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A Facile Asymmetric Synthesis of Either Enantiomer of 2-Substituted Pyrrolidines

Leleti Rajender Reddy,* Sonia G. Das,† Yugang Liu, and Mahavir Prashad

Chemical Research and Development, Novartis Pharmaceuticals Corporation, One Health Plaza, East Hanover, New Jersey 07936. †Current address: Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, 308 Harvard St. SE, Minneapolis, MN 55455.

rajender.leleti@novartis.com

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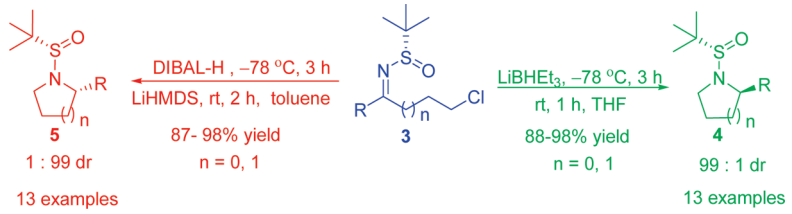

A new and general method for asymmetric synthesis of either enantiomer of 2-substituted pyrrolidines from a single starting material is described. Reductive cyclization of (S_S)-γ-chloro-*N*-*tert*-butanesulfinyl ketimines with $LiBHEt_3$ in THF at −78 to 23 °C afforded (S_S,*R*)-*N*-*tert*-butanesulfinyl-2-substituted pyrrolidines in excellent yields (88−98%) and with high diastereoselectivity (99:1). The diastereoselectivity is controlled effectively by the choice of reducing agent. Thus, the corresponding epimers of (S_S,*S*)-2-substituted pyrrolidines were synthesized in good yields (87−98%) and with high diastereoslectivity (1:99) by simply switching the reducing agent from $LiBHEt_3$ to DIBAL-H/LiHMDS. Deprotection of *N*-*tert*-butanesulfinyl-2-substituted pyrrolidines using 4 N HCl in dioxane and MeOH gave the corresponding enantiomers of 2-substituted pyrrolidines in quantative yield. This method was found to be effective for a variety of substrates including aromatic, heteroaromatic, and aliphatic substituents. Extension of this methodology to the formation of 2-substituted piperidines is also illustrated. Reductive cyclization of (S_S)-δ-chloro-*N*-*tert*-butanesulfinyl ketimine with $LiBHEt_3$ in THF at −78 to 23 °C or DIBAL-H/LiHMDS in toluene at −78 to 0 °C afforded the (S_S,*R*)-*N*-*tert*-butanesulfinyl-2-substituted piperidines in excellent yield (98%) and with high diastereoselectivity (99:1) or (S_S,*S*)-*N*-*tert*-butanesulfinyl-2-substituted piperidines in good yield (98%) and with high diastereoselectivity (1:99), respectively.

Introduction

Enantiomerically pure 2-substituted pyrrolidines are ubiquitous structural motifs found in a wide variety of natural products[1−3] and pharmaceutical drugs.[4−12] Over 4000 compounds containing this pharmacophore are currently in advanced stages of biological testing.[13] In addition, these compounds are effective chiral controllers and thus play an important role in asymmetric synthesis.[14] As a result, the

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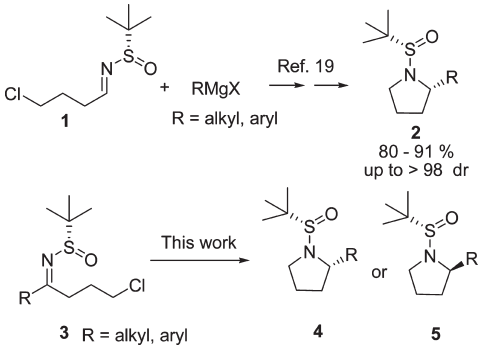
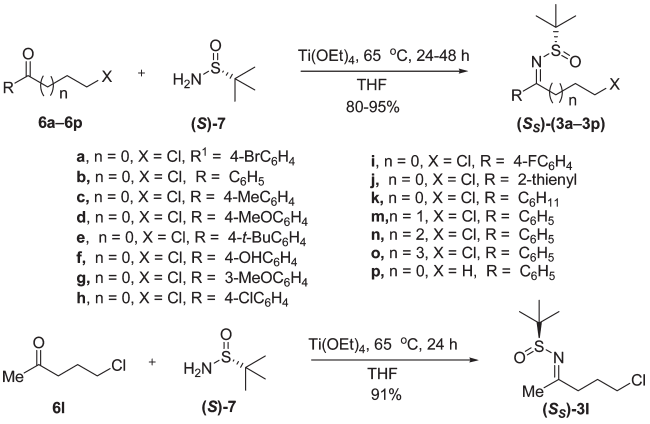
SCHEME 1



synthesis of these compounds has been an active area of research. Known synthetic methods of these privileged structures suffer from either long synthetic sequences, low yields, lack of generality, or modest selectivity.[15,16] The classical approach to obtain enantiomerically pure 2-substitued pyrrolidines is by resolution of the racemate via diastereoselective salt formation. However, the maximum theoretical yield for resolution is only 50%. Campos et al. have reported[17] an elegant method for asymmetric synthesis of 2-substituted pyrrolidines in a highly enantioselective manner. This method employs (−)-sparteine mediated enantioselective lithiation of *N*-Boc-pyrrolidine, followed by transmetalation and Pd-catalyzed Negishi coupling. This method is limited to the synthesis of (*R*)-aryl pyrrolidines due to the lack of inexpensive alternatives for (+)-sparteine.[21] In addition, it utilizes *s*-BuLi, which is a pyrophoric liquid and restricted from use on a large scale.[18] Recently, we reported[19] an asymmetric synthesis of 2-substituted pyrrolidines by addition of Grignard reagents to γ-chloro *N*-*tert*-butanesulfinyl aldimine followed by base-catalyzed cyclization. This method provides either enantiomer of 2-substituted pyrrolidines by changing the chiral starting material. Thus, development of an asymmetric synthesis to provide either enantiomer of 2-substituted pyrrolidines from the same starting material still remains an elusive challenge. We reasoned that a direct method to access either enantiomer of 2-substituted pyrrolidines would be via asymmetric reductive cyclization of γ-chloro-*N*-*tert*-butanesulfinyl ketimines **3**, and this asymmetric reductive cyclization of **3** to either diastereomers of 2-substituted pyrrolidines has not been described to our knowledge.[20] Herein, we report a versatile and practical method for diastereoselective reductive cyclization of (S_S)-γ-chlorinated *N*-*tert*-butanesulfinyl ketimines (**3**) to give either diastereomer of 2-substituted pyrrolidines (**4** or **5**) in a single step with high yields (Scheme 1). The *tert*-butanesulfinyl group not only induces excellent diastereoselectivity but also serves as an efficient low molecular weight protecting group for the nitrogen for future modifications of the 2-substituted pyrrolidines, if needed.

SCHEME 2. Synthesis of Chlorinated *N*-*tert*-Butanesulfinyl Ketimines (S_S)-3a−3p



Results and Discussion

Synthesis of γ-Chlorinated *N*-*tert*-Butanesulfinyl Ketimines (S_S)-3a−3p. Two methodologies were investigated for the synthesis of γ-chlorinated *N*-*tert*-butanesulfinyl ketimines (S_S)-**3a**−**3p** by condensation of appropriate ketones **6a**−**6p**[21] with (*S*)-*tert*-butanesulfinamide[22] **7** (Scheme 2). An initial attempt to synthesize **3a** under heterogeneous conditions[23] using pyridinium *p*-toluenesulfonate as a catalyst and magnesium sulfate as a water scavenger was unsuccessful. However, a subsequent trial using homogeneous conditions[24] that utilized $Ti(OEt)_4$ as both a Lewis acid and a water scavenger furnished **3a** in 90% yield. Since this approach was straightforward and provided **3a** with excellent yields, it was employed to prepare aryl sulfinyl ketimines **3a**−**3i**, heteroaryl sulfinyl ketimine **3j**, and aliphatic sulfinyl ketimines **3k** and **3p**. In the same way, the δ-chlorinated *N*-*tert*-butanesulfinyl ketimine (S_S)-**3m**, ε-chlorinated *N*-*tert*-butanesulfinyl ketimine (S_S)-**3n**, ζ-chlorinated *N*-*tert*-butanesulfinyl ketimine (S_S)-**3o**, and dechlorinated *N*-*tert*-butanesulfinyl ketimine (S_S)-**3p** were synthesized via condensation of (*S*)-*tert*-butanesulfinamide **7** with ketones 6m−**6p,** respectively. In all cases, the products were isolated in analytically pure form by extractive workup followed by flash chromatography. ^{1}H NMR analysis revealed that sulfinyl ketimines **3a**−**3p** existed solely as the (*E*)-isomer,

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(21) Ketones are commercially available from several companies.
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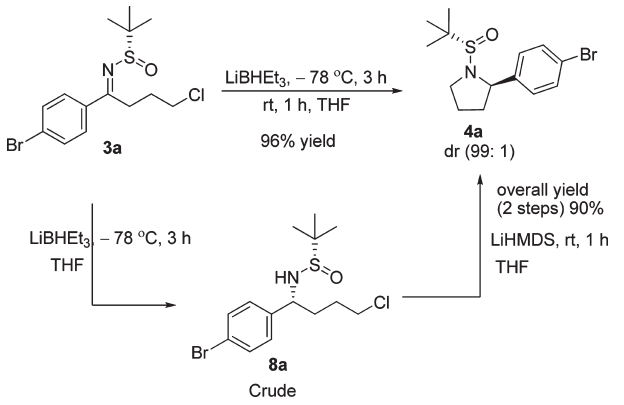
SCHEME 3. Asymmetric Reductive Cyclization of γ-Chlorinated *N-tert*-Butanesulfinyl Ketimine (S_S)-3a by using $LiBHEt_3$

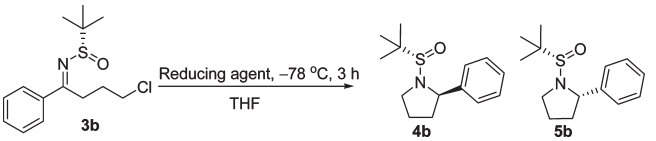


and the corresponding (*Z*)-sulfinyl ketimines were not observed.

Asymmetric Reductive Cyclization of γ-Chlorinated *N-tert*-Butanesulfinyl Ketimines (S_S)-3a−3p. With the sulfinyl ketimines in hand, the preparation of 2-substituted pyrrolidines via asymmetric reduction of the γ-chloro *N-tert*-butanesulfinyl ketimines was explored. Reduction of sulfinyl ketimine (S_S)-**3a** with 1.1 equiv of $LiBHEt_3$ in dry THF at −78 °C for 3 h followed by extractive workup afforded the crude γ-chloro sulfinamide (S_S,*R*)-**8a** in quantitative yield with little or no formation of the ring-closed product, i.e., pyrrolidine (S_S,*R*)-**4a** (Scheme 3). Gratifyingly, further stirring the crude γ-chloro sulfinamide **8a** with a strong base such as LiHMDS in THF at rt for 1 h afforded the desired pyrrolidine (S_S,*R*)-**4a** in 90% overall yield from **3a** with a high diastereomeric ratio of 99:1 (Scheme 3). The diastereoselectivity of the reaction was determined on the basis of ^1H NMR analysis of the crude product. The (*R*)-1-((*S*)-*tert*-butylsulfinyl)-2-(4-bromophenyl)pyrrolidine (**4a**) was obtained as a colorless crystalline solid (mp 120−122 °C). The structure and absolute configuration of (S_S,*R*)-**4a** was confirmed by single crystal X-ray diffraction analysis (see Supporting Information). Further optimization of this (**3a** to **4a**) two-step process to one step was achieved by warming the reaction mixture at −78 to 23 °C followed by stirring for 1 h, yielded pyrrolidine (S_S,*R*)-**4a** in a single step in 96% yield with a high diastereoselectivity of 99:1.

Thrilled with these results, a series of metal hydrides were screened to further elaborate this reduction and test the possibility of stereoselectivity reversal. A series of reducing agents, such as L-Selectride, $NaBH_4$, $LiBH_4$, 9-BBN, $NaBH_3CN$, $LiAlH_4$, and DIBAL-H, were studied in the reduction of γ-chloro *N-tert*-butanesulfinyl ketimines **3b** in THF for 3 h at −78 °C. Selectivity was monitored after cyclization of crude sulfinamide **8b** to the desired crude pyrrolidines **4b** and **5b** by using 1.5 equiv of LiHMDS. (Table 1). Reduction with L-Selectride provided a similar result as $LiBHEt_3$ (99:1 dr, Table 1, entry 1). We were gratified to find the reversal of diastereoselectivity with a ratio of 40:60 (**4b**/**5b**) when $NaBH_4$ was used as a reducing agent (Table 1, entry 2). Replacing $NaBH_4$ with $LiBH_4$ resulted in a slightly better outcome with a 35:65 dr (Table 1, entry 3). Reduction using a sterically hindered

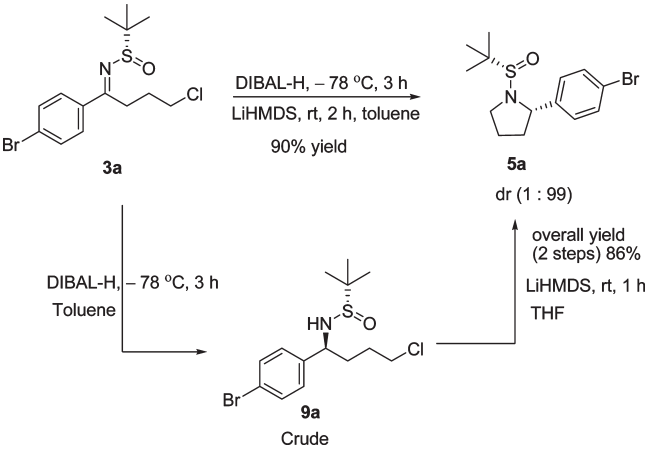
TABLE 1. Reductive Cyclization of Sulfinyl Ketimine (S_S)-3b Using Various Metal Hydrides



entry	reducing agent	solvent	conversion (%)	**4b**:**5b**[a,c]
1	L-Selectride	THF	100	99:1
2[b]	$NaBH_4$	THF	98	40:60
3	$LiBH_4$	THF	100	35:65
4	9-BBN	THF	100	38:62
5	$LiAlH_4$	THF	100	18:82
6	DIBAL-H	THF	100	4:96
7	DIBAL-H	toluene	100	1:99

[a]All reactions were performed using 1.5 equiv of reducing agent at −78 °C for 3 h, followed by isolation of crude product and cyclization using LiHMDS, rt, 1 h in dry THF, unless stated otherwise indicated. [b]10 equiv of MeOH was used. [c]The diastereoselectivity was determined by ^1H NMR analysis. The "99:1 or 1:99" denotes that signals for only one diastereomer were observed.

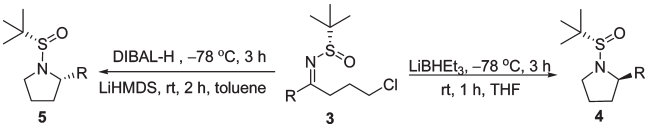
SCHEME 4. Asymmetric Reductive Cyclization of γ-Chlorinated *N-tert*-Butanesulfinyl Ketimine (S_S)-3a using DIBAL-H and LiHMDS



reducing agent like 9-borabicyclo[3.3.1]nonane (9-BBN) failed to show any improvement (38:62 dr, Table 1, entry 4). Interestingly, $LiAlH_4$ showed an improved diastereoselectivity of 18:82 dr, (Table 1, entry 6). To our delight, when DIBAL-H was used, a marked enhancement in diastereoselectivity was observed with a diastereomeric ratio of 4:96 (Table 1, entry 7). The diastereoselectivity was further improved to 1:99 when the reduction was conducted in toluene instead of THF (Table 1, entry 8).

Pleased with these results, we focused our efforts on developing a single-step method to yield **5b** with high diastereoselectivity. Unlike the $LiBHEt_3$ conditions, pyrrolidine **5b** was not observed during the reduction of sulfinyl ketimine **3a** with DIBAL-H at −78 °C for 3 h followed by warming to rt and stirring for 1−12 h. We reasoned that the low basicity of the corresponding aluminum complex may inhibit the cyclization. With this rationale the addition of LiHMDS to the reaction mixture followed by warming the reaction mixture from −78 to 23 °C led to complete cyclization. Thus, in one pot we were able to synthesize (S_S,*S*)-**5a** in a 90%

TABLE 2. Asymmetric Reductive Cyclization of γ-Chlorinated *N*-*tert*-Butanesulfinyl Ketimine (S_S)-3a−3l with $LiBHEt_3$ and DIBAL-H/LiHMDS



		$LiBHEt_3$		DIBAL-H	
entry	R	product	yield[a] (dr)[b]	product	yield[a] (dr)[b]
1	4-BrC_6H_4	**4a**	96 (99:1)	**5a**	90 (1:99)
2	C_6H_5	**4b**	94 (99:1)	**5b**	92 (1:99)
3	4-MeC_6H_4	**4c**	92 (99:1)	**5c**	93 (1:99)
4	4-$MeOC_6H_4$	**4d**	90 (99:1)	**5d**	87 (1:99)
5	4-*t*BuC_6H_4	**4e**	93 (99:1)	**5e**	91 (1:99)
6	4-HOC_6H_4	**4f**	98 (99:1)	**5f**	94 (1:99)
7	3-$MeOC_6H_4$	**4g**	92 (99:1)	**5g**	90 (1:99)
8	4-ClC_6H_4	**4h**	98 (99:1)	**5h**	93 (1:99)
9	4-FC_6H_4	**4i**	93 (99:1)	**5i**	98 (1:99)
10	2-thienyl	**4j**	93 (99:1)	**5j**	95 (1:99)
11	C_6H_{11}	**4k**	94 (99:1)	**5k**	95 (1:99)
12	Me	**4l**	88 (8:92)	**5l**	89 (91:9)

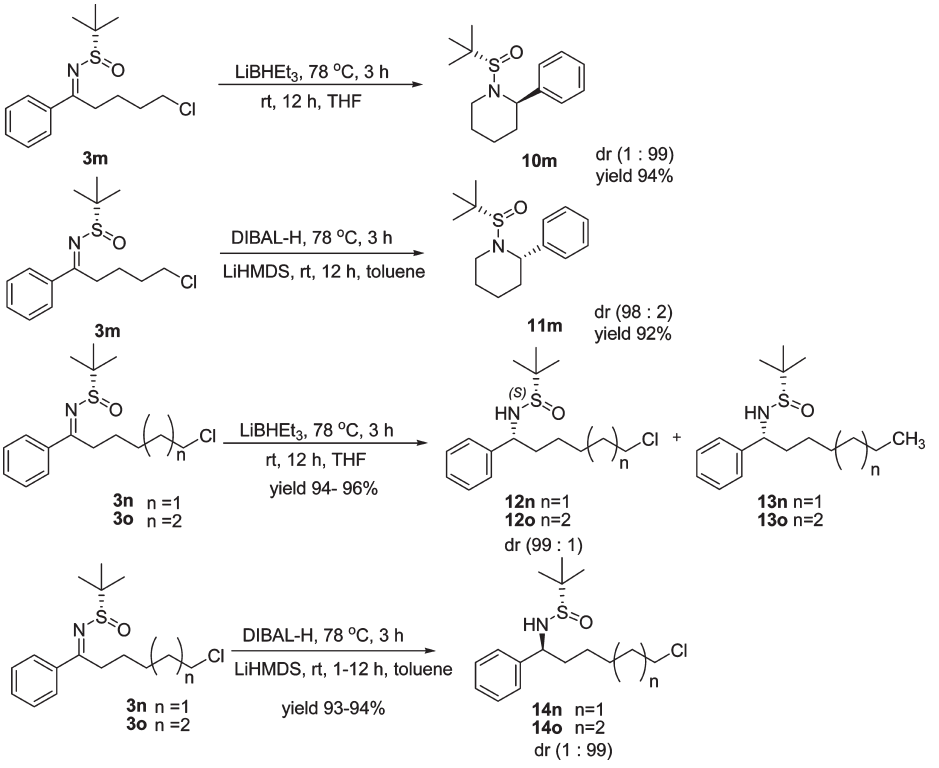
[a]Isolated yield of analytically pure products. [b]The diastereoselectivity was determined by ^1H NMR analysis. The "99:1 or 1:99" denotes that signals for only one diastereomer were observed; *dr* relative to sulfur.

yield with a high diastereomeric ratio of 1:99 (Scheme 4). The structure and absolute configuration of (S_S,*S*)-**5a** was confirmed by comparing the ^1H NMR, ^{13}C NMR, and specific rotation data with literature data.[19]

Scope of the Reaction. With optimized one-step processes to access either of the two diastereomers of 2-substituted pyrrolidines (S_S,*R*)-**4** and (S_S,*S*)-**5** starting from *N*-sulfinyl ketimines **3**, a variety of γ-chlorinated *N*-*tert*-butanesulfinyl ketimines (S_S)-**3** were used as substrates to probe the general applicability (Table 2). In the $LiBHEt_3$ mediated reductive cyclization of phenyl γ-chloro *N*-*tert*-butanesulfinyl ketimine **3b**, substitiuents such as OMe, Me, *t*-Bu, OH, Cl, Br, F, etc. in the *para* and *meta* positions of the phenyl ring (**3c**−**3i**) were well tolerated, and high diastereoselectivity (99:1 dr) and high yields were obtained in every instance. (Table 2, entries 3−6). Similarly, treatment **3c**−**3i** with DIBAL-H/LiHMDS afforded the corresponding 2-aryl substituted pyrrolidines (**5c**−**5i**) in 88−94% yields with high diastereoselectivity (99:1 dr). Furthermore, heteroaryl ketimine **3j**, when treated with $LiBHEt_3$ or DIBAL-H/LiHMDS, also underwent stereoselective reductive cyclization to afford **4j** or **5j** with diastereomeric ratio of 99:1 and 1:99 in 93% and 95% yields, respectively (Table 2, entry 10). In addition, these reactions were also found to be tolerant to aliphatic ketimines (Table 2, entries 11 and 12). Treatment of cyclohexyl sulfinyl ketimine **3k** with $LiBHEt_3$ or DIBAL-H/LiHMDS also afforded the corresponding pyrrolidines **4k** or **5k** in 94% and 95% yield with diastereomeric ratios of 99:1 and 1:99, respectively (Table 2, entry 10). However, when methyl ketimine **3l** was subjected to $LiBHEt_3$ conditions, the reverse stereoselective product, i.e., (*R*)-1-((*S*)-*tert*-butylsulfinyl)-2-methylpyrrolidine (S_S,*R*-**5l**) was obtained with slightly lower diastereoselectivities (8:92 dr) in 88% yield (Table 2, entry 12). In the same way, treatment of **3l** with DIBAL-H/LiHMDS afforded the reverse stereoselective product, i.e., (*S*)-1-((*S*)-*tert*-butylsulfinyl)-2-methyl-pyrrolidine (S_S,*S*-**4l**) with 89% yield and diastereomeric ratio of 91:9 (Table 2, entry 12). Thus, as summarized in Table 2, all reactions took place readily and afforded the corresponding pyrrolidines in good to excellent yields with high diastereoselectivities.

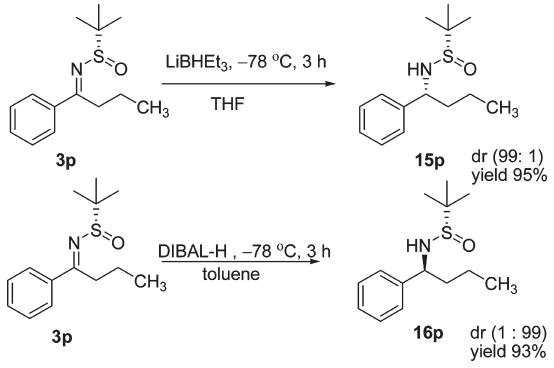
Asymmetric Synthesis of 2-Substituted Piperidines and Azepanes. Extension of this methodology to the asymmetric

SCHEME 5. Asymmetric Synthesis of 2-Subtituted Piperidines



synthesis of 2-substituted piperidines, azepanes, and azocines was investigated. Reduction of δ-chlorinated *N-tert*-butanesulfinyl ketimine (**3m**) with $LiBHEt_3$ at −78 °C for 3 h followed by increasing the reaction temperature to rt and stirring overnight led to the desired 2-phenyl piperidine **10m** with high diastereoselectivity (99:1) and 94% yield (Scheme 5). Likewise, treatment of **3m** with DIBAL-H/LiHMDS afforded reversal of diastereofacial selectivity, and 2-phenyl piperidine **11m** was obtained with dr of 1:99 in 92% yield (Scheme 5). Excited by these results, we moved on to the preparation of larger ring systems like azepanes (seven-membered) and azocines (eight-membered). Treatment of ε-chlorinated *N-tert*-butanesulfinyl ketimine (**3n**) with $LiBHEt_3$ at −78 °C for 3 h afforded the ε-chloro sulfinamide **12n** in quantitative yield and high diastereoselectivity (99:1 dr). However, ensuing efforts to cyclize **12n** by warming the reaction to rt and stirring for 2 days failed to afford the cyclized azepane ring. Prolonged stirring of **12n** with $LiBHEt_3$ at rt led to the dechlorinated side product **13n** (Scheme 5). Similarly, treatment of **3n** with DIBAL-H at −78 °C for 3 h also led to complete conversion of **3n** to **14n**, but subsequent treatment with LiHMDS at rt and stirring for 2 days did not result in the cyclized azepane (Scheme 5). A series of other bases (BuLi, NaH, LiHMDS, Et_3N, and KOH) were investigated in different solvents to promote cyclization of **12n** and **14n** to the seven-membered ring; however, no cyclization was occurred (see the Supporting Information). We reasoned that the increased strain coupled with high activation energy of the transition state may inhibit the cyclization. Similar results were obtained with ζ-chlorinated *N-tert*-butanesulfinyl ketimine(S_S)-**3o**.

SCHEME 6. Reduction of Dechlorinated *N-tert*-Butanesulfinyl Ketimine (S_S)-3p



Mechanistic Rationale/Reasoning. Intrigued by the reversal of diastereofacial selectivity upon changing reducing agents from $LiBHEt_3$ to DIBAL-H, we pursued the reason for this diastereoselective switch. To exclude the role of the chloro group in the diastereoselectivity of the reducing agents, we synthesized the dechlorinated ketimine **3p** (Scheme 6). Reduction of **3p** with DIBAL-H and $LiBHEt_3$ using the conditions mentioned earlier resulted in the formation of **15p** and **16p**, respectively, with high diastereoselectivity (Scheme 6), demonstrating that the chloro group does not play a role. We propose that the DIBAL-H reaction proceeds through a closed transition state where the aluminum metal coordinates with the sulfinyl oxygen directing the hydride attack from the *si* face of the imine bond to give the (S_S,*S*) diastereomer (Figure 1, TS 1). Alternatively,

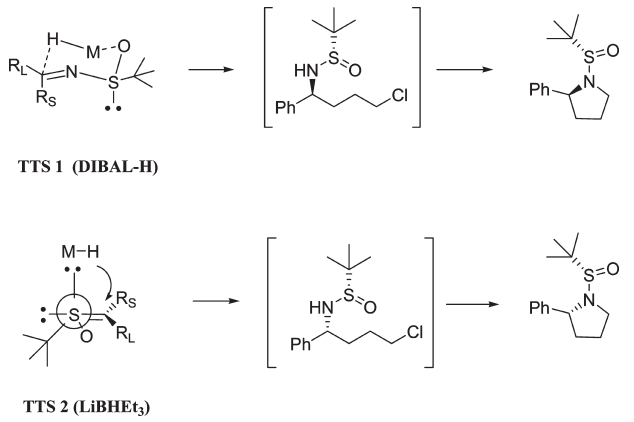
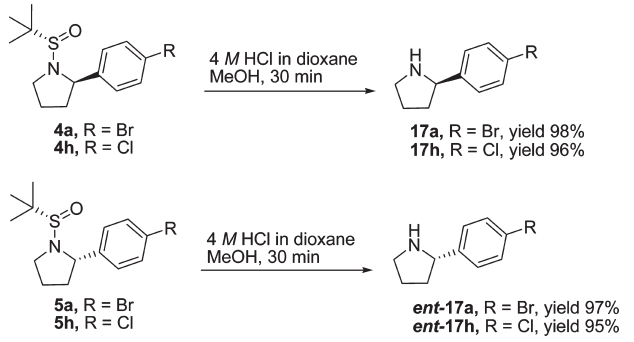


FIGURE 1. Proposed transition states for the reduction of sulfinyl ketimines (S_S)-**3**.

poorly coordinating and rapidly reacting $LiBHEt_3$ was posed to attack the electrophilic carbon atom in a sterically controlled fashion via an open transition state. Hence, delivery of the hydride would occur from the same face as the sulfur lone pair to give the (S_S,*R*) diastereomer (Figure 1, TS 2).

SCHEME 7. Selective Deprotection of Sulfinyl Group

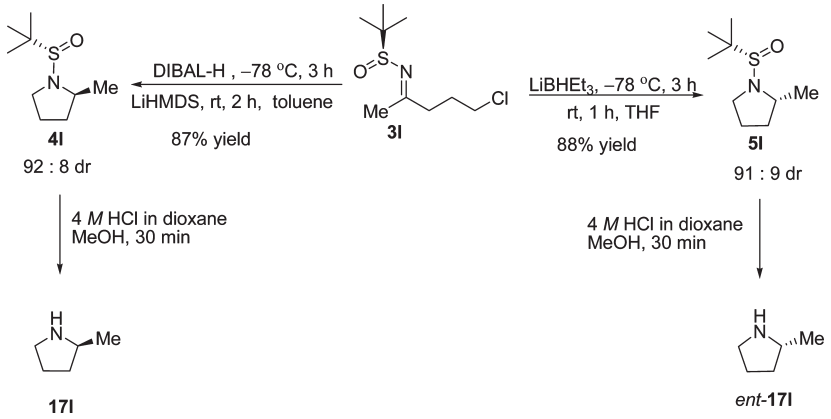


Deprotection To Generate Single Enantiomers of 2-Substituted Pyrrolidines. Finally, dissolving **4a** in methanol followed by treatment with 4 M HCl for 30 min led to cleavage of the sulfinyl group resulting in the formation of the (*R*)-2-(4-bromophenyl) pyrrolidine (**17a**) as a single enantiomer in 98% yield (Scheme 7). The other diastereomer **5a** also underwent smooth deprotection to afford (*S*)-2-(4-bromophenyl)pyrrolidine (*ent*-**17a**) in 97% yield. The chloro substituted pyrrolidine **4h** and **5h** were also tested under these conditions and were found to give similar results. In the same way, treatment of **4l** or **5l** with 4 M HCl (dioxane) in methanol for 30 min afforded the (*S*)-2-(4-bromophenyl)-pyrrolidine (**17l**) or (*R*)-2-(4-bromophenyl)pyrrolidine (*ent*-**17l**) in 95% and 92% yields, respectively. The absolute configuration of (*S*)-**17l** and (*R*)-*ent*-**17l** was confirmed by comparing the specific rotation data with literature data.[25]

Thus, the sulfinyl group can be cleaved readily under mild acidic conditions to provide the respective amines in excellent yields.

(25) (a) Kim, M.-J.; Lim, G-B; Whang, S-Y; Ku, B.-C.; Choi, J.-Y. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 71. (b) Kostyanovsky, R. G.; Gella, I. M.; Markov, V. I; Samojlova, Z. E. *Tetrahedron* **1974**, *30*, 39.

SCHEME 8. Asymmetric Reductive Cyclization of Methyl Ketimine 3l and Selective Deprotection of Sulfinyl Group



Conclusion. In conclusion, we have developed a highly efficient, versatile one-step process for asymmetric synthesis of either stereoisomer of 2-substituted pyrrolidines from the same starting material with excellent yields and high diastereoselectivity. This method was also applied for the asymmetric synthesis of both diastereomers of 2-substituted piperidines with good yields and excellent diastereoselectivity. This method was found to be effective for a variety of substrates incorporating various aromatic and aliphatic substituents. Extension of this work is currently underway in our laboratory.

Experimental Section

General Procedure (GP1) for the Synthesis of γ-Chloro *N*-Sulfinyl Ketimine 3. A 500 mL, three-necked, round-bottomed flask was charged with 1-(4-bromophenyl)-4-chlorobutan-1-one **6a** (40.0 mmol), THF (100 mL), *tert*-butanesulfinamide **7** (60.0 mmol), and $Ti(OEt)_4$ (80.0 mmol) under nitrogen atm. The reaction mixture was then heated at reflux at 65 °C for 48 h. After completion, the reaction was allowed to cool to rt. Isopropyl acetate (100 mL) and saturated NaCl solution (100 mL) were then added to this mixture and stirred for 1 h. The solids were removed by filtration, and the filtrate was washed with water (2 × 50 mL). The organic phase was evaporated under vacuum to dryness to obtain the crude product. The crude product was purified by flash column chromatography (silica gel, 10% ethyl acetate in heptanes) to afford the pure γ-chloro *N*-sulfinyl ketimine **3a**.

(*S,E*)-*N*-(4-Chloro-1-(4-bromophenyl)butylidene)-2-methylpropane-2-sulfinamide (3a). Following the general procedure (GP1), the reaction of 4-chloro-1-(4-bromophenyl)-butan-1-one (**6b**) (25.5 g, 100.0 mmol) with (S_S)-*tert*-butanesulfinamide (13.3 g, 110.0 mmol) and $Ti(OEt)_4$ (34.5 g, 150.0 mmol) gave 30.6 g (84%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3a** as white solid, mp = 48−50 °C, $[\alpha]^{25}_D$ = −24.2 (*c* 1.10, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.66−7.86 (m, 2 H), 7.56 (d, *J* = 8.51 Hz, 2 H), 3.57−3.70 (m, 2 H), 3.19−3.51 (m, 2 H), 2.01−2.28 (m, 2 H), 1.24−1.42 (m, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 176.8, 136.3, 131.9, 128.9, 126.5, 58.0, 44.5, 31.5, 29.8, 22.7. HRMS (EI) calcd for $C_{14}H_{20}NOSBrCl$ [M + H] 364.0120, found 364.0138.

(*S,E*)-*N*-(4-chloro-1-phenyl)butylidene)--2-methylpropane-2-sulfinamide (3b). Following the general procedure (GP1), the reaction of 4-chloro-1-phenyl-butan-1-one (**6b**) (18.2 g, 100.0 mmol) with (S_S)-*tert*-butanesulfinamide (13.3 g, 110.0 mmol) and $Ti(OEt)_4$ (34.5 g, 150.0 mmol) gave 25.9 g (91%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3b** as white solid, mp = 35−36 °C, $[\alpha]^{25}_D$ = −20.9 (*c* 1.10, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.79−7.96 (m, 2 H), 7.33−7.56 (m, 3 H), 3.57−3.72 (m, 2 H), 3.23−3.54 (m, 2 H), 2.07−2.28 (m, 2 H), 1.36 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 178.0, 137.5, 131.7, 128.7, 127.4, 57.9, 44.6, 31.6, 30.0, 22.7. HRMS (EI) calcd for $C_{14}H_{21}NOSl$ [M + H] 286.1024, found 286.1032.

(*S,E*)-*N*-(4-Chloro-1-*p*-tolylbutylidene)-2-methylpropane-2-sulfinamide (3c). Following the general procedure (GP1), the reaction of 4-chloro-1-*p*-tolyl-butan-1-one (**6c**) (25 g, 127.0 mmol) with (S_S)-*tert*-butanesulfinamide (23.1 g, 190.6 mmol) and $Ti(OEt)_4$ (57.9 g, 254.2 mmol) gave 34.3 g (90%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3c** as viscous oil, $[\alpha]^{25}_D$ = −17.5 (*c* 1.03, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.74−7.83 (m, 2 H), 7.24 (d, *J* = 8.20 Hz, 2 H), 3.59−3.67 (m, 2 H), 3.22−3.49 (m, 2 H), 2.40 (s, 3 H), 2.08−2.25 (m, 2 H), 1.34 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 178.0, 142.4, 134.8, 129.4, 127.5, 57.7, 53.4, 44.7, 31.7, 30.0, 22.7, 21.4. HRMS (EI) calcd for $C_{15}H_{23}NOSCl$ [M + H] 300.1189, found 300.1176.

(*S,E*)-*N*-(4-Chloro-1-(4-methoxyphenyl)butylidene)-2-methylpropane-2-sulfinamide (3d). Following the general procedure (GP1), the reaction of 4-chloro-1-(4-methoxyphenyl)butan-1-one (**6d**) (25 g, 117.5 mmol) with (S_S)-*tert*-butanesulfinamide (21.37 g, 176.32 mmol) and $Ti(OEt)_4$ (57.9 g, 235.1 mmol) gave 31.56 g (85%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3d** as viscous oil, $[\alpha]^{25}_D$ = −28.3 (*c* 1.15, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.83−7.91 (m, 2 H), 6.88−6.97 (m, 2 H), 3.86 (s, 3 H), 3.59−3.68 (m, 2 H), 3.19−3.47 (m, 2 H), 2.07−2.27 (m, 2 H), 1.32 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 178.0, 162.6, 130.0, 129.4, 114.4, 57.5, 55.4, 53.4, 44.8, 31.7, 29.9, 22.6. HRMS (EI) calcd for $C_{15}H_{23}NO_2SCl$ [M + H] 316.1138, found 316.1125.

(*S,E*)-*N*-(1-(4-*tert*-Butylphenyl)-4-chlorobutylidene)-2-methylpropane-2-sulfinamide (3e). Following the general procedure (GP1), the reaction of 1-(4-tert-butylphenyl)-4-chlorobutan-1-one (**6e**) (10 g, 41.885 mmol) with (S_S)-*tert*-butanesulfinamide (7.614 g, 62.83 mmol) and $Ti(OEt)_4$ (19.112 g, 83.77 mmol) gave 13.6 g (90%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3e** as viscous oil, $[\alpha]^{25}_D$ = −18.9 (*c* 1.0, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.76−7.90 (m, 2 H), 7.45 (d, *J* = 7.57 Hz, 2 H), 3.59−3.69 (m, 2 H), 3.21−3.51 (m, 2 H), 2.08−2.27 (m, 2 H), 1.34 (s, 18 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 177.8, 155.3, 134.7, 127.3, 125.6, 57.7, 53.4, 44.7, 34.9, 31.7, 31.1, 28.1, 22.7. HRMS (EI) calcd for $C_{18}H_{29}NOSCl$ [M + H] 342.1653, found 342.1657.

(*S,E*)-*N*-(4-Chloro-1-(4-hydroxyphenyl)butylidene)-2-methylpropane-2-sulfinamide (3f). Following the general procedure (GP1), the reaction of 5-chloro-1-(4-hydroxy-phenyl)butan-1-one (**6f**) (10 g, 50.34 mmol) with (S_S)-*tert*-butanesulfinamide (9.15 g, 75.51 mmol) and $Ti(OEt)_4$ (22.969 g, 100.68 mmol) gave 9.87 g (65%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3f** as a solid, mp = 88−90 °C, $[\alpha]^{25}_D$ = −52.0 (*c* 1.04, MeOH). ^{1}H

NMR (400 MHz, DMSO-d_6) δ ppm 10.26 (s, 1 H), 7.81 (d, J = 7.58 Hz, 2 H), 6.86 (d, J = 8.84 Hz, 2 H), 3.71 (t, J = 6.57 Hz, 2 H), 3.10−3.33 (m, 2 H), 1.88−2.12 (m, 2 H), 1.21 (s, 9 H). ^{13}C NMR (125 MHz, DMSO-d_6)) δ ppm 178.9, 161.2, 129.6, 127.7, 115.4, 56.3, 44.7, 31.5, 29.4 22.0. HRMS (EI) calcd for $C_{14}H_{21}NO_2SCl$ [M + H] 302.0982, found 302.1011.

(*S,E*)-*N*-(4-Chloro-1-(3-methoxyphenyl)butylidene)-2-methylpropane-2-sulfinamide (3g). Following the general procedure (GP1), the reaction of 5-chloro-1-(3-methoxyphenyl)butan-1-one (**6g**) (5 g, 23.51 mmol) with (S_S)-*tert*-butanesulfinamide (4.27 g, 35.26 mmol) and Ti(OEt)$_4$ (10.72 g, 47.02 mmol) gave 6.08 g (82%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3g** as a viscous liquid, $[\alpha]^{25}_D$ = −10.4 (*c* 1.42, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.40−7.49 (m, 2 H), 7.34 (t, J = 7.88 Hz, 1 H), 7.03 (d, J = 7.25 Hz, 1 H), 3.83 (s, 3 H), 3.60−3.66 (m, 2 H), 3.23−3.48 (m, 2 H), 2.08−2.25 (m, 2 H), 1.33 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 177.7, 159.7, 138.9, 129.6, 119.8, 117.5, 112.6, 57.9, 55.3, 44.6, 31.7, 30.0, 22.7. HRMS (EI) calcd for $C_{15}H_{23}NO_2SCl$ [M + H] 316.1133, found 316.1134.

(*S,E*)-*N*-(4-Chloro-1-(4-chlorophenyl)butylidene)-2-methylpropane-2-sulfinamide (3h). Following the general procedure (GP1), the reaction of 4-chloro-1-(4-chlorophenyl)butan-1-one (**6h**) (10 g, 46.06 mmol) with (S_S)-*tert*-butanesulfinamide (8.374 g, 69.95 mmol) and Ti(OEt)$_4$ (21.018 g, 92.12 mmol) gave 13.7 g (93%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3h** as a white color solid, mp = 40−42 °C, $[\alpha]^{25}_D$ = −26.9 (*c* 1.12, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.75−7.88 (m, 2 H), 7.41 (d, J = 8.51 Hz, 2 H), 3.59−3.69 (m, 2 H), 3.23−3.49 (m, 2 H), 2.04−2.25 (m, 2 H), 1.32 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 176.8, 138.0, 135.9, 129.0, 128.7, 58.0, 44.6, 31.6, 29.8, 22.7. HRMS (EI) calcd for $C_{14}H_{20}NOSCl_2$ [M + H] 320.06378, found 320.0638.

(*S,E*)-*N*-(4-Chloro-1-(4-fluorophenyl)butylidene)-2-methylpropane-2-sulfinamide (3i). Following the general procedure (GP1), the reaction of 4-chloro-1-(4-fluorophenyl)butan-1-one (**6i**) (10 g, 49.84 mmol) with (S_S)-*tert*-butanesulfinamide (9.06 g, 74.76 mmol) and Ti(OEt)$_4$ (22.74 g, 99.68 mmol) gave 14.2 g (94%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3i** as a white color solid, mp = 38−40 °C, $[\alpha]^{25}_D$ = −40.7 (*c* 1.05, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.85−7.96 (m, 2 H), 7.12 (t, J = 8.51 Hz, 2 H), 3.60−3.70 (m, 2 H), 3.23−3.49 (m, 2 H), 2.08−2.26 (m, 2 H), 1.35 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 176.8, 165.9, 163.9, 133.7, 129.8, 129.7, 115.8, 115.7, 115.4, 57.8, 44.6, 31.6, 29.9, 22.7. HRMS (EI) calcd for $C_{14}H_{20}NOSClF$ [M + H] 304.0938, found 304.0926.

(*S,E*)-*N*-(4-Chloro-1-(thiophen-2-yl)butylidene)-2-methylpropane-2-sulfinamide (3j). Following the general procedure (GP1), the reaction of 4-chloro-1-(thiophen-2-yl)butan-1-one (**6j**) (5 g, 26.5 mmol) with (S_S)-*tert*-butanesulfinamide (4.817 g, 39.75 mmol) and Ti(OEt)$_4$ (12.09 g, 53.0 mmol) gave 7.5 g (97%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3j** as a viscous liquid, $[\alpha]^{25}_D$ = −90.0 (*c* 1.06, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.58 (d, J = 3.15 Hz, 1 H), 7.50 (d, J = 5.04 Hz, 1 H), 7.07−7.12 (m, 1 H), 3.60−3.70 (m, 2 H), 3.33−3.42 (m, 1 H), 3.23 (dd, J = 10.72, 5.67 Hz, 1 H), 2.15−2.35 (m, 2 H), 1.30 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 172.3, 144.9, 132.3, 129.6, 128.0, 58.0, 44.6, 32.1, 30.6, 22.5. HRMS (EI) calcd for $C_{12}H_{19}NOS_2Cl$ [M + H] 292.0597, found 292.0573.

(*S,E*)-*N*-(4-Chloro-1-cyclohexyl-butylidene)-2-methylpropane-2-sulfinamide (3k). Following the general procedure (GP1), the reaction of 4-chloro-1-cyclohexyl-butan-1-one (**6k**) (9.1 g, 50.0 mmol) with (S_S)-*tert*-butanesulfinamide (9.06 g, 74.76 mmol) and Ti(OEt)$_4$ (22.74 g, 99.68 mmol) gave 13.2 g (90%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3k** as a viscus oil, $[\alpha]^{25}_D$ = −32.8 (*c* 1.02, MeOH). ^{1}H NMR (501 MHz, DMSO-d_6) δ ppm 3.63−3.76 (m, 2 H), 2.62−2.74 (m, 2 H), 2.20−2.33 (m, 1 H), 2.00−2.11 (m, 2 H), 1.76−1.87 (m, 2 H), 1.53−1.69 (m, 3 H), 1.16−1.36 (m, 5 H), 1.12 (s, 9 H). ^{13}C NMR (125 MHz, DMSO-d_6) δ ppm 168.7, 55.9, 48.7, 44.5, 32.7, 27.68, 25.4, 24.4, 21.7. HRMS (EI) calcd for $C_{14}H_{27}NOSCl$ [M + H] 292.8883, found 292.8885.

(*S,E*)-*N*-(4-Chloro-1-methyl)-2-methylpropane-2-sulfinamide (3l). Following the general procedure (GP1), the reaction of 4-chloro-1-methyl-butan-1-one (**6l**) (12.0 g, 100.0 mmol) with (S_S)-*tert*-butanesulfinamide (13.3 g, 110.0 mmol) and Ti(OEt)$_4$ (34.5 g, 150.0 mmol) gave 18.8 g (85%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3l** as a viscous liquid, $[\alpha]^{25}_D$ = −21.1 (*c* 1.60, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 3.60 (t, J = 6.31 Hz, 2 H), 2.60 (t, J = 7.09 Hz, 2 H), 2.35 (s, 3 H), 2.00−2.16 (m, 2 H), 1.24 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 183.8, 56.3, 44.2, 39.9, 27.9, 23.3, 22.1. HRMS (EI) calcd for $C_9H_{19}ClNOS$ [M + H] 224.0876, found 224.0861.

(*S,E*)-*N*-(5-Chloro-1-phenylpentylidene)-2-methylpropane-2-sulfinamide (3m). Following the general procedure (GP1), the reaction of 5-chloro-1-phenylpentan-1-one (**6m**) (10 g, 50.84 mmol) with (S_S)-*tert*-butanesulfinamide (9.24 g, 76.26 mmol) and Ti(OEt)$_4$ (23.2 g, 101.68 mmol) gave 13.72 g (90%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3m** as a viscous liquid, $[\alpha]^{25}_D$ = +23.6 (*c* 1.02, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.78−7.91 (m, 2 H), 7.39−7.51 (m, 3 H), 3.51−3.61 (m, 2 H), 3.14−3.37 (m, 2 H), 1.78−1.95 (m, 4 H), 1.33 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 179.0 137.7, 131.5, 128.6, 127.3, 57.7, 44.3, 32.3, 31.3, 25.9, 22.7. HRMS (EI) calcd for $C_{15}H_{23}NOSCl$ [M + H] 300.1183, found 300.1184.

(*S,E*)-*N*-(6-Chloro-1-phenylhexylidene)-2-methylpropane-2-sulfinamide (3n). Following the general procedure (GP1), the reaction of 6-chloro-1-phenylhexan-1-one (**6n**) (10 g, 47 mmol) with (S_S)-*tert*-butanesulfinamide (8.6 g, 71.4 mmol) and Ti(OEt)$_4$ (20.71 g, 94 mmol) gave 13.42 g (90%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3n** as a viscous liquid, $[\alpha]^{25}_D$ = +12.4 (*c* 1.22, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.83 (br. s., 2 H), 7.40−7.51 (m, 3 H), 3.57 (none, 1 H), 3.51 (t, J = 6.46 Hz, 2 H), 3.23−3.34 (m, 1 H), 3.12−3.22 (m, 1 H), 1.77−1.85 (m, 2 H), 1.65−1.74 (m, 2 H), 1.54−1.63 (m, 2 H), 1.35 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 179.5, 137.8, 131.5, 128.6, 127.3, 57.3, 44.7, 32.2, 32.0, 27.9, 27.0, 22.7. HRMS (EI) calcd for $C_{16}H_{25}NOSCl$ [M + H] 314.1345, found 314.1347.

(*S,E*)-*N*-(7-Chloro-1-phenylhexylidene)-2-methylpropane-2-sulfinamide (3o). Following the general procedure (GP1), the reaction of 7-chloro-1-phenylheptan-1-one (**6o**) (11.5 g, 50.0 mmol) with (S_S)-*tert*-butanesulfinamide (9.0 g, 75.0 mmol) and Ti(OEt)$_4$ (22.8 g, 100.0 mmol) gave 14.5 g (89%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3o** as a viscous liquid, $[\alpha]^{25}_D$ = +29.0 (*c* 1.02, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.74−7.92 (m, 2 H), 7.35−7.53 (m, 3 H), 3.51 (t, J = 6.78 Hz, 2 H), 3.06−3.36 (m, 2 H), 1.62−1.85 (m, 4 H), 1.40−1.54 (m, 4 H), 1.32 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 179.8, 137.9, 131.4, 128.5, 127.4, 57.5, 44.9, 32.4, 29.0, 28.4, 26.5, 22.7. HRMS (EI) calcd for $C_{17}H_{27}ClNOS$ [M + H] 328.1502, found 328.1504.

(*S,E*)-2-Methyl-*N*-(1-phenylbutylidene)propane-2-sulfinamide (3p). Following the general procedure (GP1), the reaction of 1-phenylpentan-1-one (**6p**) (10 g, 67.47 mmol) with (S_S)-*tert*-butanesulfinamide (12.16 g, 101.20 mmol) and Ti(OEt)$_4$ (30.786 g, 134.94 mmol) gave 15.6 g (92%) of pure γ-chloro *N*-sulfinyl ketimine (S_S) **3p** as a viscous liquid, $[\alpha]^{25}_D$ = +30.4 (*c* 1.63, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.78−7.92 (m, 2 H), 7.37−7.52 (m, 3 H), 3.20−3.32 (m, 1 H), 3.07−3.20 (m, 1 H), 1.65−1.78 (m, 2 H), 1.32 (s, 9 H), 1.03 (t, J = 7.41 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 180.0, 138.2, 131.4, 128.5, 127.4, 57.3, 34.3, 22.6, 22.2, 14.2. HRMS (EI) calcd for $C_{14}H_{22}NOS$ [M + H] 252.1422, found 252.1414.

General Procedure (GP2) for the Synthesis of 2-Substituted Pyrrolidines 4. $LiBHEt_3$ was added to a solution of ketimine **3a** (5 mmol) in THF (15 mL) at −78 °C under nitrogen. After stirring for 3 h at −78 °C, the reaction mixture was warmed to rt and stirred for 1 h. On completion, the reaction was quenched

with saturated NH_4Cl solution (20 mL). The organic layer was then separated, washed with water, and dried under vacuum to give crude product. The crude product was purified by column chromatography (silica gel, ethyl acetate/hexanes) to afford the pure 2-substituted pyrrolidines **4**.

General Procedure (GP3) for the Synthesis of 2-Substituted Pyrrolidines 5. To a solution of ketimine **3a** (5 mmol) in toluene (15 mL) at −78 °C was added DIBAL-H under nitrogen. After stirring for 3 h at −78 °C, the reaction mixture was warmed to rt followed by addition of LiHMDS (7.5 mmol) and stirred for 1 h. On completion, the reaction was quenched with saturated K^+Na^+ tartarate solution (20 mL). The organic layer was then separated, washed with water, and dried under vacuum to give crude product. The crude product was purified by column chromatography (silica gel, ethyl acetate/hexanes) to afford the pure 2-substituted pyrrolidines **5**.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-bromophenyl)-pyrrolidine (4a). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3a** (1.82 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4a** (1.58 g, 96%) as white solid, mp = 120−122 °C, $[\alpha]^{25}_D$ = +152.3 (*c* 1.13, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.44 (d, *J* = 8.51 Hz, 2 H), 7.17 (d, *J* = 8.51 Hz, 2 H), 4.59 (t, *J* = 7.25 Hz, 1 H), 3.83−3.96 (m, 1 H), 2.89−3.05 (m, 1 H), 2.17−2.30 (m, 1 H), 1.68−2.02 (m, 3 H), 1.10 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 142.3, 131.4, 128.9, 121.0, 68.7, 57.2, 42.1, 35.9, 26.3, 23.8. HRMS (EI) calcd for $C_{14}H_{21}BrNOS$ [M + H] 330.0522, found 330.0527.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-bromophenyl)-pyrrolidine (5a). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3a** (3.65 g, 10.0 mmol) with DIBAL-H (12.0 mL, 12.0 mmol, 1.0 M in toluene) and followed by LiHMDS (15.0 mL, 15.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5a** (2.91 g, 90%) as white solid, mp = 100−112 °C, $[\alpha]^{25}_D$ = −164.3 (*c* 1.13, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.38−7.49 (m, 2 H), 7.14 (d, *J* = 8.51 Hz, 2 H), 5.02 (dd, *J* = 8.20, 2.84 Hz, 1 H), 3.49−3.69 (m, 2 H), 2.16 (dd, *J* = 11.98, 9.14 Hz, 1 H), 1.64−1.96 (m, 3 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.7, 131.4, 128.2, 120.3, 57.4, 56.9, 54.8, 36.4, 24.1, 23.0. HRMS (EI) calcd for $C_{14}H_{21}BrNOS$ [M + H] 330.0527, found 330.0539.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-phenyl-pyrrolidine (4b). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3b** (1.42 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4b** (1.17 g, 94%) as a viscous liquid, $[\alpha]^{25}_D$ = +121.6 (*c* 1.05, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.14−7.40 (m, 5 H), 4.64 (t, *J* = 7.25 Hz, 1 H), 3.83−3.99 (m, 1 H), 2.91−3.04 (m, 1 H), 2.19−2.34 (m, 1 H), 1.71−2.01 (m, 3 H), 1.10 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.3, 128.2, 127.2, 69.3, 57.2, 42.1, 35.9, 26.3, 23.8. HRMS (EI) calcd for $C_{14}H_{22}NOS$ [M + H] 252.1439, found 252.1422.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-phenyl-pyrrolidine (5b). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3b** (1.42 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5b** (1.15 g, 92%) as white solid, mp = 80−81 °C, $[\alpha]^{25}_D$ = −140.0 (*c* 1.07, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.16−7.34 (m, 5 H), 5.07 (dd, *J* = 8.04, 2.68 Hz, 1 H), 3.61−3.71 (m, 1 H), 3.52−3.60 (m, 1 H), 2.16 (dd, *J* = 11.35, 8.51 Hz, 1 H), 1.71−1.92 (m, 3 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.1, 126.8, 125.0, 55.9, 55.9, 53.3, 35.1, 22.6, 21.5. HRMS (EI) calcd for $C_{14}H_{22}NOS$ [M + H] 252.1402, found 252.1413.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-methylphenyl)-pyrrolidine (4c). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3c** (1.49 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4c** (1.21 g, 92%) as a white solid, mp = 62−64 °C, $[\alpha]^{25}_D$ = +144.6 (*c* 1.03, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.17 (d, *J* = 8.2 Hz, 2 H), 7.11 (d, *J* = 8.2 Hz, 2 H), 4.60 (t, *J* = 7.41 Hz, 1 H), 3.83−3.92 (m, 1 H), 2.92−3.01 (m, 1 H), 2.32 (s, 3 H), 2.15−2.25 (m, 1 H), 1.93−2.01 (m, 1 H), 1.72−1.90 (m, 2 H), 1.10 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 140.2, 136.7, 128.9, 127.1, 69.0, 57.1, 42.0, 35.9, 26.3, 23.8, 21.0. HRMS (EI) calcd for $C_{15}H_{24}NOS$ [M + H] 266.1573, found 266.1574.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-mehtylphenyl)-pyrrolidine (5c). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3b** (1.49 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5c** (1.39 g, 93%) as white solid, mp = 96−98 °C, $[\alpha]^{20}_D$ = −159.0 (*c* 0.8, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.09−7.17 (m, 4 H), 5.02 (dd, *J* = 8.04, 2.68 Hz, 1 H), 3.62−3.70 (m, 1 H), 3.50−3.57 (m, 1 H), 2.32 (s, 3 H), 2.08−2.18 (m, 1 H), 1.77−1.90 (m, 2 H), 1.70−1.78 (m, 1 H), 1.06 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 141.5, 136.0, 129.0, 126.4, 57.5, 57.4, 54.5, 36.6, 24.1, 23.1, 23.0. HRMS (EI) calcd for $C_{15}H_{24}NOS$ [M + H] 266.1579, found 266.1569.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-methoxyphenyl)-pyrrolidine (4d). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3d** (1.57 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4d** (1.26 g, 90%) as a white solid, mp = 61−63 °C, $[\alpha]^{25}_D$ = +123.2 (*c* 1.0, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.18−7.23 (m, 2 H), 6.82−6.87 (m, 2 H), 4.52−4.61 (m, 1 H), 3.83−3.90 (m, 1 H), 3.78 (s, 3 H), 2.91−3.00 (m, 1 H), 2.14−2.24 (m, 1 H), 1.92−2.02 (m, 1 H), 1.70−1.90 (m, 2 H), 1.09 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 158.7, 135.0, 128.3, 113.6, 68.6, 57.0, 55.1, 41.9, 35.9, 26.3, 23.8. HRMS (EI) calcd for $C_{15}H_{24}NO_2S$ [M + H] 282.1528, found 282.1527.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-methoxyphenyl)-pyrrolidine (5d). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3d** (1.57 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5d** (1.22 g, 87%) as white solid, mp = 85−87 °C, $[\alpha]^{25}_D$ = −140.8 (*c* 1.09, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.16 (d, *J* = 8.83 Hz, 2 H), 6.83−6.87 (m, 2 H), 4.99 (dd, *J* = 7.88, 2.84 Hz, 1 H), 3.79 (s, 3 H), 3.62−3.70 (m, 1 H), 3.47−3.55 (m, 1 H), 2.07−2.17 (m, 1 H), 1.78−1.91 (m, 2 H), 1.69−1.76 (m, 1 H), 1.06 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 158.2, 136.6, 127.6, 113.7, 57.4, 55.1, 54.2, 36.6, 24.1, 23.1. HRMS (EI) calcd for $C_{15}H_{24}NO_2S$ [M + H] 282.1528, found 282.1532.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-*tert*-butylphenyl)-pyrrolidine (4e). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3e** (1.70 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4e** (1.42 g, 93%) as a white solid, mp = 45−50 °C, $[\alpha]^{25}_D$ = 110.5 (*c* 1.0, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.33 (d, *J* = 8.34 Hz, 2 H), 7.21 (d, *J* = 8.34 Hz, 2 H), 4.64 (t, *J* = 6.95 Hz, 1 H), 3.85−3.92 (m, 1 H), 2.93−3.01 (m, 1 H), 2.17−2.25 (m, 1 H), 1.91−2.00 (m, 1 H), 1.74−1.91 (m, 2 H), 1.31 (s, 9 H), 1.11 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 150.0, 140.1, 126.7, 125.1, 57.2, 42.0, 35.8, 34.4, 31.5, 31.4, 26.2, 23.9. HRMS (EI) calcd for $C_{18}H_{30}NOS$ [M + H]308.2043, found 308.2046.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-*tert*-butylphenyl)-pyrrolidine (5e). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3e** (1.70 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and

followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5e**(1.39 g, 91%) as white solid, mp = 55−60 °C, $[\alpha]^{25}_D$ = −141.0 (*c* 1.12, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.31 (d, *J* = 8.20 Hz, 2 H), 7.16 (d, *J* = 8.20 Hz, 2 H), 5.02 (dd, *J* = 8.04, 2.36 Hz, 1 H), 3.63−3.70 (m, 1 H), 3.48−3.54 (m, 1 H), 2.09−2.16 (m, 1 H), 1.74−1.88 (m, 3 H), 1.31 (s, 9 H), 1.07 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 149.3, 141.2, 126.1, 125.1, 57.8, 57.4, 54.1, 36.4, 34.4, 31.3, 24.1, 23.1. HRMS (EI) calcd for $C_{18}H_{30}NOS$ [M + H] 308.2048, found 308.2043.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-hydroxylphenyl)-pyrrolidine (4f). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3f** (1.50 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4f** (1.30 g, 98%) as a white solid, mp = 150 °C, $[\alpha]^{25}_D$ = +137.4 (*c* 0.93, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.13 (d, *J* = 8.51 Hz, 2 H), 6.82 (d, *J* = 8.51 Hz, 2 H), 6.50 (br. s., 1 H), 4.53−4.56 (m, 1 H), 3.84−3.89 (m, 1 H), 2.94−3.01 (m, 1 H), 2.18−2.23 (m, 1 H), 1.95−2.01 (m, 1 H), 1.74−1.87 (m, 2 H), 1.12 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 155.6, 134.4, 128.5, 115.2, 68.7, 57.2, 42.2, 35.7, 26.3, 23.8. HRMS (EI) calcd for $C_{14}H_{22}NO_2S$ [M + H] 268.1371, found 268.1364.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-hydroxyphenyl)-pyrrolidine (5f). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3f** (1.50 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5f** (1.25 g, 94%) as white solid, mp = 185 °C, $[\alpha]^{25}_D$ = −124.4 (*c* 1.02, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 8.07 (s, 1 H), 7.08 (d, *J* = 8.51 Hz, 2 H), 6.83 (d, *J* = 8.83 Hz, 2 H), 4.87 (dd, *J* = 7.57, 3.15 Hz, 1 H), 3.69−3.76 (m, 1 H), 3.40−3.47 (m, 1 H), 2.13 (dd, *J* = 11.98, 7.88 Hz, 1 H), 1.81−1.92 (m, 2 H), 1.73−1.81 (m, 1 H), 1.13 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 155.8, 134.6, 127.8, 115.5, 60.0, 57.8, 51.9, 36.2, 24.0, 23.4. HRMS (EI) calcd for $C_{14}H_{22}NO_2S$ [M + H] 268.1371, found 268.1365.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(3-methoxyphenyl)-pyrrolidine (4g). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3g** (1.57 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4g** (1.28 g, 92%) as a white solid, mp = 45−50 °C, $[\alpha]^{25}_D$ = +152.8 (*c* 1.12, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.23 (t, *J* = 7.88 Hz, 1 H), 6.82−6.91 (m, 2 H), 6.75−6.81 (m, 1 H), 4.63 (t, *J* = 7.09 Hz, 1 H), 3.86−3.92 (m, 1 H), 3.80 (s, 3 H), 2.95−3.00 (m, 1 H), 2.22−2.27 (m, 1 H), 1.94−2.00 (m, 1 H), 1.77−1.89 (m, 2 H), 1.12 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 159.2, 145.0, 129.3, 119.5, 112.9, 112.4, 69.2, 57.2, 55.1, 42.1, 35.8, 26.2, 23.8. HRMS (EI) calcd for $C_{15}H_{24}NO_2S$ [M + H] 282.1528, found 282.1519.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(3-methoxyphenyl)-pyrrolidine (5g). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3g** (1.57 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5g** (1.26 g, 90%) as a viscous liquid, $[\alpha]^{25}_D$ = −131.0 (*c* 1.21, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.22 (t, *J* = 7.88 Hz, 1 H), 6.80−6.86 (m, 2 H), 6.75 (dd, *J* = 8.20, 2.52 Hz, 1 H), 5.03−5.05 (m, 1 H), 3.80 (s, 3 H), 3.61−3.68 (m, 1 H), 3.53−3.58 (m, 1 H), 2.11−2.19 (m, 1 H), 1.72−1.92 (m, 3 H), 1.07 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 159.6, 146.4, 129.4, 118.9, 112.4, 111.6, 57.4, 55.1, 54.9, 36.5, 24.2, 23.0. HRMS (EI) calcd for $C_{15}H_{24}NO_2S$ [M + H] 282.1528, found 282.1516.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-chlorophenyl)-pyrrolidine (4h). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3h** (1.59 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4h** (1.39 g, 98%) as a white solid, mp = 75−77 °C, $[\alpha]^{25}_D$ = +111.9 (*c* 1.09, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21 (dd, 4 H), 4.55 (t, 1 H), 3.79−3.87 (m, 1 H), 2.87−2.96 (m, 1 H), 2.14−2.23 (m, 1 H), 1.63−1.97 (m, 3 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 141.8, 132.9, 128.6, 128.4, 68.6, 57.2, 42.1, 36.0, 26.3, 23.8. HRMS (EI) calcd for $C_{14}H_{21}NOSCl$ [M + H] 286.1032, found 286.1028.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-chlorophenyl)-pyrrolidine (5h). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3h** (1.59 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5h** (1.32 g, 93%) as white solid, mp = 95−102 °C, $[\alpha]^{25}_D$ = −145.6 (*c* 0.75, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.26−7.31 (m, 2 H), 7.16−7.21 (m, 2 H), 5.04 (dd, *J* = 7.96, 2.65 Hz, 1 H), 3.50−3.69 (m, 1 H), 2.07−2.23 (m, 1 H), 1.65−1.94 (m, 3 H), 1.05 (s, 9 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.2, 132.2, 128.5, 127.9, 57.5, 56.9, 54.9, 36.5, 24.1, 23.0. HRMS (EI) calcd for $C_{14}H_{21}NOSCl$ [M + H] 286.1032, found 286.1034.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-fluorophenyl)-pyrrolidine (4i). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3i** (1.51 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4i** (1.25 g, 93%) as a white solid, $[\alpha]^{25}_D$ = +127.4 (*c* 1.18, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21−7.30 (m, 2 H), 6.95−7.04 (m, 2 H), 4.58−4.64 (m, 1 H), 3.82−3.93 (m, 1 H), 2.92−3.01 (m, 1 H), 2.20−2.29 (m, 1 H), 1.93−2.01 (m, 1 H), 1.70−1.91 (m, 2 H), 1.09 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 163.2, 160.8, 138.9, 128.8, 128.7, 115.2, 115.0, 68.5, 57.2, 42.0, 36.0, 26.3, 23.8. HRMS (EI) calcd for $C_{14}H_{21}NOSF$ [M + H] 270.1322, found 270.1321.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-(4-chlorophenyl)-pyrrolidine (5i). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3i** (1.51 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5i** (1.31 g, 98%) as white solid, mp = 80 °C, $[\alpha]^{25}_D$ = −146.5 (*c* 1.0, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.19−7.24 (m, 2 H), 6.97−7.02 (m, 2 H), 5.04 (dd, *J* = 7.88, 2.84 Hz, 1 H), 3.62−3.69 (m, 1 H), 3.51−3.56 (m, 1 H), 2.12−2.19 (m, 1 H), 1.76−1.92 (m, 2 H), 1.68−1.76 (m, 1 H), 1.05 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 162.5, 160.5, 140.3, 128.0, 128.0, 115.2, 115.0, 57.4, 57.0, 54.5, 36.5, 24.1, 23.0. HRMS (EI) calcd for $C_{14}H_{21}NOSF$ [M + H] 270.1322, found 270.1320.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-thiophenyl-pyrrolidine (4j). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3j** (1.45 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4j** (1.19 g, 93%) as a viscous liquid, $[\alpha]^{25}_D$ = +98.5 (*c* 1.21, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.19 (dd, *J* = 4.26, 1.73 Hz, 1 H), 6.90−6.96 (m, 2 H), 4.94 (t, *J* = 6.46 Hz, 1 H), 3.78−3.86 (m, 1 H), 2.91−2.98 (m, 1 H), 2.22−2.30 (m, 1 H), 1.85−2.03 (m, 3 H), 1.14 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 147.9, 126.6, 124.4, 65.1, 57.5, 41.4, 35.8, 26.7, 23.7. HRMS (EI) calcd for $C_{12}H_{20}NOS_2$ [M + H] 258.0986, found 258.0979.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2thiophenyl-pyrrolidine (5j). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3j** (1.45 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded pyrrolidine **5j** (1.22 g, 95%) as white solid, mp = 125−130 °C, $[\alpha]^{25}_D$ = −130.2 (*c* 0.98, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.15 (d, *J* = 5.04 Hz, 1 H), 6.91−6.95 (m, 1 H), 6.87 (d, *J* = 3.15 Hz, 1 H), 5.24−5.28 (m, 1 H), 3.60−3.66 (m, 1 H), 3.43−3.49 (m, 1 H), 2.07−2.15 (m, 1 H), 1.87−1.96 (m, 3 H), 1.12 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 148.9, 126.7, 123.8, 123.6, 57.6, 54.1, 53.9, 36.7, 24.2, 22.9. HRMS (EI) calcd for $C_{12}H_{20}NOS_2$ [M + H] 258.0981, found 258.0979.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-cyclohexyl-pyrrolidine (4k). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3k** (1.44 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4k** (1.20 g, 94%) as a viscous liquid, $[\alpha]^{25}_D$ = +106.0 (*c* 0.75, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 3.68−3.79 (m, 1 H), 3.45−3.52 (m, 1 H), 2.59−2.69 (m, 1 H), 1.73−1.83 (m, 4 H), 1.65−1.72 (m, 4 H), 1.54−1.63 (m, 1 H), 1.40−1.51 (m, 1 H), 1.21 (s, 9 H), 1.07−1.18 (m, 3 H), 0.89−1.05 (m, 2 H), ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 70.7, 57.7, 42.6, 42.3, 30.4, 27.2, 26.8, 26.7, 26.6, 26.5, 26.2, 24.0. HRMS (EI) calcd for $C_{14}H_{28}NOS$ [M + H] 258.1892, found 258.1890.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-cyclohexyl-pyrrolidine (5k). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3k** (1.45 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 M in THF) afforded pyrrolidine **5k** (1.22 g, 95%) as a viscous liquid, $[\alpha]^{25}_D$ = −40.9 (*c* 1.05, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 3.53−3.63 (m, 1 H), 3.30−3.39 (m, 1 H), 3.14−3.23 (m, 1 H), 1.60−1.83 (m, 10 H), 1.23−1.32 (m, 2 H), 1.20 (s, 9 H), 1.05−1.17 (m, 1 H), 0.89−1.06 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.7, 57.5, 50.0, 41.5, 30.7, 27.4, 27.2, 26.6, 26.5, 26.3, 25.2, 23.4. HRMS (EI) calcd for $C_{14}H_{28}NOS$ [M + H] 258.1892, found 258.1858.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-methyl-pyrrolidine (4l). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3l** (1.11 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded pyrrolidine **4l** (0.83 g, 88%) as a viscous liquid, $[\alpha]^{25}_D$ = +32.5 (*c* 0.89, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 3.77−3.84 (m, 1 H), 3.49−3.57 (m, 1 H), 3.04−3.14 (m, 1 H), 1.77−1.95 (m, 3 H), 1.47−1.54 (m, 1 H), 1.22 (d, *J* = 6.62 Hz, 3 H), 1.19 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 60.7, 57.2, 54.7, 47.1, 41.3, 33.5, 24.0, 23.5, 20.4. HRMS (EI) calcd for $C_9H_{20}NOS$ [M + H] 190.1258, found 190.1266.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-methyl-pyrrolidine (5l). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3l** (1.11 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 M in THF) afforded pyrrolidine **5l** (0.85 g, 89%) as a viscous liquid, $[\alpha]^{25}_D$ = +83.6 (*c* 1.38, $CHCl_3$). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 3.69−3.75 (m, 1 H), 2.73−2.80 (m, 1 H), 1.96−2.04 (m, 1 H), 1.82−1.91 (m, 1 H), 1.67−1.78 (m, 1 H), 1.34−1.45 (m, 1 H), 1.18 (s, 9 H), 1.17 (d, *J* = 5.99 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 60.6, 56.6, 41.2, 33.7, 25.9, 23.7, 22.0. HRMS (EI) calcd for $C_9H_{20}NOS$ [M + H] 190.1258, found 190.1260.

(*R*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-phenyl-piperidine (10m). Following the general procedure (GP2), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3m** (1.49 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded piperidine **10m** (1.24 g, 94%) as a white solid, mp = 45−50 °C, $[\alpha]^{25}_D$ = −116.9 (*c* 1.16, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.43 (d, *J* = 8.20 Hz, 2 H), 7.36 (t, *J* = 7.72 Hz, 2 H), 7.20−7.27 (m, 1 H), 4.68 (t, *J* = 4.10 Hz, 1 H), 3.29 (dd, *J* = 8.04, 3.31 Hz, 2 H), 2.16−2.23 (m, 1 H), 2.00−2.09 (m, 1 H), 1.56−1.70 (m, 4 H), 1.42−1.52 (m, 1 H), 1.15 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 140.2, 128.5, 127.4, 126.6, 58.7, 31.2, 25.6, 23.0, 20.4. HRMS (EI) calcd for $C_{15}H_{24}NOS$ [M + H] 266.1579, found 266.1563.

(*S*)-1-((*S*)-2-Methyl-propane-2-sulfinyl)-2-phenyl-piperidine (11m). Following the general procedure (GP3), the reaction of γ-chloro *N*-sulfinyl ketimine (S_S) **3m** (1.49 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded piperidine **11m** (1.21 g, 92%) as white solid, mp = 50−55 °C, $[\alpha]^{25}_D$ = −108.0 (*c* 1.04, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.22−7.36 (m, 5 H), 4.14 (dd, *J* = 8.51, 4.10 Hz, 1 H), 3.31−3.36 (m, 1 H), 2.93−3.01 (m, 1 H), 1.89−1.97 (m, 2 H), 1.73−1.84 (m, 2 H), 1.57−1.66 (m, 1 H), 1.43−1.55 (m, 1 H), 1.13 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 141.8, 128.4, 128.2, 127.3, 65.4, 58.1, 43.8, 34.4, 25.5, 24.1, 23.2. HRMS (EI) calcd for $C_{15}H_{24}NOS$ [M + H] 266.1579, found 266.1550.

(*S*)-2-Methyl-propane-2-sulfinic Acid [(*R*)-6-Chlro-1-phenyl-hexyl]amide (12n). Following the general procedure (GP2), the reaction of chloro *N*-sulfinyl ketimine (S_S) **3m** (1.56 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded amide **12n** (1.48 g, 94%) as a viscous liquid. ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.24−7.35 (m, 5 H), 4.32−4.38 (m, 1 H), 3.46 (t, *J* = 6.62 Hz, 2 H), 3.40 (d, *J* = 2.84 Hz, 1 H), 1.75−1.88 (m, 2 H), 1.66−1.75 (m, 2 H), 1.37−1.47 (m, 2 H), 1.27−1.37 (m, 1 H), 1.19−1.24 (m, 1 H), 1.17 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 141.9, 128.4, 127.5, 59.2, 55.4, 44.8, 38.5, 32.2, 26.5, 25.2, 22.5. HRMS (EI) calcd for $C_{16}H_{27}NOSCl$ [M + H] 316.1502, found 316.1499.

(*S*)-2-Methyl-propane-2-sulfinic Acid [(*S*)-6-Chlro-1-phenyl-hexyl]amide (14n). Following the general procedure (GP3), the reaction of chloro *N*-sulfinyl ketimine (S_S) **3m** (1.56 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded amide **14n** (1.20 g, 93%) as a viscous liquid. ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.25−7.37 (m, 5 H), 4.31−4.35 (m, 1 H), 3.46 (t, *J* = 6.62 Hz, 2 H), 3.40 (d, *J* = 3.47 Hz, 1 H), 1.98−2.07 (m, 1 H), 1.66−1.78 (m, 3 H), 1.35−1.47 (m, 2 H), 1.25−1.32 (m, 1 H), 1.23 (s, 9 H), 1.09−1.19 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 142.4, 128.7, 127.8, 127.1, 58.9, 55.6, 44.8, 36.3, 32.3, 26.6, 24.9, 22.6. HRMS (EI) calcd for $C_{16}H_{27}NOSCl$ [M + H] 316.1502, found 316.1498.

(*S*)-2-Methyl-propane-2-sulfinic Acid [(*R*)-1-Phenyl-butyl]amide (15p). Following the general procedure (GP2), the reaction of chloro *N*-sulfinyl ketimine (S_S) **3p** (1.26 g, 5.0 mmol) with $LiBHEt_3$ (6.0 mL, 6.0 mmol, 1.0 M in THF) afforded amide **15p** (1.20 g, 95%) as a viscous liquid, $[\alpha]^{25}_D$ = +89.3 (*c* 1.05, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.31−7.35 (m, 2 H), 7.26−7.30 (m, 3 H), 4.35−4.40 (m, 1 H), 3.36 (br. s., 1 H), 1.72−1.83 (m, 2 H), 1.24−1.36 (m, 1 H), 1.19 (s, 9 H), 0.89 (t, *J* = 7.25 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 142.1, 128.3, 127.6, 127.5, 59.2, 55.4, 40.9, 22.5, 19.2, 13.8. HRMS (EI) calcd for $C_{14}H_{24}NOS$ [M + H] 254.1579, found 254.1569.

(*S*)-2-Methyl-propane-2-sulfinic Acid [(*S*)-1-Phenyl-butyl]amide (16p). Following the general procedure (GP3), the reaction of chloro *N*-sulfinyl ketimine (S_S) **3p** (1.26 g, 5.0 mmol) with DIBAL-H (6.0 mL, 6.0 mmol, 1.0 M in toluene) and followed by LiHMDS (7.5 mL, 7.5 mmol, 1.0 mL in THF) afforded amide **16p** (1.18 g, 93%) as a viscous liquid, $[\alpha]^{25}_D$ = +20.2 (*c* 1.02, MeOH). ^{1}H NMR (501 MHz, $CDCl_3$) δ ppm 7.24−7.35 (m, 5 H), 4.31−4.37 (m, 1 H), 3.43 (d, *J* = 3.47 Hz, 1 H), 1.94−2.04 (m, 1 H), 1.67−1.75 (m, 1 H), 1.21 (s, 9 H), 1.10−1.20 (m, 1 H), 0.88 (t, *J* = 7.41 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 142.6, 128.6,127.7, 127.1, 58.9, 55.6, 38.8, 22.6, 18.9, 13.8. HRMS (EI) calcd for $C_{14}H_{24}NOS$ [M + H] 254.1579, found 254.1574.

General Procedure (GP4) for Deprotection of the *tert*-Butanesulfinyl Group from 4 and 5. To a solution of **4** or **5** (2 mmol) in MeOH (10 mL) was added 4 M HCl solution (in dioxane, 2 mL). After the mixture was stirred at room temperature for 30 min, the mixture was concentrated to dryness and carefully dissolved in water (20 mL). The aqueous layer was washed with ethyl acetate (2 × 20 mL) and neutralized with 6 N NaOH solution to pH ∼13. Then, the resulting aqueous solution was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. The organic layer was concentrated to dryness to obtained pure 2-substituted pyrrolidins **17** or ***ent*-17**.

(*R*)-2-(4-Bromophenyl)-pyrrolidine (17a). Following the general procedure (GP4), the reaction of **4a** (658 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*R*)-2-(4-bromophenyl)-pyrrolidine **17a** (440 mg, 97%) as viscous oil,

$[\alpha]^{25}_D$ = +52.1 (*c* 1.01, CH_2Cl_2). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 7.40 (d, *J* = 8.51 Hz, 2 H), 7.22 (d, *J* = 8.20 Hz, 2 H), 4.05 (t, *J* = 7.72 Hz, 1 H), 3.10−3.24 (m, 1 H), 2.92−3.04 (m, 1 H), 2.08−2.23 (m, 1 H), 1.72−2.01 (m, 3 H), 1.43−1.67 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 131.2, 128.2, 120.2, 61.8, 46.9, 34.4, 25.5. HRMS (EI) calcd for $C_{10}H_{13}BrN$ [M + H] 226.0231, found 226.0229.

(*S*)-2-(4-Bromophenyl)-pyrrolidine (*ent*-17a). Following the general procedure (GP4), the reaction of **5a** (658 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*S*)-2-(4-bromophenyl) pyrrolidine ***ent*-17a** (442 mg, 98%) as viscous oil, $[\alpha]^{25}_D$ = −51.9 (*c* 1.27, CH_2Cl_2). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 7.41 (d, *J* = 8.20 Hz, 2 H), 7.22 (d, *J* = 8.20 Hz, 2 H), 4.05 (t, *J* = 7.57 Hz, 1 H), 3.11−3.21 (m, 1 H), 2.91−3.05 (m, 1 H), 2.08−2.27 (m, 2 H), 1.69−1.98 (m, 2 H), 1.43−1.67 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 131.3, 126.2, 120.3, 61.8, 46.9, 34.4, 25.5. HRMS (EI) calcd for $C_{10}H_{13}BrN$ [M + H] 226.0226, found 226.0228.

(*R*)-2-(4-Chlorophenyl)-pyrrolidine (17h). Following the general procedure (GP4), the reaction of **4h** (570 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*R*)-2-(4-chlorophenyl)-pyrrolidine **17h** (347 mg, 96%) as viscous oil, $[\alpha]^{25}_D$ = +41.1 (*c* 1.05, CH_2Cl_2). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 7.21−7.38 (m, 4 H), 4.09 (t, *J* = 7.72 Hz, 1 H), 3.09−3.27 (m, 1 H), 2.90−3.07 (m, 1 H), 2.08−2.27 (m, 1 H), 1.70−2.03 (m, 3 H), 1.49−1.71 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.5, 132.2, 128.9, 127.8, 61.8, 46.9, 34.4, 25.5. HRMS (EI) calcd for $C_{10}H_{13}ClN$ [M + H] 182.0697, found 182.0696.

(*S*)-2-(4-Chlorophenyl)-pyrrolidine (*ent*-17h). Following the general procedure (GP4), the reaction of **5h** (570 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*S*)-2-(4-bromophenyl) pyrrolidine ***ent*-17 h** (343 mg, 95%) as viscous oil, $[\alpha]^{25}_D$ = −40.9 (*c* 1.15, CH_2Cl_2). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 7.21−7.36 (m, 4 H), 4.09 (t, *J* = 7.72 Hz, 1 H), 3.11−3.28 (m, 1 H), 2.85−3.08 (m, 1 H), 2.10−2.25 (m, 1 H), 1.74−1.99 (m, 3 H), 1.45−1.69 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 143.6, 132.2, 128.3, 127.8, 61.8, 46.9, 34.5, 25.5. HRMS (EI) calcd for $C_{10}H_{13}ClN$ [M + H] 182.0731, found 182.0733.

(*R*)-2-Methyl-pyrrolidine (*ent*-17l). Following the general procedure (GP4), the reaction of **5l** (378 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*R*)-2-methyl-pyrrolidine ***ent*-17l** (138 mg, 92%) as viscous oil, $[\alpha]^{25}_D$ = −31.2 (*c* 1.19, hexane). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 2.97−3.13 (m, 2 H), 2.82 (q, *J* = 8.41 Hz, 1 H), 1.81−1.92 (m, 1 H), 1.66−1.82 (m, 2 H), 1.59 (br. s., 1 H), 1.18 (m and d, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 54.5, 46.7, 33.7, 25.7, 21.2. HRMS (EI) calcd for $C_5H_{12}N$ [M + H] 86.0954, found 86.0970.

(*S*)-2-Methyl-pyrrolidine (17l). Following the general procedure (GP4), the reaction of **4l** (378 mg, 2.0 mmol) with 4 M HCl solution (in dioxane, 2 mL) gives the (*S*)-2-methyl-pyrrolidine **17l** (142 mg, 95%) as viscous oil, $[\alpha]^{25}_D$ = +30.9 (*c* 1.02, hexane). ^1H NMR (501 MHz, $CDCl_3$) δ ppm 2.97−3.13 (m, 2 H), 2.76−2.88 (m, 1 H), 1.81−1.93 (m, 1 H), 1.56−1.81 (m, 3 H), 1.07−1.25 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 54.4, 46.7, 33.6, 25.6, 21.1. HRMS (EI) calcd for $C_5H_{12}N$ [M + H] 86.0947, found 86.0970.

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Supporting Information Available: Complete experimental procedures, characterization data, copies of NMR spectra, and single X-ray crystallographic data for compound **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.