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# Asymmetric synthesis of cyclic α-amino acid derivatives by the intramolecular reaction of magnesium carbenoid with an *N*-magnesio arylamine

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ABSTRACT

The synthesis of pipecolic acid and homopipecolic acid derivatives was developed from ω-(2-aminophenyl)-1-chloroalkyl *p*-tolyl sulfoxides by treatment with *i*-PrMgCl. An intramolecular nucleophilic substitution reaction of a magnesium carbenoid with an *N*-magnesio arylamine is the key step of this reaction. Proline and pipecolic acid derivatives were also synthesized from ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxides by the same chemistry. Starting from enantiomerically pure (1*S*,$R_S$)-1-chloro-3-[2-(*N*-methylamino)phenyl]propyl *p*-tolyl sulfoxide, enantiomerically pure (*R*)-pipecolic acid derivative was obtained. The intramolecular nucleophilic substitution reaction of the magnesium carbenoid with *N*-magnesio arylamine was proven to take place with inversion of the carbenoid carbon. The stereochemistry of these reactions is also discussed.

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## 1. Introduction

α-Amino acids are obviously one of the most important sets of compounds in organic chemistry. They are fundamental building blocks of peptides, proteins, and many natural products and play essential roles in living organisms. Innumerable studies concerning the chemistry and synthesis of α-amino acids and their derivatives have been performed and reviewed.[1] Cyclic α-amino acids and their derivatives have recently received considerable attention. They are conformationally constrained, and used in controlling peptide secondary structures in medicinal chemistry.[2]

We have also been interested in the synthesis of α-amino acid derivatives and reported several new methods for their synthesis.[3] In addition, we recently reported a novel one-pot synthesis of α-amino acid derivatives **4** from 1-chloroalkyl phenyl sulfoxides **1** by the intermolecular nucleophilic substitution of magnesium carbenoid with *N*-lithio arylamines as the key reaction (Scheme 1). Thus, magnesium carbenoid **2** was generated from **1** with *i*-PrMgCl via the sulfoxide–magnesium exchange reaction; compound **2** was then treated with an *N*-lithio arylamine to afford *N*-α-magnesioalkyl arylamine **3**. Finally, the α-amino carbanion **3** was trapped with ethyl chloroformate to give α-amino acid ester **4** in good yield.[4]

In continuation of our interest in the synthesis of α-amino acids by our original method, we recently investigated an intramolecular version of the aforementioned reaction and found that it was successful.[5] The essence of this investigation is shown in Scheme 1. Thus, treatment of ω-(2-aminophenyl)-1-chloroalkyl *p*-tolyl sulfoxide **5** with *i*-PrMgCl followed by ethyl chloroformate gave cyclic α-amino acid derivative **7** through α-amino-substituted alkylmagnesium intermediate **6**. When enantiomerically pure (1*S*,$R_S$)-1-chloro-3-[2-(*N*-methylamino)phenyl]propyl *p*-tolyl sulfoxide **5** ($n = 1$) was used as the starting material, enantiomerically pure (*R*)-pipecolic acid derivative **7** ($n = 1$) was obtained. In a similar manner, treatment of ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxide **8** with *i*-PrMgCl followed by ethyl chloroformate gave the proline derivative and pipecolic acid derivative **10** through α-amino-substituted alkylmagnesium intermediate **9**. Details of the aforementioned procedure and the stereochemistry of the reactions are described herein.

## 2. Results and discussion

### 2.1. Synthesis of cyclic α-amino acid derivatives from ω-(2-aminophenyl)-1-chloroalkyl *p*-tolyl sulfoxides

In order to examine the feasibility of the intramolecular version of the key reaction, we first synthesized ω-(2-aminophenyl)-1-chloroalkyl *p*-tolyl sulfoxides with different lengths of the methylene chain **5a**–**5d** as shown in Scheme 2. 2-(2-Aminophenyl)-1-chloroethyl *p*-tolyl sulfoxide **5a** was synthesized from the known benzyl bromide **11**.[6] Alkylation of the α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxide with **11** in THF containing HMPA

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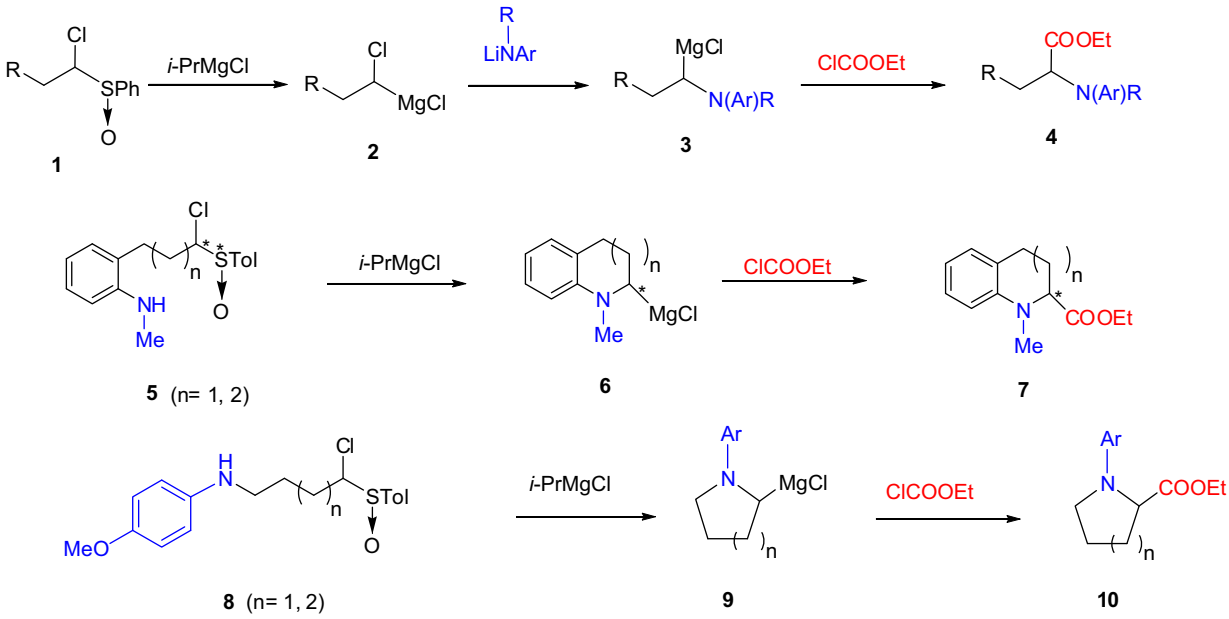



**Scheme 1.**

afforded **12** in 65% yield. The Boc group was removed with trifluoroacetic acid (TFA) to give the desired **5a** in high yield.

3-(2-Aminophenyl)-1-chloropropyl *p*-tolyl sulfoxide **5b** was synthesized from 3,4-dihydro-2(1*H*)-quinolinone **13**. Thus, a methoxymethyl group was introduced on the nitrogen of **13** and the product was reduced with $NaBH_4$ to give aminoalcohol **14** in high overall yield.[7] The nitrogen in **14** was protected by a Boc group to afford **l5**, which was converted to sulfide **16** via a conventional procedure. Chlorination followed by oxidation of **16** gave sulfoxide **17** in good overall yield. Finally, the Boc protecting group was removed to afford the desired **5b**.

4-(2-Aminophenyl)-1-chlorobutyl *p*-tolyl sulfoxide **5c** was synthesized from **15**. Thus, the hydroxyl group in **15** was converted to an iodo group to give iodide **18**. Alkylation of lithium α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxide with **18** in THF afforded **19**, which was treated with TFA to give the desired **5c** in good overall yield.

5-(2-Aminophenyl)-1-chloropentyl *p*-tolyl sulfoxide **5d** was synthesized from **18**. At first, *tert*-butyl acetate was alkylated with iodide **18** to give ester **20** in quantitative yield. The ester group was reduced with DIBAL-H to give an alcohol, which was converted to sulfide to give **21**. Sulfide **21** was chlorinated and then oxidized as above to give sulfoxide **22** in high overall yield. Finally, the Boc group was removed with TFA to afford the desired **5d**.

The key reaction, intramolecular nucleophilic substitution reaction of the magnesium carbenoid with *N*-magnesio arylamine, was at first investigated with amino sulfoxide **5b** as a representative example (Scheme 3). Examination for the optimized conditions was carried out and the results were reported.[5] Thus, to a solution of **5b** in toluene at −40 °C was added *t*-BuMgCl (1.3 equiv) and the reaction mixture was stirred for 5 min to generate magnesium amide. Then, *i*-PrMgCl (2.5 equiv) was added to the reaction mixture and the reaction mixture was stirred for 5 min (the magnesium carbenoid was generated and the intramolecular reaction proceeded to afford intermediate **6a**) after which ethyl chloroformate (5 equiv) was added. By these treatments the desired pipecolic acid derivative **7a** was obtained in 66% yield. The same treatment of **5c** gave homopipecolic acid derivative **7b**, via intermediate **6b**, in 68% yield.

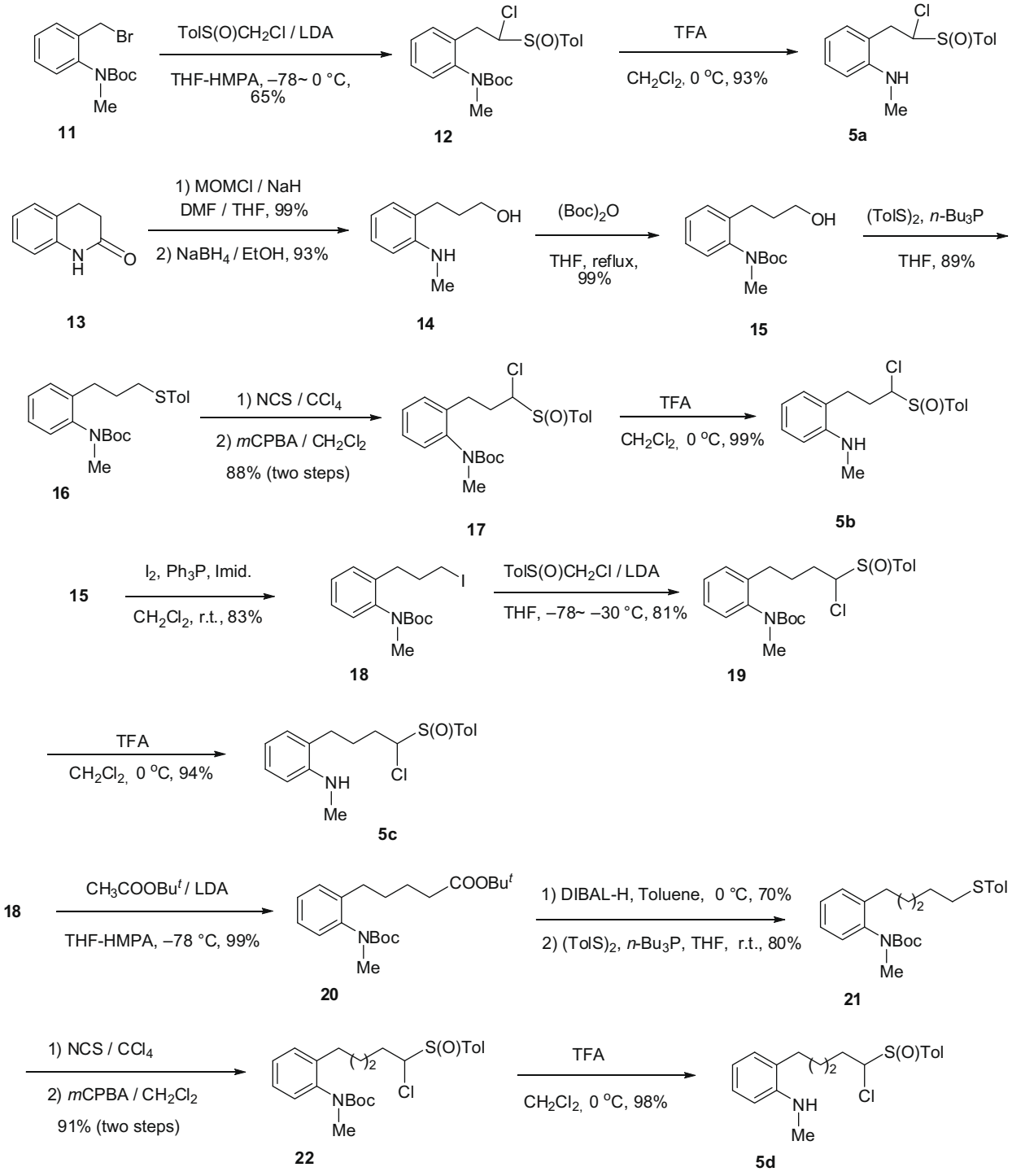
Although the synthesis of six- and seven-membered cyclic α-amino acid derivatives **7a** and **7b** was successful, the synthesis of five- and eight-membered cyclic α-amino acid derivatives from **5a** and **5d** was problematic. The same treatment of **5a** with *i*-PrMgCl followed by ethyl chloroformate gave styrene derivative **23** in 83% yield. Production of the thermodynamically stable olefin conjugated with an aromatic ring is thought to be the reason for the difficulty of the cyclization. The same treatment of **5d** again did not give the desired cyclic α-amino acid derivative but instead gave olefin **24** in 46% yield. From this result, it was proven that the formation of 8-membered ring by this method is quite difficult.

### 2.2. Synthesis of cyclic α-amino acid derivatives from ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxides

In continuation of the study described above, we investigated the intramolecular reaction with ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxides **8**. Starting materials **8a–c** were synthesized from 4-iodoanisole and ω-amino-1-alkanols as shown in Scheme 4. The synthesis of **8a** is described as a representative example. Thus, coupling of 4-iodoanisole and 3-amino-1-propanol promoted by L-proline gave aminoalcohol **25**.[8] The nitrogen in **25** was protected with Boc group and the hydroxyl group was converted to an iodo group to give iodide **26** in quantitative yield. Alkylation of the lithium α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxide with **26** followed by deprotection of the Boc group with TFA afforded the desired **8a** in 77% overall yield from 3-amino-1-propanol. 5-(4-Methoxyphenylamino)-1-chloropentyl *p*-tolyl sulfoxide **8b** and 6-(4-methoxyphenylamino)-1-chlorohexyl *p*-tolyl sulfoxide **8c** were synthesized from 4-iodoanisole and 4-amino-1-butanol and 5-amino-1-pentanol, respectively, in the same way as described above.

The intramolecular nucleophilic substitution reaction of the magnesium carbenoid with *N*-magnesio arylamine, the key reaction, was investigated using **8a** as a representative example (Scheme 4). Examination for the optimized conditions was carried out and the results were reported.[5] Thus, 3.5 equiv of *i*-PrMgCl was added to a solution of **8a** in THF at −78 °C and the temperature of the reaction mixture was allowed to warm to −40 °C. Ethyl chloroformate (5 equiv) was added to the reaction mixture to give the desired proline derivative **10a** in 59% yield.

The reaction is thought to proceed as follows: Removal of the hydrogen on the nitrogen and the sulfoxide–magnesium exchange reaction proceeded simultaneously to afford magnesium carbenoid



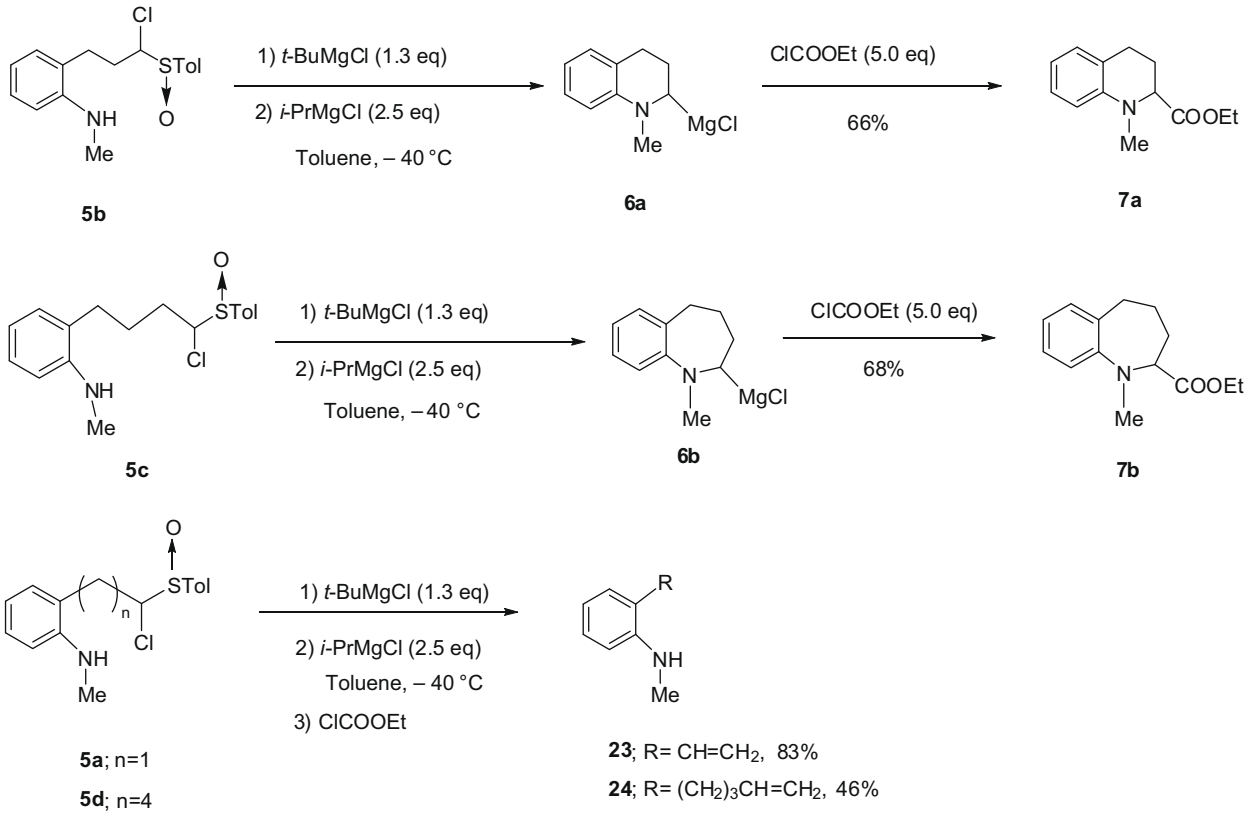

**Scheme 2.** Synthesis of ω-(2-aminophenyl)-1-chloroalkyl *p*-tolyl sulfoxides **5a**–**5d**.

intermediate **27**. The nucleophilic substitution reaction of the magnesium carbenoid with *N*-magnesio arylamine took place intramolecularly to afford α-aminoalkylmagnesium intermediate **9a**, which reacted with ethyl chloroformate to give proline derivative **10a**.

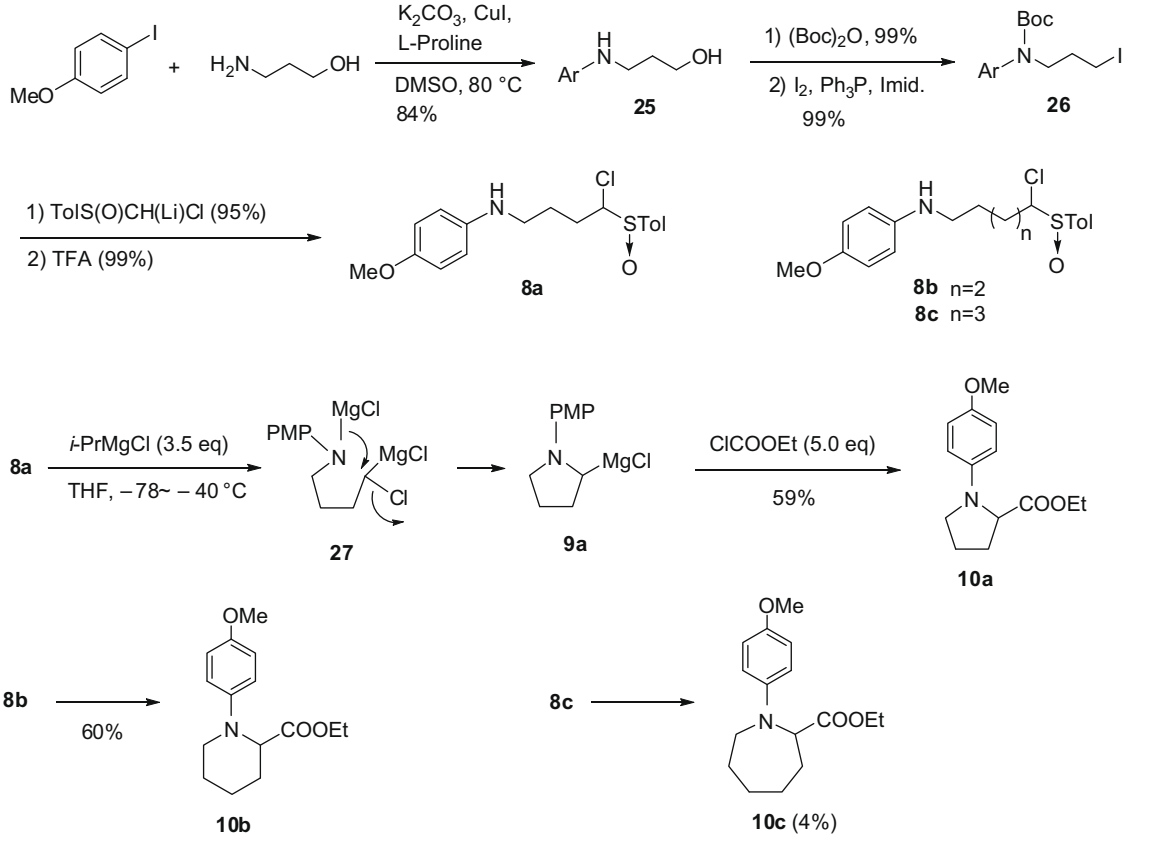
In order to investigate the scope and limitations of this reaction, ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxides with a longer carbon chain than **8a** were treated with *i*-PrMgCl followed by ethyl chloroformate (Scheme 4). Treatment of **8b** with *i*-PrMgCl followed by ethyl chloroformate afforded the desired *N*-arylpipecolic acid ethyl ester **10b** in 60% yield. Unfortunately, similar treatment of the one-carbon homologated sulfoxide **8c** gave a rather complex mixture from which the desired **10c** was obtained in only 4% yield.

### 2.3. Asymmetric synthesis of pipecolic acid derivative from enantiomerically pure (1*S*,$R_S$)-1-chloro-3-(2-methylaminophenyl)-propyl *p*-tolyl sulfoxide through a chiral magnesium carbenoid

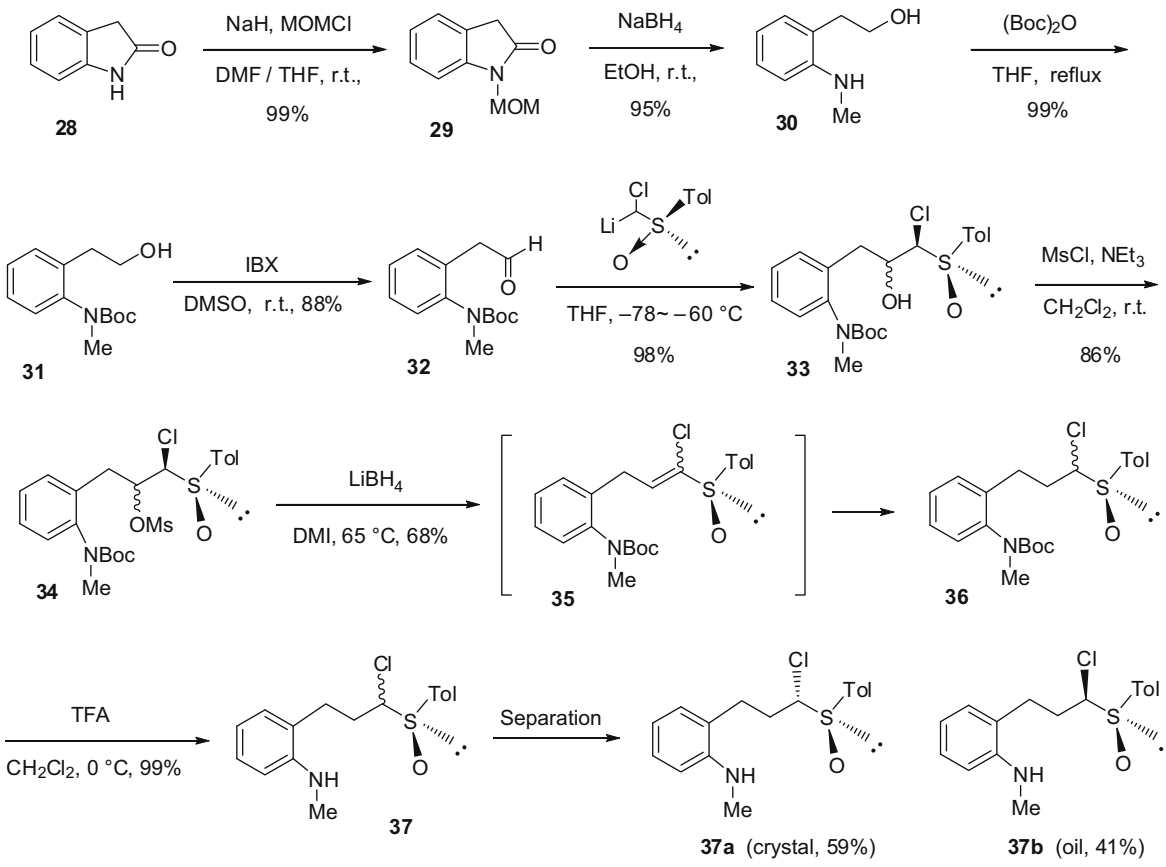
In order to investigate if the above-mentioned procedure could be expanded to an asymmetric synthesis of cyclic α-amino acid derivatives and to investigate the stereochemistry of the key




**Scheme 3.** Intramolecular reaction of magnesium carbenoid with *N*-magnesio arylamine.




**Scheme 4.** Synthesis of ω-(arylamino)-1-chloroalkyl *p*-tolyl sulfoxides and the intramolecular reaction.




**Scheme 5.** Synthesis of (1*S*,$R_S$)-3-(2-methylaminophenyl)-1-chloropropyl *p*-tolyl sulfoxide **37a**.

reaction, we tried the procedure with optically active starting material. At first, enantiomerically pure starting material, (1*S*,$R_S$)-1-chloro-3-(2-methylaminophenyl)propyl *p*-tolyl sulfoxide **37a** was synthesized from oxindole **28** (Scheme 5).

A methoxymethyl group was introduced on the nitrogen of **28** to give **29**, which was reduced with $NaBH_4$ to give aminoalcohol **30** in high overall yield.[7] The nitrogen of **30** was protected with a Boc group and the hydroxyl group was oxidized with IBX in DMSO to give aldehyde **32** in good yield. Aldehyde **32** was treated with the lithium α-sulfinyl carbanion of (*R*)-chloromethyl *p*-tolyl sulfoxide[9] to afford a mixture of adducts **33**,[10] which was treated with methanesulfonyl chloride to give mesylate **34** as a mixture of two diastereomers.

Reductive removal of the mesyl group was found to be problematic. After some investigation, treatment of **34** with $LiBH_4$ in 1,3-dimethylimidazolidin-2-one (DMI) at 65 °C was found to be the conditions of choice. This reduction gave 1-chloroalkyl *p*-tolyl sulfoxide **36**; however, unexpectedly, the product was an inseparable mixture of two diastereomers with respect to the carbon bearing the chlorine atom. This reduction was thought to proceed via β-elimination (to give vinyl sulfoxide **35**)[11] followed by conjugate addition of the hydride to the double bond. The evidence for the above assumption is that in some experiments, a trace of vinyl sulfoxide **35** was obtained. Deprotection of the Boc group in **36** gave **37** and, fortunately, diasteromers **37a** and **37b** were separable by silica gel column chromatography. Main product **37a** is a crystalline compound and its absolute configuration was determined by X-ray crystallographic analysis and the ORTEP drawing is shown in Figure 1.[12]

Finally, enantiomerically pure 1-chloroalkyl-*p*-tolyl sulfoxide **37a** was treated with *t*-BuMgCl followed by *i*-PrMgCl and ethyl

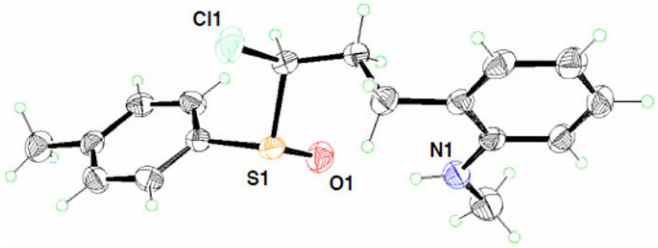
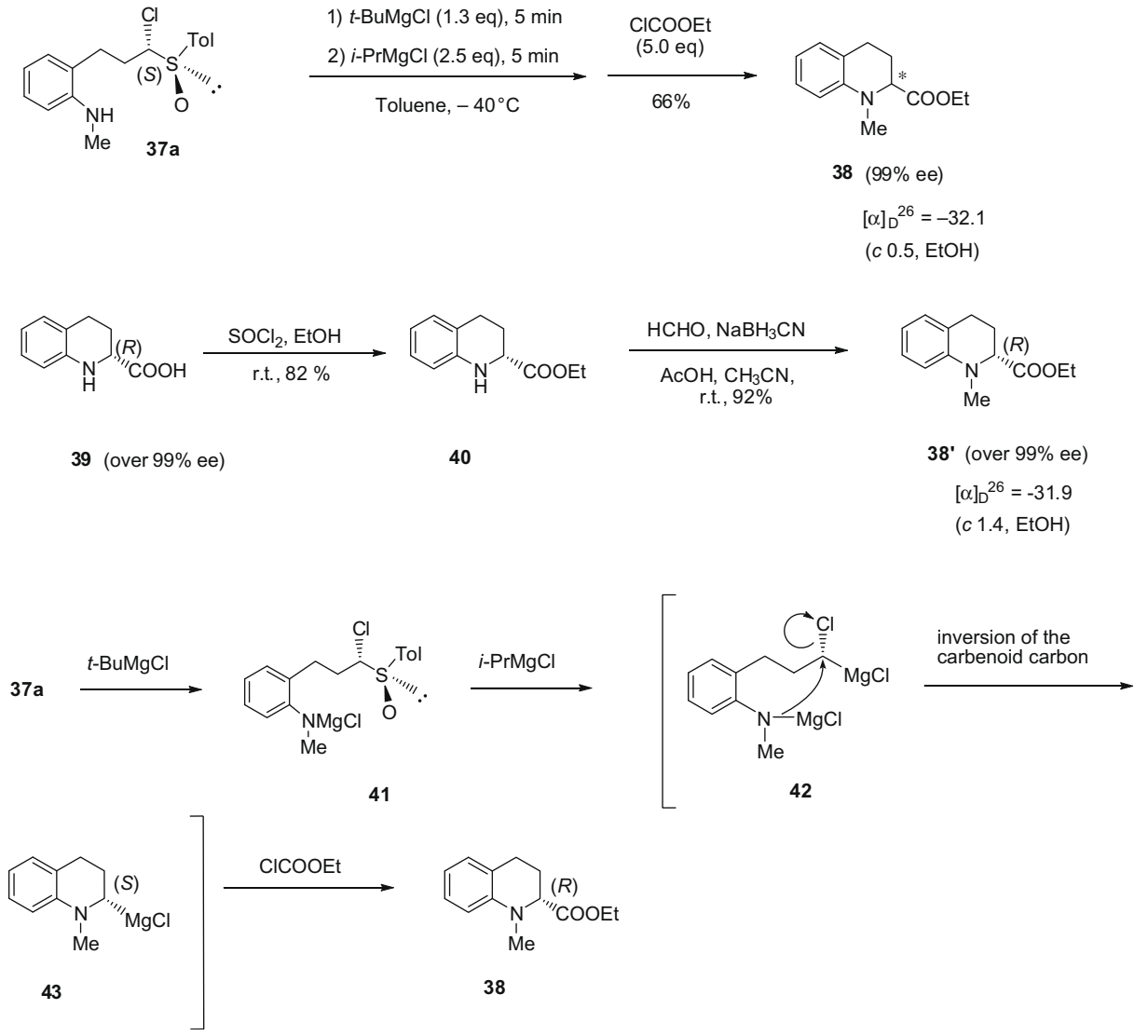



**Figure 1.** Crystal structure of **37a**.

chloroformate under the conditions described above to give the optically active pipecolic acid derivative **38** in 66% yield (Scheme 6). The enantiomeric excess was measured by a chiral stationary column, CHIRALCEL-OD (hexane/*i*-PrOH = 30:1), and was found to be over 99%. The high enantiomeric excess of product **38** means that almost no racemization occurred throughout the reactions. At this point, the absolute configuration of the product was unclear.

The absolute configuration of **38** was determined by comparing **38** with the compound whose absolute configuration is known as follows: At first, (*R*)-1,2,3,4-tetrahydroquinoline-2-carboxylic acid **39** was synthesized from quinaldinic acid by Nagata's procedure.[13] The carboxylic acid was converted to ethyl ester **40** in ethanol with thionyl chloride. Methylation of the nitrogen in **40** was carried out with the conventional procedure to afford **38′** in high yield. Both the sign and value of the specific rotation of **38** derived from **37a** were consistent with those of **38′**. From these results, product **38** derived from **37a** was determined to be (*R*)-1-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ethyl ester.[14]




**Scheme 6.**

As we could determine the absolute configuration of **38**, the whole stereochemistry of the reaction can be inferred as shown in Scheme 6. At first, treatment of **37a** with *t*-BuMgCl resulted in the formation of magnesium amide **41**. As the sulfoxide–magnesium exchange reaction is known to take place with retention of the configuration of the carbon bearing the sulfinyl group,[15,16] sulfoxide **41** gave magnesium carbenoid **42** with an (*S*)-absolute configuration. The key intramolecular cyclization proceeds with inversion of the carbenoid carbon[16] to afford α-amino carbanion **43** with an (*S*)-absolute configuration. Finally, the anion was trapped by ethyl chloroformate with retention of configuration of the carbanion to afford the final product **38**.

## 3. Conclusion

In conclusion, a novel synthesis of cyclic α-amino acid derivatives (proline, pipecolic acid,[14] and homopipecolic acid derivatives) was achieved by the intramolecular reaction of magnesium carbenoids with *N*-magnesio arylamine as the key reaction. An asymmetric synthesis of an enantiomerically pure (*R*)-pipecolic acid derivative was achieved starting from enantiomerically pure (1*S*,$R_S$)-1-chloro-3-[2-(*N*-methylamino)phenyl]propyl *p*-tolyl sulfoxide **37a**. The intramolecular nucleophilic substitution reaction of the magnesium carbenoid with *N*-magnesio arylamine was proven to take place with inversion of the carbenoid carbon. The results described in this paper contribute to the further development of the synthesis, including asymmetric synthesis, of cyclic α-amino acid derivatives and also the chemistry of magnesium carbenoids.

## 4. Experimental

Melting points were measured on a Yanaco MP-S3 apparatus and are uncorrected. $^1$H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 500 and BRUKER UltraShield 400, 300 spectrometer. IR spectra were recorded on a Perkin–Elmer spectrum One FT-IR instrument. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion with JEOL JMS-SX102A. Silica gel 60N (KANTO CHEMICAL) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry solvent and reagents, toluene and DMF were distilled from $CaH_2$. Diethyl ether was distilled from Na and THF was distilled from diphenylketyl. HMPA was dried over $CaSO_4$ and distilled before use. In the $^1$H NMR spectra, br s refers to a broad singlet.

### 4.1. *N*-{2-[2-Chloro-2-(toluene-4-sulfinyl)ethyl]phenyl}-*N*-methylcarbamic acid *tert*-butyl ester 12

To a solution of LDA (3 mmol) and HMPA (5 mmol) in 13 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added a solution of chloromethyl *p*-tolyl sulfoxide (0.47 g; 2.5 mmol) in 2 mL of dry THF dropwise with stirring. After 10 min, to the solution of lithio chloromethyl *p*-tolyl sulfoxide was added a solution of **11** (0.77 g; 3.01 mmol) in 2 mL of dry THF with stirring. The reaction mixture was stirred and slowly allowed to warm to 0 °C for 2 h. The reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$ and the organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **12** (0.79 g; 65%) as a colorless oil; IR (neat) 3006, 2978, 2930, 1694 (CO), 1598, 1583, 1495, 1477, 1454, 1392, 1436, 1367, 1305, 1279, 1255, 1217, 1155, 1088, 1058 (SO), 1017, 977, 926, 864, 811 $cm^{-1}$. $^1H$ NMR $\delta$ 1.27 (5H, br s, *t*-Bu), 1.51 (4H, br s, *t*-Bu), 2.43 (3H, s), 2.68–3.28 (4H, m), 3.36–3.76 (1H, m), 4.62–5.06 (1H, m), 6.95–7.40 (6H, m), 7.42–7.68 (2H, m). MS *m*/*z* (%) 407 ($M^+$, trace), 212 (50), 140 (25), 132 (95), 91 (23), 57 (81). Calcd for $C_{21}H_{26}ClNO_3S$: *M*, 407.1322. Found: *m*/*z* 407.1322.

### 4.2. *N*-{2-[2-Chloro-2-(toluene-4-sulfinyl)ethyl]phenyl}-*N*-methylamine 5a

A solution of **12** (0.66 g; 1.62 mmol) in 4 mL of $CH_2Cl_2$ was cooled in an ice bath. To this solution was added TFA (1.54 mL) with stirring. After 3 h, the reaction was quenched with 5% aq NaOH. The whole was extracted with $CH_2Cl_2$ and the organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **5a** (0.47 g; 93%; approximately a 7:3 mixture of two diastereomers) as a colorless oil; IR (neat) 3392 (NH), 3044, 2922, 2814, 1606, 1586, 1517, 1469, 1450, 1426, 1307, 1270, 1171, 1085, 1045 (SO), 1016, 938, 921, 811, 750 $cm^{-1}$. $^1H$ NMR $\delta$ 2.41 (3H, s), 2.82 (3H, d, *J* = 11.3 Hz), 3.02 (0.5H, d, *J* = 9.4 Hz), 3.08 (0.5H, d, *J* = 9.3 Hz), 3.53–3.64 (1H, m), 3.98–4.38 (1H, br s), 4.52 (0.3H, dd, *J* = 9.3, 2.2 Hz), 4.76 (0.7H, q, *J* = 4.2 Hz), 6.58–6.70 (2H, m), 7.00 (0.7H, d, *J* = 7.4 Hz), 7.09 (0.3H, d, *J* = 7.4 Hz), 7.16–7.24 (1H, m), 7.30–7.36 (2H, m), 7.58 (1.4H, d, *J* = 8.3 Hz), 7.64 (0.6H, d, *J* = 8.2 Hz). MS *m*/*z* (%) 307 ($M^+$, 20), 168 (60), 132 (100), 118 (45), 91 (18), 77 (8), 65 (5). Calcd for $C_{16}H_{18}ClNOS$: *M*, 307.0797. Found: *m*/*z* 307.0796.

### 4.3. *N*-[2-(3-Hydroxypropyl)phenyl]-*N*-methylcarbamic acid *tert*-butyl ester 15

To a solution of **14**[7] (0.547 g; 3.31 mmol) in 3 mL of THF was added $(Boc)_2O$ (0.8 mL; 3.48 mmol) with stirring. After the mixture was refluxed overnight, the solvent was evaporated. The residue was purified by silica gel column chromatography to afford **15** (0.866 g; 99%) as a colorless oil; IR (neat) 3435 (OH), 2976, 1698 (CO), 1063, 1581, 1494, 1454, 1367, 1305, 1255, 1155, 1094, 1060, 979, 916, 867, 760 $cm^{-1}$. $^1H$ NMR $\delta$ 1.25 (5H, br s, *t*-Bu), 1.52 (4H, br s, *t*-Bu), 1.82–2.10 (2H, br s), 2.64 (2H, t, *J* = 7.1 Hz), 3.15 (3H, s), 3.50–3.72 (2H, br s), 7.00–7.34 (4H, m). MS *m*/*z* (%) 265 ($M^+$, 5), 209 (30), 165 (100), 120 (55), 118 (25), 57 (93). Calcd for $C_{15}H_{23}NO_3$: *M*, 265.1678. Found: *m*/*z* 265.1697.

### 4.4. *N*-Methyl-*N*-[2-(3-*p*-tolylsulfanylpropyl)phenyl]carbamic acid *tert*-butyl ester 16

A solution of **15** (0.69 g; 2.60 mmol) and ditolyl disulfide (0.833 g; 3.38 mmol) in 8.7 mL of THF was cooled in an ice bath. To this solution was added tributylphosphine (0.9 mL; 3.64 mmol) with stirring. The reaction mixture was stirred at 0 °C for 5 min and at room temperature for 18 h. The reaction mixture was diluted with benzene and the organic layer was washed twice with 5% aq NaOH followed by satd aq $NH_4Cl$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by silica gel column chromatography to afford **16** (0.86 g; 89%) as a colorless oil; IR (neat) 2975, 2929, 1699 (CO), 1602, 1581, 1494, 1454, 1366, 1305, 1254, 1154, 1120, 1090, 1043, 1018, 977, 869, 805, 761 $cm^{-1}$. $^1H$ NMR $\delta$ 1.30 (7H, br s, *t*-Bu), 1.51 (2H, br s, *t*-Bu), 1.82–2.00 (2H, m), 2.31 (3H, s), 2.65 (2H, t, *J* = 7.5 Hz), 2.86 (2H, t, *J* = 7.2 Hz), 3.11 (3H, s), 7.08 (3H, d, *J* = 7.9 Hz), 7.12–7.27 (5H, m). MS *m*/*z* (%) 371 ($M^+$, 37), 315 (53), 148 (95), 120 (28), 57 (36). Calcd for $C_{22}H_{29}NO_2S$: *M*, 371.1919. Found: *m*/*z* 371.1918.

### 4.5. *N*-{2-[3-Chloro-3-(toluene-4-sulfinyl)propyl]phenyl}-*N*-methylcarbamic acid *tert*-butyl ester 17

*N*-Chlorosuccinimide (NCS; 0.32 g; 2.38 mmol) was added to a solution of **16** (0.81 g; 2.17 mmol) in 3.5 mL of carbon tetrachloride and the suspension was stirred at room temperature overnight. The precipitate was filtered off and the solvent was evaporated to afford crude α-chlorosulfide.

A solution of the crude α-chlorosulfide in 4.3 mL of $CH_2Cl_2$ was cooled to −40 °C. To this solution was added *m*-CPBA (0.56 g; 2.38 mmol) and the reaction mixture was stirred for 1 h. The reaction was quenched with satd aq $Na_2SO_3$ and the reaction mixture was diluted with $CH_2Cl_2$. The organic layer was washed twice with 5% aq NaOH followed by satd aq $NH_4Cl$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The product was purified by silica gel column chromatography to afford **17** (0.81 g; 88%) as a colorless oil; IR (neat) 2977, 1702 (CO), 1598, 1494, 1453, 1367, 1304, 1255, 1155, 1087, 1056 (SO), 1017, 977, 867, 812, 759, 664 $cm^{-1}$. $^1H$ NMR $\delta$ 1.26, 1.32, 1.45, 1.48 (each br s, total 9H, *t*-Bu), 1.70–2.24 (1H, m), 2.42 (3H, s), 2.48–2.64 (1H, m), 2.65–2.80 (1H, m), 2.82–3.00 (1H, m), 3.07 (1.5H, s), 3.13 (1.5H, s), 4.49 (1H, d, *J* = 9.3 Hz), 7.02–7.36 (6H, m), 7.52 (2H, d, *J* = 7.4 Hz).

### 4.6. *N*-{2-[3-Chloro-3-(toluene-4-sulfinyl)propyl]phenyl}-*N*-methylamine 5b

A solution of **17** (0.69 g; 1.63 mmol) in 4 mL of $CH_2Cl_2$ was cooled in an ice bath. To this solution was added TFA (1.55 mL) with stirring. After 3 h, the reaction was quenched with 5% aq NaOH. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **5b** (0.53 g; 99%; approximately a 7:3 mixture of two diastereomers) as a colorless oil; IR (neat) 3398 (NH), 2924, 2814, 1914, 1734, 1605, 1585, 1516, 1494, 1471, 1427, 1400, 1375, 1310, 1265, 1218, 1170, 1085, 1048 (SO), 1016, 927, 841, 811, 750 $cm^{-1}$. $^1H$ NMR $\delta$ 1.87–1.97 (0.3H, m), 2.24–2.34 (0.7H, m), 2.40–2.88 (9H, m), 3.60–4.20 (1H, m), 4.46 (0.7H, dd, *J* = 7.7, 3.5 Hz), 4.53 (0.3H, dd, *J* = 9.5, 4.1 Hz), 6.58–6.68 (2H, m), 6.96–7.02 (1H, m), 7.16 (1H, t, *J* = 7.4 Hz), 7.27–7.34 (2H, m), 7.51 (0.6H, d, *J* = 8.2 Hz), 7.60 (1.4H, d, *J* = 8.2 Hz). MS *m*/*z* (%) 321 ($M^+$, 43), 182 (25), 146 (33), 120 (100), 118 (10), 91 (23), 65 (6). Calcd for $C_{17}H_{20}ClNOS$: *M*, 321.0954. Found: *m*/*z* 321.0954.

### 4.7. *N*-[2-(3-Iodopropyl)phenyl]-*N*-methylcarbamic acid *tert*-butyl ester 18

To a solution of **15** (0.86 g; 3.23 mmol) in 13 mL of $CH_2Cl_2$ at room temperature were successively added imidazole (0.33 g; 4.85 mmol), $Ph_3P$ (1.27 g; 4.85 mmol), and $I_2$ (1.23 g; 4.85 mmol) with stirring. After 2 h, the reaction was quenched with satd aq $Na_2SO_3$. The whole was extracted with $CH_2Cl_2$ and the organic layer was successively washed with satd aq $Na_2SO_3$ and satd aq $NaHCO_3$. The organic layer was dried over $MgSO_4$. The product was purified

by silica gel column chromatography to afford **18** (1.0 g; 83%) as a colorless oil; IR (neat) 3063, 3004, 2975, 2931, 1697 (CO), 1602, 1581, 1494, 1478, 1453, 1390, 1365, 1305, 1256, 1215, 1153, 1112, 1084, 1042, 977, 869, 771, 760, 663, 605, 582, 499 $cm^{-1}$. $^1H$ NMR $\delta$ 1.33 (6H, br s, *t*-Bu), 1.52 (3H, br s, *t*-Bu), 2.00–2.23 (2H, m), 2.66 (2H, t, $J$ = 7.5 Hz), 3.15 (3H, s), 3.16–3.26 (2H, m), 7.02–7.28 (4H, m). MS *m/z* (%) 375 ($M^+$, 5), 319 (95), 275 (22), 192 (24), 148 (65). Calcd for $C_{15}H_{22}INO_2$: *M*, 375.0695. Found: *m/z* 375.0702.

### 4.8. *N*-{2-[4-Chloro-4-(toluene-4-sulfinyl)butyl]phenyl}-*N*-methylcarbamic acid *tert*-butyl ester 19

To a solution of LDA (0.64 mmol) in 2 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added dropwise a solution of chloromethyl *p*-tolyl sulfoxide (0.12 g; 0.64 mmol) in 0.8 mL of dry THF with stirring. After 10 min, to the solution of the α-lithio chloromethyl *p*-tolyl sulfoxide was added a solution of **18** (0.2 g; 0.533 mmol) in 0.8 mL of dry THF with stirring. The reaction mixture was stirred and slowly allowed to warm to −30 °C for 1.5 h. The reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$ and the organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **19** (approximately a 1:1 mixture of two diastereomers; 0.19 g; 81%) as a colorless oil; IR (neat) 2978, 1917, 1694 (CO), 1598, 1581, 1495, 1455, 1367, 1305, 1253, 1155, 1088, 1056 (SO), 1017, 978, 868, 812, 757 $cm^{-1}$. $^1H$ NMR $\delta$ 1.30 (6H, br s, *t*-Bu), 1.30 (3H, br s, *t*-Bu), 1.60–2.12 (3H, m), 2.27 (1H, br s), 2.44 (3H, s), 2.48–2.66 (2H, m), 3.09–3.17 (3H, m), 4.40 (0.5H, dd, $J$ = 8.8, 3.2 Hz), 4.52 (0.5H, br s), 7.02–7.24 (4H, m), 7.34 (2H, d, $J$ = 7.7 Hz), 7.54 (1H, d, $J$ = 8.1 Hz), 7.62 (1H, d, $J$ = 8.1 Hz). MS *m/z* (%) 435 ($M^+$, trace), 240 (95), 204 (60), 160 (70), 120 (75), 57 (85). Calcd for $C_{23}H_{30}ClNO_3S$: *M*, 435. 1635. Found: *m/z* 435.1627.

### 4.9. *N*-{2-[4-Chloro-4-(toluene-4-sulfinyl)butyl]phenyl}-*N*-methylamine 5c

A solution of **19** (0.22 g; 0.5 mmol) in 1.2 mL of $CH_2Cl_2$ was cooled in an ice bath. To this solution was added TFA (0.47 mL) with stirring. After 3 h, the reaction was quenched with 5% aq NaOH. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **5c** (approximately a 1:1 mixture of two diastereomers; 0.157 g; 94%) as a colorless oil; IR (neat) 3401 (NH), 2929, 2813, 1605, 1585, 1515, 1470, 1307, 1265, 1169, 1086, 1049 (SO), 1016, 811, 788, 749 $cm^{-1}$. $^1H$ NMR $\delta$ 1.56–2.12 (3H, m), 2.25–2.40 (1H, m), 2.43 (3H, s), 2.46–2.54 (2H, m), 2.87 (3H, d, $J$ = 2.3 Hz), 3.65 (1H, br s), 4.43 (0.5H, dd, $J$ = 9.0, 3.4 Hz), 4.54 (0.5H, dd, $J$ = 9.0, 4.0 Hz), 6.60–6.71 (2H, m), 6.99 (1H, t, $J$ = 8.7 Hz), 7.16 (1H, t, $J$ = 7.7 Hz), 7.33 (2H, d, $J$ = 7.9 Hz), 7.53 (1H, t, $J$ = 8.3 Hz), 7.62 (1H, d, $J$ = 8.1 Hz). MS *m/z* (%) 335 ($M^+$, 65), 196 (55), 160 (100), 139 (20), 120 (95), 118 (48), 91 (46), 77 (15), 65 (13), 39 (3). Calcd for $C_{18}H_{22}ClNOS$: *M*, 335.1110. Found: *m/z* 335.1111.

### 4.10. 5-[2-(*N*-*tert*-Butoxycarbonyl-*N*-methylamino)phenyl] pentanoic acid *tert*-butyl ester 20

To a solution of LDA (14.1 mmol) and HMPA (14.1 mmol) in 44 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added dropwise a solution of *tert*-butyl acetate (1.89 mL; 14.1 mmol) with stirring. After 10 min, to the solution of the α-lithio *tert*-butyl acetate was added a solution of **18** (1.76 g; 4.70 mmol) in 3 mL of dry THF with stirring. The reaction mixture was stirred at −78 °C for 15 min, then the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **20** (1.70 g; 99%) as a colorless oil; IR (neat) 2976, 1702 (CO), 1602, 1580, 1493, 1458, 1365, 1305, 1255, 1155, 1092, 977, 869, 759 $cm^{-1}$. $^1H$ NMR $\delta$ 1.32, 1.52 (each br s, total 9H, *t*-Bu), 1.44 (9H, s), 1.58–1.68 (4H, br s), 2.20–2.27 (2H, m), 2.50–2.60 (2H, m), 3.14 (3H, s), 7.02–7.27 (4H, m). MS *m/z* (%) 363 ($M^+$, 1), 307 (5), 262 (20), 251 (32), 234 (40), 207 (100), 120 (28), 57 (46). Calcd for $C_{21}H_{33}NO_4$: *M*, 363.2410. Found: *m/z* 363.2412.

### 4.11. *N*-Methyl-*N*-{2-[5-(*p*-tolylsulfanyl)pentyl]phenyl}carbamic acid *tert*-butyl ester 21

To a solution of **20** (90 mg; 0.248 mmol) in 2.5 mL of dry toluene in a flame-dried flask at 0 °C under an argon atmosphere was added a solution of DIBAL-H (0.98 M; 0.98 mL; 0.744 mmol) with stirring. After 30 min, the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with 5% HCl and dried over $MgSO_4$. The produced alcohol was purified by silica gel column chromatography to afford an alcohol (51 mg; 70%) as a colorless oil; IR (neat) 3436 (OH), 2932, 1701 (CO), 1603, 1581, 1495, 1455, 1367, 1305, 1255, 1155, 1042, 979, 868, 761 $cm^{-1}$. $^1H$ NMR $\delta$ 1.20–1.76 (15H, m), 2.54 (2H, t, $J$ = 7.7 Hz), 3.14 (3H, s), 3.64 (2H, t, $J$ = 6.5 Hz), 7.02–7.28 (4H, m). MS *m/z* (%) 293 ($M^+$, 2), 237 (32), 193 (100), 120 (63), 57 (63), 28 (29). Calcd for $C_{17}H_{27}NO_3$: *M*, 293.1988. Found: *m/z* 293.1991.

To a solution of the alcohol (0.45 g; 1.54 mmol) was added ditolyl disulfide (0.5 g; 2 mmol) in 5 mL of THF and cooled in an ice bath. To this solution was added tributylphosphine (0.55 mL; 2 mmol) with stirring. The reaction mixture was stirred at 0 °C for 5 min and at room temperature for 18 h. The reaction mixture was diluted with benzene and the organic layer was washed twice with 5% NaOH followed by satd aq $NH_4Cl$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by silica gel column chromatography to afford **21** (0.49 g; 80%) as a colorless oil; IR (neat) 2930, 2860, 1698 (CO), 1602, 1580, 1493, 1454, 1364, 1304, 1254, 1154, 1092, 1038, 1018, 977, 869, 804, 760 $cm^{-1}$. $^1H$ NMR $\delta$ 1.31 (6H, s, *t*-Bu), 1.51 (3H, br s, *t*-Bu), 1.40–1.70 (6H, m), 2.31 (3H, s), 2.52 (2H, t, $J$ = 7.7 Hz), 2.87 (2H, t, $J$ = 7.4 Hz), 3.13 (3H, s), 7.01–7.28 (8H, m). MS *m/z* (%) 399 ($M^+$, 30), 343 (50), 299 (45), 176 (97), 120 (60), 57 (46). Calcd for $C_{24}H_{33}NO_2S$: *M*, 399.2232. Found: *m/z* 399.2230.

### 4.12. *N*-{2-[5-Chloro-5-(toluene-4-sulfinyl)pentyl]phenyl}-*N*-methylcarbamic acid *tert*-butyl ester 22

*N*-Chlorosuccinimide (0.176 g; 1.32 mmol) was added to a solution of **21** (0.48 g; 1.2 mmol) in 1.8 mL of carbon tetrachloride and the suspension was stirred at room temperature overnight. The precipitate was filtered off and the solvent was evaporated to afford the crude α-chlorosulfide.

A solution of the crude α-chlorosulfide in 3 mL of $CH_2Cl_2$ was cooled to −40 °C. To this solution was added *m*-chloroperbenzoic acid (0.31 g; 1.32 mmol) and the reaction mixture was stirred for 1 h. The reaction was quenched with satd aq $Na_2SO_3$ and the solution was diluted with $CH_2Cl_2$. The organic layer was washed twice with 5% NaOH followed by satd aq $NH_4Cl$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The product was purified by silica gel column chromatography to afford **22** (0.493 g; 91%; approximately a 3:1 mixture of two diastereomers) as a colorless oil; IR (neat) 2932, 2685, 1695 (CO), 1598, 1580, 1495, 1455, 1367, 1305, 1255, 1155, 1088, 1055 (SO), 1017, 977, 868, 812, 759 $cm^{-1}$. $^1H$ NMR $\delta$ 1.31 (6H, br s, *t*-Bu), 1.51 (3H, br s, *t*-Bu), 1.58–2.04 (4H, m), 2.19–2.34 (1H, m), 2.43 (3H, s), 2.55 (2H, t, $J$ = 7.5 Hz), 3.13 (3H, s), 4.38 (0.75H, d, $J$ = 9.8 Hz), 4.50 (0.25H, dd, $J$ = 9.5, 3.8 Hz), 7.02–7.23 (4H, m), 7.34 (2H, d, $J$ = 7.9 Hz), 7.55

(0.5H, d, $J$ = 8.1 Hz), 7.62 (1.5H, d, $J$ = 7.9 Hz). MS $m/z$ (%) 449 ($M^+$, 1), 392 (10), 349 (20), 254 (100), 210 (45), 174 (27), 120 (41), 57 (62). Calcd for $C_{24}H_{32}ClNO_3S$: $M$, 449.1791. Found: $m/z$ 449.1799.

### 4.13. *N*-{2-[5-Chloro-5-(toluene-4-sulfinyl)pentyl]phenyl}-*N*-methylamine 5d

A solution of **22** (0.474 g; 1.05 mmol) in 2.5 mL of $CH_2Cl_2$ was cooled in an ice bath. To this solution was added TFA (1 mL) with stirring. After 3 h, the reaction was quenched with 5% aq NaOH and the whole was extracted with $CH_2Cl_2$. The organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **5d** (0.361 g; 98%; approximately a 3:1 mixture of two diastereomers) as a colorless oil; IR (neat) 3403 (NH), 3003, 2931, 2863, 2813, 1912, 1604, 1584, 1515, 1494, 1463, 1427, 1400, 1379, 1306, 1263, 1217, 1168, 1086, 1050 (SO), 1016, 839, 811, 751 $cm^{-1}$. $^1H$ NMR $\delta$ 1.22–1.32 (0.25H, m), 1.44–1.89 (4H, m), 1.94–2.10 (0.75H, m), 2.20–2.36 (1H, m), 2.36–2.54 (2H, m), 2.43 (3H, s), 2.88 (3H, s), 3.64 (1H, br s), 4.39 (0.75H, dd, $J$ = 9.7 Hz, 3.0 Hz) , 4.51 (0.25H, dd, $J$ = 13.5 Hz, 4.0 Hz), 6.60–6.74 (2H, m), 6.97–7.03 (1H, m), 7.16 (1H, t, $J$ = 7.9 Hz), 7.34 (2H, d, $J$ = 7.9 Hz), 7.54 (0.5H, d, $J$ = 8.3 Hz), 7.63 (1.5H, d, $J$ = 6.6 Hz). MS $m/z$ (%) 349 ($M^+$, 73), 210 (85), 174 (45), 172 (7), 133 (13), 120 (100), 91 (38), 77 (8). Calcd for $C_{19}H_{24}ClNOS$: $M$, 349.1267. Found: $m/z$ 349.1266.

### 4.14. 1-Methyl-1,2,3,4-tetrahydroquinoline-2-carboxylic acid ethyl ester 7a

To a solution of **5b** (20 mg; 0.062 mmol) in 3 mL of dry toluene in a flame-dried flask at −40 °C under an argon atmosphere was added a solution of *t*-BuMgCl (1.0 M solution in THF, 0.08 mL; 0.08 mmol) dropwise with stirring. After 5 min, a solution of *i*-PrMgCl (2.0 M solution in $Et_2O$, 0.078 mL; 0.155 mmol) was added dropwise to the reaction mixture with stirring. After 5 min, to the solution of α-aminoalkylmagnesium intermediate **6a** was added ethyl chloroformate (0.03 mL; 0.31 mmol) dropwise at −40 °C with stirring. After 10 min, the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **7a** (9 mg; 66%) as a colorless oil; IR (neat) 2935, 1740 (CO), 1604, 1502, 1374, 1336, 1185, 1102, 1038, 746 $cm^{-1}$. $^1H$ NMR $\delta$ 1.24 (3H, t, $J$ = 7.1 Hz), 2.07–2.16 (1H, m), 2.26–2.32 (1H, m), 2.68–2.72 (2H, m), 2.95 (3H, s), 4.01 (1H, dd, $J$ = 5.2, 4.5 Hz), 4.10–4.24 (2H, m), 6.60–6.66 (2H, m), 6.93 (1H, d, $J$ = 7.6 Hz), 7.10 (1H, t, $J$ = 7.8 Hz). MS $m/z$ (%) 219 ($M^+$, 14), 146 (100), 130 (10). Calcd for $C_{13}H_{17}NO_2$: $M$, 219.1259. Found: $m/z$ 219.1261.

### 4.15. 1-Methyl-2,3,4,5-tetrahydro-1*H*-benzo[b]azepine-2-carboxylic acid ethyl ester 7b

Colorless oil; IR (neat) 2936, 1732 (CO), 1599, 1492, 1179, 1056, 756 $cm^{-1}$. $^1H$ NMR $\delta$ 1.23 (3H, t, $J$ = 7.1 Hz), 1.54–1.85 (3H, m), 1.91–2.03 (1H, m), 2.70 (1H, quintet, $J$ = 6.8 Hz), 2.90 (1H, quintet, $J$ = 6.8 Hz), 2.93 (1H, s), 3.76 (1H, dd, $J$ = 5.3, 4.0 Hz), 4.05–4.22 (2H, m), 6.88 (1H, t, $J$ = 7.4 Hz), 6.98 (1H, d, $J$ = 7.9 Hz), 7.04 (1H, d, $J$ = 7.4 Hz), 7.17 (1H, dt, $J$ = 7.9, 1.7 Hz). MS $m/z$ (%) 233 ($M^+$, 10), 160 (100), 144 (10), 132 (9), 117 (8), 91 (10). Calcd for $C_{14}H_{19}NO_2$: $M$, 233.1415. Found: $m/z$ 233.1416.

### 4.16. *N*-Methyl-*N*-(2-vinylphenyl)amine 23

Colorless oil; IR (neat) 3436 (NH), 2917, 2814, 1623, 1603, 1577, 1510, 1461, 1426, 1307, 1262, 1166, 1064, 993, 910, 747 $cm^{-1}$. $^1H$ NMR $\delta$ 2.87 (3H, s), 3.74–3.96 (1H, br s), 5.31 (1H, dd, $J$ = 10.9, 1.5 Hz), 5.60 (1H, dd, $J$ = 17.5, 1.7 Hz), 6.58–6.79 (3H, m), 7.15–7.28 (2H, m). MS $m/z$ (%) 133 ($M^+$, 55), 118 (100), 105 (7), 91 (35), 77 (20), 63 (13). Calcd for $C_9H_{11}N$: $M$, 133.0890. Found: $m/z$ 133.0887.

### 4.17. *N*-Methyl-*N*-[2-(4-pentenyl)phenyl]amine 24

Colorless oil; IR (neat) 3444 (NH), 2929, 1639, 1605, 1585, 1508, 1461, 1307, 1262, 1167, 1044, 911, 747 $cm^{-1}$. $^1H$ NMR $\delta$ 1.71 (2H, quintet, $J$ = 7.0 Hz), 2.15 (2H, q, $J$ = 7.0 Hz), 2.47 (2H, t, $J$ = 7.9 Hz), 2.88 (3H, s), 3.65 (1H, br s, NH), 5.01 (1H, m), 5.03 (1H, m), 5.78–5.93 (1H, m), 6.62 (1H, dd, $J$ = 8.1, 2.1 Hz), 6.69 (1H, dt, $J$ = 8.5, 2.0 Hz), 7.04 (1H, dd, $J$ = 7.4, 1.2 Hz), 7.15 (1H, dt, $J$ = 7.9, 1.2 Hz). MS $m/z$ (%) 175 ($M^+$, 30), 134 (12), 120 (100), 106 (15), 91 (25), 77 (10), 65 (9). Calcd for $C_{12}H_{17}N$: $M$, 175.1366. Found: $m/z$ 175.1360.

### 4.18. 3-(4-Methoxyphenylamino)-1-propanol 25

To a solution of 4-iodoanisole (4.68 g; 20 mmol) in 12 mL of dry DMSO in a flame-dried flask at 80 °C under an argon atmosphere was successively added a solution of 3-aminoalcohol (2.3 mL; 30 mmol), $K_2CO_3$ (5.53 g; 40 mmol), CuI (381 mg; 2 mmol), and L-proline (461 mg; 4 mmol) with stirring. After 12 h, the reaction was quenched with water. The whole was extracted with AcOEt. The organic layer was washed with $H_2O$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **25** (3.05 g; 84%) as a colorless oil; IR (neat) 3367 (OH, NH), 2937, 2062, 1849, 1729, 1618, 1591, 1514, 1465, 1409, 1374, 1235, 1180, 1124, 1036, 930, 821 $cm^{-1}$. $^1H$ NMR $\delta$ 1.83–1.91 (2H, m), 2.20–3.15 (2H, br s), 3.24 (2H, t, $J$ = 6.3 Hz), 3.75 (3H, s), 3.82 (2H, t, $J$ = 5.8 Hz), 6.61–6.65 (2H, m), 6.77–6.84 (2H, m).

### 4.19. *N*-(3-Iodopropyl)-*N*-(4-methoxyphenyl)carbamic acid *tert*-butyl ester 26

To a solution of **25** (3.05 g; 16.8 mmol) in 160 mL of $CH_2Cl_2$ in a flask at room temperature was added a solution of TEA (3.5 mL; 25.2 mmol) followed by $(Boc)_2O$ (5.79 mL; 25.2 mmol) with stirring. After being stirred at room temperature for 12 h, the solvent was evaporated. The crude product was purified by silica gel column chromatography to afford carbamic acid *tert*-butyl ester (5.8 g; 99%) as a colorless oil; IR (neat) 3445 (OH), 2977, 1695 (CO), 1611, 1586, 1515, 1456, 1394, 1368, 1269, 1249, 1166, 1107, 1037, 999, 836, 768 $cm^{-1}$. $^1H$ NMR $\delta$ 1.38 (9H, s), 1.60–1.68 (3H, m), 3.65–3.72 (2H, m), 3.75 (2H, t, $J$ = 6.2 Hz), 3.81 (3H, s), 6.86 (2H, d, $J$ = 6.8 Hz), 7.04 (2H, d, $J$ = 8.0 Hz).

To a solution of the carbamic acid *tert*-butyl ester (4.29 g; 15.2 mmol) in 60 mL of $CH_2Cl_2$ at room temperature were successively added imidazole (2.07 g; 30.4 mmol), $Ph_3P$ (7.97 g; 30.4 mmol), and $I_2$ (7.72 g; 30.4 mmol) with stirring. After 2 h, the reaction was quenched with satd aq $Na_2SO_3$. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with satd aq $Na_2SO_3$ followed by satd aq $NaHCO_3$ and brine and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **26** (5.8 g; 99%) as a colorless oil; IR (neat) 2975, 1694 (CO), 1610, 1512, 1458, 1391, 1247, 1153, 1036, 835, 768, 475 $cm^{-1}$. $^1H$ NMR $\delta$ 1.42 (9H, s), 2.02–2.12 (2H, m), 3.13 (2H, t, $J$ = 7.0 Hz), 3.66 (2H, t, $J$ = 7.0 Hz), 3.80 (3H, s), 6.86 (2H, d, $J$ = 8.9), 7.02–7.15 (2H, m).

### 4.20. *N*-[4-Chloro-4-(toluene-4-sulfinyl)butyl]-*N*-(4-methoxyphenyl)amine 8a

To a solution of LDA (12.7 mmol) in 35 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added dropwise a solution of chloromethyl *p*-tolyl sulfoxide (2.0 g;

10.6 mmol) in 10 mL of dry THF with stirring. After 10 min, to the solution of the α-lithio chloromethyl *p*-tolyl sulfoxide was added a solution of **26** (4.95 g; 12.7 mmol) in 8 mL of dry THF at −75 °C with stirring. The reaction mixture was slowly allowed to warm to 0 °C for 2 h and the reaction was quenched with satd aq $NH_4Cl$. The product was purified by silica gel column chromatography to afford the sulfoxide as approximately a 1:1 mixture of two diastereomers (4.5 g; 95%) as a colorless oil; IR (neat) 2931, 1694 (CO), 1514, 1455, 1394, 1367, 1295, 1248, 1159, 1086, 1055 (SO), 835, 812, 756 $cm^{-1}$. $^1H$ NMR $\delta$ 1.39 (9H, s), 1.55–1.75 (1.5H, m), 1.75–2.05 (1.5H, m), 2.15–2.30 (1H, m), 2.43 (3H, s), 3.50–3.78 (2H, m), 3.80 (3H, s), 4.35–4.45 (0.5H, m), 4.50–4.70 (0.5H, m), 6.84 (2H, d, $J$ = 8.8 Hz), 6.95–7.10 (2H, m), 7.33 (2H, d, $J$ = 8.0 Hz), 7.53 (1H, d, $J$ = 8.2 Hz), 7.61 (1H, d, $J$ = 8.2 Hz).

To a solution of the sulfoxide (3.25 g; 7.2 mmol) in 17 mL of $CH_2Cl_2$ at room temperature was added TFA (17 mL) with stirring. After 2 h, the reaction was quenched with 5% aq NaOH. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **8a** as a 1:1 mixture of two diastereomers (2.5 g; 99%) as a colorless oil; IR (neat) 3360 (NH), 2945, 1732, 1620, 1596, 1516, 1374, 1235, 1179, 1086, 1044 (SO), 821 $cm^{-1}$. $^1H$ NMR $\delta$ 1.26–2.11 (4H, m), 2.33–2.42 (1H, m), 2.43 (3H, s), 3.10–3.17 (2H, m), 3.75 (3H, s), 4.43 (0.5H, dd, $J$ = 9.4, 3.2 Hz), 4.58 (0.5H, dd, $J$ = 9.8, 3.8 Hz), 6.54–6.58 (2H, m), 6.78 (2H, d, $J$ = 8.8 Hz), 7.33 (2H, d, $J$ = 10.0 Hz), 7.53 (1H, d, $J$ = 8.2 Hz), 7.62 (1H, d, $J$ = 8.2 Hz). MS *m/z* (%) 351 ($M^+$, 95), 350 (100), 335 (10), 297 (13) 278 (15), 246 (20), 214 (95), 200 (90), 175 (70), 136 (65). Calcd for $C_{18}H_{22}ClNO_2S$: *M*, 351.1060. Found: *m/z* 351.1048.

### 4.21. *N*-[5-Chloro-5-(toluene-4-sulfinyl)pentyl]-*N*-(4-methoxyphenyl)amine 8b

Colorless oil (approximately a 7:3 mixture of two diastereomers); IR (neat) 3361 (NH), 3052, 2862, 2832, 2934, 1729, 1596, 1516, 1235, 1179, 1085, 1044 (SO), 817, 737 $cm^{-1}$. $^1H$ NMR $\delta$ 1.59–1.73 (6H, m), 2.43 (3H, s), 3.06–3.11 (2H, m), 3.75 (3H, s), 4.39 (0.3H, dd, $J$ = 9.5, 3.0 Hz), 4.51–4.54 (0.7H, m), 6.55–6.58 (2H, m), 6.78 (2H, d, $J$ = 7.7 Hz), 7.33 (2H, d, $J$ = 7.9 Hz), 7.54 (1.4H, d, $J$ = 8.2 Hz), 7.63 (0.6H, d, $J$ = 8.2 Hz). MS *m/z* (%) 365 ($M^+$, 15), 313 (15), 226 (48), 189 (30), 174 (20), 136 (100), 124 (18). Calcd for $C_{19}H_{24}ClNO_2S$: *M*, 365.1216. Found: *m/z* 365.1212.

### 4.22. *N*-[6-Chloro-6-(toluene-4-sulfinyl)hexyl]-*N*-(4-methoxyphenyl)amine 8c

Colorless oil (approximately a 1:1 mixture of two diastereomers); IR (neat) 3355 (NH), 2995, 2935, 1596, 1515, 1463, 1304, 1235, 1179, 1085, 1048 (SO), 816, 756 $cm^{-1}$. $^1H$ NMR $\delta$ 1.33–1.81 (7H, m), 1.65–2.00 (1H, m), 2.23–2.27 (1H, m), 2.43 (3H, s), 3.03–3.08 (2H, m), 3.74 (3H, s), 4.39 (0.5H, dd, $J$ = 9.7, 3.0 Hz), 4.51 (0.5H, dd, $J$ = 9.5, 3.7 Hz), 6.55–6.59 (2H, m), 6.77 (2H, d, $J$ = 7.8 Hz), 7.33 (2H, d, $J$ = 8.0 Hz), 7.54 (1H, d, $J$ = 8.2 Hz), 7.63 (1H, d, $J$ = 8.2 Hz). MS *m/z* (%) 379 ($M^+$, 10), 327 (5), 239 (30), 162 (15), 136 (100). Calcd for $C_{20}H_{26}ClNO_2S$: *M*, 379.1372. Found *m/z* 379.1373.

### 4.23. 1-(4-Methoxyphenyl)pyrrolidine-2-carboxylic acid ethyl ester 10a

To a solution of **8a** (43 mg; 0.12 mmol) in 6 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added a solution of *i*-PrMgCl (2.0 M solution in THF, 0.22 mL; 0.43 mmol) with stirring. After 1 min, ethyl chloroformate (0.058 mL; 0.6 mmol) was added dropwise to the reaction mixture at −78 °C with stirring. After 10 min, the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **10a** (18 mg; 59%) as a colorless oil; IR (neat) 2978, 2833, 1746 (CO), 1621, 1515, 1464, 1367, 1242, 1178, 1094, 1039, 978, 813 $cm^{-1}$. $^1H$ NMR $\delta$ 1.24 (3H, t, $J$ = 7.1 Hz), 2.02–2.30 (4H, m), 3.28–3.34 (1H, m), 3.52–3.57 (1H, m), 3.74 (3H, s), 4.11–4.23 (3H, m), 6.50 (2H, d, $J$ = 9.1 Hz), 6.82 (2H, d, $J$ = 9.1 Hz). MS *m/z* (%) 249 ($M^+$, 20), 176 (100). Calcd for $C_{14}H_{19}NO_3$: *M*, 249.1363. Found: *m/z* 249.1361.

### 4.24. 1-(4-Methoxyphenyl)piperidine-2-carboxylic acid ethyl ester 10b

Colorless oil; IR (neat) 2934, 2856, 1738 (CO), 1511, 1465, 1248, 1180, 1034, 820 $cm^{-1}$. $^1H$ NMR $\delta$ 1.13 (3H, t, $J$ = 7.1 Hz), 1.48–1.70 (3H, m), 1.75–1.88 (1H, m), 1.92–2.00 (1H, m), 2.06–2.11 (1H, m), 3.12–3.18 (1H, m), 3.35–3.42 (1H, m), 3.75 (3H, s), 4.00–4.12 (2H, m), 4.24 (1H, t, $J$ = 4.8 Hz), 6.81 (2H, d, $J$ = 6.8 Hz), 6.91 (2H, d, $J$ = 6.8 Hz). MS *m/z* (%) 263 ($M^+$, 15), 190 (100), 134 (10). Calcd for $C_{15}H_{21}NO_3$: *M*, 263.1519. Found: *m/z* 263.1519.

### 4.25. 1-(4-Methoxyphenyl)azepane-2-carboxylic acid ethyl ester 10c

Colorless oil; IR (neat) 2930, 1743 (CO), 1514, 1465, 1388, 1244, 1180, 1041, 812 $cm^{-1}$. $^1H$ NMR $\delta$ 1.26 (3H, t, $J$ = 7.1 Hz), 1.31–1.43 (2H, m), 1.62–1.90 (5H, m), 2.35–2.42 (1H, m), 3.46–3.60 (2H, m), 3.74 (3H, s), 3.98–4.03 (1H, m), 4.10–4.25 (2H, m), 6.60 (2H, d, $J$ = 9.2 Hz), 6.81 (2H, d, $J$ = 9.2 Hz). MS *m/z* (%) 277 ($M^+$, 15), 204 (100), 149 (5), 134 (5). Calcd for $C_{16}H_{23}NO_3$: *M*, 277.1676. Found: *m/z* 277.1677.

### 4.26. *N*-[2-(2-Hydroxyethyl)phenyl]-*N*-methylcarbamic acid *tert*-butyl ester 31

To a solution of **30** (1.1 g; 7.26 mmol) in 6.6 mL of THF was added $(Boc)_2O$ (1.75 mL; 7.62 mmol) with stirring. The mixture was refluxed overnight and the solvent was evaporated. The crude product was purified by silica gel column chromatography to afford **31** (1.8 g; 99%) as a colorless oil; IR (neat) 3431 (OH), 3064, 2977, 2933, 1683 (CO), 1603, 1581, 1495, 1454, 1369, 1305, 1278, 1255, 1155, 1092, 1047, 979, 867, 760 $cm^{-1}$. $^1H$ NMR $\delta$ 1.33 (5H, br s, *t*-Bu), 1.52 (4H, br s, *t*-Bu), 1.68 (0.5H, br s), 2.62 (0.5H, br s), 2.73–2.90 (2H, m), 3.16 (3H, s), 3.78–3.98 (2H, m), 7.04–7.38 (4H, m). MS *m/z* (%) 251 ($M^+$, 13), 221 (13), 195 (6), 178 (13), 165 (58), 151 (55), 132 (39), 120 (90), 118 (20), 91 (13), 77 (10), 57 (100). Calcd for $C_{14}H_{21}NO_3$: *M*, 251.1522. Found: *m/z* 251.1520.

### 4.27. *N*-Methyl-*N*-[2-(2-oxoethyl)phenyl]carbamic acid *tert*-butyl ester 32

To a solution of **31** (1.79 g; 7.13 mmol) in 28 mL of DMSO at room temperature was added IBX (2.39 g; 8.55 mmol) with stirring. After the reaction mixture was stirred for 2 h, the reaction was quenched with ice water. The whole was filtered off and extracted with AcOEt. The organic layer was washed twice with water and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **32** (1.54 g; 88%) as a colorless oil; IR (neat) 2978, 2725 (CHO), 1699 (CO), 1603, 1496, 1367, 1306, 1255, 1155, 1091, 1044, 977, 866 $cm^{-1}$. $^1H$ NMR $\delta$ 1.32 (6H, br s, *t*-Bu), 1.50 (3H, br s, *t*-Bu), 3.14 (3H, s), 3.63 (2H, s), 7.13–7.37 (4H, m), 9.69 (1H, s). MS *m/z* (%) 249 ($M^+$, trace), 235 (trace), 221 (10), 176 (8), 165 (90), 149 (23), 120 (45), 118 (13), 91 (22), 77 (7), 57 (100). Calcd for $C_{14}H_{19}NO_3$: *M*, 249.1365. Found: *m/z* 249.1368.

### 4.28. Mesylate 34

To a solution of LDA (2.46 mmol) in 8 mL of dry THF in a flame-dried flask at −78 °C under an argon atmosphere was added dropwise a solution of (*R*)-chloromethyl *p*-tolyl sulfoxide (0.422 g; 2.24 mmol; over 99% ee) in 2 mL of dry THF with stirring. After 10 min, to the solution of the (*R*)-α-lithio chloromethyl *p*-tolyl sulfoxide was added dropwise a solution of **32** (1.39 g; 5.59 mmol) in 2 mL of dry THF with stirring. The reaction mixture was slowly allowed to warm to −60 °C for 35 min, then the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford adduct **33** (0.96 g; 98%; a mixture of 2,3-*syn* and 2,3-*anti* diastereomers). IR (neat) 3379 (OH), 2977, 1931, 1699 (CO), 1598, 1581, 1495, 1478, 1454, 1367, 1305, 1255, 1156, 1089, 1047 (SO), 1015, 978, 862, 814, 757, 664, 624, 604, 581, 514, 472 $cm^{-1}$. $^1H$ NMR $\delta$ 1.22–1.62 (9H, m), 2.40–2.45 (3H, m), 2.75–3.27 (5H, m), 4.10–4.80 (1.5H, m), 4.98–5.15 (0.5H, m), 7.05–7.59 (7.7H, m), 7.70 (0.3H, d, $J$ = 8.2 Hz). MS *m/z* (%) 437 ($M^+$, 3), 381 (5), 337 (8), 298 (4), 242 (65), 198 (58), 164 (60), 139 (40), 120 (100), 118 (27), 57 (68), 41 (9), 28 (8). Calcd for $C_{22}H_{28}NO_4SCl$: *M*, 437.1427. Found: *m/z* 437.1427.

To a solution of adduct **33** (1.10 g; 2.51 mmol) in 14 mL of $CH_2Cl_2$ at room temperature was added a solution of MsCl (0.77 mL; 8.77 mmol) followed by TEA (1.2 mL; 7.52 mmol) with stirring. After 45 min, the reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **34** (1.12 g; 86%; a mixture of 1,2-*syn* and 1,2-*anti* diastereomers). IR (neat) 3008, 2977, 2931, 1683 (CO), 1597, 1496, 1480, 1455, 1367, 1305, 1279, 1255, 1176, 1093, 1065 (SO), 1016, 963, 905, 809, 772, 758 $cm^{-1}$. $^1H$ NMR $\delta$ 1.21–1.53 (9H, m), 2.33–2.50 (6H, m), 2.96–3.32 (5H, m), 3.45 (1H, dt, $J$ = 14.1, 2.0 Hz), 4.78–5.14 (1H, m), 7.12–7.56 (8H, m). MS *m/z* (%) 515 ($M^+$, 5), 442 (5), 415 (20), 363 (5), 347 (4), 320 (27), 276 (10), 266 (18), 224 (92), 180 (56), 144 (100), 120 (85), 91 (19). Calcd for $C_{23}H_{30}NO_6S_2Cl$: *M*, 515.1204. Found: *m/z* 515.1198.

### 4.29. (*Rs*)-*N*-{2-[3-Chloro-3-(toluene-4-sulfinyl)propyl]phenyl}-*N*-methylcarbamic acid *tert*-butyl ester 36

To a solution of **34** (27 mg; 0.052 mmol) in 0.52 ml of DMI at room temperature was added a solution of $LiBH_4$ (2.0 M solution in THF, 0.078 mL; 0.156 mmol) with stirring. The reaction mixture was allowed to warm to 65 °C for 2.5 h. The reaction was quenched with satd aq $NH_4Cl$. The whole was extracted with $CHCl_3$. The organic layer was washed with satd aq $NH_4Cl$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **36** (16 mg; 68%) as a mixture of *syn* and *anti* diastereomers (*syn*:*anti* = 2:3); IR (neat) 2929, 1695 (CO), 1598, 1495, 1455, 1368, 1305, 1257, 1154, 1088, 1058 (SO), 1017, 977, 907, 867, 811, 760 $cm^{-1}$. $^1H$ NMR $\delta$ 1.26, 1.29, 1.32, 1.49 (each br s, total 9H, *t*-Bu), 1.70–1.91 (0.4H, br s), 2.08–2.24 (0.6H, br s), 2.42 (2.3H, s), 2.43 (0.7H, s), 2.50–2.62 (1H, m), 2.66–2.80 (1H, m), 2.82–3.02 (1H, m), 3.04–3.16 (3H, m), 4.34–4.46 (0.6H, m), 4.47–4.56 (0.4H, m), 7.04–7.40 (6H, m), 7.46–7.64 (2H, m). MS *m/z* (%) 421 ($M^+$, 5), 365 (13), 348 (7), 321 (9), 226 (100), 190 (15), 164 (34), 146 (38), 120 (37), 118 (11). Calcd for $C_{22}H_{28}ClNO_3S$: *M*, 421.1479. Found: *m/z* 421.1483.

### 4.30. (*S,Rs*)-*N*-{2-[3-Chloro-3-(toluene-4-sulfinyl)propyl]phenyl}-*N*-methylamine 37a

A solution of **36** (117 mg; 0.278 mmol) in 0.7 mL of $CH_2Cl_2$ was cooled in an ice bath. To this solution was added TFA (0.265 mL) with stirring. After 3 h, the reaction was quenched with 5% aq NaOH. The whole was extracted with $CH_2Cl_2$. The organic layer was washed with 5% aq NaOH and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **37a** (52 mg; 59%) and **37b** (37 mg; 41%). Compound **37a**: Colorless crystals; mp 92.5–93.5 °C (AcOEt–hexane); IR (neat) 3395 (NH), 2923, 2813, 1605, 1585, 1516, 1493, 1470, 1427, 1363, 1310, 1266, 1172, 1085, 1047(SO), 1016, 905, 841, 811, 750, 623, 515 $cm^{-1}$. $^1H$ NMR $\delta$ 2.24–2.39 (1H, m), 2.43 (3H, s), 2.41–2.55 (1H, m), 2.68–3.02 (2H, m), 2.87 (3H, s), 4.07 (1H, br s), 4.47 (1H, dd, $J$ = 7.0, 3.6 Hz), 6.64 (2H, dq, $J$ = 7.8, 1.0 Hz), 7.02 (1H, d, $J$ = 7.4 Hz), 7.18 (1H, t, $J$ = 7.8 Hz), 7.34 (2H, d, $J$ = 8.0 Hz), 7.48 (2H, d, $J$ = 8.2 Hz). MS *m/z* (%) 321 ($M^+$, 43), 182 (25), 146 (33), 120 (100), 118 (10), 91 (23). Calcd for $C_{17}H_{20}ClNOS$: *M*, 321.0954. Found: *m/z* 321.0954. $[\alpha]_D^{29} = -158$ (*c* 1.35, $CHCl_3$). Both diastereomeric excess and enantiomeric excess of **37a** were determined to be over 99% by HPLC using CHIRALCEL OD (hexane/*i*-PrOH = 9:1) as a chiral stationary column.

### 4.31. (*R,Rs*)-*N*-{2-[3-Chloro-3-(toluene-4-sulfinyl)propyl]phenyl}-N-methylamine 37b

Colorless oil; IR (neat) 3400 (NH), 3044, 2924, 1604, 1584, 1515, 1470, 1308, 1265, 1170 1086, 1049, 910, 810 $cm^{-1}$. $^1H$ NMR $\delta$ 1.88–1.96 (1H, m), 2.42 (3H, s), 2.52–2.58 (1H, m), 2.65–2.70 (1H, m), 2.79–2.84 (1H, m), 2.85 (3H, s), 3.73 (1H, br s), 4.54 (1H, dd, $J$ = 9.6, 3.6 Hz), 6.62 (1H, dd, $J$ = 8.4, 0.6 Hz), 6.67 (1H, dt, $J$ = 12.0, 1.2 Hz), 7.01 (1H, dd, $J$ = 7.8, 1.8 Hz), 7.18 (1H, dt, $J$ = 6.0, 1.8 Hz), 7.32 (2H, d, $J$ = 7.8 Hz), 7.52 (2H, d, $J$ = 8.4 Hz). MS *m/z* (%) 321 ($M^+$, 43), 182 (25), 146 (48), 130 (17), 120 (100), 91 (37). Calcd for $C_{17}H_{20}ClNOS$: *M*, 321.0954. Found *m/z* 321.0949. $[\alpha]_D^{25} = -80.8$ (*c* 0.45, ethanol).

### 4.32. (*R*)-(−)-1-Methyl-1,2,3,4-tetrahydroquinoline-2-carboxylic acid ethyl ester 38

Colorless oil; $[\alpha]_D^{26} = -32.1$ (*c* 0.5, ethanol). All spectral data were consistent with those of **7a**.

### 4.33. (*R*)-1,2,3,4-Tetrahydroquinoline-2-carboxylic acid ethyl ester 40

Thionyl chloride (1.14 g; 14.8 mmol) was added to a solution of **39** (1.81 g; 10.2 mmol) in 10 mL of ethanol at 0 °C and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with satd aq $K_2CO_3$ and the whole was extracted with AcOEt. The organic layer was washed with satd aq $K_2CO_3$ and dried over $MgSO_4$. The product was purified by silica gel column chromatography to afford **40** (1.72 g; 82%) as a colorless oil. IR (neat) 3400 (NH), 2979, 2933, 1733 (CO), 1608, 1587, 1497, 1371, 1341, 1299, 1209, 1028, 748 $cm^{-1}$. $^1H$ NMR $\delta$ 1.29 (3H, t, $J$ = 7.1 Hz), 1.91–2.05 (1H, m), 2.24–2.35 (1H, m), 2.69–2.90 (2H, m), 4.01 (1H, dd, $J$ = 9.0, 3.7 Hz), 4.15–4.31 (2H, m), 4.32–4.42 (1H, br s), 6.56–6.70 (2H, m), 6.92–7.05 (2H, m). MS *m/z* (%) 205 ($M^+$, 18), 132 (100), 130 (13), 117 (7), 103 (3), 77 (4). Calcd for $C_{12}H_{15}NO_2$: *M*, 205.1105. Found: *m/z* 205.1103.

### 4.34. (*R*)-1-Methyl-1,2,3,4-tetrahydroquinoline-2-carboxylic acid ethyl ester 38′

To a solution of **40** (13 mg; 0.063 mmol) and 37% aqueous formaldehyde (0.077 mL; 0.95 mmol) in 0.7 mL of acetonitrile was added $NaBH_3CN$ (19 mg; 0.29 mmol) with stirring. Acetic acid (0.019 mL) was added to the reaction mixture and the whole was stirred at room temperature for 30 min. Acetic acid (0.019 mL) was added to the reaction mixture and the whole was stirred for

another 30 min. The reaction mixture was diluted with ether and the organic layer was washed with aq NaOH followed by brine. The organic layer was dried over $MgSO_4$ and the product was purified by silica gel column chromatography to afford **38′** (13 mg; 92%) as a colorless oil. $[\alpha]_D^{26} = -31.9$ (*c* 1.4, ethanol). All spectroscopic data were consistent with those of **7a**.

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