 127.5, 127.7, 127.9, 128.2, 128.3, 133.3, 137.2, 141.5; HRMS (TOF ES$^+$) $m/z$ calcd for $C_{19}H_{24}NOS$ [(M + H)$^+$] 314.1579, found 314.1573.


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*Compound* ***9b:*** Pale yellow solid; mp 114−116 °C; $[\alpha]_D^{25}$ −99.7 (*c* = 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.58 (s, 3 H), 1.65 (s, 3 H), 2.34−2.41 (m, 1H), 2.56−2.60 (m, 1H), 3.24 (d, *J* = 2.3 Hz, 1H), 4.79−4.87 (m, 2H), 5.11−5.14 (m, 1H), 5.41−5.46 (m, 1H), 7.27−7.28 (m, 1H), 7.34−7.51 (m, 8H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.83−7.85 (m, 1H), 8.05−8.07 (m, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.5, 23.1, 42.1, 52.7, 61.8, 119.1, 122.9, 124.8, 125.1, 125.5, 126.0, 127.7, 127.9, 128.3, 128.9, 130.7, 133.3, 133.8, 137.0, 137.3; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{23}H_{26}NOS$ [(M + H)$^+$] 364.1735, found 364.1733.

*Compound* ***9c:*** White solid; mp 75−78 °C; $[\alpha]_D^{25}$ −76. 0 (*c* = 2.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.56 (s, 3 H), 1.64 (s, 3 H), 2.11−2.20 (m, 1H), 2.31−2.36 (m, 4H), 3.05 (s, 1H), 4.51−4.53 (m, 1H), 4.78−4.84 (m, 2H), 5.37−5.44 (m, 1H), 7.09−7.15 (m, 4H), 7.35−7.42 (m, 3H), 7.46−7.48 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 19.2, 22.2, 23.4, 42.0, 51.8, 61.6, 118.9, 125.9, 126.7, 127.1, 127.6, 127.8, 128.2, 130.3, 133.3, 135.6, 137.1, 139.3; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{20}H_{26}NOS$ [(M + H)$^+$] 328.1735, found 328.1734.

*Compound* ***9d:*** Colorless liquid; $[\alpha]_D^{25}$ −52.8 (*c* = 1.4, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.56 (s, 3 H), 1.63 (s, 3 H), 2.13−2.20 (m, 1H), 2.31−2.37 (m, 4H), 3.03 (s, 1H), 4.21−4.23 (m, 1H), 4.76−4.83 (m, 2H), 5.37−5.41 (m, 1H), 7.02−7.09 (m, 4H), 7.35−7.41 (m, 3H), 7.45−7.47 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.1, 22.3, 23.3, 43.3, 56.0, 61.6, 118.9, 127.2, 127.7, 127.8, 128.2, 129.0, 133.4, 137.1, 137.2, 138.4; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{20}H_{26}NOS$ [(M + H)$^+$] 328.1735, found 328.1745.

*Compound* ***9e:*** Crystalline solid; mp 76−81 °C; $[\alpha]_D^{25}$ −72.5 (*c* = 1.35, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.55 (s, 3 H), 1.63 (s, 3 H), 2.10−2.18 (m, 1H), 2.29−2.34 (m, 1H), 3.06 (s, 1H), 4.21−4.24 (m, 1H), 4.77−4.85 (m, 2H), 5.33−5.40 (m, 1H), 6.92−6.97 (m, 2H), 7.05−7.09 (m, 2H), 7.35−7.45 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.4, 22.9, 43.2, 55.6, 61.7, 115.1, 115.3, 119.2, 127.6, 127.9, 128.3, 128.8, 128.9, 133.1, 137.1, 137.2, 160.8, 163.3; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{19}H_{23}NOFS$ [(M + H)$^+$] 332.1484, found 332.1492.

*Compound* ***9f:*** Light yellow liquid; $[\alpha]_D^{25}$ −52.3 (*c* = 1.18, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.55 (s, 3 H), 1.65 (s, 3 H), 2.36−2.45 (m, 2H), 2.94 (d, *J* = 4 Hz, 1H), 4.34−4.38 (m, 1H), 4.78−4.86 (m, 2H), 5.36−5.43 (m, 1H), 6.06−6.07 (m, 1H), 6.26−6.27 (m, 1H), 7.31−7.46 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.0, 23.7, 39.6, 51.3, 61.8, 107.2, 109.9, 119.2, 127.6, 127.8, 128.2, 132.6, 136.9, 141.9, 153.9; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{17}H_{22}NO_2S$ [(M + H)$^+$] 304.1371, found 304.1371.

*Compound* ***9g:*** Colorless liquid; $[\alpha]_D^{25}$ −56.4 (*c* = 2.25, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 0.74−0.84 (m, 6H), 1.05−1.21 (m, 2H), 1.44−1.51 (m, 1H), 1.56 (s, 3H), 1.65 (s, 3H), 2.12−2.16 (m, 2H), 2.56 (d, *J* = 7.3 Hz, 1H), 3.19−3.22 (m, 1H), 4.75−4.86 (m, 2H), 5.45−5.52 (m, 1H), 7.28−7.37 (m, 3H), 7.41−7.43 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 21.9, 22.6, 22.9, 23.1, 24.3, 40.7, 44.2, 52.8, 61.9, 118.6, 127.5, 127.7, 128.1, 133.4, 137.5; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{17}H_{28}NOS$ [(M + H)$^+$] 294.1892, found 294.1890.

*Compound* ***9h:*** Colorless liquid; $[\alpha]_D^{25}$ −70.4 (*c* = 2.25, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 0.69−0.88 (m, 2H), 0.96−1.14 (m, 3H), 1.27−1.32 (m, 1H), 1.44−1.53 (m, 2H), 1.57−1.65 (m, 9H), 2.01−2.17 (m, 2H), 2.55 (d, *J* = 6.4 Hz, 1H), 2.93−2.98 (m, 1H), 4.69−4.83 (m, 2H), 5.43−5.51 (m, 1H), 7.27−7.32 (m, 1H), 7.34−7.38 (m, 2H), 7.42−7.44 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.8, 22.9, 26.1, 26.2, 26.4, 28.3, 28.8, 36.9, 40.9, 58.9, 62.0, 118.3, 127.5, 127.6, 128.1, 134.0, 137.6; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{19}H_{30}NOS$ [(M + H)$^+$] 320.2048, found 320.2058.

*Compound* ***9i:*** Pale yellow liquid; $[\alpha]_D^{25}$ −76.4 (*c* = 2.15, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.66 (s, 3 H), 1.72 (s, 3 H), 2.14−2.21 (m, 1H), 2.30−2.36 (m, 1H), 2.9 (s, 1H), 4.87−4.95 (m, 2H), 5.51−5.58 (m, 1H), 5.90−5.95 (m, 1H), 6.49−6.53 (m, 1H), 7.27−7.31 (m, 1H), 7.33−7.45 (m, 7H), 7.50−7.52 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.4, 23.4, 41.1, 55.1, 61.6, 118.9, 126.4, 127.6, 127.8, 128.2, 128.4, 129.6, 132.1, 133.0, 136.4, 137.2; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{21}H_{26}NOS$ [(M + H)$^+$] 340.1735, found 340.1729.

*Compound* ***9j:*** Light pink liquid; mp 116−119 °C; $[\alpha]_D^{25}$ −52.5 (*c* = 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ = 1.62 (d, *J* = 4.1 Hz, 6H), 1.67 (s, 3 H), 2.37−2.49 (m, 2H), 3.22 (br, 1H), 4.82−4.87 (m, 2H), 5.23−5.31 (m, 1H), 7.15−7.24 (m, 5H), 7.32−7.42 (m, 3H), 7.47−7.50 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ = 22.5, 23.1, 27.7, 49.0, 59.7, 62.4, 120.3, 126.1, 126.7, 127.6, 127.7, 128.1, 128.3, 132.4, 137.9, 145.4; HRMS (TOF ES$^+$) *m*/*z* calcd for $C_{20}H_{26}NOS$ [(M + H)$^+$] 328.1735, found 328.1741.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1H$ and $^{13}C$ NMR spectra of all pure products. 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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