Article

Asymmetric Synthesis of #-(diarylmethyl) alkyl amines through Regioselective Lithiation of #-Diarylmethanes and Diastereoselective Addition to Ellman's Imines.

Leleti Rajender Reddy, Sharadsrikar Kotturi, Yogesh Waman, Chirag Patel, Megha Danidharia, and Rajesh Shenoy

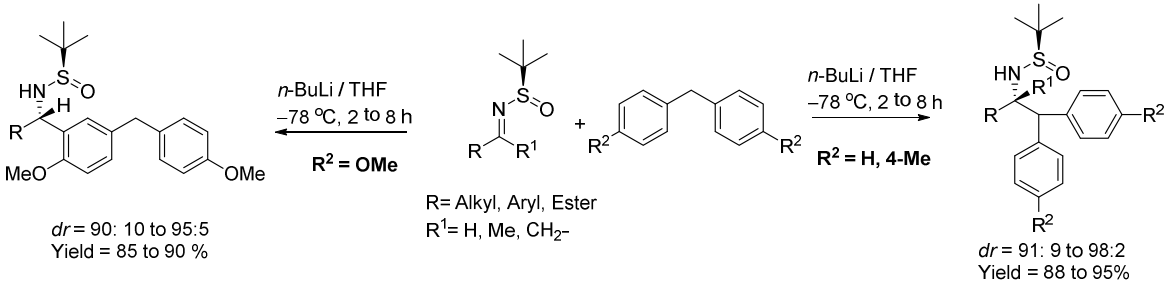
J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b00879 • Publication Date (Web): 29 May 2018

Asymmetric Synthesis of α-(diarylmethyl) alkyl amines through Regioselective Lithiation of α-Diarylmethanes and Diastereoselective Addition to Ellman's Imines.

Leleti Rajender Reddy,* Sharadsrikar Kotturi, Yogesh Waman, Chirag Patel, Megha Danidharia, and Rajesh Shenoy.

Piramal Discovery Solutions, Pharmaceutical Special Economic Zone, Sarkhej Bavla Highway, Ahmedabad, Gujarat 382213, India.

rajender.leleti@piramal.com



Abstract:

A highly regio- and diastereo- selective lithiation/addition of α-diarylmethanes to *N-tert*-butanesulfinylimines is reported. This methodology also affords the preparation of enantiomerically pure α-(diarylmethyl) alkyl amines bearing quaternary centers.

Introduction

For an ongoing program within our research group we needed to synthesize asymmetric amines of the type **1**. These type of chiral amines are ubiquitous structural motifs present in many drugs and drug candidates (Fig. 1).[1] Such amines are also effective chiral polydentate ligands in asymmetric synthesis.[2] While the synthesis of these compounds have been an active area of research, currently available synthetic methods of these privileged structures suffer from long

synthetic sequences, low yields, or lack of broad substrate scope (Scheme 1).[2] We reasoned that an asymmetric addition of diarylmethyl anion to Ellman's Imines could afford a direct access to enantioenriched α–(diarylmethyl) alkyl amines, such a methodology has not been reported to the best of our knowledge.[3] Herein, we report a straightforward and scalable synthesis of enantioenriched α-(diarylmethyl) alkyl amines in high yield with broad substrate scope (Scheme 1). We envisaged that this synthetic effort could be of value in a variety of research applications, including the discovery of new bioactive substances.

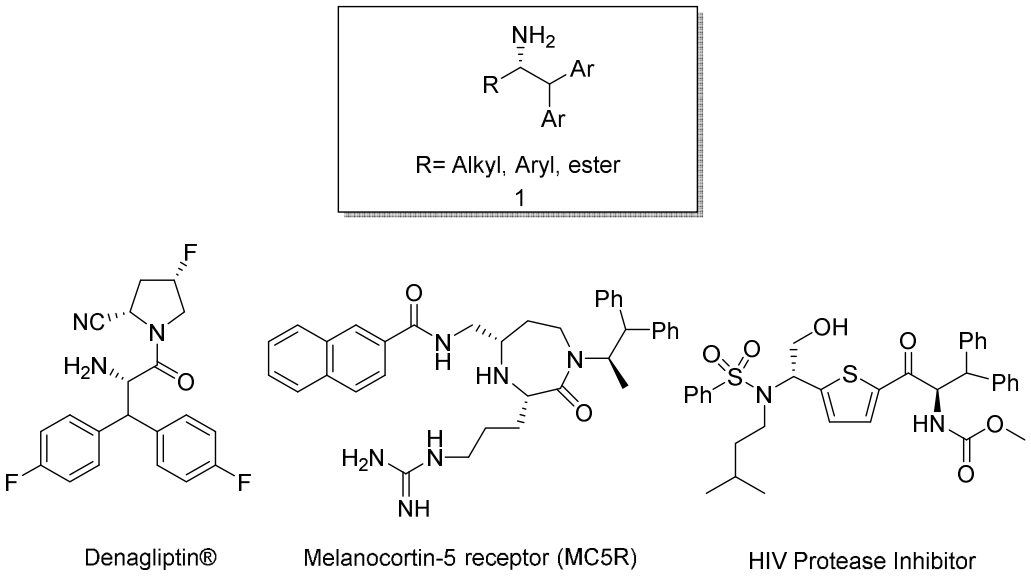


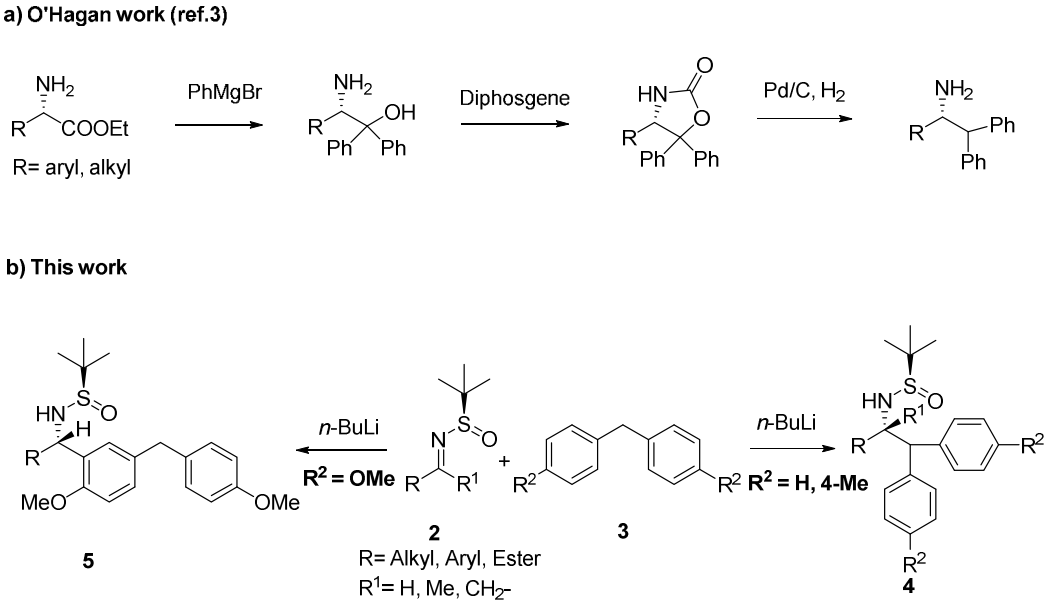
Fig. 1. α-(Diarylmethyl) alkyl amines containing biologically important molecules.

Results and discussion

At the outset of our investigation, we chose diphenylmethane (**3a**) as our model substrate for the lithiation reactions. We were interested in using *n*-BuLi under mild conditions instead of less stable, more expensive and highly pyrophoric *t*-BuLi and *s*-BuLi for the deprotonation at low temperature. The lithiation of **3a**[5] at 0 °C for 1 h in the absence of a ligand and followed by addition to *N*-*tert*-butanesulfinylphenyl aldimine (R_S) **2a**[4] in THF at −78 °C for 2 h afforded α-

(dipheylmethyl) phenyl amine derivative **4a** in 93% yield and with a high diastereomeric ratio (*dr* 98:2). The diastereoselectivity of the reaction was determined to be 98:2 by ^{1}H NMR analysis of the crude product.

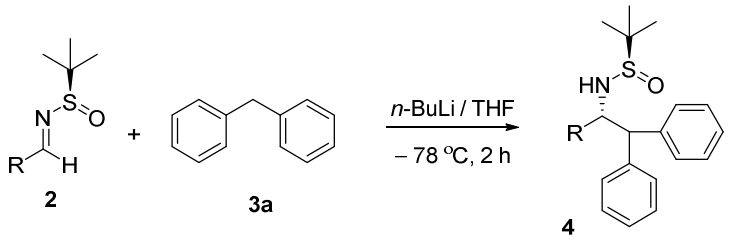
Scheme 1. Approaches to α-(diarylmethyl) alkyl amines.



Once we identified the optimal reaction conditions, the scope of the methodology was investigated by various aldimines (Table 1) with different diarylmethyl lithium reagents. Interestingly, a large variety of substituted aromatic *N*-*tert*-butanesulfinyl aldimines, such as *o*-chloro, *o*-chloro-*p*-fluoro, *p*-methyl, *p*-methoxy derivatives (**2b–e**), reacted with **3a-Li** to lead the corresponding α-(diphenylmethyl) alkyl amines **4b–e** (Table 1, entries 2-5) in yields of 90 – 95% with high diastereomeric ratios (*dr* 98:2). Likewise, heterocyclic *N*-*tert*-butanesulfinyl aldimines, such as 2-furyl (**2f**) and 2-thiophenyl (**2g**) reacted with **3a-Li** to afford the corresponding α-(diarylmethyl) alkyl amines **4f** and **4g** (Table 1, entries 6, 7) in 91% and 92% yields with *dr* 98:2 respectively. Similarly, several aliphatic *N*-*tert*-butanesulfinyl aldimines,

such as cinnamyl, 3-phenyl ethyl, isopropyl, isobutyryl, *n*-propyl derivatives (**2h–l**) were also reacted with **3a-Li** to form α-(diphenylmethyl) alkyl amines **4h–l** in yields of 90-94% with high diastereomeric ratios (*dr* 98:2).

Table 1. Addition of diarylmethyl nucleophile to various *N-tert*-butanesulfinyl aldimines.[a]



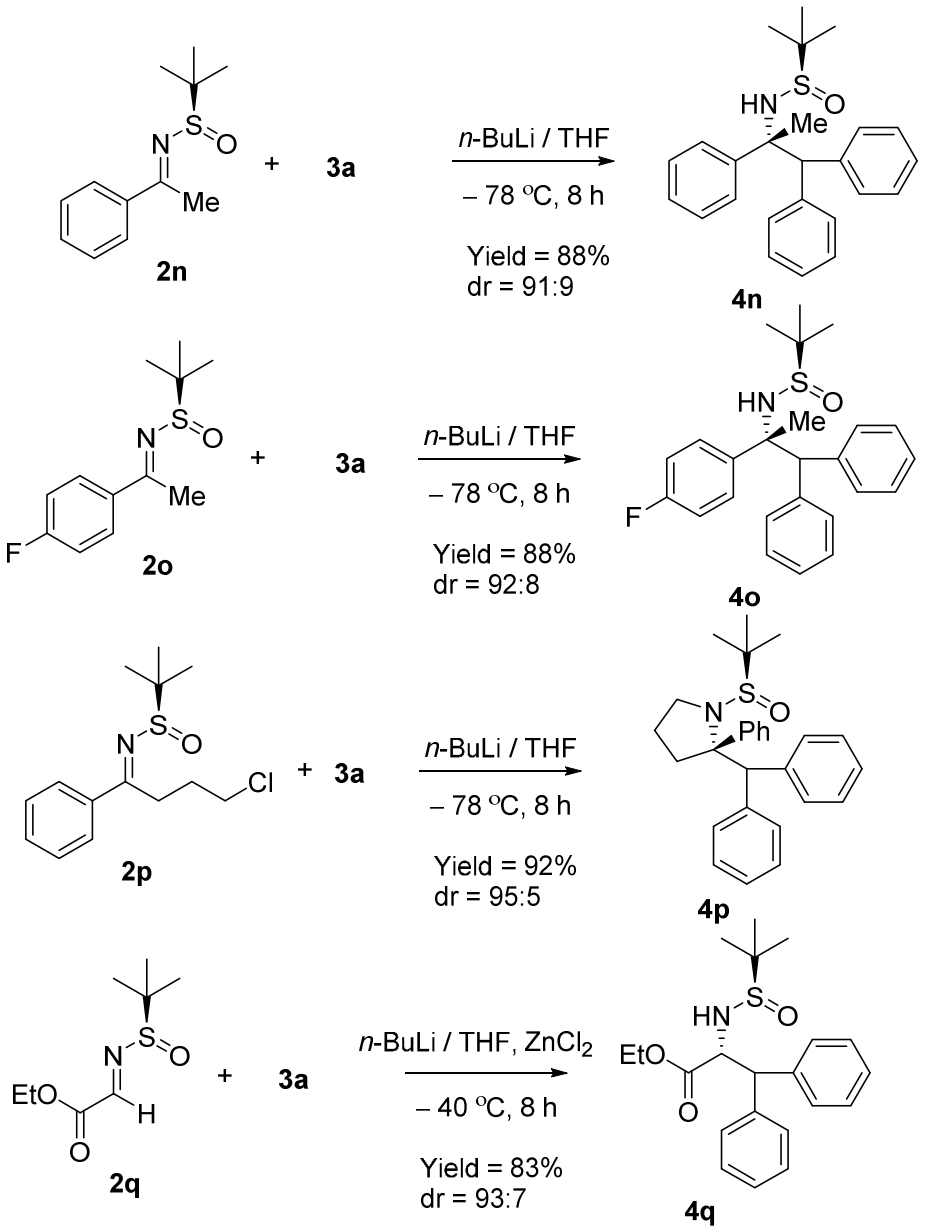
entry	Substrate (R)	product	yield (%)[b]	dr[c]
1	**2a**: R= Ph	**4a**	93	>98:2
2	**2b**: R= *o*-ClC_6H_5	**4b**	90	>98:2
3	**2c**: R= *o*-Cl-*p*-FC_6H_4	**4c**	91	>98:2
4	**2d**: R= *p*-MeC_6H_5	**4d**	90	>98:2
5	**2e**: R= *p*-$MeOC_6H_5$	**4e**	95	>98:2
6	**2f**: R= 2-Furyl	**4f**	91	>98:2
7	**2g**: R= 2-Thiophenyl	**4g**	92	>98:2
8	**2h**: R= Cinnamyl	**4h**	92	>98:2
9	**2i**: R= $PhCH_2CH_2$	**4i**	90	>98:2
10	**2j**: R= Isopropyl	**4j**	93	>98:2
11	**2k**: R= Isobutyryl	**4k**	94	>98:2
12	**2l**: R= *n*-Propyl	**4l**	90	>98:2

[a] All the reactions performed with 1.0 equiv of **2** and 2.0 equiv of **3a** at –78 °C for 2 h. [b] Isolated yield. [c] The diastereoselectivity was determined by ^{1}H NMR analysis. The ">98:2" *dr* denotes that signal for only one diastereomer were observed

To broaden the scope of this method, we investigated the various *N-tert*-butanesulfinyl ketimines **2** under optimal reaction conditions to generate the quaternary α-(diphenylmethyl) alkyl amines. Similarly, the reaction of **3a-Li** with *N-tert*-butanesulfinyl methyl ketimines **2n** and **2o** in THF at –78 °C for 8 h afforded **4n** and **4o** bearing a quaternary center in 88 and 90% yields with *dr* 91:9

and 92:8 diastereomeric ratios respectively. Likewise, reaction of **3a-Li** with *γ*-chlorinated *N*-*tert*-butanesulfinyl ketimine **2p** also proceeded under optimal reaction conditions afford the cyclized pyrrolidine derivative **4p** with a quaternary center in 92% yield with *dr* >95:5 (Scheme 2).

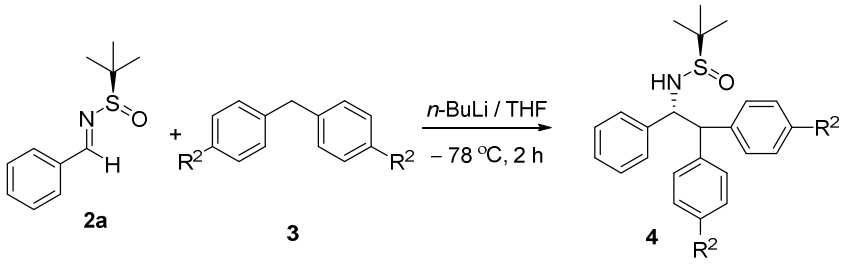
Scheme 2. Addition of diarylmethyl nucleophile to various *N*-*tert*-butanesulfinyl ketimines.



Further we extended this methodology to the asymmetric amino acid derivatives. The reaction

of **3a-Li** with *N-tert*-butanesulfinyl imino acetate **2q** in THF at −78 °C for 2 h did not yield the expected product, probably due to *N-tert*-butanesulfinyl imino acetate **2q** being a complex electrophile with multiple reacting centers. However, the reaction of **3a-ZnCl$_2$** with **2q** in THF at –40 °C for 8 h proceeded in a facile manner with 82% yield and diastereomeric ratios of 93:7 (Table 2).

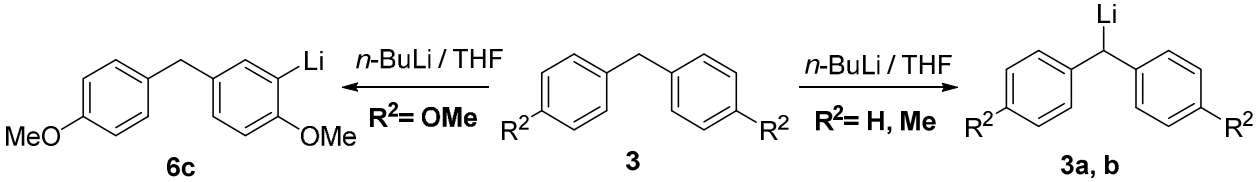
Table 2. Addition of various diarylmethyl nucleophile to *N-tert*-butanesulfinylphenyl aldimine (R_S) **2a.**



entry	reagent (R)	product	yield (%)[b]	dr[c]
1	**3a**: R= H	**4a**	93	>98:2
2	**3b**: R= *p*-Me	**4m**	90	>98:2

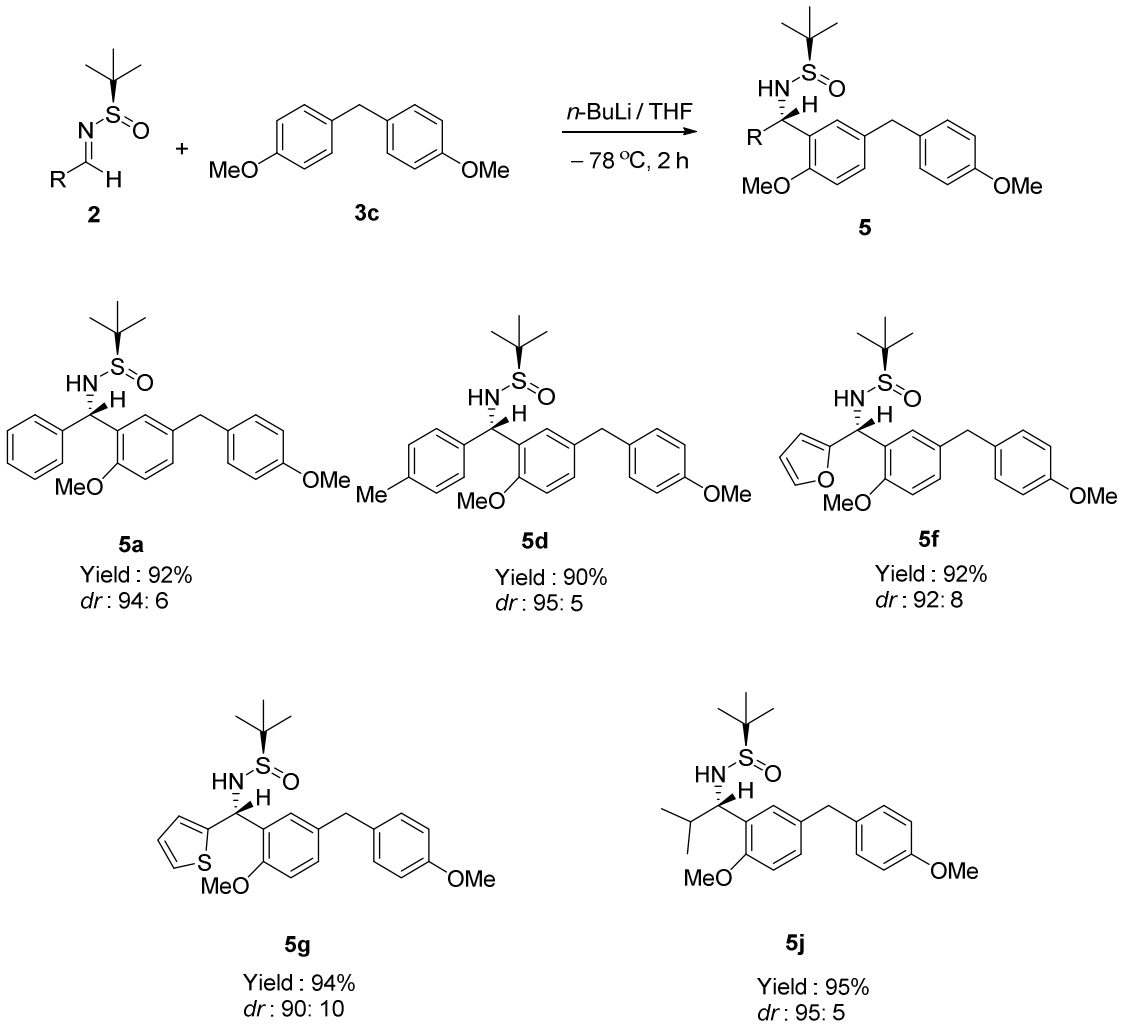
Encouraged by these results, we examined other substituted **3a-Li** reagents. In a similar manner, *p*-methyl substituted **3b-Li** reacted smoothly with **2a** to obtain the corresponding **4m** in 90% yield with high diastereomeric ratio (>98:2). However, surprisingly the reaction of di(*p*-methoxy phenyl)methane **3c** with *n*-BuLi generated the *o*-lithiated intermediate **6c**[6] instead of **3c-Li** intermediate (Scheme 3).

Scheme 3. Reactive species.



Treatment of *o*-lithiated intermediate **6c** with several *N*-*tert*-butanesulfinylphenyl aldimines such as **2a, 2d, 2f, 2g** and **2j** lead to the corresponding amines **5a−j** (Scheme 4, entries 1−5) in excellent yields (90−95%) and good diastereomeric ratios (*dr* 90:10 to 95:5). The structure and absolute configuration of *(R_S,S)*-**5j** was confirmed by single crystal X-ray diffraction analysis (Fig. 2).

Scheme 4. Addition of *o*-lithiated intermediate **6c** to various *N*-*tert*-butanesulfinyl Aldimines (**2**).



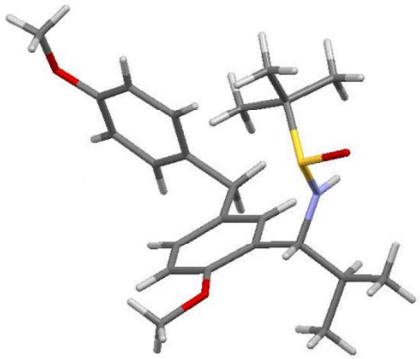
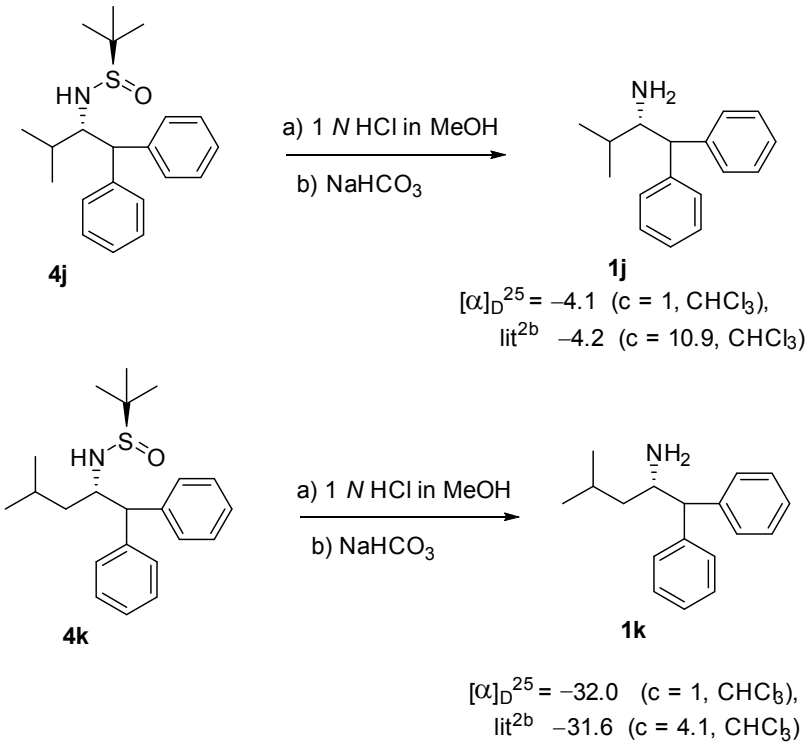


Fig. 2. X-ray crystal structure of **5j (CCDC No. 1835984)**.

Finally, the sulfinyl group was readily cleaved under mild acidic conditions (1*N* HCl in Methanol at 0 ^{o}C for 30 min.) to provide free amine **1** in quantitative yield. The absolute configuration of newly generated center in **1j**, **k** were confirmed as "*S*" by comparison with literature (Scheme 5).[2b]

Scheme 5. Cleavage of Sulfinyl Group.



Conclusions

In conclusion, a regioselective lithiation of α-Diarylmethanes and followed by highly diastereoselective addition to various chiral *N*-*tert*-butanesulfinylimines has been developed. This method is also found to be efficient for the preparation of enantiomerically and diastereomerically pure α-(diarylmethyl) alkyl amines bearing quaternary centers. Extension of this work is currently in progress.

Experimental Section

General Information. All the reactions were performed under dry nitrogen gas in glassware that was flame-dried and equipped with a magnetic stirring bar. Thin-layer chromatography (TLC) was performed using silica gel 60 F254 pre-coated plates (0.25 mm). Flash chromatography was performed using silica gel (40 μm particle size). All compounds were judged pure by TLC analysis (single spot/ two solvent systems) using a UV lamp or PMA for detection purposes. ^{1}H and ^{13}C NMR spectra were recorded on a FT-NMR spectrometer at 400 and 100 MHz, respectively. Mass spectra (HRMS) were obtained using an electrospray ionization (ESI-TOF) mass spectrometer. The reaction temperatures refer to internal reaction temperatures. All the Ellman's Imines (2a-q) were synthezied using known procedures.[4]

General procedure (GP1):

A solution of biphenyl methane (5.0 mmol) in THF (2.5 mL) was cooled to 0 ^{o}C, then *n*-BuLi (1.6 M in cyclohexane, 3.0 mmol) was added dropwise via syringe and the resulting solution was stirred for 1 h at 0 ^{o}C. After that the reaction was cooled to -78 ^{o}C and *N*-*tert*-butanesulfinyl aldimine (R_S) **2** (1.0 mmol in 0.5 mL of THF) was added dropwise via syringe over the period of

30 min. The reaction mixture was stirred for 1 h at -78 °C. After completion of the reaction, it was quenched with water (5 mL) and warmed to room temperature over the period of 30 min. The reaction mixture was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was removed in vacuo to give crude product. The crude product was purified by column chromatography using ethyl acetate/hexanes afforded the pure Compound **4**.

(*R*)-2-methyl-*N*-((*R*)-1,2,2-triphenylethyl)propane-2-sulfinamide (4a): Following the general procedure (GP1), the reaction of *N*-*tert*-butanesulfinyl aldimine (R_S) **2a** (200 mg, 0.95 mmol) with biphenyl methane (4.77 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.86 mmol) afforded amine **4a** as white solid (330 mg, 93%). mp =150–152 °C, $[\alpha]^{20}_D$ = 46.7 (c. 0.25, $CHCl_3$). IR: 3273, 3057, 1452, 1045, 700. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.54 (d, *J*=7.6 Hz, 2H), 7.47 (d, *J*=7.2 Hz, 2H), 7.30-7.24 (m, 4H), 7.18-7.10 (m, 3H), 7.05-7.02 (m, 3H), 6.94-6.92 (m, 1H), 5.30 (d, *J*=10.4 Hz, 1H), 5.12 (t, *J*=11.2 Hz, 1H), 4.48 (d, *J*=11.6 Hz, 1H), 0.73 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 149.2, 148.4, 147.6, 133.6, 133.6, 133.3, 133.2, 133.1, 132.8, 131.7, 131.1, 130.9, 69.6, 63.1, 60.5, 27.3. HRMS (ESI) Calcd for $C_{24}H_{28}NOS$ $[M+H]^+$: 378.1886, Found 378.1872

(*R*)-N-((*R*)-1-(2-chlorophenyl)-2,2-diphenylethyl)-2-methylpropane-2-sulfinamide (4b): Following the general procedure (GP1), the reaction of *N*-*tert*-butanesulfinyl aldimine (R_S) **2b** (200 mg, 0.82 mmol) with biphenyl methane (4.10 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.46 mmol) afforded amine **4b** as white solid (300 mg, 90%). mp = 145–147 °C, $[\alpha]^{20}_D$ = 16.3 (c. 0.25 in $CHCl_3$). IR: 3172, 3062, 2953, 1494, 1450, 1055, 756, 700. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.88-7.86 (m, 1H), 7.50 (d, *J*=7.6 Hz, 2H), 7.33-7.14 (m, 7H), 7.10-7.04 (m, 3H), 6.99-6.95 (m, 1H), 5.55 (dd, *J*=21.6, 10.8 Hz, 1H), 5.38 (d, *J*=9.6 Hz, 1H), 4.59 (d, *J*=11.2 Hz, 1H), 0.74 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 143.6, 142.0, 141.9, 132.8, 129.5,

129.1, 128.8, 128.7, 128.5, 128.4, 127.6, 126.6, 126.6, 60.0, 57.8, 56.0, 22.5. HRMS (ESI) Calcd for $C_{24}H_{27}ClNOS$ $[M+H]^+$: 412.1496, Found 412.1490.

(*R*)-N-((*R*)-1-(2-chloro-4-fluorophenyl)-2,2-diphenylethyl)-2-methylpropane-2-sulfinamide (4c): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2c** (200 mg, 0.76 mmol) with biphenyl methane (3.82 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.29 mmol) afforded amine **4c** as white solid (290 mg, 91%). mp =125–127 ^oC, $[\alpha]^{20}_D$ = 24.9 (c. 0.25 in $CHCl_3$). IR: 3174, 2958, 1604, 1494, 1039, 744, 702. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.96-7.89 (m, 1H), 7.50 (d, *J*=7.6 Hz, 2H), 7.32 (t, *J*=7.6 Hz, 2H), 7.29- 7.13 (m, 5H), 7.13-7.08 (m, 2H), 7.02-6.98 (m, 1H), 5.54 -5.42 (m, 2H), 4.57 (d, *J*=11.2 Hz, 1H), 0.76 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 162.0, 159.6, 143.4, 141.9, 137.6, 133.4, 131.1, 128.8, 128.7, 128.6, 128.4, 126.7, 116.1, 115.9, 115.1, 114.9, 59.6, 57.8, 56.0, 34.0, 22.5, 22.2, 14.3. HRMS (ESI) Calcd for $C_{24}H_{26}ClFNOS$ $[M+H]^+$: 430.1407, Found 430.1410.

(*R*)-N-((*R*)-2, 2-diphenyl-1-(p-tolyl)ethyl)-2-methylpropane-2-sulfinamide (4d): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2d** (250 mg, 1.11 mmol) with biphenyl methane (5.59 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.35 mmol) afforded amine **4d** as white solid (390 mg, 90%). mp =162–164 ^oC, $[\alpha]^{20}_D$ = 50.8 (c. 0.25 in $CHCl_3$). IR: 3290, 3028, 2947, 1494, 1452, 1066, 704. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.52 (d, *J*=7.2 Hz, 2H), 7.35 (d, *J*=7.6 Hz, 2H), 7.34-7.22 (m, 4H), 7.16-7.05 (m, 3H), 7.01-6.94 (m, 3H), 5.18 (d, *J*=10.0 Hz, 1H), 5.07 (t, *J*=10.8 Hz, 1H), 4.47 (d, *J*=11.6 Hz, 1H), 2.17 (s, 3H), 0.72 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.5, 143.0, 140.7, 135.8, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 126.3, 126.2, 64.5, 58.3, 55.7, 22.5, 21.1. HRMS (ESI) Calcd for $C_{25}H_{30}NOS$ $[M+H]^+$: 392.2043, Found 392.2026.

(*R*)-N-((*R*)-1-(4-methoxyphenyl)-2,2-diphenylethyl)-2-methylpropane-2-sulfinamide (4e): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2e** (200 mg, 0.835 mmol) with biphenyl methane (4.17 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.50 mmol) afforded amine **4e** as white solid (323 mg, 95%). mp = 164–166 ^{o}C, $[\alpha]^{20}_{D}$ = 58.6 (c. 0.25 in $CHCl_3$). IR: 3280, 2947, 1585, 1514, 1454, 1244, 1043, 705. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.52 (d, *J*=7.6 Hz, 2H), 7.38 (d, *J*=8.8 Hz, 2H), 7.35-7.21 (m, 4H), 7.16-7.04 (m, 3H), 7.03-6.92 (m, 1H), 6.71 (d, *J*=8.4 Hz, 2H), 5.15 (d, *J*=10.4 Hz, 1H), 5.06 (t, *J*=11.2 Hz, 1H), 4.46 (d, *J*=11.2 Hz, 1H), 3.66 (s, 3H), 0.72 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 158.1, 144.6, 143.1, 135.8, 129.5, 128.9, 128.9, 128.5, 128.5, 126.3, 126.1, 113.5, 64.2, 58.5, 55.7, 55.2, 22.6. HRMS (ESI) Calcd for $C_{25}H_{30}NO2S$ $[M+H]^+$: 408.1992, Found 408.1981.

(*R*)-N-((*R*)-1-(furan-2-yl)-2,2-diphenylethyl)-2-methylpropane-2-sulfinamide (4f): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2f** (250 mg, 1.25 mmol) with biphenyl methane (6.27 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.76 mmol) afforded amine **4f** as white solid (420 mg, 91%). mp =141–143 ^{o}C, $[\alpha]^{20}_{D}$ = 79.7 (c. 0.25 in $CHCl_3$). IR: 3261, 2956, 1496, 1450, 1161, 1060, 705. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.44 (d, *J*=7.2 Hz, 2H), 7.41-7.31 (m, 4H), 7.29-7.21 (m, 2H), 7.19-7.03 (m, 4H), 6.48 (s, 1H), 5.22-5.08 (m, 2H), 4.32 (d, *J*=10.8 Hz, 1H), 0.72 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.3, 143.3, 142.7, 140.5, 128.8, 128.6, 128.6, 128.6, 127.9, 126.4, 126.3, 110.7, 58.2, 56.3, 55.7, 22.6. HRMS (ESI) Calcd for $C_{22}H_{26}NO2S$ $[M+H]^+$: 368.1679, Found 368.1666.

(*R*)-N-((*R*)-2,2-diphenyl-1-(thiophen-2-yl)ethyl)-2-methylpropane-2-sulfinamide (4g): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2g** (200 mg, 0.93 mmol) with biphenyl methane (4.64 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.78 mmol) afforded amine **4g** as white solid (327 mg, 92%). mp =140–142 ^{o}C, $[\alpha]^{20}_{D}$ = 82.7 (c.

0.25 in $CHCl_3$). IR: 3333, 3028, 2985, 1452, 1060, 704. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.49 (d, *J*=7.6 Hz, 2H), 7.36 (d, *J*=7.2 Hz, 2H), 7.32-7.18 (m, 3H), 7.17-7.06 (m, 4H), 7.05-6.95 (m, 1H), 6.82-6.76 (m, 1H), 5.47-5.35 (m, 2H), 4.46 (d, *J*=11.2 Hz, 1H), 0.72 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 147.1, 144.2, 143.0, 128.7, 128.6, 128.5, 126.4, 126.4, 126.3, 125.1, 59.8, 59.3, 55.9, 22.6. HRMS (ESI) Calcd for $C_{22}H_{26}NOS_2$ $[M+H]^+$: 384.1450 Found 384.1438.

(*R*)-2-methyl-N-((*S*,*E*)-1,1,4-triphenylbut-3-en-2-yl)propane-2-sulfinamide (4h): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2h** (300 mg, 1.27 mmol) with biphenyl methane (6.37 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.82 mmol) afforded amine **4h** as white solid (473 mg, 92%). mp =128–130 ^{o}C, $[\alpha]^{20}_D$ = 20.0 (c. 0.25 in $CHCl_3$). IR: 3446, 2922, 1450, 1354, 1047, 748, 700. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.46-7.39 (m, 5H), 7.31-7.15 (m, 8H), 7.15-7.05(m, 2H), 6.55 (d, *J*=15.9 Hz, 1H), 6.18-6.08 (m, 1H), 5.32 (d, *J*=10.0 Hz, 1H), 4.79-4.68 (m, 1H), 4.15 (d, *J*=11.2 Hz, 1H), 0.75 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.0, 143.0, 137.2, 132.4, 131.0, 129.0, 128.9, 128.8, 128.7, 128.5, 127.7, 126.6, 126.4, 126.3, 63.2, 57.9, 55.7, 22.6. HRMS (ESI) Calcd for $C_{26}H_{30}NOS$ $[M+H]^+$: 404.2043, Found 404.2036.

(*R*)-2-methyl-N-((*S*)-1,1,4-triphenylbutan-2-yl)propane-2-sulfinamide (4i): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2i** (300 mg, 1.26 mmol) with biphenyl methane (6.31 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.79 mmol) afforded amine **4i** as white solid (461 mg, 90%). mp = 112–114 ^{o}C, $[\alpha]^{20}_D$ = –34.8 (c. 0.25 in $CHCl_3$). IR: 3481, 3120, 1452, 1016, 700. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.34 (d, *J*=7.6 Hz, 2H), 7.31-7.18 (m, 8H), 7.17-7.12 (m, 2H), 7.11-7.04 (m, 3H), 4.98 (d, *J*=8.8 Hz, 1H), 4.1-4.02 (m, 1H), 3.97 (d, *J*=11.2 Hz, 1H), 2.92- 2.80 (m, 1H), 2.76-2.64 (m, 1H), 1.74-1.66 (m, 2H),

0.75 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.4, 144.0, 142.7, 129.0, 128.9, 128.7, 128.6, 128.6, 128.2, 126.6, 126.3, 126.0, 60.3, 58.7, 55.7, 36.9, 31.2, 22.8. HRMS (ESI) Calcd for $C_{26}H_{32}NOS$ $[M+H]^+$: 406.2199, Found 406.2180.

(*R*)-2-methyl-N-((*S*)-3-methyl-1,1-diphenylbutan-2-yl)propane-2-sulfinamide (4j): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2j** (300 mg, 1.71 mmol) with Biphenyl methane (8.55 mmol) and *n*-Butyllithium (1.6 M in cyclohexane, 5.13 mmol) afforded amine **4j** as white solid (546 mg, 93%). mp =169–171 °C, $[\alpha]^{20}_D$ = 31.7 (c. 0.25 in $CHCl_3$). IR: 3300, 2949, 1450, 1047, 704. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.48-7.38 (m, 4H), 7.32-7.18 (m, 4H), 7.16-7.06 (m, 2H), 4.44-4.37 (m, 1H), 4.06-4.01 (m, 2H), 1.70-1.62 (m, 1H), 1.03 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.8 Hz, 3H), 0.68 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.8, 144.3, 129.0, 129.0, 128.6, 128.3, 126.5, 126.3, 65.7, 56.8, 55.9, 29.3, 22.6, 21.3, 15.3. HRMS (ESI) Calcd for $C_{21}H_{30}NOS$ $[M+H]^+$: 344.2043, Found 344.2027.

(*R*)-2-methyl-N-((*S*)-4-methyl-1,1-diphenylpentan-2-yl)propane-2-sulfinamide (4k): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2k** (300 mg, 1.58 mmol) with biphenyl methane (7.92 mmol) and *n*-BuLi (1.6 M in cyclohexane, 4.75 mmol) afforded amine **4k** as white solid (532 mg, 94%). mp =113–115 °C, $[\alpha]^{20}_D$ = –32.0 (c. 0.25 in $CHCl_3$). IR: 3493, 3103, 1450, 1028, 704. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.42-7.33 (m, 4H), 7.31-7.18 (m, 4H), 7.15-7.05 (m, 2H), 4.76 (d, *J*=8.8 Hz, 1H), 4.09-3.99 (m, 1H), 3.85 (d, *J*=10.6 Hz, 1H), 2.09-2.05 (m, 1H), 1.48-1.39 (m, 1H), 1.09 -1.01 (m, 1H), 0.83 (d, *J*=6.4 Hz, 3H), 0.75 (d, *J*=6.8 Hz, 3H), 0.68 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.6, 144.5, 129.1, 129.0, 128.6, 128.2, 126.6, 126.2, 60.1, 58.9, 55.6, 44.5, 24.4, 23.2, 22.8, 21.7. HRMS (ESI) Calcd for $C_{22}H_{32}NOS$ $[M+H]^+$: 358.2199, Found 358.2188.

(*R*)-N-((*S*)-1,1-diphenylpentan-2-yl)-2-methylpropane-2-sulfinamide (4l): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2l** (200 mg, 1.14 mmol) with biphenyl methane (5.70 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.42 mmol) afforded amine **4l** as white solid (358 mg, 90%). mp = 100–102 ^{o}C, $[\alpha]^{20}_{D}$ = –5.8 (c. 0.25 in $CHCl_3$). IR: 3425, 3107, 1454, 1030, 704. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.41-7.36 (m, 4H), 7.28-7.18 (m, 4H), 7.17-7.06 (m, 2H), 4.77 (d, *J*=9.2 Hz, 1H), 4.04-4.01 (m, 1H), 3.90 (d, *J*=11.2 Hz, 1H),1.59-1.52 (m, 1H), 1.42-1.35 (m, 3H), 0.76 (t, *J*=6.8 Hz, 3H), 0.70 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.6, 144.3, 129.0, 128.9, 128.5, 128.2, 126.5, 126.2, 60.5, 59.1, 55.6, 37.0, 24.4, 22.7, 18.3, 14.4. HRMS (ESI) Calcd for $C_{21}H_{30}NOS$ $[M+H]^+$: 344.2043, Found 344.2027.

(*R*)-2-methyl-N-((*R*)-1-phenyl-2,2-di-p-tolylethyl)propane-2-sulfinamide (4m): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2m** (200 mg, 0.95 mmol) with di-*p*-tolylmethane (4.77 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.86 mmol) afforded amine **4m** as white solid (438 mg, 90%). mp =143–145 ^{o}C, $[\alpha]^{20}_{D}$ = 45.9 (c. 0.25 in $CHCl_3$). IR: 3334, 2978, 2954, 1597, 1494, 1350, 1066, 709. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.45 (d, *J*=7.6 Hz, 2H), 7.37 (d, *J*=7.6 Hz, 2H), 7.20-7.01 (m, 7H), 6.84 (d, *J*=8 Hz, 2H), 5.23 (d, *J*=10.4 Hz, 1H), 5.03 (t, *J*=11.2Hz, 1H), 4.40 (d, *J*=11.2 Hz, 1H), 2.22 (s, 3H), 2.08 (s, 3H), 0.74 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 143.4, 141.2, 141.1, 135.6, 130.9, 130.4, 128.2, 128.1, 128.0, 127.8, 126.8, 126.6, 63.3, 63.2, 56.1, 24.6, 22.7, 20.9. HRMS (ESI) Calcd for $C_{26}H_{32}NOS$ $[M+H]^+$: 406.2199, Found 406.2180.

(*R*)-2-methyl-N-((*R*)-1,1,2-triphenylpropan-2-yl)propane-2-sulfinamide (4n): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl ketimines (R_S) **2n** (200 mg, 0.89 mmol) with Biphenyl methane (4.47 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.68 mmol)

afforded amine **4n** as white solid (438 mg, 88%). mp = 107–109 °C, $[\alpha]^{20}_{D}$ = 108.2 (c. 0.25 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41-7.36 (m, 2H), 7.32-7.18 (m, 10H), 7.03-6.98 (m, 2H), 4.39 (s, 1H), 4.12 (s, 1H), 1.84 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 144.7, 140.1, 139.1, 130.4, 128.1, 128.0, 127.9, 127.4, 127.1, 126.9, 65.3, 63.7, 56.5, 27.2, 22.8. HRMS (ESI) Calcd for $C_{25}H_{30}NOS$ $[M+H]^+$: 392.2043, Found 392.2027.

(*R*)-N-((*R*)-2-(4-fluorophenyl)-1,1-diphenylpropan-2-yl)-2-methylpropane-2-sulfinamide (4o): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl ketimines (R_S) **2o** (200 mg, 0.83 mmol) with biphenyl methane (4.14 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.48 mmol) afforded amine **4o** as white solid (438 mg, 88%). mp = 101–103 °C, $[\alpha]^{20}_{D}$ = 78.3 (c. 0.25 in $CHCl_3$). IR: 3304, 2960, 1598, 1510, 1450, 1348, 1072, 835, 705. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46-7.37 (m, 4H), 7.32-7.22 (m, 4H), 7.22-7.06 (m, 4H), 7.03-6.94 (m, 2H), 5.08 (s, 1H), 4.61 (s, 1H), 1.77 (s, 3H), 0.98 (s, 9H), ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 147.5, 145.7, 145.7, 135.7, 135.1, 134.7, 134.6, 133.0, 132.8, 131.6, 131.4, 118.9, 118.6, 68.0, 67.9, 60.9, 28.9, 27.4. HRMS (ESI) Calcd for $C_{25}H_{29}FNOS$ $[M+H]^+$:410.1948, Found 410.1929.

(*R*)-2-benzhydryl-1-((*R*)-tert-butylsulfinyl)-2-phenylpyrrolidine (4p): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl ketimines **2p** (200 mg, 0.7 mmol) with biphenyl methane (3.50 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.10 mmol) afforded amine **4p** as white solid (438 mg, 92%). mp =128–130 °C, $[\alpha]^{20}_{D}$ = 73.2 (c. 0.25 in $CHCl_3$). IR: 3088, 2929, 1494, 1450, 1359, 1064, 714. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.31-7.20 (m, 8H), 7.16-7.08 (m, 5H), 7.05-6.98 (m, 2H), 5.14 (s, 1H), 3.67-3.58 (m, 1H), 2.73-2.64 (m, 1H), 2.33-2.25 (m, 1H), 2.21-2.09 (m, 1H), 1.47-1.39 (m, 1H), 1.12-1.08 (m, 1H), 0.79 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 146.5, 146.2, 146.0, 136.3, 136.0, 133.8, 132.7, 132.7, 132.3, 132.3,

131.9, 131.2, 82.5, 63.6, 63.1, 28.6, 28.1. HRMS (ESI) Calcd for $C_{27}H_{32}NOS$ $[M+H]^+$: 418.2199, Found 418.2179.

Ethyl (*R*)-2-(((*R*)-tert-butylsulfinyl)amino)-3,3-diphenylpropanoate (4q): A solution of biphenyl methane (4.87 mmol) in THF (2.5 mL) was cooled to 0 ^oC then *n*-BuLi (1.6 M in cyclohexane, 2.92 mmol) was added dropwise via syringe and the resulting reaction mixture was stirred for 1 h at 0 ^oC. To the reaction mixture $ZnCl_2$ (0.5 M solution in THF, 4.87 mmol) was added at 0 ^oC and stirred for 1 h. After that the reaction mixture was cooled to -78 ^oC and *N-tert*-butanesulfinyl aldimine (R_S) **2q** (200 mg, 0.97 mmol in 0.5 mL of THF) was added dropwise via syringe over the period of 30 min. The reaction mixture was allowed to come at -40 ^oC and stirred for 8 h at -40 ^oC. After completion of reaction, it was quenched with water (5 mL) and warmed to room temperature over the period of 30 min. The reaction mixture was extracted with ethyl acetate (3 X 5 mL) and combined organic layers was washed with water (1 X 5 mL) and oncentrated under vacum to dryness to obtained crude compound. The crude compound was purified by column chromatography using ethyl acetate/hexanes to afford amine **4q** as white solid (438 mg, 83%). mp =89–91 ^oC, $[\alpha]^{20}_D$ = 44.1 (c. 0.25 in $CHCl_3$). IR: 3028, 2927, 1735, 1598, 1494, 1452, 1346, 1037, 702. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.46-7.34 (m, 4H), 7.31-7.22 (m, 4H), 7.21-7.13 (m, 2H), 5.73 (dd, *J*=10.4, 7.2 Hz, 1H), 4.70-4.51 (m, 1H), 4.40-4.33 (m, 1H), 3.89-3.81 (m, 2H), 0.87-0.78 (m, 12H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 172.7, 142.1, 141.1, 129.0, 128.8, 128.6, 128.5, 127.2, 126.7, 63.1, 60.5, 56.1, 54.5, 22.6, 13.9. HRMS (ESI) Calcd for $C_{21}H_{28}NO_3S$ $[M+H]^+$: 374.1784, Found 374.1778.

(*R*)-N-((S)-(2-methoxy-5-(4-methoxybenzyl)phenyl)(phenyl)methyl)-2-methylpropane-2-sulfinamide (5a): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2a** (200 mg, 0.95 mmol) with bis(4-methoxyphenyl)methane (4.77 mmol) and *n*-

BuLi (1.6 M in cyclohexane, 2.86 mmol) afforded amine **5a** as white solid (384 mg, 92%). mp = 98–100 °C, $[\alpha]^{20}_D$ = –6.7 (c. 0.25 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.42-7.36 (m, 2H), 7.36-7.21 (m, 3H), 7.13-7.05 (m, 3H), 6.84-6.77 (m, 3H), 6.02 (s, 1H), 3.91(s, 2H), 3.82 (s, 3H), 3.77(s, 3H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.9, 155.3, 142.5, 133.6, 133.4, 129.8, 129.6, 128.7, 128.5, 127.5, 127.4, 113.8, 110.9, 56.3, 55.8, 55.6, 55.3, 40.3, 22.6. HRMS (ESI) Calcd for $C_{26}H_{32}NO_3S$ $[M+H]^+$: 438.2097, Found 438.2078.

(*R*)-N-((*S*)-(2-methoxy-5-(4-methoxybenzyl)phenyl)(p-tolyl)methyl)-2-methylpropane-2-sulfinamide (5d): Following the general procedure (GP1), the reaction of *N*-*tert*-butanesulfinyl aldimine (R_S) **2d** (247 mg, 1.11 mmol) with bis(4-methoxyphenyl)methane (5.59 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.35 mmol) afforded amine **5d** as white solid (460 mg, 92%). mp =107–108 °C, $[\alpha]^{20}_D$ = –61.8 (c. 0.25 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.32 (s, 1H), 7.21-7.15 (m, 2H), 7.12-7.02 (m, 5H), 6.90-6.80 (m, *3*H), 5.75 (d, *J*=5.6 Hz, 1H), 5.58 (d, *J*=5.6 Hz, 1H), 3.79 (s, 2H), 3.71(s, 6H), 2.25 (s, 3H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.9, 155.3, 139.5, 137.1, 133.7, 133.4, 129.8, 129.7, 129.2, 128.6, 128.6, 127.4, 113.8, 110.8, 56.0, 55.8, 55.6, 55.3, 40.3, 22.6, 21.1. HRMS (ESI) Calcd for $C_{27}H_{34}NO_3S$ $[M+H]^+$: 452.2260, Found 452.2284.

(*R*)-N-((*R*)-furan-2-yl(2-methoxy-5-(4-methoxybenzyl)phenyl)methyl)-2-methylpropane-2-sulfinamide (5f): Following the general procedure (GP1), the reaction of *N*-*tert*-butanesulfinyl aldimine (R_S) **2f** (248 mg, 1.25 mmol) with bis(4-methoxyphenyl)methane (6.27 mmol) and *n*-BuLi (1.6 M in cyclohexane, 3.76 mmol) afforded amine **5f** as white solid (490 mg, 92%). mp =113–115 °C, $[\alpha]^{20}_D$ = –24.2 (c. 0.25 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.38-7.17 (m, 3H), 7.14-7.06 (m, 3H), 6.88-6.80 (m, 3H), 6.40 (s, 1H), 5.87 (s, 1H), 3.90 (s, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.9, 155.1, 143.2, 140.2,

133.6,133.5, 129.7, 129.4, 128.8, 128.5, 127.8, 113.8, 110.9, 110.0, 55.8, 55.6, 55.3, 50.1, 40.2, 22.5. HRMS(ESI) Calcd for $C_{24}H_{30}NO_4S$ $[M+H]^+$: 428.1890, Found 428.1874.

(*R*)-N-((*R*)-(2-methoxy-5-(4-methoxybenzyl)phenyl)(thiophen-2-yl)methyl)-2-methylpropane-2-sulfinamide (5g): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2g** (200 mg, 0.93 mmol) with bis(4-methoxyphenyl)methane (4.64 mmol) and *n*- BuLi (1.6 M in cyclohexane, 2.78 mmol) afforded amine **5g** as white solid (387 mg, 94%). mp =117–119 ^oC, $[\alpha]^{20}_D$ = –24.5 (c. 0.25 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.22 (m, 2H), 7.17-7.05 (m, 4H), 6.94-6.91 (m, 1H), 6.90-6.80 (m, 3H), 6.26-6.21 (m, 1H), 3.97-3.93 (m, 1H), 3.91 (s, 2H), 3.82 (s, 6H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.8, 155.2, 146.7, 133.6, 133.5, 129.8, 129.5, 129.1, 128.5, 126.7, 125.4, 125.0, 113.8, 111.0, 55.9, 55.6, 55.2, 52.6, 40.2, 22.5. HRMS (ESI) Calcd for $C_{24}H_{30}NO_3S_2$ $[M+H]^+$: 444.1662, Found 444.1647.

(*R*)-N-((*S*)-1-(2-methoxy-5-(4-methoxybenzyl)phenyl)-2-methylpropyl)-2-methylpropane-2-sulfinamide (5j): Following the general procedure (GP1), the reaction of *N-tert*-butanesulfinyl aldimine (R_S) **2j** (170 mg, 0.95 mmol) with bis(4-methoxyphenyl)methane (4.77 mmol) and *n*-BuLi (1.6 M in cyclohexane, 2.86 mmol) afforded amine **5j** as white solid (365 mg, 95%). mp =122–124 ^oC, $[\alpha]^{20}_D$ = –52.8(c. 0.25 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.10-7.02 (m, 3H), 6.99 (s, 1H), 6.85-6.81 (m, 3H), 4.50-4.46 (m, 1H), 3.88 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.74-3.70 (m, 1H), 2.10-2.04 (m, 1H), 1.10 (s, 9H), 1.01(d, *J*=6.4 Hz, 3H), 0.86 (d, *J*=6.8 Hz,3H), . ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.8, 155.5, 133.7, 133.1, 129.7, 129.5, 128.2, 113.8, 110.7, 55.5, 55.5, 55.3, 40.2, 33.8, 22.4, 19.6, 19.0. HRMS (ESI) Calcd for $C_{23}H_{34}NO_3S$ $[M+H]^+$: 404.2254, Found 404.2244.

General procedure (GP2): A solution of α-(diarylmethyl) alkyl amines (1.0 mmol) in 1,4-Dioxane (1 mL) was added HCl (4.0 M solultion in 1,4-Dioxane, 10.0 mmol) at room temperature. It was stirred at room temperature for 2 h and then reaction mixture was concentrated under vacuo. The crude was diluted with water (2 ml) and ethyl acetate (5 mL) and pH was adjust to 12-13 using 6 *M* NaOH aqueous solution. It was extracted with ethyl acetate (3 x 5 mL) and combined organic layer was concentrated under vacuum to obtain product.

(*S*)-3-methyl-1,1-diphenylbutan-2-amine (1j): Following the general procedure (GP2), the reaction of α-(diarylmethyl) alkyl amines **4j** (100 mg, 0.29 mmol) with HCl (4.0 M in dioxane, 2.9 mmol, 0.72 mL) afforded amine **1j** as white solid (69 mg, 99%). mp = 70–71 ^{o}C, $[\alpha]^{20}_{D}$ = –4.1 (c. 1.0 in $CHCl_3$), reported –4.2 (c, 10.9 in $CHCl_3$). IR: 3361, 30 64, 3024, 2958, 2926, 1597, 1490, 1450, 1361, 748, 702. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.48-7.42 (m, 2H), 7.40-7.34 (m, 2H), 7.27-7.21 (m, 4H), 7.18-7.08 (m, 2H), 3.74 (d, *J*=10.8 Hz, 1H), 3.50 (dd, *J*=10.8, 2.0 Hz, 1H), 1.54-1.47 (m, 1H), 0.98 (bs, 2H), 0.90 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.7, 144.5, 128.9, 128.7, 128.3, 126.4, 126.3, 57.9, 57.7, 28.9, 21.5, 14.1. HRMS (ESI) Calcd for $C_{17}H_{22}N$ $[M+H]^{+}$: 240.1747, Found 240.1750.

(*S*)-4-methyl-1,1-diphenylpentan-2-amine (1k): Following the general procedure (GP2), the reaction of α-(diarylmethyl) alkyl amines **4k** (100 mg, 0.28 mmol) with HCl in dioxane (4.0 M in dioxane, 2.8 mmol, 0.7 mL) afforded amine **1k** as white solid (70 mg, 99%). mp = 48–50 ^{o}C, $[\alpha]^{20}_{D}$ = –32.0 (c. 1.0 in $CHCl_3$) reported –31.6 (c, 4.1 in $CHCl_3$). IR: 3379, 3026, 2953, 2900, 1597, 1494, 1450, 1355, 1080, 744, 704. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.44-7.39 (m, 2H), 7.36-7.24 (m, 6H), 7.19-7.10 (m, 2H), 3.62-3.53 (m, 2H), 1.83-1.78 (m, 1H), 1.25-1.17 (m,

2H), 1.10- 0.96 (m, 2H), 0.83-0.75 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 144.6, 144.3, 128.9, 128.8, 128.8, 128.3, 126.5, 126.4, 61.1, 51.8, 45.3, 24.6, 24.6, 21.7. HRMS (ESI) Calcd for $C_{18}H_{24}N$ $[M+H]^+$: 254.1903, Found 254.1898

Supporting Information Available: Copies of NMR spectra of all the compounds and X-ray crystallography data of compound **5j**. This material is available free of charge via the Internet at http://pubs.acs.org.

Acknowledgment

We thank Mr.Vivek Sharma and Suresh Raghava (Piramal Enterprises Limited) for valuable support.

References

(1) (a) Harris, J. M.; Neustadt, B. R.; Sorota, S. C.; Stamford, A. W.; Tulshian, D.; Mckittrick, *PCT Int. Appl.* **2008**, WO 2008033460 (b) Appell, R. B.; Boulton, L. T.; Daugs, E. D.; Hansen, M.; Hanson, C. H.; Heinrich, J.; Kronig, C.; Lloyd, R. C.; Louks, D.; Nitz, M. The Large-Scale Synthesis of (S)-N-Boc-bis(4-fluorophenyl)alanine. *Organic Process Research & Development* **2013**, *17*, 69. (c) Michael, J. E.; Alan, S.; Erik, J. S.; & Benjamin, F. C. Target discovery in small-molecule cell-based screens by in situ proteome reactivity profiling. *Nature Biotechnology* **2005**, *23*, 1303. (d) Daniel, P. I.; Christian, W. A Stereodynamic Probe Providing a Chiroptical Response to Substrate-Controlled Induction of an Axially Chiral Arylacetylene Framework. *J. Am. Chem. Soc*. **2011**, *133*, 2414.

(2) (a) Bailey, D. J.; O'Hagan, D.; Tavasli, M. A short synthesis of (*S*)-2-(diphenylmethyl)pyrrolidine, a chiral solvating agent for NMR analysis. Tetrahedron: Asymmetry **1997**, *8*, 149. (b) O'Hagan, D.; Tavasli, M. A short synthesis of (*S*)-α-

(diphenylmethyl)alkyl amines from amino acids. Tetrahedron: Asymmetry **1999**, *10*, 1189.

(3) (a) Ellman, J. A.; Owens, T. D.; Tang, T. P. *N-tert*-Butanesulfinyl Imines: Versatile Intermediates for the Asymmetric Synthesis of Amines. *Acc. Chem. Res*. **2002**, *35*, 984. (b) Ellman, J. A. Applications of tert-butanesulfinamide in the asymmetric synthesis of amines. *Pure Appl. Chem*. **2003**, *75*, 39. (c) Ferreira, F.; Botuha, C.; Chemla, F.; Perez-Luna, A. tert-Butanesulfinimines: structure, synthesis and synthetic applications. *Chem. Soc. Rev*. **2009**, *38*, 1162 (d) Robak, M. T.; Herbage, M. A.; Ellman, J. A. Synthesis and Applications of tert-Butanesulfinamide. *Chem. Rev*. **2010**, *110*, 3600.

(4) *N-tert*-butanesulfinyl aldimines and Ketimines are prepared as per our previously reported procedures (a) Rajender, L.R.; Bin, H.; Prashad, M.; Prasad, K. Asymmetric Synthesis of Homoallylic Amines Bearing Adjacent Stereogenic Centers by Addition of Substituted Allylic Zinc Reagents to *N-tert*-Butanesulfinylimines. *Org. Lett.,* **2008**, *10*, 3109. (b) Reddy, L.R.; Sonia, G. D.; Liu, Y.; Prashad, M. A Facile Asymmetric Synthesis of Either Enantiomer of 2-Substituted Pyrrolidines. *J. Org. Chem*. **2010**, *75*, 2236. (c) Reddy, L.R.; Aditya, P.G.; Eric, V.; Liu, Y. Rhodium-Catalyzed Asymmetric Arylation of *N*-(*tert*-Butanesulfinyl)imines with Sodium Tetraarylborates. *J. Org. Chem*. **2012**, *77*, 1095. (d) Reddy, L.R.; Aditya, P.G.; Liu, Y.Asymmetric Synthesis of α-Amino Acids by Reduction of N-tert-Butanesulfinyl Ketimine Esters. *J. Org. Chem*. **2011**, *76*, 3409. (e) Reddy, L.R.; Prashad, M.; Prasad, K. A Protocol for an Asymmetric Synthesis of γ-Amino Acids. *J. Org. Chem*. **2012**, *77*, 6296 (f) Reddy, L.R.; Prashad, M. Asymmetric synthesis of 2-substituted pyrrolidines by addition of Grignard reagents to γ-chlorinated *N-tert*-butanesulfinyl imine. *Chem. Commun*. **2010**, *46*, 222.

(5) **Preparation 3-Li**: To stirred solution of **3** (2.0 mmol) in THF at 0 ^{o}C *n*-BuLi (1.9 mmol) was added dropwise and stirred for 1 h at the same temperature afford **3-Li** reagent.

(6) (a) Snieckus, V. Directed ortho metalation. Tertiary amide and O-carbamate directors in synthetic strategies for polysubstituted aromatics. *Chem. Rev.* **1990**, *90*, 879. (b) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. Beyond Thermodynamic Acidity: A Perspective on the Complex-Induced Proximity Effect (CIPE) in Deprotonation Reactions. *Angew. Chem. Int. Ed*. **2004**, *43*, 2206. (c) Steffen, P.; Unkelbach, C.; Christmann, M.; Hiller, W.; Strohmann, C. Catalytic and Stereoselective ortho-Lithiation

of a Ferrocene Derivative. *Angew. Chem. Int. Ed*. **2013**, *52*, 9836. (d) Jastrzebski, J. T.; Arink, A. M.; Kleijn, H.; Braam, T. W.; Lutz, M.; Spek, A. L.; van Koten, G. Directed *ortho*-Lithiation: Observation of an Unexpected 1-Lithio to 3-Lithio Conversion of 1-Lithio-naphthyllithium Compounds with an *ortho*-Directing 2-(Dimethylamino)methyl Group.*J. Am. Chem. Soc*. **2013**, *135*, 13371. (e) Mallardo, V.; Rizzi, R.; Sassone, F. C.; Mansueto, R.; Perna, F. M.; Salomone, A.; Capriati, V. Regioselective desymmetrization of diaryltetrahydrofurans *via* directed *ortho*-lithiation: an unexpected help from green chemistry. *Chem. Commun*. **2014**, *50*, 8655. (f) Rouquet, G.; Blakemore, D. C.; Ley, S. V. Highly regioselective lithiation of pyridines bearing an oxetane unit by *n*-butyllithium. *Chem. Commun*. **2014**, *50*, 8908. (g) Slocum, D. W.; Reinscheld, T. K.; White, C. B.; Timmons, M. D.; Shelton, P. A.; Slocum, M. G.; Sandlin, R. D.; Holland, E. G.; Kusmic, D.; Jennings, J. A.; Tekin, K. C.; Nguyen, Q.; Bush, S. J.; Keller, J. M.; Whitley, P. E. *ortho*-Lithiations Reassessed: the Advantages of Deficiency Catalysis in Hydrocarbon Media. *Organometallics* **2013**, *32*, 1674.