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Regio- and stereoselective synthesis of 1,3-aminoalcohol derivatives from allylamine derivatives via internal sulfinyl group participation ☆

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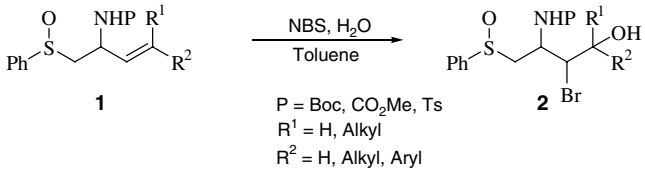
Abstract—The regio- and stereoselective preparation of 1,3-aminoalcohol derivatives from protected allylamines via intramolecular participation by the sulfinyl group is reported. A carbamate protecting group on nitrogen leads to products arising from nucleophilic participation by both the sulfinyl and carbamate groups, while protection as the sulfonamide affords the product arising from sulfinyl group participation alone.

1. Introduction

1,3-Aminoalcohols are structural units present in many synthetic[1] and natural products[2] possessing potent biological activity. Their potential as chiral auxiliaries and ligands in asymmetric synthesis is also well recognized.[3] Not surprisingly, 1,3-aminoalcohols have attracted the attention of synthetic chemists with a number of different strategies being devised for their construction.[4] 1,2-/1,3-Stereocontrol, in the reaction of acyclic allylic and homoallylically substituted olefins with electrophiles, by asymmetric induction, constitutes a valuable synthetic tactic.[5] We report herein a novel methodology for the regio- and stereoselective synthesis of 1,3-aminoalcohol derivatives **2** from β-protected amino-γ,δ-unsaturated sulfoxides **1**, by 1,2-asymmetric induction via intramolecular nucleophilic assistance by the sulfinyl group[6] (Eq. 1).



(1)

2. Results and discussion

The diastereomeric unsaturated sulfoxides **7**–**9** were prepared in a short sequence of straightforward reactions from acetonide **3**.[7] Thus deprotection of the acetonide group in **3** via treatment with cat. amounts of camphor-10-sulfonic acid (CSA) in methanol afforded the aminoalcohol **4**. Compound **4** was further converted into the sulfide **6** in a single step using the Hata protocol[8] or in two steps by initial mesylation of the hydroxy group followed by displacement of the mesylate with thiophenol. Oxidation of the sulfide **6** with $NaIO_4$[9] afforded an equimolar mixture of sulfoxides **7***a* and **7***s*, which were separated by column chromatography (Scheme 1). Deprotection of the carbamate group of **7***a* and **7***s* individually with trifluoroacetic acid, followed by reprotection of the resulting ammonium salt as the

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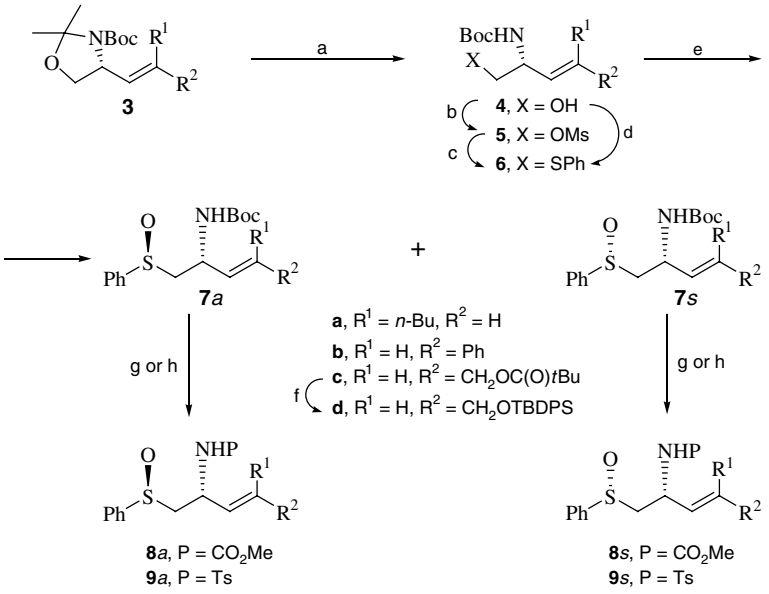


Scheme 1. Preparation of diastereomeric β-protected amino unsaturated sulfoxides. Reagents and conditions: (a) CSA (cat.), MeOH, rt, 16 h, **4a**: 72%; **4b** 75%; **4c**: 70%; (b) MsCl, Et_3N, CH_2Cl_2, rt, 30 min; (c) PhSH, DBU, PhH, rt, 30 min, **6a**: 91%; **6b**: 87%; (d) PhSSPh, PBu_3P, THF, 72 °C, 76 h, **6c**: 63%; (e) $NaIO_4$, MeOH, H_2O, rt, 16 h, **7a***a* and **7a***s*: 94%; **7b***a* and **7b***s*: 92%; **7c***a* and **7c***s*: 90%; (f) i. 0.5 M NaOH, MeOH, H_2O, rt, 16 h, 95%; ii. TBDPS–Cl, imidazole, DMF, rt, 2 h, 80%; (g) i. TFA/DCM, 0 °C, 30 min, 95%; ii. $ClCO_2Me$, Et_3N, 0 °C to rt, 1 h, 86%; (h) i. TFA/DCM, 0 °C, 30 min, 95%; ii. *p*-TsCl, Et_3N, 0 °C to rt, 1 h.

methyl carbamate or sulfonamide afforded sulfoxides **8***a*/**8***s* and **9***a*/**9***s*, respectively.

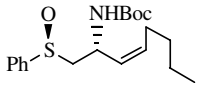
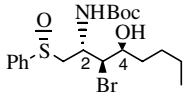
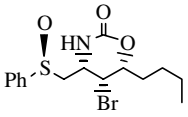
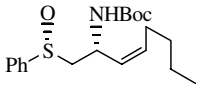
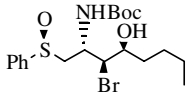
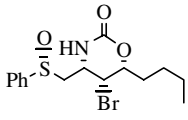
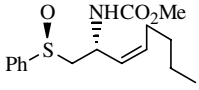
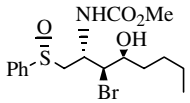
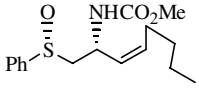
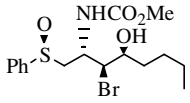
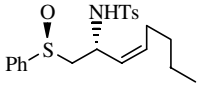
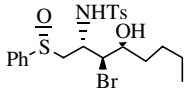
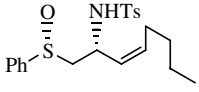
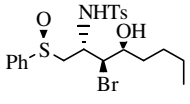
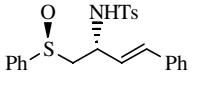
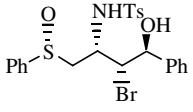
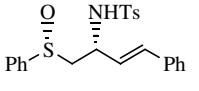
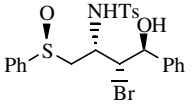
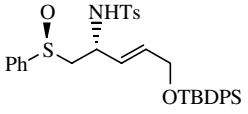
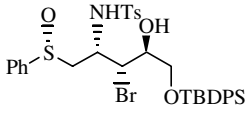
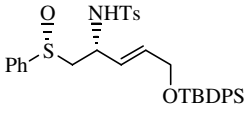
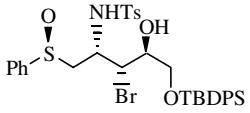
The diastereomeric sulfoxides **7**–**9** were prepared in order to study their reaction with *N*-bromosuccinimide (NBS), which would allow us to understand the influence of the relative stereochemistry of the sulfinyl and allylic amino substituent on the regio- and stereochemical outcome of the reaction. The diastereomerically pure sulfoxides were reacted at ambient temperature with NBS in toluene as the solvent, in the presence of water to afford the aminoalcohol derivatives (Table 1).

Sulfoxides **7a**, wherein the allylic amino substituent was protected as the *tert*-butyl carbamate, afforded products arising from internal participation of both the carbamate[10] and sulfinyl groups with the former pathway being slightly favoured. The methyl carbamate moiety is known to be a poorer nucleophile[10e] when compared to the *tert*-butyl carbamate group. Thus sulfoxides **8a** were prepared and reacted with NBS. It is clear from entries 3 and 4 in Table 1 that the products resulting from the sulfinyl group participation, although not formed exclusively, are the predominant component of the reaction mixture. The nucleophilicity of the sulfinyl group can therefore be assumed to be inbetween that of the *tert*-butyl and methyl carbamate group. In the search for a protecting group for the amino substituent that would not function as a nucleophile, the toluenesulfonamides **9** were prepared and treated with NBS. Inspection of the table reveals the following trends: (1) The products resulting from sulfinyl group participation were formed exclusively in the reaction of **9** with NBS. (2) The reaction is highly regioselective affording products from a 6-*endo* nucleophilic attack, probably as a consequence of the inductive electron withdrawing nature of the allylic amino substituent, which would destabilize any partial positive charge developing at C3. (3) The reaction is general, stereoselective and proceeds to afford a product in good yield. (4) The protecting group on the amino substituent has very little influence on the stereoselectivity of the reaction (i.e., compare entries 1, 3, 5 and 2, 4, 6). (5) Opposite stereo- selectivity is observed in products arising via carbamate and sulfinyl group participation, indicating different reaction pathways. The asymmetric induction in the pathway proceeding via carbamate participation is very high. (6) The sulfoxides with a relative *syn*-orientation of the sulfinyl and amino substituents react more stereoselectively than sulfoxides with an *anti*-disposition of sulfinyl and amino substituents (compare entries 1, 3, 5, 7 and 9 with 2, 4, 6, 8 and 10). It is noteworthy that diastereomers **7***s*–**9***s* with the relative *syn*-disposition of the sulfinyl and amino substituent can be selectively prepared from **6** following the protocol reported by Lewanowicz et al.[11]

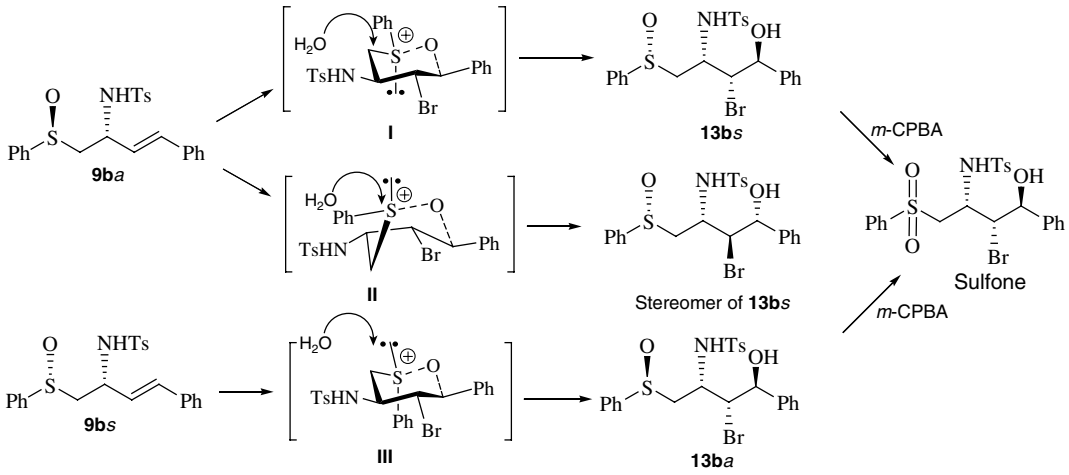
The regio- and stereoselectivity of the reaction can be rationalized (as illustrated for sulfoxides **9b**) by invoking the sulfoxonium ion intermediate (**I**, **II** and **III**), formed by the nucleophilic attack of the sulfinyl group on the olefin π-complexed to the bromonium ion[12] in a 6-*endo* fashion followed by hydrolysis by the attack of water on sulfur[13] (Scheme 2). There is a net inversion of sulfur configuration in going from the starting material to the product.

The isomeric nature of products **10a***s*/**10a***a*, **11a***s*/**11a***a*, **12a***s*/**12a***a*, **13a***s*/**13a***a*, **13b***s*/**13b***a* and **13d***s*/**13d***a* were established by individually oxidizing the sulfoxides to yield the identical sulfones.

Table 1. Regio- and stereoselective formation of bromohydrins[a]

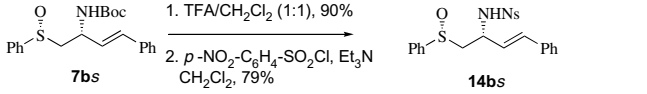
S. No.	Allyl amino derivative	Product from sulfinyl participation	C2/C3 *syn*/*anti*	Product from carbamate participation	C2/C3 *syn*/*anti*	Ratio[b] (yield, %)[c]
1	 **7a*a***	 **10a*s***	17:83	 **11a*a***	>95:<5	3:2 (81)
2	 **7a*s***	 **10a*a***	10:90	 **11a*s***	>95:<5	1:2 (78)
3	 **8a*a***	 **12a*s***	8:92	**11a*a***	>95:<5	8:2 (70)
4	 **8a*s***	 **12a*a***	<5:>95	**11a*s***	>95:<5	8.5:1.5 (70)
5	 **9a*a***	 **13a*s***	15:85			100:0 (76)
6	 **9a*s***	 **13a*a***	<5:>95			100:0 (82)
7	 **9b*a***	 **13b*s***	85:15			100:0 (75)
8	 **9b*s***	 **13b*a***	>95:<5			100:0 (80)
9	 **9d*a***	 **13d*s***	70:30[d]			100:0 (70)
10	 **9d*s***	 **13d*a***	85:15[d]			100:0 (70)

[a] All reactions were carried out on 0.5 mmol scale in the presence of 1.2 equiv of NBS and 1.5 equiv of water.
[b] Ratio refers to the products arising from sulfinyl versus carbamate participation, respectively.
[c] Yield refers to the combined yield of all the products resulting from the reaction.
[d] Approx. 10–15% of the regiomer was also formed.



Scheme 2. Reaction pathways affording stereoisomeric products.

Suitable crystals were obtained from the *p*-nitrobenzenesulfonamide derivative **14b***s*, derived from **7b***s* (Eq. 2), with its structure deduced by X-ray diffraction[14] (Fig. 1). Based on the crystal structure of **14b***s*, a structure could be assigned to **9b***s* since it was also derived from **7b***s*. The relationship between the absolute configuration of sulfoxides and the chiroptical properties is well known.[11,15] The positive sign observed for the primary band (235–255 nm) in the Cotton effect curve of **9b***s* also confirms the (*R*)-configuration for the sulfinyl group (Fig. 2). The positive sign for the primary band in the cotton effect curve of **9a***s* and **9d***s* (Fig. 2) supports the structure assigned to it. The CD spectra of **9a***a*, **9b***a* and **9d***a* were almost mirror images of **9a***s*, **9b***s* and **9d***s*, respectively (Fig. 2).



(2)

Structures were assigned to **7a***s* and **7d***s* by the comparison of their ^{1}H NMR data with **7b***s*.[16] Similarly the ^{1}H NMR of **7a***a* and **7d***a* were similar to the ^{1}H NMR of **7b***a*.[16] The chemical shifts of the methine proton (C2-H) of the diastereomeric sulfoxides are diagnostic; the C2-H proton in the *anti*-series appears downfield.[16]

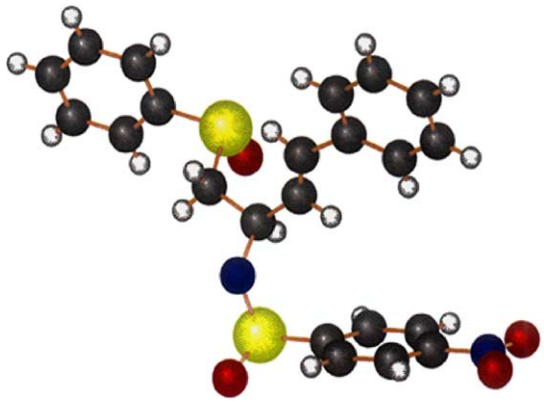


Figure 1. X-ray structure of **14b***s*.

The structure of **10a***a*, the major stereoisomer arising from **7a***s*, was assigned by inspection of the ^{1}H NMR data of the derived oxazinone **15**[17] (Scheme 3). The C3 methine proton coupling with C2 and C4 methine protons were 8.7 and 3.5 Hz, respectively. The ^{1}H NMR data of oxazinone **11a***a* supported the structure assigned to it as well. An NOE was observed between the methine protons at C2 and C4. In addition the *J* values for C3 methine proton coupling with the C2 and C4 methine protons were 3.5 and 2.5 Hz, respectively. The oxazinone derived from the minor isomer arising from **7a***s* was found to be identical to that of **11a***a* (Scheme 3). This proves beyond doubt that there is inversion of sulfur configuration[6c,d] in going from **7a***s* to **10a***a* and its minor stereoisomer due to intramolecular sulfinyl group participation.[18] Deprotection of the Boc group in **10a***s* and its subsequent treatment with methyl chloroformate and *p*-toluenesulfonyl chloride in the presence of a base afforded products identical to **12a***s* and **13a***s*, thus proving their structure (Scheme 3). The relative orientation of the substituents at C2–C4 in **13b***s* and **10a***a* was proven by transforming them into tetrahydrofuran derivatives **16** and **17**, respectively.[19] Compound **16** revealed NOE's between the C2 and C4 methine protons and C1 and C3 methine protons, thus proving the assigned structure. Compound **17** revealed NOE between C2 and C4 methine protons. The structure of **13d***s*/**13d***a* was assigned based on an analogy with **13b***s*/**13b***a*, respectively, since the *trans*-olefins **9b** and **9d** were expected to react similarly.

3. Conclusion

In conclusion we have disclosed a methodology for the regio- and stereoselective synthesis of 1,3-aminoalcohols from allylamine derivatives via efficient asymmetric induction and intramolecular nucleophilic participation by the sulfinyl group. Highly functionalized products are obtained, which can be further elaborated by carbon–

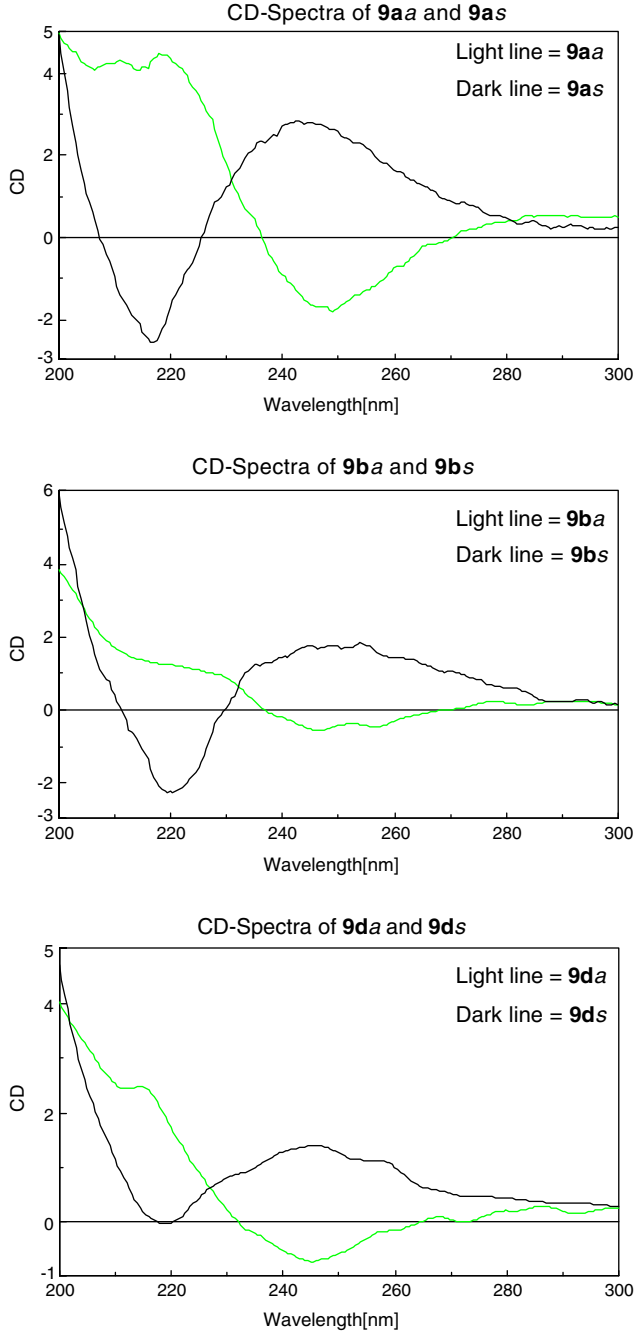


Figure 2. CD spectra. These were recorded in acetonitrile in the concentration range of 10^{-4}–10^{-5} M.

carbon and carbon–heteroatom bond formations into bioactive target molecules. The potential of the methodology to synthesize natural products possessing the 1,3-aminoalcohol subunit is currently in progress and shall be disclosed in due course.

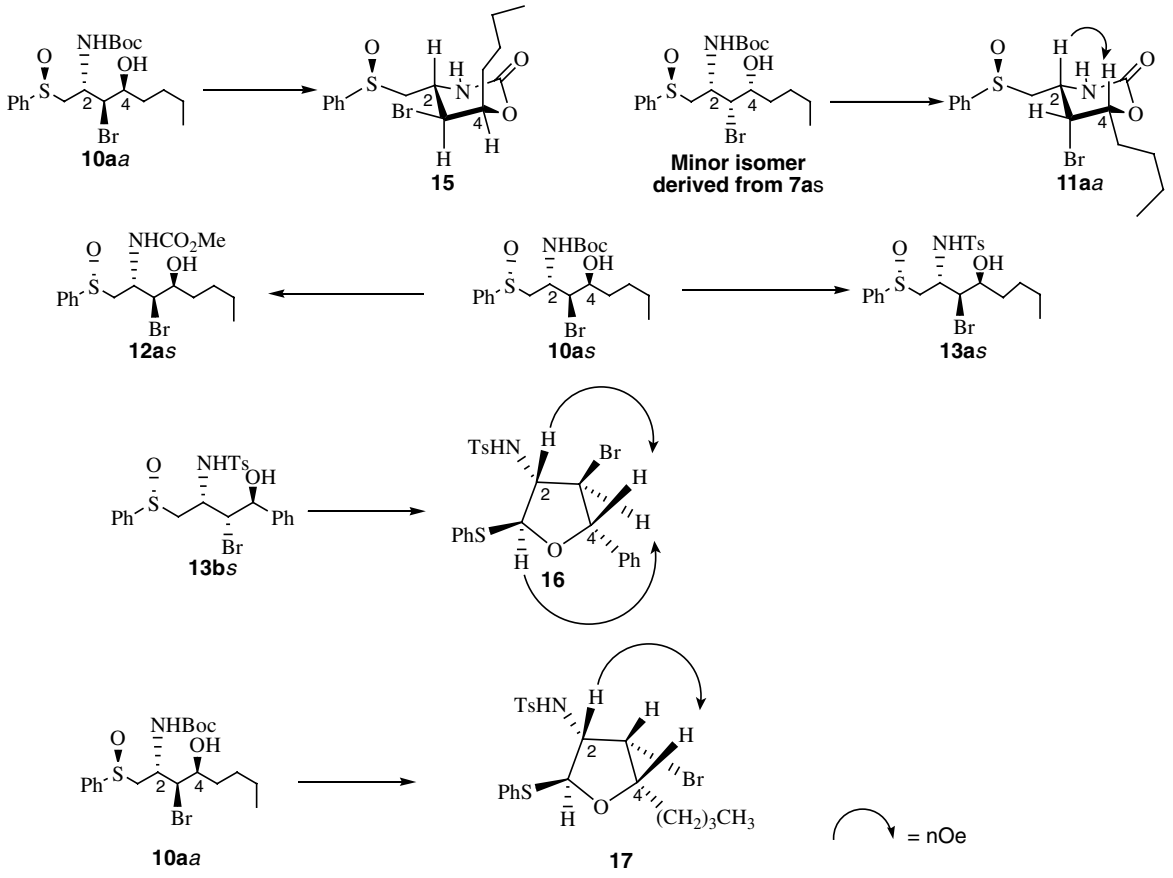
4. Experimental section

4.1. General

All air or moisture sensitive reactions were carried out under nitrogen atmosphere. Solvents were distilled freshly, THF over Na/benzophenone ketyl, DCM over P_2O_5 followed by CaH_2 and toluene over P_2O_5. Commercially available reagents were used without further purification except NBS, which was freshly recrystallized from hot water before use. Thin layer chromatography was performed with precoated silica gel plates. Column chromatography was carried out using silica gel (60–120 mesh). NMR spectra were recorded on a 200, 300 or 400 MHz spectrometer. ^{1}H NMR and ^{13}C NMR samples were internally referenced to TMS (0.00 ppm). Melting points are uncorrected.

4.1.1. Preparation of *tert*-butyl 4-[(*Z*)-1-hexenyl]-2,2-dimethyl-(4*S*)-1,3-oxazolane-3-carboxylate, 3a. *n*-Pentylphosphonium bromide (4.45 g, 11 mmol) was suspended in dry THF (44 mL) in a round bottom flask under N_2, cooled to −78 °C at which point *n*-BuLi (5 mL, 2 M in hexane, 10 mmol) was added dropwise over 10 min. The mixture was stirred for 30 min while gradually allowing the temperature to reach 0 °C after which stirring continued for a further period of 1 h at the same temperature. The resulting dark red solution was cooled to −78 °C and a solution of Garner's aldehyde (2.3 g, 10 mmol) in THF (10 mL) added dropwise over 10 min. The reaction mixture was gradually allowed to return to room temperature and stirred for a further period of 4 h at room temperature. The reaction mixture was then quenched with water and washed successively with an aq 1 M HCl solution, brine and dried over Na_2SO_4. Purification on a silica gel column using AcOEt/petroleum ether (1:19, v/v) afforded **3a** (1.26 g, 6.2 mmol) in 62% yield. Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.52–5.32 (m, 2H), 4.72–4.50 (br s, 1H), 4.02 (dd, $J = 9.0$, 6.7 Hz, 1H), 3.61 (dd, $J = 9.0$, 4.2 Hz, 1H), 2.24–1.98 (m, 2H), 1.56 (s, 3H), 1.54–1.24 (m, 16H), 0.91 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3010$–2830, 1695, 1375, 1250, 1175, 1090, 1050, 850. $[\alpha]_D^{25} = +55.0$ (*c* 0.95, $CHCl_3$). MS (EI) 203 $[M]^+$. Anal. Calcd for $C_{16}H_{29}NO_3$: C, 67.81; H, 10.31; N, 4.94. Found: C, 67.75; H, 10.13; N, 4.72.

4.1.2. Preparation of *tert*-butyl 2,2-dimethyl-4-[2-phenyl-(*E*)-1-ethenyl]-1,3-oxazolane-3-carboxylate, 3b. Benzylphosphonium bromide (3.92 g, 11 mmol) was suspended in dry THF (44 mL) in a round bottom flask under N_2, cooled to −78 °C and *n*-BuLi (5 mL, 2 M in hexanes, 10 mmol) added dropwise over 10 min. The mixture was stirred for 30 min gradually allowing the temperature to reach 0 °C and stirred further for a period of 1 h at the same temperature. The resulting dark red solution was cooled to −78 °C and a solution of Garner's aldehyde (2.3 g, 10 mmol) in THF (10 mL) added dropwise over 10 min. The reaction mixture was gradually allowed to return to room temperature and then stirred for a further period of 4 h. The reaction mixture was then quenched with water and washed successively with aq 1 M HCl solution, brine and dried over Na_2SO_4. ^{1}H NMR of the crude product revealed the presence of *cis*- and *trans*-olefins in a ratio of 4:1. The product mixture was subjected to isomerization following the



Scheme 3. Elucidation of the structure of aminoalcohols.

protocol previously reported by Schwarz et al.[7a] Thus, PhSH (37 mg, 0.33 mmol) and AIBN (54 mg, 0.33 mmol) were added to the olefin mixture (2.0 g, 6.6 mmol) in benzene (25 mL) and refluxed for 16 h. The reaction mixture was diluted with benzene and washed successively with 0.2 M NaOH soln, water, brine and dried over Na_2SO_4. Evaporation of the volatiles under reduced pressure followed by column chromatography using AcOEt/petroleum ether (1:19, v/v) as the eluent afforded **3b** (2.0 g, 6.6 mmol) in 66% overall yield for 2 steps. Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35–7.10 (m, 5H), 6.49 (d, $J = 12.2$ Hz, 1H), 5.68 (dd, $J = 12.2$, 9.5 Hz, 1H), 4.91–4.75 (m, 1H), 4.23–4.08 (m, 1H), 3.86–3.72 (m, 1H), 1.62 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H). IR (neat) $\nu = 3060$–2880, 1700, 1480, 1455, 1380, 1255, 1175, 1100. $[\alpha]_D^{25} = -63.6$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 304 $[M+H]^+$. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 70.97; H, 8.13; N, 4.83.

4.1.3. *tert*-Butyl 4-[3-(*tert*-butylcarbonyloxy)-(*E*)-1-propenyl]-2,2-dimethyl-1,3-oxazolane-3-carboxylate, 3c. Ethyl-(triphenylphosporanilidine)acetate (8.3 g, 20 mmol) was added portionwise to a solution of Garner aldehyde (4.6 g, 20 mmol) in benzene (60 mL) at room temperature and then stirred for 30 min. After evaporation of the solvent under reduced pressure, ether was added to the residue and cooled to 0 °C. Most of the triphenylphosphine oxide formed in the reaction precipitated out and was removed by filtration. The filtrate was concentrated and the residue purified by column chromatography using AcOEt/petroleum ether (1:9, v/v) as the eluent to afford the unsaturated ester (5.68 g, 19 mmol) in 95% yield. Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.83 (dd, $J = 15.8$, 8.7 Hz, 1H), 5.87 (d, $J = 15.8$ Hz, 1H), 4.59–4.34 (m, 1H), 4.20 (q, $J = 7.0$ Hz, 2H), 4.12–3.98 (m, 1H), 3.73–3.68 (m, 1H), 1.68–1.39 (m, 15H), 1.25 (t, $J = 7.0$ Hz, 3H). IR (neat) $\nu = 2928$, 1742, 1698, 1390, 1256, 1176. MS (LSIMS) 300 $[M+H]^+$. In a dry round bottom flask containing dry toluene (32 mL), diisobutylaluminium hydride (47.5 mmol, 47.5 mL, 1 M soln in toluene) was added, followed by *n*-BuLi (47.5 mmol, 23.75 mL, 2 M in hexanes) dropwise over a period of 10 min at ambient temperature. The above prepared ate complex was added to a solution of the unsaturated ester (5.68 g, 19 mmol) in toluene (38 mL) and cooled at −78 °C, over a period of 10 min. The reaction mixture was stirred for 40 min while gradually allowing it to return to rt and then left to stir for a further period of 30 min. The reaction mixture was diluted with ether (100 mL) and small ice pieces added to quench the reaction. The gel that precipitated out was filtered through a sintered funnel and the gel washed with hot ethyl acetate. Evaporation of the filtrate under reduced pressure and column chromatography of the residue using AcOEt/petroleum ether (3:7, v/v) afforded the allylalcohol (3.55 g, 13.87 mmol) in 73% yield. Liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.78–5.60 (m, 2H), 4.40–4.23 (m, 1H), 4.16–4.07 (m, 2H), 4.02–3.72 (m, 2H), 3.90 (br

s, OH), 1.61–1.42 (m, 15H). $[\alpha]_D^{25} = +23.6$ (*c* 0.75, $CHCl_3$). IR (neat) $\nu = 3445$, 2980, 1696, 1392, 1255, 1170. MS (EI) 257 $[M]^+$.

To the stirred solution of allylalcohol (3.55 g, 13.9 mmol) in dry dichloromethane (56 mL) was added successively Et_3N (2.10 g, 20.8 mmol) and pivaloyl chloride (1.81 g, 15 mmol) at 0 °C. The reaction mixture was gradually allowed to attain rt and stirred for a further period of 25 min. The reaction mixture was diluted with DCM, washed successively with water, 10% aq citric acid soln, brine and dried over Na_2SO_4. The organic layer was evaporated under reduced pressure, and the crude residue purified by column chromatography using AcOEt/petroleum ether (1:9, v/v) as the eluent to afford the ester **3c** (3.91 g, 11.51 mmol) in 83% yield (58% overall yield from Garner aldehyde). Liquid. ^1H NMR (200 MHz, $CDCl_3$) δ 5.74–5.53 (m, 2H), 4.60–4.47 (m, 2H), 4.30–4.16 (m, 1H), 4.02 (dd, $J = 8.9$, 6.7 Hz, 1H), 3.72 (dd, $J = 8.9$, 2.2 Hz, 1H), 1.59 (s, 3H), 1.51–1.31 (br s, 12H), 1.17 (s, 9H). IR (neat) $\nu = 3378$, 2977, 2877, 1699, 1479, 1383, 1254, 1159, 1097. $[\alpha]_D^{25} = +1.6$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 342 $[M+H]^+$. Anal. Calcd for $C_{18}H_{31}NO_5$: C, 63.32; H, 9.15; N, 4.10. Found: C, 63.49; H, 9.42; N, 3.87.

4.1.4. General procedure for the cleavage of the acetonide group in 3 to yield 4. To the substrate **3** (5 mmol) in methanol (20 mL) was added camphor-10-sulfonic acid (62.5 mg, 0.25 mmol) at room temperature and stirred for 16 h under N_2 atmosphere. The reaction mixture was quenched by the addition of a few drops of Et_3N and the solvent evaporated under reduced pressure. The crude product mixture was chromatographed on a silica gel column using AcOEt/petroleum ether (1:24, v/v) as the eluent to afford the aminoalcohol **4**.

4.1.4.1. 2-(*tert*-Butyloxycarbonylamido)-(2*R*,3*Z*)-3-octen-1-ol, 4a. Solid, 72%, mp 65–66 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 5.57 (dt, $J = 10.9$, 7.4 Hz, 1H), 5.25 (dd, $J = 10.9$, 9.1 Hz, 1H), 4.72–4.53 (br s, NH), 4.52–4.35 (m, 1H), 3.64–3.48 (m, 2H), 2.25–2.05 (m, 2H), 1.45 (s, 9H), 1.45–1.26 (m, 4H), 0.91 (distorted t, 3H). IR (neat) $\nu = 3460$–3380, 3040–2860, 1701, 1500, 1387, 1258, 1145. $[\alpha]_D^{25} = +29.6$ (*c* 1.0, $CHCl_3$). MS (EI) 243 $[M]^+$. Anal. Calcd for $C_{13}H_{25}NO_3$: C, 64.17; H, 10.35; N, 5.76. Found: C, 64.21; H, 10.28; N, 5.72.

4.1.4.2. 2-(*tert*-Butyloxycarbonylamido)-4-phenyl-(2*R*,3*E*)-3-buten-1-ol, 4b. Solid, 75%, mp 95–96 °C. ^1H NMR (200 MHz, $CDCl_3$) δ 7.41–7.17 (m, 5H), 6.60 (d, $J = 15.8$ Hz, 1H), 6.14 (dd, $J = 15.8$, 6.3 Hz, 1H), 4.95–4.82 (br s, NH), 4.47–4.32 (m, 1H), 3.78 (dd, $J = 10.2$, 4.1 Hz, 1H), 3.73 (dd, $J = 10.2$, 4.9 Hz, 1H), 1.46 (s, 9H). IR (neat) $\nu = 3600$–3280, 3005, 1700, 1500, 1270, 1170. $[\alpha]_D^{25} = -40.6$ (*c* 1.0, $CHCl_3$). MS (EI) 263 $[M]^+$. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.32; H, 8.17; N, 5.70.

4.1.4.3. 4-(*tert*-Butyloxycarbonylamido)-5-hydroxy-(*E*,4*R*)-2-pentenyl pivalate, 4c. Liquid, 70%. ^1H NMR (200 MHz, $CDCl_3$) δ 5.82–5.60 (m, 2H), 4.78 (d, $J = 6.0$ Hz, NH), 4.57 (d, $J = 4.0$ Hz, 2H), 4.26–4.22 (m, 1H), 3.72–3.53 (m, 2H), 1.47 (s, 9H), 1.22 (s, 9H). IR (neat) $\nu = 3369$, 2975, 1712, 1699, 1518, 1367, 1284, 1163, 1059. $[\alpha]_D^{25} = +3.6$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 302 $[M+H]^+$. Anal. Calcd for $C_{16}H_{29}NO_3$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.66; H, 9.14; N, 4.77.

4.1.5. General procedure for mesylation. To a solution of **4** (1 mmol) in dichloromethane (2 mL) cooled at 0 °C was added successively Et_3N (131 mg, 1.3 mmol), DMAP (cat.) and methanesulfonyl chloride (115 mg, 1 mmol) at 0 °C and stirred for 10 min at the same temperature. The reaction mixture was quenched by the addition of water and then extracted into dichloromethane. The organic layer was washed successively with 10% aq citric acid, aq $NaHCO_3$, water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and taken to the next step without further purification.

4.1.5.1. 2-(*tert*-Butyloxycarbonylamido)-(*Z*)-3-octenyl methanesulfonate, 5a. Viscous liquid, 95%. ^1H NMR (200 MHz, $CDCl_3$) δ 5.63 (dt, $J = 10.8$, 7.4 Hz, 1H), 5.31 (dd, $J = 10.8$, 8.8 Hz, 1H), 4.75–4.54 (m, 1H and NH), 4.23 (dd, $J = 9.7$, 3.7 Hz, 1H), 4.14 (dd, $J = 9.7$, 5.6 Hz, 1H), 2.99 (s, 3H), 2.23–2.02 (m, 2H), 1.54–1.22 (m, 13H), 0.92 (t, $J = 6.7$ Hz, 3H).

4.1.5.2. 2-(*tert*-Butyloxycarbonylamido)-4-phenyl-(*E*)-3-butenyl methanesulfonate, 5b. Liquid, 98%. ^1H NMR (200 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H), 6.63 (d, $J = 15.6$ Hz, 1H), 6.12 (dd, $J = 15.6$, 6.2 Hz, 1H), 4.92 (d, $J = 8.6$ Hz, NH), 4.60–4.56 (m, 1H), 4.37 (dd, $J = 9.8$, 4.4 Hz, 1H), 4.29 (dd, $J = 9.8$, 5.1 Hz, 1H), 3.02 (s, 3H), 1.47 (s, 9H).

4.1.6. General procedure for preparation of sulfides. To a solution of **5** (1 mmol) in benzene (2 mL) was added successively PhSH (110 mg, 1 mmol) and DBU (228 mg, 1.5 mmol) under N_2 and stirred for 30 min. The reaction mixture was diluted with ether and washed successively with 0.2 M aq NaOH solution, water, brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure followed by purification on silica gel column using AcOEt/petroleum ether (3:97, v/v) afforded the thioether **6**.

4.1.6.1. 1-Phenylsulfanyl-(2*R*,3*Z*)-3-octen-2-*tert*-butyloxycarbonylamide, 6a. Viscous liquid, 91%. ^1H NMR (200 MHz, $CDCl_3$) δ 7.50–7.12 (m, 5H), 5.51 (dt, $J = 10.8$, 6.7 Hz, 1H), 5.34–5.27 (m, 1H), 4.65–4.45 (m, 1H and NH), 3.18 (dd, $J = 14.1$, 4.7 Hz, 1H), 2.95 (dd, $J = 14.1$, 7.0 Hz, 1H), 2.12–1.96 (m, 2H), 1.43 (s, 9H), 1.36–1.20 (m, 4H), 0.88 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3312$, 2927, 2897, 1698, 1503, 1400, 1245, 1163, 1023. $[\alpha]_D^{25} = -4.0$ (*c* 0.75, $CHCl_3$). MS (LSIMS) 336 $[M+H]^+$. Anal. Calcd for $C_{19}H_{29}NO_2S$: C, 68.02; H, 8.71; N, 4.17; S, 9.56. Found: C, 67.85; H, 8.43; N, 4.47; S, 9.23.

4.1.6.2. 3-Phenyl-1-phenylsulfanylmethyl-(1*R*,2*E*)-2-*tert*-butyloxycarbonylamide, 6b. Solid, 87%, mp 64–66 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40–7.10 (m, 4H), 7.33–7.12 (m, 6H), 6.53 (d, $J = 15.6$ Hz, 1H), 6.13 (dd, $J = 15.6$, 5.9 Hz, 1H), 4.90–4.77 (br s, NH), 4.54–4.50 (m, 1H), 3.27 (dd, $J = 13.4$, 5.2 Hz, 1H), 3.12 (dd, $J = 13.4$, 5.9 Hz, 1H), 1.46 (s, 9H). IR (neat) $\nu = 3375$, 2928, 1696, 1500, 1366, 1247, 1167, 1022, 745. $[\alpha]_D^{25} = +14.2$ (c 1.1, $CHCl_3$). MS (LSIMS) 356 $[M+H]^+$. Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94; S, 9.02. Found: C, 70.67; H, 7.19; N, 3.73; S, 9.27.

4.1.7. 4-(*tert*-Butyloxycarbonylamido)-5-phenylsulfanyl-(*E*,4*R*)-2-pentenyl pivalate, 6c. A hard glass tube containing the alcohol **4** (2.41 g, 8 mmol), PhSSPh (5.2 g, 24 mmol) and PBu_3 (6.46 g, 32 mmol) in dry THF (32 mL) was sealed at the top at −78 °C and after attaining room temperature, heated to 72 °C for 36 h. After evaporating the solvent on a rotary evaporator the crude product mixture was chromatographed on a silica gel column using AcOEt/petroleum ether (1:9, v/v) as the eluent to afford **6c** in 63% yield. Low melting solid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.42–7.15 (m, 5H), 5.79–5.77 (m, 2H), 4.75–4.65 (m, 1H), 4.52 (s, 2H), 4.43–4.32 (m, 1H), 3.12 (dd, $J = 14.1$, 5.8 Hz, 1H), 2.98 (dd, $J = 14.1$, 5.8 Hz, 1H), 1.39 (s, 9H), 1.15 (s, 9H). IR (neat) $\nu = 3403$, 2953, 1714, 1698, 1510, 1365, 1267, 1159, 1039. $[\alpha]_D^{25} = +7.8$ (c 1.0, $CHCl_3$). MS (LSIMS) 394 $[M+H]^+$. Anal. Calcd for $C_{21}H_{31}NO_4S$: C, 64.09; H, 7.94; N, 3.56; S, 8.15. Found: C, 64.35; H, 7.63; N, 3.76; S, 8.53.

4.1.8. General procedure for the preparation of sulfoxides from sulfides. To a solution of the substrate (1 mmol) in methanol (10 mL) was added dropwise a solution of $NaIO_4$ (1 mmol) in water (5 mL) at 0 °C and allowed to attain room temperature during a period of 30 min. After stirring for 16 h, the reaction mixture was filtered and the resulting filtrate then evaporated to remove most of methanol under reduced pressure. The aq residue was extracted into ethyl acetate, dried over Na_2SO_4 and evaporated. The diastereomers were separated by column chromatography using AcOEt/petroleum ether (1:3, v/v) as the eluent.

4.1.8.1. 1-(S_S)-Phenylsulfinyl-(2*R*,3*Z*)-3-octen-2-*tert*-butyloxycarbonylamide, 7a*a*. Solid, 47%, mp 107–109 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.68–7.58 (m, 2H), 7.56–7.46 (m, 3H), 5.76–5.41 (m, 2H and NH), 4.90–4.70 (m, 1H), 3.17–3.03 (m, 1H), 2.89 (dd, $J = 13.5$, 4.1 Hz, 1H), 2.25–2.01 (m, 2H), 1.60–1.28 (m, 13H), 0.91 (distorted t, 3H). IR (neat) $\nu = 3207$, 2972, 2925, 2837, 1703, 1537, 1175, 1044. $[\alpha]_D^{25} = -168.0$ (c 1.0, $CHCl_3$). MS (LSIMS) 353 $[M+H]^+$. Anal. Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32; N, 3.98; S, 9.12. Found: C, 65.13; H, 8.14; N, 3.63; S, 9.34.

4.1.8.2. 1-(R_S)-Phenylsulfinyl-(2*R*,3*Z*)-3-octen-2-*tert*-butyloxycarbonylamide, 7a*s*. Solid, 47%, mp 68–69 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.66 (m, 2H), 7.56–7.45 (m, 3H), 5.60–5.36 (m, 2H), 4.95–4.81 (br s, NH), 4.71 (quintet, $J = 6.9$ Hz, 1H), 3.10 (dd, $J = 13.9$, 6.9 Hz, 1H), 2.98–2.85 (m, 1H), 2.11–1.95 (m, 2H), 1.45 (s, 9H), 1.39–1.09 (m, 4H) 0.85 (distorted t, 3H). IR (neat) $\nu = 3243$, 2975, 2928, 1700, 1540, 1169. $[\alpha]_D^{25} = +72.4$ (c 1.0, $CHCl_3$). MS (LSIMS) 353 $[M+H]^+$. Anal. Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32; N, 3.98; S, 9.12. Found: C, 64.73; H, 8.47; N, 3.73; S, 9.29.

4.1.8.3. 4-Phenyl-1-(S_S)-phenylsulfinyl-(2*R*,3*E*)-3-buten-2-*tert*-butyloxycarbonylamide, 7b*a*. Solid, 46%, mp 147–148 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.68–7.59 (m, 2H), 7.56–7.46 (m, 3H), 7.41–7.10 (m, 5H), 6.65 (d, $J = 16.3$ Hz, 1H), 6.37 (dd, $J = 16.3$, 5.9 Hz, 1H), 5.90–5.76 (br s, NH), 4.74 (quintet, $J = 5.9$ Hz, 1H), 3.22–3.02 (m, 2H), 1.48 (s, 9H). IR (neat) $\nu = 3290$, 2978, 2925, 1709, 1525, 1147, 1040. $[\alpha]_D^{25} = -167.0$ (c 1.04, $CHCl_3$). MS (LSIMS) 372 $[M+H]^+$. Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.90; H, 6.78; N, 3.77; S, 8.63. Found: C, 67.45; H, 7.04; N, 3.77; S, 8.53.

4.1.8.4. 4-Phenyl-1-(R_S)-phenylsulfinyl-(2*R*,3*E*)-3-buten-2-*tert*-butyloxycarbonylamide, 7b*s*. Solid, 46%, mp 133–134 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72–7.61 (m, 2H), 7.58–7.46 (m, 3H), 7.36–7.15 (m, 5H), 6.55 (d, $J = 15.2$ Hz, 1H), 6.19 (dd, $J = 15.2$, 7.0 Hz, 1H), 5.18–5.04 (br s, NH), 4.63 (quintet, $J = 7.0$ Hz, 1H), 3.16 (d, $J = 7.0$ Hz, 2H), 1.46 (s, 9H). IR (neat) $\nu = 3284$, 2968, 1710, 1523, 1157, 1037. $[\alpha]_D^{25} = +13.5$ (c 0.70, $CHCl_3$). MS (LSIMS) 372 $[M+H]^+$. Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.90; H, 6.78; N, 3.77; S, 8.63. Found: C, 67.73; H, 6.64; N, 3.84 S, 8.67.

4.1.8.5. 4-(*tert*-Butyloxycarbonylamido)-5-(S_S)-phenylsulfinyl-(*E*,4*R*)-2-pentenyl pivalate, 7c*a*. Liquid, 45%. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.68–7.50 (m, 5H), 7.30 (d, $J = 8.4$ Hz, NH), 5.76–5.62 (m, 2H), 4.57–4.32 (m, 3H), 3.0–2.80 (m, 2H), 1.40 (s, 9H), 1.12 (s, 9H). IR (neat) $\nu = 3312$, 2968, 1725, 1699, 1517, 1360, 1157, 1037. $[\alpha]_D^{25} = -93.0$ (c 0.75, $CHCl_3$). MS (LSIMS) 410 $[M+H]^+$. Anal. Calcd for $C_{21}H_{31}NO_5S$: C, 61.59; H, 7.63; N, 3.42; S, 7.83. Found: C, 61.23; H, 7.54; N, 3.57; S, 7.87.

4.1.8.6. 4-(*tert*-Butyloxycarbonylamido)-5-(R_S)-phenylsulfinyl-(*E*,4*R*)-2-pentenyl pivalate, 7c*s*. Liquid, 45%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73–7.46 (m, 5H), 5.92–5.75 (m, 2H), 5.10–4.95 (br s, NH), 4.65–4.41 (m, 3H), 3.12–2.96 (m, 2H), 1.46 (s, 9H), 1.22 (s, 9H). IR (neat) $\nu = 3310$, 2970, 1728, 1695, 1510, 1457, 1245, 1159, 1040. $[\alpha]_D^{25} = +66.1$ (c 0.66, $CHCl_3$). MS (LSIMS) 410 $[M+H]^+$. Anal. Calcd for $C_{21}H_{31}NO_5S$: C, 61.59; H, 7.63; N, 3.42; S, 7.83. Found: C, 61.42; H, 7.64; N, 3.33; S, 7.93.

4.1.9. General procedure for the preparation of methyl carbamates and sulfonamides from *tert*-butylcarbamates. To a stirred solution of sulfoxide **7** (0.5 mmol) in dichloromethane (0.5 mL) was added dropwise a solution of trifluoroacetic acid/dichloromethane (1:1, 0.5 mL) at 0 °C and stirred for 30 min. The solvent was evaporated under reduced pressure, dried under vacuum and without further purification, the ammonium salt was taken into dichloromethane (2 mL) and treated with triethylamine (101 mg, 1 mmol) followed by methylchloroformate (47 mg, 0.5 mmol), *p*-TsCl (95 mg,

0.5 mmol) or *p*-nitrobenzenesulfonyl chloride (111 mg, 0.5 mmol) at 0 °C. After stirring for 1 h at room temperature, the reaction mixture was diluted with dichloromethane and washed successively with aq citric acid, water, brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure followed by purification on a silica gel column using AcOEt/petroleum ether (9:11, v/v) afforded the products **8**, **9** or **14**, respectively.

4.1.9.1. 1-(S_S)-Phenylsulfinyl-(2*R*,3*Z*)-3-octen-2-methoxycarbonylamide, 8a*a*. Solid, 78%, mp 115–117 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.65–7.58 (m, 2H), 7.54–7.45 (m, 3H), 5.93 (d, $J = 7.5$ Hz, NH), 5.75–5.45 (m, 2H), 4.90–4.74 (m, 1H), 3.67 (s, 3H), 3.20–3.03 (m, 1H), 2.88 (dd, $J = 12.9$, 2.8 Hz, 1H), 2.21–2.00 (m, 2H), 1.42–1.25 (m, 4H), 0.92 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3262$, 2963, 2921, 1726, 1698, 1527, 1252, 1035. $[\alpha]_D^{25} = -276.4$ (*c* 1.16, $CHCl_3$). MS (LSIMS) 310 $[M+H]^+$. Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53; S, 10.36. Found: C, 61.98; H, 7.13; N, 4.43; S, 10.09.

4.1.9.2. 1-(R_S)-Phenylsulfinyl-(2*R*,3*Z*)-3-octen-2-methoxycarbonylamide, 8a*s*. Solid, 80%, mp 143–146 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72–7.65 (m, 2H), 7.60–7.44 (m, 3H), 5.60–5.39 (m, 2H), 5.26 (d, $J = 7.1$ Hz, NH), 4.75 (quintet, $J = 7.1$ Hz, 1H), 3.64 (s, 3H), 3.12 (dd, $J = 13.0$, 7.1 Hz, 1H), 2.91 (dd, $J = 13.0$, 5.7 Hz, 1H), 2.12–1.91 (m, 2H), 1.41–1.17 (m, 4H), 0.88 (distorted t, 3H). IR (neat) $\nu = 3310$, 2970, 2923, 1716, 1520, 1040, 750, 683. $[\alpha]_D^{25} = +89.4$ (*c* 0.70, $CHCl_3$). MS (LSIMS) 310 $[M+H]^+$. Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53; S, 10.36. Found: C, 62.58; H, 7.33; N, 4.59; S, 10.77.

4.1.9.3. 1*N*-[1-(S_S)-Phenylsulfinylmethyl-(1*R*,2*E*)-2-heptenyl]-4-methyl-1-benzenesulfonamide, 9a*a*. Solid, 82%, mp 112–114 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, $J = 8.2$ Hz, 2H), 7.55–7.40 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 2H), 6.31 (d, $J = 5.9$ Hz, NH), 5.45–5.30 (m, 2H), 4.49–4.40 (m, 1H), 3.03 (dd, $J = 13.4$, 7.5 Hz, 1H), 2.69 (dd, $J = 13.4$, 3.0 Hz, 1H), 2.44 (s, 3H), 1.81–1.69 (m, 2H), 1.23–1.10 (m, 4H), 0.86 (distorted t, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.4, 22.2, 27.0, 31.1, 48.2, 60.4, 123.9, 127.1, 127.4, 129.2, 129.4, 131.2, 133.5, 137.6, 142.6, 143.2. IR (neat) $\nu = 3342$, 2928, 2855, 1330, 1159. $[\alpha]_D^{25} = -118.8$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 406 $[M+H]^+$. Anal. Calcd for $C_{21}H_{27}NO_3S_2$: C, 62.19; H, 6.71; N, 3.45; S, 15.81. Found: C, 61.86; H, 6.97; N, 3.71; S, 16.10.

4.1.9.4. 1*N*-[1-(R_S)-Phenylsulfinylmethyl-(1*R*,2*E*)-2-heptenyl]-4-methyl-1-benzenesulfonamide, 9a*s*. Solid, 84%, mp 114–116 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, $J = 8.2$ Hz, 2H), 7.70–7.45 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 2H), 5.49–5.23 (m, 2H), 4.46–4.33 (m, 1H), 3.13 (dd, $J = 13.4$, 6.7 Hz, 1H), 2.75 (dd, $J = 13.4$, 6.7 Hz, 1H), 2.42 (s, 3H), 1.80–1.60 (m, 2H), 1.28–1.08 (m, 4H), 0.91 (distorted t, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.4, 22.2, 27.1, 31.1, 48.0, 62.9, 124.0, 126.4, 127.4, 129.3, 129.5, 131.2, 134.7, 143.4, 143.7. IR (neat) $\nu = 3258$, 2924, 2847, 1455, 1327, 1160. $[\alpha]_D^{25} = +168.7$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 406 $[M+H]^+$. Anal. Calcd for $C_{21}H_{27}NO_3S_2$: C, 62.19; H, 6.71; N, 3.45; S, 15.81. Found: C, 62.56; H, 6.38; N, 3.01; S, 16.13.

4.1.9.5. 1*N*-[3-Phenyl-1-(S_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-propenyl]-4-methyl-1-benzenesulfonamide, 9b*a*. Solid, 80%, mp 177–178 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74 (d, $J = 8.2$ Hz, 2H), 7.62–7.43 (m, 5H), 7.38–7.11 (m, 7H), 6.45–6.40 (m, 1H and NH), 6.04 (dd, $J = 16.3$, 7.4 Hz, 1H), 4.52 (quintet, $J = 5.2$ Hz, 1H), 2.98–2.92 (d, $J = 5.2$ Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 51.4, 62.2, 123.4, 125.9, 127.4, 127.8, 128.9, 130.6, 131.8, 135.3, 142.5, 143.1. IR (neat) $\nu = 3258$, 2924, 2847, 1455, 1327, 1160. $[\alpha]_D^{25} = -115.9$ (*c* 0.5, $CHCl_3$). MS (LSIMS) 426 $[M+H]^+$. Anal. Calcd for $C_{23}H_{23}NO_3S_2$: C, 64.92; H, 5.45; N, 3.29; S, 15.07. Found: C, 64.67; H, 5.66; N, 3.14; S, 14.90.

4.1.9.6. 1*N*-[3-Phenyl-1-(R_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-propenyl]-4-methyl-1-benzenesulfonamide, 9b*s*. Solid, 87%, mp 152–153 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, $J = 8.2$ Hz, 2H), 7.62–7.46 (m, 5H), 7.30–7.08 (m, 7H), 6.35 (d, $J = 16.3$ Hz, 1H), 5.90 (dd, $J = 16.3$, 9.2 Hz, 1H), 4.44–4.32 (m, 1H), 3.16 (dd, $J = 13.4$, 7.4 Hz, 1H), 2.92 (dd, $J = 13.4$, 5.9 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 53.2, 62.3, 124.1, 125.8, 127.4, 129.4, 129.5, 131.4, 133.2, 137.5, 143.2, 143.4. IR (neat) $\nu = 3062$, 2927, 1445, 1331, 1159. $[\alpha]_D^{25} = +9.2$ (*c* 0.7, $CHCl_3$). MS (LSIMS) 426 $[M+H]^+$. Anal. Calcd for $C_{23}H_{23}NO_3S_2$: C, 64.92; H, 5.45; N, 3.29; S, 15.07. Found: C, 65.07; H, 5.26; N, 3.55; S, 15.20.

4.1.9.7. 1*N*-[3-Phenyl-1-(R_S)-phenylsulfinylmethyl-(1*R*,2*E*)-propenyl]-4-nitro-1-benzenesulfonamide, 14b*s*. Solid, 88%, mp 164–165 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.05 (d, $J = 9.1$ Hz, 2H), 7.89 (d, $J = 9.1$ Hz, 2H), 7.62–7.38 (m, 5H), 7.18–6.90 (m, 5H), 6.12 (d, $J = 15.6$ Hz, 1H), 5.64 (dd, $J = 15.6$, 8.2 Hz, 1H), 4.48–4.26 (br s, NH), 4.23–4.18 (m, 1H), 3.06 (dd, $J = 12.6$, 6.7 Hz, 1H), 2.83 (dd, $J = 12.6$, 7.4 Hz, 1H). IR (neat) $\nu = 3421$, 2927, 1587, 1520, 1327, 1160. MS (LSIMS) 457 $[M+H]^+$. Anal. Calcd for $C_{22}H_{20}N_2O_5S_2$: C, 57.88; H, 4.42; N, 6.14; S, 14.05. Found: C, 57.92; H, 4.57; N, 6.14; S, 14.12.

4.1.9.8. 4-(4-Methylphenylsulfonamido)-5-(S_S)-phenylsulfinyl-(*E*,4*R*)-2-pentenyl pivalate, 9c*a*. Viscous liquid, 79%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, $J = 8.2$ Hz, 2H), 7.55–7.44 (m, 5H), 7.26 (d, $J = 8.2$ Hz, 2H), 6.50 (d, $J = 8.2$ Hz, NH), 5.72–5.65 (m, 2H), 4.43–4.38 (m, 3H), 2.94–2.74 (m, 2H), 2.43 (s, 3H), 1.18 (s, 9H). IR (neat) $\nu = 3325$, 1732, 1332, 1159. $[\alpha]_D^{25} = -90.1$ (*c* 0.75, $CHCl_3$). MS (LSIMS) 464 $[M+H]^+$. Anal. Calcd for $C_{23}H_{29}NO_5S_2$: C, 59.59; H, 6.30; N, 3.02; S, 13.83. Found: C, 59.69; H, 5.92; N, 3.27; S, 14.22.

4.1.9.9. 4-(4-Methylphenylsulfonamido)-5-(R_S)-phenylsulfinyl-(*E*,4*R*)-2-pentenyl pivalate, 9c*s*. Viscous liquid, 81%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73 (d, $J = 8.2$ Hz, 2H), 7.62–7.46 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 2H), 6.03 (d, $J = 5.9$ Hz, NH), 5.62–5.58 (m, 2H), 4.38

(d, $J = 3.72$ Hz, 2H), 4.23–4.20 (m, 1H), 3.03 (dd, $J = 13.4$, 7.4 Hz, 1H), 2.83 (dd, $J = 13.4$, 5.9 Hz, 1H), 2.44 (s, 3H), 1.17 (s, 9H). IR (neat) $\nu = 3250$, 1725, 1337, 1161. $[\alpha]_D^{25} = +92.3$ (c 0.25, $CHCl_3$). MS (LSIMS) 464 $[M+H]^+$. Anal. Calcd for $C_{23}H_{29}NO_5S_2$: C, 59.59; H, 6.30; N, 3.02; S, 13.83. Found: C, 59.93; H, 6.08; N, 3.40; S, 13.62.

4.1.10. General procedure for the preparation of the silyl ether from the pivaloyl esters. To the pivaloyl ester **9c***a* (820 mg, 2 mmol) in methanol (15 mL) cooled at 0 °C was added dropwise a solution of 0.2 M aq NaOH (15 mL). The reaction mixture was allowed to attain rt gradually and then stirred for 4 h. The solvent was removed under reduced pressure and the product alcohol extracted into ethyl acetate. The organic layer was washed with water, brine and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography, using AcOEt/petroleum ether (2:3, v/v) as the eluent, afforded the alcohol (589 mg, 1.9 mmol) in 95% yield.

To the solution of the above alcohol (570 mg, 1.5 mmol) in dichloromethane (6 mL) was added imidazole (204 mg, 3 mmol) followed by TBDPSCl (453 mg, 1.65 mmol) and stirred at rt for 1 h. Dichloromethane (10 mL) was added to the reaction mixture and the organic layer washed with water, brine and dried over Na_2SO_4. Column chromatography using AcOEt/petroleum ether (1:4, v/v) as the eluent afforded the **7d***a* (857 mg, 1.52 mmol) in 80% yield (76% overall yield for 2 steps).

Following the similar procedure detailed for the conversion of **9c***a* into **9d***a*, **9c***s* yielded **9d***s* in 75% overall yield for 2 steps.

4.1.10.1. Hydrolyzed product of 9c*a*: 1*N*-[4-hydroxy-1-(S_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-butenyl]-4-methyl-1-benzenesulfonamide. Solid, 76%, mp 143–145 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74 (d, $J = 8.2$ Hz, 2H), 7.50–7.44 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 2H), 6.30 (d, $J = 8.9$ Hz, NH), 5.86–5.64 (m, 2H), 4.31–4.29 (m, 1H), 4.08–3.96 (m, 2H), 2.92–2.78 (m, 2H), 2.43 (s, 3H). IR (neat) $\nu = 3270$, 1537, 1458, 1328, 1158. $[\alpha]_D^{25} = -119.8$ (c 0.25, $CHCl_3$). MS (LSIMS) 380 $[M+H]^+$. Anal. Calcd for $C_{18}H_{21}NO_4S_2$: C, 56.97; H, 5.58; N, 3.69; S, 16.90. Found: C, 56.69; H, 5.52; N, 3.97; S, 16.85.

4.1.10.2. Hydrolyzed product of 9c*s*: 1*N*-[4-hydroxy-1-(R_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-butenyl]-4-methyl-1-benzenesulfonamide. Low melting solid, 75%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, $J = 8.2$ Hz, 2H), 7.60–7.40 (m, 5H), 7.25 (d, $J = 8.2$ Hz, 2H), 6.66 (d, $J = 6.7$ Hz, NH), 5.75–5.55 (m, 2H), 4.17–4.13 (m, 1H), 3.94–3.91 (m, 2H), 3.06 (dd, $J = 13.4$, 6.7 Hz, 1H), 2.92 (dd, $J = 13.4$, 7.4, 1H), 2.38 (s, 3H). IR (neat) $\nu = 3145$, 2926, 1460, 1330, 1159. $[\alpha]_D^{25} = +112.6$ (c 1.0, $CHCl_3$). MS (LSIMS) 380 $[M+H]^+$. Anal. Calcd for $C_{18}H_{21}NO_4S_2$: C, 56.97; H, 5.58; N, 3.69; S, 16.90. Found: C, 57.11; H, 5.72; N, 3.47; S, 16.99.

4.1.10.3. 1*N*-[4-Hydroxy-1-(S_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-butenyl]-4-methyl-1-benzenesulfonamide, 9d*a*. Solid, 83%, mp 115–116 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.62–7.54 (m, 4H), 7.48–7.45 (m, 5H), 7.38–7.28 (m, 6H), 7.18 (d, $J = 8.2$ Hz, 2H), 5.80–5.56 (m, 2H), 4.41–4.26 (m, 1H), 4.06 (s, 2H), 2.76 (d, $J = 5.2$ Hz, 2H), 2.33 (s, 3H), 1.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 21.2, 26.6, 51.6, 61.8, 63.0, 123.8, 126.1, 127.1, 127.5, 129.2, 129.3, 129.5, 131.0, 132.4, 133.2, 135.2, 137.9, 142.9. IR (neat) $\nu = 3421$, 2927, 1451, 1168, 1109, 1043. $[\alpha]_D^{25} = -75.8$ (c 0.3, $CHCl_3$). MS (LSIMS) 618 $[M+H]^+$. Anal. Calcd for $C_{34}H_{39}NO_4S_2Si$: C, 66.09; H, 6.36; N, 2.27; S, 10.38. Found: C, 66.29; H, 5.94; N, 2.63; S, 10.62.

4.1.10.4. 1*N*-[4-Hydroxy-1-(R_S)-phenylsulfinylmethyl-(1*R*,2*E*)-2-butenyl]-4-methyl-1-benzenesulfonamide, 9d*s*. Low melting solid, 81%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.69 (d, $J = 8.2$ Hz, 2H), 7.60–7.44 (m, 9H), 7.35–7.24 (m, 6H), 7.20 (d, $J = 8.2$ Hz, 2H), 5.58–5.52 (m, 2H), 4.20–4.07 (m, 1H), 4.03 (s, 2H), 2.98 (dd, $J = 13.4$, 7.4 Hz, 1H), 2.70 (dd, $J = 13.4$, 5.9 Hz, 1H), 2.35 (s, 3H), 0.98 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 21.4, 26.7, 52.4, 62.4, 63.1, 124.0, 126.3, 127.3, 127.6, 129.3, 129.5, 129.6, 131.3, 133.1, 135.3, 137.3, 143.3. IR (neat) $\nu = 3489$, 2925, 2853, 1367, 1157, 1111, 1029. $[\alpha]_D^{25} = +64.5$ (c 0.55, $CHCl_3$). MS (LSIMS) 618 $[M+H]^+$. Anal. Calcd for $C_{34}H_{39}NO_4S_2Si$: C, 66.09; H, 6.36; N, 2.27; S, 10.38. Found: C, 65.78; H, 6.77; N, 2.23; S, 10.72.

4.1.11. General procedure for the reaction of the sulfoxides with NBS. To the solution of the sulfoxide (0.5 mmol) in toluene (2.5 mL) was added water (18 mg, 1 mmol) followed by freshly recrystallized *N*-bromosuccinimide (0.107 g, 0.6 mmol) and stirred at rt under nitrogen atmosphere. The progress of the reaction was monitored by TLC. When no starting material could be detected (30 min to 6 h), the reaction mixture was taken into ethyl acetate (10 mL) and washed with aqueous saturated sodium bicarbonate (10 mL), water (2×10 mL) and brine (10 mL). The organic layer was dried over sodium sulfate and evaporated under vacuum to afford the crude product mixture. Purification of the crude product by column chromatography on silica gel using AcOEt/petroleum ether as eluent afforded products in 70–85% combined yield.

4.1.11.1. Products from 7a*a*

4.1.11.1.1. 2-(tert-Butyloxycarbonylamido)-3-bromo-1-(R_S)-phenylsulfinyl-(2S,3S,4S)-octan-4-ol, **10a***s*. Viscous liquid, 40%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.64–7.54 (m, 2H), 7.50–7.40 (m, 3H), 5.38 (d, $J = 6.9$ Hz, NH), 4.13–3.89 (m, 2H), 3.75–3.63 (m, 1H), 3.40–3.10 (m, 2H), 1.51–1.10 (m, 15H), 0.82 (t, $J = 6.8$ Hz, 3H). IR (neat) $\nu = 3310$, 2974, 2923, 1697, 1540, 1030. $[\alpha]_D^{25} = +31.7$ (c 0.8, $CHCl_3$). MS (LSIMS) 448 $[M+H]^+$. Anal. Calcd for $C_{19}H_{30}BrNO_4S$: C, 50.89; H, 6.74; N, 3.12; S, 7.15. Found: C, 50.64; H, 6.99; N, 3.19; S, 6.89.

4.1.11.1.2. 2-(tert-Butyloxycarbonylamido)-3-bromo-1-(R_S)-phenylsulfinyl-(2S,3R,4R)-octan-4-ol, stereoisomer of **10a***s*. Liquid, 8%. ^{1}H NMR (200 MHz, $CDCl_3$)

δ 7.72–7.60 (m, 2H), 7.58–7.45 (m, 3H), 5.12 (d, $J = 7.2$ Hz, NH), 4.41–4.23 (m, 2H), 3.72 (br s, 1H), 3.31–3.06 (m, 2H), 1.62–1.40 (m, 6H), 1.41 (s, 9H), 0.91 (distorted t, 3H). IR (neat) $\nu = 3310$, 2947, 1696, 1546, 1153, 1029. $[\alpha]_D^{25} = +25.2$ (*c* 0.64, $CHCl_3$). MS (LSIMS) 448 $[M+H]^+$. Anal. Calcd for $C_{19}H_{30}BrNO_4S$: C, 50.89; H, 6.74; N, 3.12; S, 7.15. Found: C, 51.04; H, 6.39; N, 3.42; S, 7.08.

4.1.11.1.3. 5-Bromo-6-butyl-4-(S_S)-phenylsulfinylmethyl-(4S,5R,6R)-1,3-oxazinan-2-one, **11a***a.* Solid, 33%, mp 129–130 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.68–7.50 (m, 5H), 6.71–6.62 (br s, NH), 4.43 (dd, $J = 3.5$, 2.5 Hz, 1H), 4.14 (dt, $J = 9.3$, 3.5 Hz, 1H), 4.02 (dt, $J = 10.4$, 2.5 Hz, 1H), 3.32 (dd, $J = 12.7$, 9.3 Hz, 1H), 2.91 (dd, $J = 12.7$, 3.5 Hz, 1H), 1.90–1.12 (m, 6H), 0.90 (t, $J = 6.9$ Hz, 3H). IR (neat) $\nu = 3262$, 2960, 2928, 2845, 1757, 1465, 1035. $[\alpha]_D^{25} = -164.8$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 375 $[M+H]^+$. Anal. Calcd for $C_{15}H_{20}BrNO_3S$: C, 48.14; H, 5.39; N, 3.45; S, 8.57. Found: C, 48.33; H, 5.08; N, 3.49; S, 8.98.

4.1.11.2. Products from 7a*s*

4.1.11.2.1. 2-(tert-Butyloxycarbonylamido)-3-bromo-1-(S_S)-phenylsulfinyl-(2S,3S,4S)-octan-4-ol, **10a***a.* Liquid, 26%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.70–7.59 (m, 2H), 7.57–7.48 (m, 3H), 5.71–5.57 (br s, NH), 4.40–4.27 (m, 1H and OH), 4.07–3.87 (m, 2H), 3.42 (dd, $J = 13.4$, 8.3 Hz, 1H), 3.17 (dd, $J = 13.4$, 2.3 Hz, 1H), 2.08–1.85 (m, 2H), 1.49 (s, 9H), 1.45–1.28 (m, 4H), 0.91 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3343$, 2965, 2855, 1700, 1259, 1043. $[\alpha]_D^{25} = -74.3$ (*c* 1.9, $CHCl_3$). MS (LSIMS) 448 $[M+H]^+$. Anal. Calcd for $C_{19}H_{30}BrNO_4S$: C, 50.89; H, 6.74; N, 3.12; S, 7.15. Found: C, 51.24; H, 6.42; N, 3.37; S, 7.49.

4.1.11.2.2. 5-Bromo-6-butyl-4-(R_S)-phenylsulfinylmethyl-(4S,5R,6R)-1,3-oxazinan-2-one, **11a***s.* Solid, 52%, mp 147–149 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78–7.54 (m, 5H), 6.08–5.95 (br s, NH), 4.57 (dd, $J = 3.4$, 2.5 Hz, 1H), 4.46 (dt, $J = 7.6$, 2.5 Hz, 1H), 4.26 (dt, $J = 9.5$, 3.4 Hz, 1H), 3.25–3.02 (m, 2H), 2.04–1.86 (m, 2H), 1.79–1.59 (m, 2H), 1.55–1.32 (m, 2H), 0.98 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3257$, 2962, 2920, 1749, 1261, 1053. $[\alpha]_D^{25} = +120.0$ (*c* 1.0, $CHCl_3$). MS (LSIMS) 375 $[M+H]^+$. Anal. Calcd for $C_{15}H_{20}BrNO_3S$: C, 48.14; H, 5.39; N, 3.45; S, 8.57. Found: C, 48.45; H, 5.78; N, 3.48; S, 8.33.

4.1.11.3. Products from 8a*a*

4.1.11.3.1. 2-(Methoxycarbonylamido)-3-bromo-1-(R_S)-phenylsulfinyl-(2S,3S,4S)-octan-4-ol, **12a***s.* Liquid, 52%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.70–7.60 (m, 2H), 7.59–7.49 (m, 3H), 5.55 (d, $J = 7.6$ Hz, NH), 4.22–4.05 (m, 2H), 3.86–3.60 (m, 4H), 3.40–3.20 (m, 2H), 2.05–1.70 (m, 2H), 1.60–1.24 (m, 4H), 0.90 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3334$, 2924, 2360, 1700, 1444, 1528, 1027. $[\alpha]_D^{25} = +47.3$ (*c* 0.47, $CHCl_3$). MS (LSIMS) 407 $[M+H]^+$. Anal. Calcd for $C_{16}H_{24}BrNO_4S$: C, 47.30; H, 5.95; N, 3.45; S, 7.89. Found: C, 47.65; H, 6.08; N, 3.79; S, 7.96.

4.1.11.3.2. 2-(Methoxycarbonylamido)-3-bromo-1-(R_S)-phenylsulfinyl-(2S,3R,4R)-octan-4-ol, stereomer of **12a***s.* Liquid, 4%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75–7.45 (m, 5H), 5.21 (d, $J = 8.9$ Hz, NH), 4.84–4.65 (m, 1H), 3.85–3.61 (m, 4H), 3.60–3.44 (m, 1H), 3.29 (dd, $J = 13.4$, 8.9 Hz, 1H), 2.97 (dd, $J = 13.4$, 5.1 Hz, 1H), 2.10–1.80 (m, 1H), 1.70–1.18 (m, 5H), 0.92 (distorted t, 3H). IR (neat) $\nu = 3289$, 2927, 1708, 1465, 1524, 1032. $[\alpha]_D^{25} = +28.4$ (*c* 0.31, $CHCl_3$). MS (LSIMS) 407 $[M+H]^+$. Anal. Calcd for $C_{16}H_{24}BrNO_4S$: C, 47.30; H, 5.95; N, 3.45; S, 7.89. Found: C, 47.13 H, 5.88; N, 3.09; S, 8.16.

4.1.11.4. Products from 8a*s*

4.1.11.4.1. 2-(Methoxycarbonylamido)-3-bromo-1-(S_S)-phenylsulfinyl-(2S,3S,4S)-octan-4-ol, **12a***a.* Viscous liquid, 59%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73–7.60 (m, 2H), 7.59–7.48 (m, 3H), 6.03 (d, $J = 7.3$ Hz, NH), 4.50–4.25 (m, 1H and OH), 4.20–3.83 (m, 2H), 3.72 (s, 3H), 3.47–3.10 (m, 2H), 2.10–1.83 (m, 2H), 1.70–1.25 (m, 4H), 0.96 (t, $J = 6.8$ Hz, 3H). IR (neat) $\nu = 3355$, 2964, 2922, 2843, 1709, 1259, 1037. $[\alpha]_D^{25} = -72.0$ (*c* 0.55, $CHCl_3$). MS (LSIMS) 407 $[M+H]^+$. Anal. Calcd for $C_{16}H_{24}BrNO_4S$: C, 47.30; H, 5.95; N, 3.45; S, 7.89. Found: C, 47.65; H, 6.28; N, 3.07; S, 7.54.

4.1.11.5. Products from 9a*a*

4.1.11.5.1. 1N-[2-Bromo-3-hydroxy-3-phenyl-1-(R_S)-phenylmethylsulfinyl-(1S,2S,3S)-heptyl]-4-methyl-1-benzenesulfonamide, **13a***s.* Solid, 65%, mp 94–96 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76 (d, $J = 8.2$ Hz, 2H), 7.69–7.47 (m, 5H), 7.29 (d, $J = 8.2$ Hz, 2H), 6.62 (d, $J = 7.4$ Hz, NH), 4.08–3.88 (m, 1H and OH), 3.79–3.61 (m, 2H), 3.47 (dd, $J = 13.4$, 2.2 Hz, 1H), 3.02 (dd, $J = 13.4$, 5.2 Hz, 1H), 2.45 (s, 3H), 1.98–1.74 (m, 1H), 1.74–1.53 (m, 1H), 1.40–1.03 (m, 4H), 0.82 (t, $J = 6.7$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.4, 21.7, 29.6, 35.5, 54.3, 59.4, 60.0, 73.5, 124.1, 127.1, 129.3, 129.7, 131.4, 137.3, 141.9, 143.7. IR (neat) $\nu = 3368$, 2928, 1331, 1159. $[\alpha]_D^{25} = +109.7$ (*c* 0.3, $CHCl_3$). MS (LSIMS) 502 $[M+H]^+$. Anal. Calcd for $C_{21}H_{28}BrNO_4S_2$: C, 50.20; H, 5.62; N, 2.79; S, 12.76. Found: C, 50.53; H, 5.22; N, 2.73; S, 12.52.

4.1.11.5.2. 1N-[2-Bromo-3-hydroxy-3-phenyl-1-(R_S)-phenylmethylsulfinyl-(1S,2R,3R)-heptyl]-4-methyl-1-benzenesulfonamide, stereoisomer of **13a***s.* Liquid, 11%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.64 (d, $J = 8.2$ Hz, 2H), 7.56–7.44 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 2H), 6.16–6.07 (br s, NH), 4.60–4.55 (m, 1H), 3.77–3.68 (m, 1H), 3.50–3.44 (m, 1H), 3.34 (dd, $J = 14.1$, 7.0 Hz, 1H), 3.20 (dd, $J = 14.0$, 5.9 Hz, 1H), 2.42 (s, 3H), 2.04–1.80 (m, 2H), 1.44–1.10 (m, 4H), 0.88 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3281$, 2925, 2854, 1367, 1158. $[\alpha]_D^{25} = +78.4$ (*c* 0.2, $CHCl_3$). MS (LSIMS) 502 $[M+H]^+$. Anal. Calcd for $C_{21}H_{28}BrNO_4S_2$: C, 50.20; H, 5.62; N, 2.79; S, 12.76. Found: C, 50.43; H, 5.98; N, 2.43; S, 12.99.

4.1.11.6. Products from 9a*s*

4.1.11.6.1. 1N-[2-Bromo-3-hydroxy-3-phenyl-1-(S_S)-phenylmethylsulfinyl-(1S,2S,3S)-heptyl]-4-methyl-1-benzenesulfonamide, **13a***a.* Solid, 82%, mp 93–95 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.83 (d, $J = 8.2$ Hz, 2H), 7.56–7.44 (m, 5H), 7.30 (d, $J = 8.2$ Hz, 2H), 4.46–4.37 (m, 1H), 3.99–3.83 (m, 1H), 3.82 (d, $J = 8.2$ Hz, 1H), 2.96 (dd, $J = 13.4$, 5.2 Hz, 1H), 2.65 (dd, $J = 13.4$, 2.3 Hz, 1H), 2.42 (s, 3H), 2.05–1.76 (m, 2H), 1.60–1.23

(m, 4H), 0.91 (t, $J = 6.7$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.4, 21.9, 29.6, 35.6, 54.5, 56.9, 61.0, 74.0, 123.7, 127.2, 129.3, 129.7, 131.3, 137.8, 143.2, 143.6. IR (neat) $\nu = 3262$, 2926, 1328, 1157. $[\alpha]_D^{25} = -89.6$ (c 0.3, $CHCl_3$). MS (LSIMS) 502 $[M+H]^+$. Anal. Calcd for $C_{21}H_{28}BrNO_4S_2$: C, 50.20; H, 5.62; N, 2.79; S, 12.76. Found: C, 50.03; H, 5.87; N, 2.59; S, 12.53.

4.1.11.7. Products from 9b*a*

4.1.11.7.1. 1N-[2-Bromo-3-hydroxy-3-phenyl-1-(R_S)-phenylmethylsulfinyl-(1S,2S,3R)-propyl]-4-methyl-1-benzenesulfonamide, **13b***s*. Solid, 64%, mp 184–186 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60 (d, $J = 8.2$ Hz, 2H), 7.53–7.40 (m, 5H), 7.32–7.20 (m, 7H), 5.27 (d, $J = 8.9$ Hz, NH), 4.84 (d, $J = 8.9$ Hz, 1H), 4.56 (d, $J = 8.9$ Hz, 1H), 4.24–4.13 (m, 1H), 3.26 (dd, $J = 14.1$, 9.7 Hz, 1H), 2.78 (dd, $J = 14.1$, 4.5 Hz, 1H), 2.44 (s, 3H). IR (neat) $\nu = 3321$, 2927, 1541, 1159. $[\alpha]_D^{25} = +118.1$ (c 0.75, $CHCl_3$). MS (LSIMS) 523 $[M+H]^+$. Anal. Calcd for $C_{23}H_{24}BrNO_4S_2$: C, 52.87; H, 4.63; N, 2.68; S, 12.27. Found: C, 53.03; H, 4.92; N, 2.63; S, 12.52.

4.1.11.8. Products from 9b*s*

4.1.11.8.1. 1N-[2-Bromo-3-hydroxy-3-phenyl-1-(S_S)-phenylmethylsulfinyl-(1S,2S,3R)-propyl]-4-methyl-1-benzenesulfonamide, **13b***a*. Solid, 80%, mp 172–174 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78 (d, $J = 8.2$ Hz, 2H), 7.56–7.46 (m, 5H), 7.38–7.14 (m, 7H), 5.40 (d, $J = 10.4$ Hz, NH), 4.84 (d, $J = 9.7$ Hz, 1H), 4.71–4.61 (m, 1H), 4.11 (d, $J = 9.7$ Hz, 1H), 2.99 (dd, $J = 13.4$, 5.2 Hz, 1H), 2.73 (dd, $J = 13.4$, 6.7 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 49.9, 62.0, 62.5, 73.5, 123.7, 127.0, 127.5, 127.8, 128.0, 129.5, 129.7, 131.2, 138.6, 142.6, 143.1, 144.2. IR (neat) $\nu = 3291$, 2925, 1455, 1157. $[\alpha]_D^{25} = -48.4$ (c 1.0, $CHCl_3$). MS (LSIMS) 523 $[M+H]^+$. Anal. Calcd for $C_{23}H_{24}BrNO_4S_2$: C, 52.87; H, 4.63; N, 2.68; S, 12.27. Found: C, 52.63; H, 4.33; N, 2.93; S, 12.42.

4.1.11.9. Products from 9d*a*

4.1.11.9.1. 1N-[2-Bromo-4-(tert-butyldiphenylsilyloxy)-3-hydroxy-1-(R_S)-phenylsulfinylmethyl-(1S,2R,3S)-butyl]-4-methyl-1-benzenesulfonamide, **13d***s*. Liquid, 42%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.42 (m, 11H), 7.40–7.16 (m, 8H), 5.10 (d, $J = 11.7$ Hz, NH), 4.46–4.42 (m, 1H), 4.28–4.10 (m, 1H), 3.82 (dd, $J = 12.4$, 1.7 Hz, 1H), 3.76–3.43 (m, 2H), 3.16 (d, $J = 13.4$, 8.2 Hz, 1H), 2.83 (dd, $J = 13.4$, 2.7 Hz, 1H), 2.35 (s, 3H), 1.01 (br s, 9H). IR (neat) $\nu = 3481$, 3047, 1465, 1324, 1154, 1108, 1019. $[\alpha]_D^{25} = +89.1$ (c 0.5, $CHCl_3$). MS (LSIMS) 714 $[M+H]^+$. Anal. Calcd for $C_{34}H_{40}BrNO_5S_2Si$: C, 59.47; H, 5.87; N, 2.04; S, 9.34. Found: C, 59.81; H, 5.62; N, 1.93; S, 9.45.

4.1.11.9.2. 1N-[3-Bromo-4-(tert-butyldiphenylsilyloxy)-2-hydroxy-1-(R_S)-phenylsulfinylmethyl-(1R,2R,3S)-butyl]-4-methyl-1-benzenesulfonamide, regiomer of **13d***s*. Liquid, 15%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.82–7.41 (m, 11H), 7.40–7.20 (m, 8H), 5.32 (d, $J = 8.2$ Hz, NH), 4.60–4.51 (m, 1H), 4.37–4.10 (m, 1H), 4.04–3.80 (m, 2H), 3.70–3.58 (m, 1H), 3.24 (dd, $J = 13.4$, 8.7 Hz, 1H), 2.88 (dd, $J = 13.4$, 3.3 Hz, 1H), 2.41 (s, 3H), 1.08 (br s, 9H). IR (neat) $\nu = 3442$, 3100, 2930, 1467, 1329, 1156, 1109, 1023. $[\alpha]_D^{25} = +33.6$ (c 0.25, $CHCl_3$). MS (LSIMS) 714 $[M+H]^+$.

4.1.11.10. Products from 9d*s*

4.1.11.10.1. 1N-[2-Bromo-4-(tert-butyldiphenylsilyloxy)-3-hydroxy-1-(S_S)-phenylsulfinylmethyl-(1S,2R,3S)-butyl]-4-methyl-1-benzenesulfonamide, **13d***a*. Solid, 51%, mp 173–175 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.51 (m, 11H), 7.56–7.20 (m, 8H), 5.38 (d, $J = 11.7$ Hz, NH), 4.57–4.40 (m, 1H), 4.34–4.15 (m, 1H), 3.97–3.70 (m, 3H), 3.12 (dd, $J = 13.4$, 3.0 Hz, 1H), 2.80–2.60 (m, 1H), 2.42 (s, 3H), 1.11 (br s, 9H). IR (neat) $\nu = 3465$, 3054, 1458, 1327, 1156, 1111, 1024. $[\alpha]_D^{25} = -108.4$ (c 0.5, $CHCl_3$). MS (LSIMS) 714 $[M+H]^+$. Anal. Calcd for $C_{34}H_{40}BrNO_5S_2Si$: C, 59.47; H, 5.87; N, 2.04; S, 9.34. Found: C, 59.11; H, 6.20; N, 1.93; S, 9.45.

4.1.11.10.2. 1N-[3-Bromo-4-(tert-butyldiphenylsilyloxy)-2-hydroxy-1-(S_S)-phenylsulfinylmethyl-(1R,2R,3S)-butyl]-4-methyl-1-benzenesulfonamide, regiomer of **13d***a*. Liquid, 10%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.40 (m, 11H), 7.38–7.18 (m, 8H), 5.18 (d, $J = 9.5$ Hz, NH), 4.30–4.20 (m, 1H), 4.16–4.12 (m, 1H), 3.97 (dd, $J = 11.6$, 2.0 Hz, 1H), 3.84 (dd, $J = 11.6$, 4.1 Hz, 1H), 3.77–3.69 (m, 1H), 3.06 (dd, $J = 13.4$, 8.2 Hz, 1H), 2.86 (dd, $J = 13.4$, 2.7 Hz, 1H), 2.32 (s, 3H), 0.98 (s, 9H). IR (neat) $\nu = 3502$, 2928, 1458, 1320, 1155, 1109, 1021. $[\alpha]_D^{25} = -28.4$ (c 0.3, $CHCl_3$). MS (LSIMS) 714 $[M+H]^+$. Anal. Calcd for $C_{34}H_{40}BrNO_5S_2Si$: C, 59.47; H, 5.87; N, 2.04; S, 9.34. Found: C, 59.84; H, 6.04; N, 2.23; S, 9.65.

4.1.12. General procedure for the conversion of bromohydrins to oxazinones. To a cooled −15 °C solution of the bromohydrin (0.1 mmol) in dichloromethane (0.5 mL) was added trifluoroacetic acid (0.5 mL) dropwise and the mixture stirred gradually allowing to attain rt and stirred further for a period of 30 min at the same temperature. The volatiles were removed and the residue taken into THF (0.5 mL). DABCO (0.3 mmol) and CDI (0.2 mmol) were added and the reaction mixture stirred at rt under nitrogen atmosphere for 24 h. The reaction mixture was concentrated under vacuum and the residue taken into ethyl acetate (15 mL). The organic layer was washed successively with water (5 mL), brine (5 mL) and dried over sodium sulfate. Evaporation of the solvent afforded the crude product, which on purification by chromatography on silica gel using AcOEt/petroleum ether (1:1, v/v) as eluent afforded the oxazinone.

4.1.12.1. 5-Bromo-6-butyl-4-(S_S)-phenylsulfinylmethyl-(4*S*,5*S*,6*S*)-1,3-oxazinan-2-one, oxazinone from 10a*a*. Viscous liquid, 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.52 (m, 5H), 6.27–6.23 (br s, NH), 4.58 (dd, $J = 8.7$, 3.6 Hz, 1H), 4.32–4.29 (m, 1H), 3.90 (dt, $J = 10.3$, 3.6 Hz, 1H), 3.78 (dd, $J = 13.4$, 10.3 Hz, 1H), 2.84 (dd, $J = 13.4$, 2.0 Hz, 1H), 2.33–2.29 (m, 1H), 2.05–1.45 (m, 5H), 0.93 (distorted t, 3H). IR (neat) $\nu = 3456$, 1745, 1457, 1276, 1120. $[\alpha]_D^{25} = +138.4$ (c 0.5, $CHCl_3$). MS (LSIMS) 375 $[M+H]^+$. Anal. Calcd for $C_{15}H_{20}BrNO_3S$: C, 48.14; H, 5.39; N, 3.45; S, 8.57. Found: C, 48.43; H, 5.08; N, 3.49; S, 8.78. Oxazinone from minor stereomer of **10a***a* identical to **11a***a*.

4.1.13. Preparation of sulfones from predominant sulfoxides formed during bromohydration. To a solution of sulfoxide (0.05 mmol) in chloroform (0.2 mL) was added *m*-CPBA (12 mg, 0.05 mmol) at 0 °C and allowed to stir for 10 min. The reaction mixture was diluted with ether and washed successively with aq sodium thiosulfate solution, aq $NaHCO_3$ solution, water, brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure followed by column chromatography using AcOEt/petroleum ether afforded the sulfone.

4.1.13.1. 2-(*tert*-Butyloxycarbonylamido)-3-bromo-1-phenylsulfonyl-(2*S*,3*S*,4*S*)-octan-4-ol, sulfone of 10a. Liquid, 90%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.92 (d, $J =$ 8.2 Hz, 2H), 7.75–7.50 (m, 3H), 5.20 (br s, NH), 4.43–3.65 (m, 4H), 3.55–3.41 (m, 1H and OH), 2.08–1.78 (m, 2H), 1.70–1.13 (m, 13H), 0.90 (t, $J = 6.7$ Hz, 3H). IR $\nu = 3189$, 2970, 2925, 1701, 1158, 1043. MS (LSIMS) 465 $[M+H]^+$. Anal. Calcd for $C_{19}H_{30}BrNO_5S$: C, 49.14; H, 6.51; N, 3.02; S, 6.90. Found: C, 49.41; H, 6.24; N, 3.34; S, 6.76.

4.1.13.2. 2-(Methoxycarbonylamido)-3-bromo-1-phenylsulfonyl-(2*S*,3*R*,4*R*)-octan-4-ol, sulfone of 12a. Liquid, 83%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.91 (d, $J =$ 8.2 Hz, 2H), 7.71–7.47 (m, 3H), 5.43 (d, $J = 9.4$ Hz, NH), 4.48–4.32 (m, 1H), 4.23 (ddd, $J = 11.2$, 3.7, 1.1 Hz, 1H), 4.13–3.94 (m, 1H), 3.89–3.45 (m, 5H and OH), 2.08–1.75 (m, 2H), 1.70–1.04 (m, 4H), 0.90 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3289$, 2955, 1699, 1543, 1034. MS (LSIMS) 423 $[M+H]^+$. Anal. Calcd for $C_{16}H_{24}BrNO_5S$: C, 45.50; H, 5.73; N, 3.32; S, 7.59. Found: C, 45.69, 5.98, 3.22, 7.89.

4.1.13.3. 5-Bromo-6-butyl-4-phenylsulfonylmethyl-(4*S*,5*R*,6*R*)-1,3-oxazinan-2-one, sulfone of 11a. Solid, 87%, mp 132–134 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.95 (d, $J = 8.6$ Hz, 2H), 7.80–7.69 (m, 3H), 6.01 (br s, NH), 4.48 (dd, $J = 4.5$, 3.2 Hz, 1H), 4.34 (q, $J = 5.9$ Hz, 1H), 4.12 (dt, $J = 10.2$, 3.2 Hz, 1H), 3.40 (d, $J = 5.9$ Hz, 2H), 2.06–1.21 (m, 6H), 0.93 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3357$, 2962, 2923, 2870, 1764, 1292, 1149. MS (LSIMS) 391 $[M+H]^+$. Anal. Calcd for $C_{15}H_{20}BrNO_4S$: C, 46.16; H, 5.16; N, 3.59; S, 8.21. Found: C, 46.31; H, 5.04; N, 3.78; S, 8.60.

4.1.13.4. 1*N*-[2-Bromo-3-hydroxy-3-phenyl-1-phenylmethylsulfonyl-(1*S*,2*R*,3*R*)-heptyl]-4-methyl-1-benzenesulfonamide, sulfone of 13a. Solid, 82%, mp 128–129 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.87–7.54 (m, 7H), 7.36 (d, $J = 8.2$ Hz, 2H), 5.86 (d, $J =$ 10.5 Hz, NH), 4.24–4.01 (m, 2H), 3.85 (d, $J = 9.7$ Hz, 1H), 3.58 (dd, $J = 14.1$, 3.7 Hz, 1H), 3.21 (dd, $J = 14.1$, 3.7 Hz, 1H), 2.48 (s, 3H), 2.18–1.73 (m, 2H), 1.62–1.24 (m, 4H), 0.93 (t, $J = 6.7$ Hz, 3H). IR (neat) $\nu = 3499$, 3288, 2929, 1304, 1157. MS (LSIMS) 518 $[M+H]^+$. Anal. Calcd for $C_{21}H_{28}BrNO_5S_2$: C, 48.65; H, 5.44; N, 2.70; S, 12.37. Found: C, 48.91; H, 5.34; N, 2.73; S, 12.65.

4.1.13.5. 1*N*-[2-Bromo-3-hydroxy-3-phenyl-1-phenylmethylsulfonyl-(1*S*,2*S*,3*R*)-propyl]-4-methyl-1-benzenesulfonamide, sulfone of 13b. Solid, 90%, mp 70–72 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73–7.40 (m, 7H), 7.37–7.13 (m, 7H), 5.27 (br s, NH), 4.82 (d, $J = 7.9$ Hz, 1H), 4.62 (d, $J = 8.6$ Hz, 1H), 4.16–4.09 (m, 1H), 3.54 (dd, $J = 14.1$, 10.2 Hz, 1H), 3.20 (d, $J = 14.1$ Hz, 1H), 2.48 (s, 3H). IR (neat) $\nu = 3475$, 3282, 2928, 1442, 1310, 1175. MS (LSIMS) 539 $[M+H]^+$. Anal. Calcd for $C_{23}H_{24}BrNO_5S_2$: C, 51.30; H, 4.49; N, 2.60; S, 11.91. Found: C, 51.47; H, 4.34; N, 2.93; S, 12.23.

4.1.13.6. 1*N*-[2-Bromo-4-(*tert*-butyldiphenylsilyloxy)-3-hydroxy-1-phenylsulfonylmethyl-(1*S*,2*R*,3*S*)-butyl]-4-methyl-1-benzenesulfonamide, sulfone of 13d. Solid, 78%, mp 173–175 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.89–7.48 (m, 11H), 7.47–7.17 (m, 8H), 4.73 (d, $J = 10.4$ Hz, NH), 4.31–4.18 (m, 1H), 3.82 (br s, 2H), 3.65–3.26 (m, 2H), 3.28–2.99 (m, 2H), 2.40 (s, 3H), 1.08 (s, 9H). IR (neat) $\nu = 3484$, 2986, 1449, 1374, 1245, 1046. MS (LSIMS) 730 $[M+H]^+$. Anal. Calcd for $C_{34}H_{40}BrNO_6S_2Si$: C, 58.11; H, 5.74; N, 1.99; S, 9.12. Found: C, 58.34; H, 5.44; N, 1.93; S, 9.43.

4.1.14. Preparation of 12a*s* and 13a*s* from 10a*s*. To a stirred solution of **10a***s* (45 mg, 0.1 mmol) in dichloromethane (0.1 mL) was added dropwise a solution of trifluoroacetic acid/dichloromethane (1:1, 0.1 mL) at 0 °C and allowed to stir for 30 min. The solvent was evaporated under reduced pressure, dried under vacuum and without further purification the aminosulfoxide in dichloromethane (0.4 mL) was treated with triethylamine (20 mg, 0.2 mmol) followed by methyl chloroformate (9 mg, 0.1 mmol) or TsCl (16 mg, 0.1 mmol) at 0 °C. After stirring for 1 h at room temperature, the reaction mixture was diluted with dichloromethane and washed successively with aq citric acid, water, brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure followed by purification on a silica gel column using AcOEt/petroleum ether (9:11, v/v) afforded the products **12a***s*/**13a***s*.

4.1.15. Procedure for the preparation of tetrahydrofuran derivatives 16 and 17. To the bromohydrin (0.1 mmol) in dry DMF (0.1 mL) was added imidazole (13 mg, 0.2 mmol) followed by TBDPSCl (27 mg, 0.1 mmol) at room temperature under a N_2 atmosphere. The reaction mixture was stirred at rt until TLC revealed complete consumption of the starting material. The reaction mixture was diluted with ether and washed successively with water, brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product mixture. Purification by column chromatography using EtOAc/petroleum ether (1:24, v/v) afforded the tetrahydrofurans.

4.1.15.1. 4-Bromo-3-(4-methylphenylsulfonamido)-5-phenyl-2-phenylsulfanyl-(2*S*,3*S*,4*R*,5*S*)-tetrahydrofuran, 16. Viscous liquid, 86%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.82 (d, $J = 8.2$ Hz, 2H), 7.38–7.13 (m, 12H), 6.07 (d, $J = 8.2$ Hz, NH), 5.30 (d, $J = 4.6$ Hz, 1H), 5.06 (d, $J = 8.9$ Hz, 1H), 4.05 (ddd, $J =$ 8.2, 6.7, 4.6 Hz, 1H), 3.69 (dd, $J = 8.9$, 6.7 Hz, 1H), 2.36 (s, 3H). IR (neat) $\nu = 3268$, 1591, 1451, 1331, 1218, 1161, 1015. MS

(LSIMS) 382 $[M-STol]^+$. Anal. Calcd for $C_{23}H_{22}BrNO_3S_2$: C, 54.76; H, 4.40; N, 2.78; S, 12.71. Found: C, 54.63; H, 4.52; N, 2.87; S, 12.62.

4.1.15.2. 4-Bromo-3-(4-methylphenylsulfonamido)-5-phenyl-2-phenylsulfanyl-(2*S*,3*S*,4*S*,5*S*)-tetrahydrofuran, 17. Low melting solid, 90%. ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, $J=8.2$ Hz, 2H), 7.36–7.19 (m, 7H), 5.14 (d, $J=10.5$ Hz, 1H), 4.99 (d, $J=8.2$ Hz, 1H), 4.24 (dd, $J=4.8$, 2.2 Hz, 1H), 3.85 (ddd, $J=10.5$, 8.2, 4.8 Hz, 1H), 3.74 (td, $J=6.7$, 2.2 Hz, 1H), 2.48 (s, 3H), 1.80–1.50 (m, 2H), 1.36–1.24 (m, 4H), 0.90 (t, $J=6.7$ Hz, 3H). IR (neat) $\nu=3310$, 2927, 1457, 1329, 1211, 1159, 1020. MS (LSIMS) 375 (M^+-STol). Anal. Calcd for $C_{21}H_{26}BrNO_3S_2$: C, 52.06; H, 5.41; N, 2.89; S, 13.24. Found: C, 50.21; H, 5.72; N, 2.83; S, 13.54.

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16.

Compound	C2-H δ (ppm)	$[\alpha]_D^{25}$	Compound	C2-H δ (ppm)	$[\alpha]_D^{25}$
7a*a*	4.81	−168.0	**7a***s*	4.71	+72.4
7b*a*	4.74	−167.0	**7b***s*	4.63	+13.5
7d*a*	4.58	−36.6	**7d***s*	4.44	+38.3
8a*a*	4.83	−276.4	**8a***s*	4.75	+89.4
9a*a*	4.45	−118.8	**9a***s*	4.38	+168.7
9b*a*	4.52	−115.9	**9b***s*	4.38	+9.2
9c*a*	4.40	−90.1	**9c***s*	4.21	+92.3
9d*a*	4.34	−75.8	**9d***s*	4.15	+64.5

17. Deprotection of the Boc group with 50% TFA/CH_2Cl_2 followed by the treatment of the resulting salt with carbonyl diimidazole in the presence of DABCO as the base in THF as the solvent afforded oxazinone **15**.
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