Toward a stereoselective synthesis of tetrahydroxy long chain base (LCB) and the synthesis of analogs of mannostatin A

Sadagopan Raghavan*, Kailash Rathore & B Sridhar

Organic Division I and Lab of X-ray Crystallography
Indian Institute of Chemical Technology, Hyderabad 500 007, India
E-mail: sraghavan@iict.res.in

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Efforts toward the stereoselective synthesis of tetrahydroxy long chain base and analogs of mannostatin A are described. The sulfinyl moiety has been efficiently utilized as an intramolecular nucleophile for oxidative functionalization of an alkene and regioselective opening of an epoxide. Nucleophilic addition to sulfinylimine has been used for the introduction of amino stereogenic center. Pummerer reaction has not been successful with a free N-H group at δ-carbon. Pummerer reaction on a N,O-acetonide furnishes an aldehyde. Attempted Wittig olefination to access the protected derivative of long chain base have failed. The analog of mannostatin could not be prepared by intramolecular addition of a sulfinyl carbanion to an imine but could be prepared by radical chemistry.

Keywords: Tetrahydroxy long chain base (LCB), mannostatin A, sulfoxide, sulfinylimine, Pummerer reaction

Sphingoid bases are the long chain amino alcohol constituent of cerebrosides, that are important mediators of biological events. Amino-1,3,4,5-tetrahydroxyoctadecene, constitutes the long chain base (LCB) of the cerebroside isolated from the latex of Euphorbia characias L. The structure of was inferred by comparing its spectral data with asteriacerebrosides and proven by total synthesis. The unique structure of LCB in particular, with four contiguous chiral centres disposed mutually anti to each other, (Z)-double bond and the biological importance of cerebrosides in general, make it an attractive target for synthesis. The synthesis reported to date utilize chiral pool starting materials including sugars, amino acid and hydroxy acid. They suffer from many drawbacks such as (i) lengthy reaction sequences, (ii) lack of stereocontrol, (iii) specialized techniques and (iv) modest yields. Thus, a practical route to LCB is highly desirable. Herein is disclosed the efforts toward the stereoselective synthesis of LCB, utilizing the sulfinyl moiety as an intramolecular nucleophile for the vicinal heterofunctionalization of an alkene in the key step of the reaction sequence.

Results and Discussion

A retrosynthetic disconnection arrived at aminotetrol as a key intermediate, the sulfinyl group of which would serve in the forward direction as the surrogate for an aldehyde, that on Wittig olefination would furnish LCB. Compound 2 was envisaged to be obtained from bromohydrin which in turn can be secured from β-hydroxy-γ,δ-unsaturated sulfoxide (Scheme I).

The synthesis began with the reaction of the carbanion of (S)-methyl phenyl sulfoxide with unsaturated ester to afford ketone 6 to afford ketone 7. Diastereoselective reduction using DIBAL-H in the presence of anhydrous zinc chloride yielded allylic alcohol (P = PMB, dr >95:<5). Oxidative functionalization of 4 using N-bromosuccinimide (NBS) as the electrophile, furnished bromohydrin regio- and stereoselectively via intramolecular participation of the sulfinyl group. To transform bromodiol 3 to compound 2, the stereogenic centres at C3 and C4 (LCB numbering) needed to be inverted. This was accomplished by a three step sequence.
Treatment of 3 with anhydrous potassium carbonate in acetonitrile furnished epoxide 8. Protection of the hydroxy group as its silyl ether 9 followed by boron trifluoride etherate (BF₃·Et₂O) mediated 5-exo opening by the sulfinyl group 13 furnished diol 14 possessing three heteroatoms that are mutually anti disposed. Protection of the hydroxy groups by treatment with methoxymethyl chloride (Mom-Cl) in the presence of Hunig's base afforded the di-Mom derivative 11 (Scheme II).

The next stage in the synthesis was the stereoselective introduction of the amino stereogenic center. Toward this end, the PMB group of 11 was deprotected with DDQ 15 to afford the alcohol 12 that on oxidation by use of Swern protocol 16 yielded aldehyde 13. Of the many methods 17 available for the stereoselective synthesis of 1,2-amino alcohols, the route employing nucleophilic addition to sulfinylimines 18 was the most attractive. Aldehyde 13 on reaction with (S)-tert-butylsulfinamide 19 furnished sulfinylimine 15. The choice of (S)-tert-butylsulfinamide was arbitrary since it was not possible to unambiguously predict the influence of the sulfinamide configuration on the newly created C-N stereogenic centre due to the likelihood of the reaction proceeding via chelation of the organometallic reagent to N-sulfinyl oxygen/OMom groups of the substrate or otherwise 21. Attempted reaction of 15 with one carbon synthons, benzoxymethylithium, derived from n-Bu₃SnCH₂OBn/n-BuLi (Ref. 22) and benzoxymethylmagnesium bromide 23, prepared from Bom-CI/Mg turnings, returned only unreacted starting material. Reaction with sterically less bulky vinylimagnesium bromide however, proceeded cleanly to yield the aminotetrol derivative 16 as the sole product 24. The amino stereogenic center at C2 was thus introduced highly selectively. The product 16 is probably formed by the attack of vinylimagnesium bromide onto the re-face of the imine via a Cram like transition state I, while the sulfinamide adopts the conformation wherein the imine hydrogen and the lone pair on the N-sulfinyl group lie in the same plane (Scheme III).

Although the absolute configuration at C2 was not known until later, we proceeded to test out further transformations. It remained to unmask the sulfinyl group to reveal an aldehyde carbonyl that could be subjected to cis-selective Wittig olefination to introduce the alkenyl side chain. Toward this goal, sulfoxide 16 was subjected to Pummerer reaction with the use of trifluoroacetic anhydride (TFAA) in the presence of triethylamine (Et₃N). A less polar spot observed during TLC examination, that was assumed to be the intermediate 17, was subjected to hydrolysis with aq saturated sodium bicarbonate in the same pot. After work-up, none of the desired aldehyde 18, but only the unsaturated ketone 23 could be isolated (Scheme IV). The formation of 23 can be rationalized by an intramolecular attack of the sulfinamide on sulfinium ion 19 to afford thioacetal 20, which then suffers elimination of the thiophenyl moiety to yield iminium ion 21. Compound 21 probably affords the more stable iminium ion 22 by a [1,3]H shift which on hydrolysis yields 23.
It was thus clear that the double bond of compound 16 had to be transformed into a hydroxymethyl derivative prior to attempting the Pummerer reaction. The sulfinamide moiety in 16 was deprotected with anhydrous 4 N HCl/dioxane, the resulting amine hydrochloride was treated with acetic anhydride in the presence of excess of triethylamine to furnish amide 24. Ozonolysis of the terminal alkene and reduction of the resultant aldehyde with the use of sodium borohydride in methanol afforded alcohol 25. The protecting groups of the hydroxy groups were removed with CSA in methanol to afford tetrol 26 (Ref. 26). Reprotection with the use of excess of acetic anhydride furnished pentaacetate 27. The stage was now set for attempting the Pummerer reaction. Thus, treatment of 27 with TFAA and Et3N afforded a less polar product (TLC) that was assumed to be the intermediate 28. Further hydrolysis of the intermediate only returned the unreacted starting material and none of the expected aldehyde 29 (Scheme V). The less polar compound observed during TLC examination is probably the sulfurane 30 that undergoes hydrolysis to afford intermediate 31 that eventually leads to the starting material 27 (Ref. 27).

The efforts to obtain an aldehyde from sulfoxide 16 were thus thwarted and therefore it was decided to attempt the Pummerer reaction before introducing the amino stereogenic center. Thus, diol 10 was protected as its acetonide 32 and subjected to Pummerer reaction, the intermediate 33 was hydrolyzed and the resulting aldehyde 34 reduced in the same pot to furnish alcohol 35. The hydroxy group was protected as its silyl ether 36. Deprotection of the PMB group in 36 with DDQ afforded alcohol 37 that was oxidized without incident under Swern conditions to yield aldehyde 38. Sulfinamide 39, readily obtained from 38 and (R)-tert-butylsulfinamide, was reacted with vinyl magnesium bromide to furnish a separable mixture of sulfinamides (dr 85:15) (Scheme VI).

The structure was assigned to major isomer 40 by X-ray crystallography of the acetate 42 prepared by a
three step sequence (Figure 1). The formation of 40 as the major product lends support to the structural assignment to 16.

Proceeding further, the alkene 40 was subjected to treatment with 4N HCl/dioxane that resulted in cleavage of the sulfinamide group. The resulting amine hydrochloride was not isolated but reacted in the same pot with di tert-butyl dicarbonate to yield the carbamate 43. Oxidative cleavage followed by reduction of the resulting aldehyde in the same pot furnished alcohol 44. The hydroxy group was protected as its N,O-acetonide 45. It remained to selectively deprotect the primary silyl ether, oxidize the resulting alcohol and submit the obtained aldehyde to Wittig olefination. Selective deprotection of the primary silyl ether proceeded cleanly using HF-pyridine29 to afford alcohol 46. Oxidation of the hydroxy group with the use of Dess-Martin periodinane30 furnished aldehyde 47 (Scheme VII).

Wittig olefination using the ylid generated from n-dodecanyltriphenylphosphonium bromide and n-BuLi in THF in the presence of HMPA afforded a complex mixture of products. Wittig olefination using other bases like LiHMDS and KHMDS both in the presence and absence of added HMPA afforded only a complex mixture of products (Scheme VII). In the meantime all the available sample of alcohol 46 had been consumed. Thus it was not possible to explore alternate routes to prepare the alkene 48. Efforts are in progress to complete the synthesis of LCB 1.
Synthesis of Mannostatin A analogs

Mannostatin A, a member of the aminocyclopentitol family of natural products, was isolated by Aoyagi and coworkers in 1989 (Ref. 31). Like other members of the family that show potent glycosidase inhibitory activity, mannostatin A too shows strong mannosidase inhibitory activity. Aminocyclopentitols are potentially useful for the treatment of viral infections and for studying polysaccharide biosynthesis. The densely functionalyzed structure and interesting biological properties have stimulated several studies focusing on the synthesis of mannostatin and their stereoisomeric analogs. We were excited by the potential of designing a stereoselective route to phenylthio analog of mannostatin A, from the enantiomer of triol derivative via the intermediacy of an imine related to 15 (Scheme VIII, retrosynthetic analysis).

Herein are presented the details of the investigation toward this goal. Ent-13 was prepared from (R)-methyl phenyl sulfoxide ent-5 in the same manner as detailed in Scheme II. Intramolecular addition of the α-sulfinyl carbanion to the imine in ent-15 was envisaged to form the C–C bond to furnish the sulfoxide derivative of 50. Since the aldehyde was readily available and was expected to be more reactive than the imine, ent-13 was subjected to treatment with lithium diisopropylamide (LDA) in THF. While no change could be observed at –78°C, warming to higher temperatures (–23°C) led to the

![Scheme VII](image-url)
formation of a complex mixture of products (Scheme IX). Examination of the crude NMR revealed the presence of unreacted starting material, epimerized aldehyde and α,β-unsaturated aldehyde. It is likely that the bulky LDA is unable to abstract the methylene proton directly bonded to sulfur, it instead abstracts the proton α to the aldehyde at higher temperature resulting in epimerization and β-elimination. The outcome was however not different with the use of a less bulky lithium diethylamide as the base in the presence or absence of added HMPA. It was therefore decided not to pursue the addition of sulfinyl carbanion on the imine ent-15.

Having been unsuccessful in forming the C–C bond using a carbanion, radical chemistry was now considered for preparing 50. Acetonide ent-32 was subjected to treatment with DDQ to afford the alcohol 51, that was oxidized with the use of Swern protocol to yield the aldehyde 52. Reaction with O-benzylhydroxylamine hydrochloride in the presence of anhydrous potassium carbonate furnished oxime ether 53. Reduction of the sulfinyl moiety using sodium iodide and TFAA in acetone35 afforded sulfide 54. α-Chlorosulfide 55 was prepared by treatment with N-chlorosuccinimide36 in benzene and without isolation was subjected to radical cyclization with the use of n-Bu3SnH (Ref. 37). A complex mixture of products resulted both in the presence and absence of added Et3N (Scheme X)38.

Exploring an alternate route, sulfoxide ent-11 was subjected to Pummerer reaction conditions, the resulting intermediate was hydrolyzed in the same pot to furnish aldehyde 56 which without purification was used in the next step. Dithioacetal formation using dimethyl disulfide and tributylphosphine39 proceeded well to afford compound 57. The p-methoxybenzyl group was deprotected to afford the alcohol 58. Oxidation using Parikh-Doering conditions40 cleanly yielded the aldehyde 59. Oxime ether formation proceeded without incident to yield compound 60 (Scheme XI).

Subjecting 60 to radical cyclization employing the conditions reported by Roberts and coworkers34 afforded an inseparable mixture of an equimolar amount of two aminocyclopentitol derivatives 61 and 62 (Scheme XI). The structures were assigned to the cyclized products based on precedent, NMR and NOE studies. Thus, it was possible to prepare two analogs of mannostatin A by radical cyclization.

Experimental Section

Compound 7: To a solution of LDA (0.08 M in solvents, 52.5 mmol) prepared from diisopropylamine (7.7 mL, 55 mmol) and n-BuLi (1.6 M in hexane, 32.8 mL, 52.5 mmol) cooled at –40°C was added a solution of (S)-methyl phenyl sulfoxide 5 (3.5 g, 25 mmol) in anhydrous THF (330 mL) and stirred at the same temperature for 30 min. The reaction mixture was gradually allowed to warm to 0°C and a solution of the unsaturated ester 6 (6.26 g, 25 mmol) in anhydrous THF (70 mL) was added dropwise and stirred further for a period of 1 hr. The reaction was quenched by the addition of a saturated aqueous NH4Cl solution (150 mL) and the pH adjusted to 2 by the addition of 5% aqueous H2SO4 solution. The two layers were separated and the aqueous phase extracted with Et3O
(3 × 70 mL). The combined organic layers were washed with water (120 mL), saturated brine (120 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent in vacuo afforded the crude product which was purified by column chromatography using 30% EtOAc/hexane (v/v) as the eluent to afford the β-keto sulfoxide 7 (5.16 g, 15 mmol) in 60% yield as a viscous oil; TLC, $R_f$ 0.25 (50% EtOAc/hexane); $[\alpha]_D^{25}$ -123.5$^\circ$ (c 2.05, CHCl$_3$); IR (KBr): 2929, 2840, 1669, 1612, 1513, 1443, 1248, 1036, 750 cm$^{-1}$; $^1$H NMR (200 MHz, CDCl$_3$): δ 7.69-7.57 (m, 2H), 7.53-7.43 (m, 3H), 7.19 (d, $J$ = 6.5 Hz, 2H), 6.89-6.73 (m, 3H), 6.34 (d, $J$ = 16.1 Hz, 1H), 4.43 (s, 2H), 4.14-4.09 (m, 2H), 4.06 (d, $J$ = 13.6 Hz,
1H), 3.88 (d, J = 13.6 Hz, 1H), 3.77 (s, 3H); $^1$C NMR (75 MHz, CDCl$_3$): δ 190.4, 159.3, 146.5, 143.0, 131.5, 129.3, 128.7, 124.1, 113.8, 72.5, 68.2, 66.6, 55.1; MS (ESI): m/z 361 [M+Na]$^+$; HRMS (ESI): m/z [M+H]$^+$ Calcd for C$_{19}$H$_{21}$O$_2$S 345.1160. Found 345.1151.

**Compound 4:** To a solution of anhydrous zinc chloride (2.45 g, 18 mmol) in THF (100 mL) maintained at ambient temperature was added a solution of the β-keto sulfoxide 7 (5.16 g, 15 mmol) in anhydrous THF (50 mL) and the mixture stirred for 15 min. The reaction mixture was cooled to −78°C and a solution of DIBAL-H (1.4 M in toluene, 4.62 g, 13.3 mmol) in dry toluene (65 mL) was added. The reaction mixture was stirred at RT for 15 min. The reaction mixture was quenched by the addition of saturated aqueous Na$_2$SO$_4$. Evaporation of the solvent afforded the crude product which was purified by column chromatography using 45% EtOAc/hexane (v/v) as the eluent to afford bromohydrin 3 (4.73 g, 10.68 mmol) as the sole product in 80% yield as a crystalline solid; m.p. 118°C; TLC, Rf 0.17 (50% EtOAc/hexane); [α]$_D^{25}$ +86.6° (c 1.35, CHCl$_3$); IR (KBr): 3329, 2925, 2864, 1708, 1513, 1448, 1249, 1027, 744 cm$^{-1}$; $^1$H NMR (200 MHz, CDCl$_3$): δ 7.63-7.52 (m, 2H), 7.50-7.40 (m, 3H), 7.17 (d, J = 8.9 Hz, 2H), 6.79 (d, J = 8.9 Hz, 2H), 4.60 (dd, J = 2.2, 10.5 Hz, 1H), 4.45 (s, 2H), 4.18 (td, J = 5.2, 9.7 Hz, 1H), 3.96-3.80 (m, 2H), 3.72 (s, 3H), 3.60 (dd, J = 4.5, 7.5 Hz, 1H), 3.21 (dd, J = 10.5, 13.5 Hz, 1H), 2.71 (dd, J = 2.2, 13.5 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 159.4, 142.8, 131.2, 129.5, 129.4, 129.3, 124.0, 113.9, 75.4, 73.2, 71.3, 66.1, 60.8, 55.3, 50.7; MS (ESI): m/z 443 [M+H]$^+$; HRMS (ESI): m/z [M+H]$^+$ Calcd for C$_{19}$H$_{23}$BrO$_2$S 443.0527. Found 443.0520.

**Compound 8:** Anhydrous K$_2$CO$_3$ (1.35 g, 9.8 mmol) was added to a solution of bromohydrin 3 (4.73 g, 10.68 mmol) in dry acetonitrile (110 mL) cooled at 0°C. The reaction mixture was then allowed to warm to RT over a period of 15 min and stirred further for 8 hr, when TLC examination revealed complete conversion of starting material. Ether (70 mL) was then added to the reaction mixture and after 10 min the precipitated solids were filtered through a plug of celite. The filtrate was evaporated to afford the crude product which was purified by column chromatography using 50% EtOAc/hexane (v/v) as the eluent to afford epoxy alcohol 8 (3.4 g, 9.4 mmol) in 88% yield as a white crystalline solid; m.p. 78°C; TLC, Rf 0.3 (60% EtOAc/hexane); [α]$_D^{25}$ +93.1° (c 2.65, CHCl$_3$); IR (KBr): 3355, 2914, 2857, 1612, 1513, 1443, 1247, 1091, 750 cm$^{-1}$; $^1$H NMR (200 MHz, CDCl$_3$): δ 7.68-7.61 (m, 2H), 7.56-7.48 (m, 3H), 7.22 (d, J = 8.3 Hz, 2H), 6.85 (d, J = 8.3 Hz, 2H), 4.46 (s, 2H), 4.34-4.25 (m, 1H), 3.78 (s, 3H), 3.70 (dd, J = 2.3, 11.3 Hz, 1H), 3.44 (dd, J = 6.0, 11.3 Hz, 1H), 3.30-3.24 (m, 1H), 3.04 (dd, J = 10.6, 13.6 Hz, 1H), 3.00-2.94 (m, 1H), 2.8 (dd, J = 2.3, 13.6 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 159.4, 143.2, 131.4, 131.2, 129.5, 123.9, 113.8, 72.9, 68.8, 65.0, 57.8, 55.3, 54.6; MS (ESI): m/z 363 [M+H]$^+$; HRMS (ESI): m/z [M+H]$^+$ Calcd for C$_{19}$H$_{23}$O$_5$S 363.1266. Found 363.1256.
**Compound 9:** To a solution of epoxy alcohol 8 (3.4 g, 9.4 mmol) in anhydrous dichloromethane (35 mL) at ambient temperature, imidazole (1.42 g, 20.7 mmol) and tert-butyldimethylsilyl chloride (1.56 g, 10.4 mmol) were added successively. The reaction mixture was then stirred for 1 hr before being diluted with dichloromethane (250 mL) and was washed with water (70 mL), saturated brine (70 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent in vacuo afforded the crude product which was purified by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to provide silyl ether 9 (4.16 g, 8.74 mmol) in 93% yield as a viscous oil; TLC, RF$_r$ 0.45 (30% EtOAc/Hexane); [α]$D$ +116° (c 1.5, CHCl$_3$). IR (KBr): 2928, 2855, 1612, 1513, 1471, 1249, 1104, 1046, 834, 780, 749 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.73-7.64 (m, 2H), 7.63-7.53 (m, 3H), 7.22 (d, $J$ = 8.6 Hz, 2H), 6.88 (d, $J$ = 8.6 Hz, 2H), 4.38 (s, 2H), 3.87-3.77 (m, 1H), 3.73 (s, 3H), 3.3-2.8 (m, 6H), 0.94 (s, 9H), 0.15 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 159.3, 144.3, 131.2, 130.9, 129.4, 123.6, 113.7, 73.0, 68.9, 68.4, 63.8, 58.5, 55.3, 55.0, 25.8, 18.2, -4.3, -5.2; MS (ESI): m/z 477 [M+H]$^+$; HRMS (ESI): m/z[M+H]$^+$ Calcd for C$_{25}$H$_{37}$OSiS 477.2130. Found 477.2128.

**Compound 10:** Boron trifluoride-diethyl ether (1.3 mL, 10.5 mmol) was added to a stirred solution of silyl ether 9 (4.16 g, 8.7 mmol) in diethyl ether/dichloromethane (9:1, 65 mL) at -78°C under nitrogen atmosphere. The reaction mixture was allowed to warm to 0°C and stirred at this temperature for 4 hr before it was quenched with saturated aqueous NaHCO$_3$ (15 mL). After being stirred at RT for a further 1 hr, two phases were separated out and the aqueous phase was extracted with chloroform (5 × 15 mL). The combined organic extracts were washed successively with water (20 mL), saturated brine (20 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent under reduced pressure afforded the crude product which was purified by column chromatography using 30% EtOAc/hexane (v/v) as the eluent to furnish diol 10 (3.15 g, 6.4 mmol) in 73% yield as a viscous oil; TLC, RF$_r$ 0.25 (50% EtOAc/hexane); [α]$D$ -67.5° (c 3.45, CHCl$_3$); IR (KBr): 3387, 2929, 2856, 1612, 1513, 1466, 1251, 1089, 1032, 835, 778, 750 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65-7.56 (m, 2H), 7.55-7.44 (m, 3H), 7.23 (d, $J$ = 8.3 Hz, 2H), 6.85 (d, $J$ = 8.3 Hz, 2H), 4.47 (s, 2H), 4.43-4.35 (m, 1H), 3.78 (s, 3H), 3.72 (dt, $J$ = 2.3, 9.8 Hz, 1H), 3.59-3.53 (m, 1H), 3.19 (dd, $J$ = 3.0, 14.3 Hz, 1H), 3.06 (dd, $J$ = 6.0, 14.3 Hz, 1H), 0.89 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 159.2, 143.5, 133.0, 131.2, 129.4, 124.2, 113.8, 74.7, 73.2, 71.4, 70.8, 69.3, 61.9, 55.3, 25.8, 18.0, -4.6; MS (ESI): m/z 495 [M+H]$^+$; HRMS (ESI): m/z[M+H]$^+$ Calcd for C$_{23}$H$_{30}$O$_4$SiS 495.2236. Found 495.2218.

**Compound 11:** To a stirred solution of the mixture of diol 10 (3.15 g, 6.4 mmol) and disopropylethyl amine (6.3 mL, 38.3 mmol) in anhydrous dichloromethane (50 mL) cooled to 0°C was added DMAP (40 mg) and methoxymethyl chloride (1.9 mL, 25.5 mmol) successively and the mixture stirred for 6 hr at ambient temperature. The reaction mixture was then quenched with water (15 mL). The layers were separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic extracts were washed with saturated brine (20 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent under reduced pressure afforded the crude product which was purified by column chromatography using 25% EtOAc/hexane (v/v) as the eluent to afford the di-MOM derivative 11 (3.05 g, 5.23 mmol) in 82% yield as a viscous oil; TLC, RF$_r$ 0.35 (50% EtOAc/hexane); [α]$D$ -30.5° (c 0.8, CHCl$_3$); IR (KBr): 2928, 2854, 1726, 1612, 1511, 1465, 1219, 1094, 1031, 772 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.68-7.58 (m, 2H), 7.53-7.44 (m, 3H), 7.20 (d, $J$ = 8.3 Hz, 2H), 6.81 (d, $J$ = 8.3 Hz, 2H), 4.73 (d, $J$ = 6.8 Hz, 1H), 4.69 (d, $J$ = 6.8 Hz, 1H), 4.65 (d, $J$ = 6.8 Hz, 1H), 4.61 (d, $J$ = 6.8 Hz, 1H), 4.43 (s, 2H), 4.37-4.29 (m, 1H), 4.01-3.95 (m, 1H), 3.90-3.83 (m, 1H), 3.79 (s, 3H), 3.63 (dd, $J$ = 3.8, 10.6 Hz, 1H), 3.53 (dd, $J$ = 6.0, 10.6 Hz, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 3.18 (dd, $J$ = 6.8, 13.6 Hz, 1H), 2.99 (dd, $J$ = 5.3, 13.6 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 156.6, 145.1, 131.0, 130.6, 129.3, 129.2, 124.3, 113.7, 97.1, 96.6, 79.1, 76.4, 73.1, 69.8, 69.0, 62.9, 56.2, 55.7, 55.2, 25.8, 18.0, -4.6, -4.4; MS (ESI): m/z 583 [M+H]$^+$; HRMS (ESI): m/z[M+Na]$^+$ Calcd for C$_{23}$H$_{30}$O$_4$NaSiS 605.2580. Found 605.2559.

**Compound 12:** DDQ (233 mg, 1.03 mmol) was added portionwise over a period of 10 min to a solution of di-Mom derivative 11 (500 mg, 0.86 mmol) in a mixture of dichloromethane/water (19:1, 5 mL) cooled at 0°C. The reaction mixture was stirred at the same temperature for 30 min and then diluted with dichloromethane (15 mL). The precipitated solid was filtered and the filtrate was washed successively with saturated aqueous NaHCO$_3$ solution (2 × 5 mL), water (5 mL), saturated brine (5 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent in
**Compound 13:** To a stirred solution of oxaly chloride (97 μL, 1.12 mmol) in anhydrous dichloromethane (4 mL) cooled at -78°C was added dropwise a solution of DMSO (0.11 mL, 1.5 mmol) in dichloromethane (4 mL) cooled at -78°C. The reaction mixture was stirred at the same temperature for 15 min. A solution of alcohol 12 (344 mg, 0.74 mmol) in anhydrous dichloromethane (2 mL) was added dropwise to the above mixture and stirring continued at -60°C for 45 min. Diisopropylethyl amine (0.64 mL, 3.7 mmol) was added and the reaction mixture was allowed to warm to -10°C. Water (3 mL) was added, the two layers were separated and the aqueous layer was extracted with dichloromethane (2 × 5 mL). The combined organic layers were washed with an IN aqueous HCl solution (5 mL), water (5 mL), saturated brine (5 mL) and dried over anhydrous Na2SO4. The solvent was evaporated under reduced pressure to afford a crude product which was purified by column chromatography using 25% EtOAc/hexane (v/v) as the eluent to afford the aldehyde 13 (320 mg, 0.69 mmol) in 93% yield as a viscous liquid; TLC, Rf 0.35 (40% EtOAc/hexane); [α]D25-16° (c 0.5, CHCl3); IR (KBr): 3331, 2924, 2855, 2310, 1729, 1444, 1258, 1079, 1029, 840, 771, 684 cm-1; 1H NMR (400 MHz, CDCl3): δ 7.68-7.58 (m, 2H), 7.56-7.44 (m, 3H), 4.80 (d, J = 6.3 Hz, 1H), 4.66 (d, J = 6.3 Hz, 1H), 4.63-4.60 (m, 2H), 4.39-4.27 (m, 1H), 3.98-3.89 (m, 1H), 3.85-3.73 (m, 1H), 3.70-3.57 (m, 2H), 3.41 (s, 3H), 3.39 (s, 3H), 3.20 (dd, J = 7.8, 14.1 Hz, 1H), 2.94 (dd, J = 4.7, 14.1 Hz, 1H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (m, 3H); 13C NMR (75 MHz, CDCl3): δ 145.3, 130.9, 129.3, 124.1, 100.0, 97.0, 80.1, 78.8, 69.0, 62.3, 56.3, 55.9, 26.0, 18.1, -4.4, -4.6; MS (ESI): m/z 485 [M+Na]+; HRMS (ESI): m/z [M+Na]+ Calcd for C21H33O2NaSSi 485.2005. Found 485.1994.

**Compound 15:** To a stirred solution of aldehyde 13 (320 mg, 0.69 mmol) in anhydrous dichloromethane (5 mL) was added (S)-tert-butylsulfinamide 14 (95 mg, 0.78 mmol) followed by neat Ti(OEt)4 (0.38 mL, 1.78 mmol). The reaction mixture was stirred for 5 hr at RT, cooled to 0°C and diluted with dichloromethane (5 mL) before it was quenched by adding ice pieces. The resulting suspension was filtered through a plug of Celite and the filter cake was washed with hot ethyl acetate (3 × 3 mL). The filtrate was evaporated under reduced pressure and the residue thus obtained was purified by column chromatography using 25% EtOAc/hexanes (v/v) as the eluent to afford the sulfinylimine 15 (339 mg, 0.61 mmol) in 86% yield as a pale yellow liquid; TLC, Rf 0.32 (40% EtOAc/hexane); [α]D33+1.8° (c 1.47, CHCl3); IR (KBr): 2929, 2860, 1727, 1595, 1447, 1305, 1160, 1080, 836, 771, 688 cm-1; 1H NMR (200 MHz, CDCl3): δ 8.01 (d, J = 4.4 Hz, 1H), 7.65-7.60 (m, 2H), 7.54-7.45 (m, 3H), 4.80 (d, J = 6.6 Hz, 1H), 4.70 (d, J = 6.6 Hz, 1H), 4.66 (s, 2H), 4.36 (q, J = 5.1 Hz, 1H), 4.21 (t, J = 5.1 Hz, 1H), 3.38-3.33 (m, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 3.14-3.05 (m, 2H), 1.21 (s, 9H), 0.91 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 167.7, 144.4, 131.1, 129.3, 124.0, 96.8, 95.7, 80.4, 77.3, 68.2, 62.1, 56.5, 56.3, 56.0, 25.7, 17.9, -4.4, -4.6; MS (ESI): m/z 564 [M+H]+. HRMS (ESI): m/z [M+Na]+ Calcd for C22H35NO2NaSSi 586.2304. Found 586.2290.

**Compound 16:** A flame dried round bottom flask equipped with a magnetic stir bar and nitrogen inlet was charged with a solution of sulfinylimine 15 (339 mg, 0.61 mmol) in anhydrous THF (6 mL). A solution of commercially available vinyl Grignard (1M in THF, 1.83 mL, 1.83 mmol) was added dropwise via a syringe to the sulfinylimine solution cooled at -78°C. The mixture was stirred for 3 hr at the same temperature, when TLC examination revealed complete consumption of the starting material. Excess organometallic reagent was quenched by the addition of saturated aqueous NH4Cl solution (2 mL). The two layers were separated, the aqueous layer was extracted with ethyl acetate (5 × 3 mL) and the combined organic layers were washed with saturated brine (5 mL) and dried over anhydrous Na2SO4. Removal of the solvent in vacuo gave the crude product which was purified by column chromatography using 60% EtOAc/hexane (v/v) as the eluent to afford the aminotetrol derivative 16 (273 mg, 0.46 mmol) as a single diastereomer in 73% yield as a viscous oil; TLC, Rf 0.25 (70% EtOAc/hexane);
[\alpha]_D^{23} -1.5^\circ (c 1.6, CHCl_3); IR (KBr): 2927, 2857, 1736, 1447, 1297, 1143, 1085, 1025, 944, 758, 690 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.66-7.62 (m, 2H), 7.51-7.44 (m, 3H), 5.93-5.83 (m, 1H), 5.28 (d, J = 17.6 Hz, 1H), 5.20 (d, J = 11 Hz, 1H), 5.06 (d, J = 9.5 Hz, 1H), 4.80 (d, J = 6.6 Hz, 1H), 4.56 (d, J = 6.1 Hz, 2H), 4.46 (d, J = 6.6 Hz, 1H), 4.27 (t, J = 6.6 Hz, 1H), 4.19-4.13 (m, 1H), 4.09-4.03 (m, 1H), 3.36 (s, 3H), 3.32 (s, 3H), 3.26 (dd, J = 6.6, 13.2 Hz, 1H), 2.89 (dd, J = 5.1, 13.2 Hz, 1H), 1.20 (s, 9H), 0.84 (s, 9H), 0.80 (s, 3H), 0.03 (s, 3H); \( ^13\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 141.5, 136.2, 131.4, 129.4, 124.3, 97.3, 97.0, 80.4, 79.0, 68.6, 56.6, 56.5, 56.3, 54.6, 25.7, 25.2, 17.9, -3.6, -5.0; MS (LC-MSD): \( m/z \) 614 [M+Na]+; HRMS (ESI): \( m/z \) Calcd for C\(_{27}\)H\(_{30}\)NO\(_2\)Na\(_2\)Si: 614.2617. Found 614.2626.

**Compound 23**: To a solution of aminotetrol derivative 16 (50 mg, 0.08 mmol) in anhydrous CH\(_2\)Cl\(_2\) (0.5 mL) cooled at 0°C was added Et\(_3\)N (36 \( \mu \)L, 0.25 mmol) followed by TFAA (49 \( \mu \)L, 0.25 mmol) under an atmosphere of nitrogen and stirred for 15 min. Then a solution of 5% aqueous NaHCO\(_3\) (0.5 mL) was added to the above reaction mixture at 0°C and stirred for a further 20 min at the same temperature. The reaction mixture was then extracted into CH\(_2\)Cl\(_2\) (3 \( \times \) 3 mL). The combined organic layers were washed successively with water (2 mL), saturated brine (2 mL) and dried over anhydrous Na\(_2\)SO\(_4\). The solvent was evaporated in vacuo and the residue was purified by column chromatography using 8% EtOAc/hexane (v/v) as the eluent to afford unsaturated ketone 23 (16 mg, 0.03 mmol) in 39% yield as a viscous oil; TLC, R\(_f\) 0.25 (15% EtOAc/hexane); [\alpha]_D^{29} +2.0^\circ (c 0.15, CHCl\(_3\)); IR (KBr): 2925, 2854, 2303, 1729, 1448, 1306, 1220, 1128, 1086, 771, 673 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 6.54-6.42 (m, 1H), 5.87 (d, J = 18.3 Hz, 1H), 5.64 (d, J = 11.7 Hz, 1H), 5.28 (d, J = 12.5 Hz, 1H), 4.70 (d, J = 6.6 Hz, 1H), 4.59-4.52 (m, 4H), 4.09-4.04 (m, 1H), 4.03-3.97 (m, 1H), 3.84-3.73 (m, 1H), 3.45-3.39 (m, 1H), 3.36 (s, 3H), 3.29 (s, 3H), 1.38 (s, 9H), 0.91 (s, 9H), 0.09 (s, 6H); MS (ESI): \( m/z \) 482 [M+H]+; HRMS (ESI): \( m/z \) [M+H]+ Calcd for C\(_{24}\)H\(_{32}\)NO\(_2\)Si: 482.2591. Found 482.2591.

**Compound 24**: To a stirred solution of the aminotetrol derivative 16 (223 mg, 0.38 mmol) in MeOH (2 mL) at 0°C was added a solution of anhydrous HCl in dioxane (4 M, 0.18 mL, 0.75 mmol) in one portion. The reaction mixture was stirred at the same temperature for 3 hr when TLC examination revealed complete consumption of the starting material. Dichloromethane (2 mL) and Et\(_3\)N (0.16 mL, 1.13 mmol) were then added, and the reaction was removed from the ice bath. After 10 min, acetic anhydride (54 \( \mu \)L, 0.56 mmol) was added in one portion. The reaction was stirred for 14 hr. Dichloromethane was removed under reduced pressure and the residue was dissolved in EtOAc (15 mL). The combined organic layer was washed with saturated aqueous NH\(_4\)Cl (3 \( \times \) 3 mL), NaHCO\(_3\) (2 \( \times \) 3 mL), saturated brine (3 mL) and dried over anhydrous Na\(_2\)SO\(_4\). The solvent was evaporated under reduced pressure to yield a crude product which was purified by column chromatography using 55% EtOAc/hexane (v/v) as the eluent to furnish acetate 24 (175 mg, 0.33 mmol) in 88% yield as a colorless viscous oil; TLC, R\(_f\) 0.3 (70% EtOAc/hexane); [\alpha]_D^{29} +5.6^\circ (c 0.7, CHCl\(_3\)); IR (KBr): 2926, 2855, 1750, 1446, 1303, 1225, 1147, 1081, 1033, 838, 765, 688 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.66-7.62 (m, 1H), 7.51-7.44 (m, 3H), 5.93-5.83 (m, 1H), 5.28 (d, J = 11 Hz, 1H), 5.06 (d, J = 9.5 Hz, 1H), 4.80 (d, J = 6.6 Hz, 1H), 4.56 (d, J = 6.1 Hz, 2H), 4.46 (d, J = 6.6 Hz, 1H), 4.27 (t, J = 6.6 Hz, 1H), 4.19-4.13 (m, 1H), 4.09-4.03 (m, 1H), 3.36 (s, 3H), 3.32 (s, 3H), 3.26 (dd, J = 6.6, 13.2 Hz, 1H), 2.89 (dd, J = 5.1, 13.2 Hz, 1H), 1.20 (s, 9H), 0.84 (s, 9H), 0.80 (s, 3H), 0.03 (s, 3H); \( ^13\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 141.5, 136.2, 131.4, 129.4, 124.3, 97.3, 97.0, 80.4, 79.0, 68.6, 56.6, 56.5, 56.3, 54.6, 25.7, 25.2, 17.9, -3.6, -5.0; MS (LC-MSD): \( m/z \) 614 [M+Na]+; HRMS (ESI): \( m/z \) Calcd for C\(_{24}\)H\(_{29}\)NO\(_2\)Na\(_2\)Si: 614.2617. Found 614.2626.

**Compound 25**: Ozone gas was bubbled into the solution of the acetate 24 (175 mg, 0.33 mmol) in DCM (10 mL) cooled at −78°C until the reaction mixture showed a pale blue coloration. Dimethyl sulfide (100 mg, 1.65 mmol) was added to the reaction mixture at the same temperature and stirred for 30 min. The reaction mixture was then brought to RT and stirred further for a period of 8 hr. The reaction mixture was then cooled to 0°C and solid NaBH\(_4\) (24 mg, 0.66 mmol) was added in small portions over a period of 10 min. The reaction mixture was then quenched with saturated aqueous NH\(_4\)Cl (2 mL) and the aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 \( \times \) 3 mL). The combined organic extracts were washed once with saturated brine (5 mL) and dried over anhydrous Na\(_2\)SO\(_4\). Evaporation of the solvent under reduced pressure afforded a crude residue, which was purified by column
chromatography using pure EtOAc as the eluent to furnish the alcohol 25 (137 mg, 0.26 mmol) in 78% yield as a viscous oil; TLC, Rf 0.2 (pure EtOAc); [α]D 30° -1.2° (c 1.35, CHCl3); IR (KBr): 3447, 2926, 2855, 1639, 1449, 1299, 1148, 1031, 837, 772 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 7.64 (d, J = 7.3 Hz, 2H), 7.57-7.44 (m, 3H), 4.80 (d, J = 6.6 Hz, 1H), 4.80 (d, J = 6.6 Hz, 1H), 4.66 (d, J = 6.6 Hz, 1H), 4.62 (d, J = 6.6 Hz, 1H), 4.59 (d, J = 6.6 Hz, 1H), 4.32-4.19 (m, 1H), 4.14-4.06 (m, 1H), 4.06-4.01 (m, 1H), 3.82-3.76 (m, 1H), 3.76-3.68 (m, 2H), 3.42 (s, 6H), 3.29 (dd, J = 7.3, 13.9 Hz, 1H), 2.96 (dd, J = 4.4, 13.9 Hz, 1H), 2.00 (s, 3H), 0.87 (s, 9H), 0.07 (s, 6H), 3.29 (dd, J = 6.2, 9.3 Hz, 1H), 3.08 (dd, J = 7.3, 13.9 Hz, 1H), 2.96 (dd, J = 4.4, 13.9 Hz, 1H), 2.00 (s, 3H), 0.87 (s, 9H), 0.07 (s, 6H), 0.04 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 170.8, 144.1, 131.2, 129.4, 124.2, 98.3, 97.0, 81.3, 78.8, 68.6, 62.7, 61.5, 56.6, 56.3, 51.2, 25.8, 23.3, 17.9, -4.5, -4.9; MS (LC-MSD): m/z 534 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C22H29NO10NaS 522.1409. Found 522.1421.

Compound 27: To a stirred solution of the alcohol 25 (137 mg, 0.26 mmol) in methanol (3 mL) was added catalytic amounts of CSA (6 mg, 0.03 mmol) and the reaction mixture stirred at ambient temperature for 30 hr. A few drops of Et3N were added to the reaction mixture and the solvent evaporated under reduced pressure to afford the crude residue which without isolation was subjected to acetylation. The crude product from above was dissolved in anhydrous CH2Cl2 (3 mL), cooled at 0°C and Et3N (0.22 mL, 1.56 mmol), DMAP (2 mg) and acetic anhydride (0.14 mL, 1.56 mmol) were added successively. The mixture was stirred at ambient temperature for 2 hr. The reaction mixture was then diluted with CH2Cl2 (10 mL), washed with 10% aqueous citric acid solution (2 × 3 mL), water (3 mL), saturated brine (3 mL) and dried over anhydrous Na2SO4. Evaporation of the solvent under reduced pressure afforded the crude product which was purified by column chromatography using 90% EtOAc/hexane (v/v) as the eluent to afford the pentaacetate 27 (148 mg, 0.32 mmol) in 62% yield as a colourless viscous oil; TLC, Rf 0.25 (pure EtOAc); [α]D 30° -38° (c 0.5, CHCl3); IR (KBr): 2923, 2853, 2302, 1744, 1452, 1220, 1149, 1038, 933, 894, 771, 678 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 7.70-7.59 (m, 2H), 7.57-7.48 (m, 3H), 6.31 (d, J = 9.3 Hz, 1H), 5.48-5.37 (m, 1H), 5.35-5.28 (m, 1H), 5.06-4.96 (m, 1H), 4.13 (dd, J = 5.3, 11.7 Hz, 1H), 4.00 (dd, J = 4.5, 11.7 Hz, 1H), 3.49-3.33 (m, 1H), 3.28-3.12 (m, 2H), 2.10 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H); MS (LC-MSD): m/z 522 [M+Na]+; HRMS (ESI): m/z [M+Na]+ Calcd for C22H29NO10NaS 522.1409. Found 522.1421.

Compound 32: To a stirred solution of diol 10 (2.47 g, 5 mmol) in dichloromethane (25 mL), was added 2,2-dimethoxypropane (3.1 mL, 25 mmol) and CSA (58 mg, 0.25 mmol) successively and the reaction mixture stirred at RT for 6 hr. Et3N (52 μL, 0.36 mmol) was added and the reaction mixture was concentrated under reduced pressure. The crude residue was purified by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to furnish the acetone 32 (2.32 g, 4.35 mmol) in 87% yield, as a viscous oil; TLC, Rf 0.25 (20% EtOAc/hexane); [α]D 23° -61.5° (c 3.05, CHCl3); IR (KBr): 2928, 2859, 2361, 1727, 1611, 1513, 1464, 1377, 1251, 1084, 1035, 833, 772, 692 cm⁻¹; 1H NMR (200 MHz, CDCl3): δ 7.59-7.53 (m, 2H), 7.50-7.43 (m, 3H), 7.18 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 4.44 (d, J = 11.6 Hz, 1H), 4.38 (d, J = 11.6 Hz, 1H), 4.35-4.28 (m, 3H), 3.78 (s, 3H), 3.65 (dd, J = 4.7, 9.3 Hz, 1H), 3.42 (dd, J = 6.2, 9.3 Hz, 1H), 3.08 (dd, J = 7.0, 13.2 Hz, 1H), 3.00 (dd, J = 3.9, 13.2 Hz, 1H), 1.44 (s, 3H), 1.36 (s, 3H), 0.84 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 159.3, 144.8, 131.0, 130.1, 129.3, 124.0, 113.8, 108.4, 79.1, 76.3, 73.0, 68.9, 66.8, 63.1, 55.2, 27.5, 25.8, 25.3, 18.0, -3.8, -4.5; MS (ESI): m/z 535 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C28H15O2NaSSi 557.2369. Found 557.2361.

Compound 35: To a solution of acetone 32 (2.32 g, 4.35 mmol) in anhydrous CH2Cl2 (25 mL) cooled at 0°C was added Et3N (1.8 mL, 13 mmol) followed by TFAA (2.5 mL, 13 mmol) under an atmosphere of nitrogen and the mixture stirred for 15 min. Then a solution of NaBH4 (658 mg, 17.4 mmol) dissolved in 5% aqueous NaHCO3 solution (35 mL) was added to the above reaction mixture at 0°C and stirred for a further 20 min at the same temperature. The layers were separated and the aqueous layer extracted with CH2Cl2 (3 × 50 mL). The combined organic layers were washed successively with water (2 × 30 mL), saturated brine (30 mL) and dried over anhydrous Na2SO4. The solvent was evaporated in vacuo and the residue was purified by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to afford alcohol 35 (1.46 g, 3.44 mmol) in 79% yield as a viscous oil; TLC, Rf 0.3 (20% EtOAc/hexane); [α]D 23° -6.8° (c 0.56, CHCl3); IR (KBr): 3472, 2934, 2858, 1613, 1575, 1513, 1463, 1373, 1250, 1082, 834, 776, 662 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 7.23 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.54 (d, J =
3.13 mmol) in 91% yield as a viscous oil; TLC, Rf 0.8 (60% EtOAc/Hexane); [α]D23 -15.6° (c 2.03, CHCl3); IR (KBrs): 3496, 2933, 2859, 1467, 1380, 1255, 1091, 836, 776, 665 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 4.22-4.09 (m, 2H), 4.08-3.99 (m, 1H), 3.76-3.59 (m, 3H), 3.58-3.44 (m, 1H), 1.42 (s, 3H), 1.32 (s, 3H), 0.89 (s, 18H), 0.13 (s, 6H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 107.6, 77.5, 76.5, 72.4, 65.0, 61.7, 28.3, 26.1, 25.9, 18.5, 18.3, -4.2, -4.5, -5.3; MS (LC-MSD): m/z 443 [M+Na]+ HRMS (ESI): m/z [M+Na]+ Calcld for C₂₂H₃₈O₈NaSi₂ 443.2625. Found 443.2636.

**Compound 38:** To a stirred solution of oxalyl chloride (0.34 mL, 3.96 mmol) in anhydrous dichloromethane (10 mL) cooled at -78°C was added dropwise a solution of DMSO (0.38 mL, 5.26 mmol) in anhydrous dichloromethane (5 mL) and the reaction mixture stirred at the same temperature for 15 min. A solution of alcohol 37 (1.11 g, 2.63 mmol) in anhydrous dichloromethane (10 mL) was added dropwise to the above mixture and stirring continued at the same temperature for 45 min. Disopropylethyl amine (2.3 mL, 13.26 mmol) was added and the reaction mixture warmed to -10°C. Water (10 mL) was added, the two layers were separated. The aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were washed with an aqueous 1N HCl solution (10 mL), water (10 mL), saturated brine (10 mL) and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure to afford a crude product which was purified by column chromatography using 2% EtOAc/hexane (v/v) as the eluent to afford the aldehyde 38 (802 mg, 1.92 mmol) in 73% yield as a viscous liquid; TLC, Rf 0.4 (10% EtOAc/hexane); [α]D23 -4.2° (c 1.97, CHCl₃); IR (KBrs): 2933, 2858, 1736, 1462, 1381, 1254, 1092, 838, 777, 674 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.57 (d, J = 2.5 Hz, 1H), 4.52 (dd, J = 7.2, 2.5 Hz, 1H), 4.33 (dd, J = 2.5, 7.2 Hz, 1H), 4.08 (dt, J = 2.5, 5.7 Hz, 1H), 3.64-3.57 (m, 2H), 1.56 (s, 3H), 1.37 (s, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.07 (s, 12H); ¹³C NMR (75 MHz, CDCl₃): δ 199.0, 109.6, 80.9, 80.8, 72.1, 64.7, 27.2, 26.1, 25.9, 25.3, 18.4, 18.2, -4.4, -4.8, -5.3; MS (LC-MSD): m/z 443 [M+Na]+ HRMS (ESI): m/z [M+Na]+ Calcld for C₂₃H₂₄O₃NaSi₂ 443.2648. Found 443.2476.

**Compound 39:** To a stirred solution of aldehyde 38 (802 mg, 1.92 mmol) in anhydrous dichloro-
methane (10 mL) was added (R)-tert-butylsulfinamide (262 mg, 2.16 mmol) followed by neat Ti(OEt)4 (1 mL, 4.9 mmol). The reaction mixture was stirred for 5 hr at RT, cooled to 0°C and diluted with dichloromethane (10 mL) before it was quenched by adding ice pieces. The resulting suspension was filtered through a plug of Celite and the filter cake was washed with hot ethyl acetate (3 × 10 mL). The filtrate was evaporated under reduced pressure and the residue thus obtained was purified by column chromatography using 5% EtOAc/hexanes (v/v) as the eluent to afford the sulfinylimine derivatives (558 mg, 1.02 mmol) and (93 mg, 0.17 mmol) as a mixture of diastereomers (dr 6:1) in 72% combined yield as colourless viscous oils.

**Compound 40**: Viscous oil; TLC, Rf 0.25 (20% EtOAc/hexane); [α]D24 +26.2° (c 1.5, CHCl3); IR (KBr): 2933, 2859, 1579, 1467, 1380, 1255, 1216, 1071, 834, 776, 692, 632 cm−1; 1H NMR (300 MHz, CDCl3): δ 8.09 (d, J = 3.4 Hz, 1H), 4.83 (dd, J = 6.4, 3.4 Hz, 1H), 4.43 (t, J = 6.4 Hz, 1H), 3.99-3.90 (m, 1H) 3.69-3.63 (m, 2H), 1.54 (s, 3H), 1.38 (s, 3H), 1.19 (s, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.10 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 167.2, 109.6, 79.0, 78.5, 72.1, 65.0, 56.7, 27.4, 26.1, 22.6, 18.4, -4.2, -4.5, -5.2, -5.4; MS (LC-MSD): m/z 522 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C23H33NO3NaSiS 572.3237. Found 572.3243.

Note: Signal for one –Si–CMe3 quaternary not picked up in 13C NMR.

**Compound 41**: Viscous oil; TLC, Rf 0.22 (20% EtOAc/hexane); [α]D33 +9.7° (c 0.85, CHCl3); IR (KBr): 2933, 2859, 1579, 1467, 1380, 1255, 1216, 1071, 834, 776, 692, 632 cm−1; 1H NMR (300 MHz, CDCl3): δ 5.91 (ddd, J = 6.8, 10.6, 17.4 Hz, 1H), 5.32 (d, J = 17.4 Hz, 1H), 5.25 (d, J = 10.6 Hz, 1H), 4.39 (dd, J = 3.0, 6.0 Hz, 1H), 4.26 (dd, J = 6.8, 8.3 Hz, 1H), 4.15-4.01 (m, 2H), 3.79 (dd, J = 3.0, 11.3 Hz, 1H), 3.68 (dd, J = 4.5, 11.3 Hz, 1H), 1.41 (s, 3H), 1.31 (s, 3H), 1.21 (s, 9H), 0.92 (s, 9H), 0.90 (s, 9H), 0.15 (s, 6H), 0.05 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 131.1, 122.9, 108.8, 75.9, 71.9, 64.6, 60.4, 53.9, 29.7, 26.1, 25.9, 25.6, 25.1, 18.6, 14.2, -3.9, -4.2, -5.3, -5.5; MS (LC-MSD): m/z 550 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C25H35NO3NaSi3S 572.3237. Found 572.3243.

Note: Signal for –S–CMe3 quaternary not picked up in 13C NMR.

**Compound 42**: To a solution of di-TBS derivative (200 mg, 0.36 mmol) in dioxane/water (3:1, 4 mL), were added 2,6-lutidine (87 µL, 0.72 mmol), OsO4 (112 µL, 2.5% in 2-methyl-2-propanol, 0.006 mmol) and NaO4 (313 mg, 1.46 mmol). The reaction mixture was stirred at 25°C and the progress monitored by TLC. After the reaction was complete, the reaction mixture was cooled to 0°C and NaBH4 (6 mg, 0.15 mmol) was added. After 30 min, the reaction mixture was diluted with CH2Cl2 (20 mL) and water (10 mL). The organic layer was separated and the water layer extracted with CH2Cl2 (3 × 10 mL). The combined organic layers were washed with water (10 mL), saturated brine (10 mL) and dried over anhydrous Na2SO4. The solvent was concentrated and the crude product was purified by column chromatography using 20% EtOAc/hexane (v/v) as the eluent to afford
corresponding alcohol (147 mg, 0.26 mmol) in 73% yield, as colorless viscous oil; TLC, Rf: 0.55 (60%, EtOAc/hexane); [α]D25 -15.2° (c 2.86, CHCl3); IR (KBr): 2933, 2859, 1641, 1463, 1375, 1255, 1209, 1091, 958, 836, 776, 662 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 4.17 (bs, 1H), 4.08-4.01 (m, 1H), 3.99-3.88 (m, 1H), 3.83-3.67 (m, 2H), 3.65-3.49 (m, 4H), 1.45 (s, 3H), 1.30 (s, 3H), 1.24 (s, 9H), 0.88 (s, 18H), 0.15 (s, 3H), 0.13 (s, 3H), 0.03 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 170.4, 108.3, 75.7, 75.4, 71.9, 65.2, 64.7, 56.6, 54.9, 26.6, 26.0, 25.9, 24.3, 22.9, 20.8, 18.4, 18.1, -3.1, -4.4, -5.4, -5.6; MS (LC-MSD): m/z 596 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C25H55NO6NaSi2S 576.3186. Found 576.3184.

To the solution of the alcohol (147 mg, 0.26 mmol) in anhydrous CH2Cl2 (1 mL) at 0°C were added Et3N (56 µL, 0.4 mmol), DMAP (1 mg) and acetic anhydride (38 µL, 0.4 mmol) successively and the mixture stirred for 2 hr at ambient temperature. The reaction mixture was diluted with CH2Cl2 (10 mL) and washed with 10% aqueous citric acid solution (2 × 3 mL), water (3 mL), saturated brine (3 mL) and dried over anhydrous Na2SO4. Evaporation of the solvent under reduced pressure afforded the crude product which was purified by column chromatography using 18% EtOAc/hexane (v/v) as the eluent to afford the acetate 42 (138 mg, 0.23 mmol) in 87% yield as a viscous oil; TLC, Rf 0.6 (60% EtOAc/hexane); [α]D26 -5.6° (c 0.74, CHCl3); IR (KBr): 2933, 2859, 1641, 1463, 1375, 1255, 1209, 1092, 958, 837, 777, 659 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 4.51 (dd, J = 5.9, 11.7 Hz, 1H), 4.31-4.21 (m, 2H), 4.06 (dd, J = 8.8, 11.0 Hz, 1H), 3.87-3.76 (m, 2H), 3.57 (d, J = 11.0 Hz, 1H), 2.05 (s, 3H), 1.45 (s, 3H), 1.32 (s, 3H), 1.22 (s, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.15 (s, 6H), 0.03 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 170.4, 108.3, 75.7, 75.4, 71.9, 65.2, 64.7, 56.6, 54.9, 26.6, 26.0, 25.9, 24.3, 22.9, 20.8, 18.4, 18.1, -3.1, -4.4, -5.4, -5.6; MS (LC-MSD): m/z 596 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C25H55NO6NaSi2S 568.3465. Found 568.3475.

**Compound 43:** To a solution of carbamate 43 (215 mg, 0.39 mmol) in dioxane/water (3:1, 4 mL), were added 2.6-lutidine (94 µL, 0.78 mmol), OsO4 (0.12 mL, 2.5% in 2-methyl-2-propanol, 0.007 mmol) and NaIO4 (336 mg, 1.56 mmol). The reaction mixture was cooled at 0°C and the progress monitored by TLC. After the reaction was complete, the reaction mixture was cooled to 0°C and NaBH4 (6 mg, 0.15 mmol) was added. After 30 min, the reaction mixture was diluted with CH2Cl2 (20 mL) and water (10 mL). The organic layer was separated and the water layer extracted with CH2Cl2 (3 × 10 mL). The combined organic layers were washed with water (10 mL), saturated brine (10 mL) and dried over anhydrous Na2SO4. The solvent was concentrated and the crude product was purified by column chromatography using 15% EtOAc/hexane (v/v) as the eluent to afford alcohol 44 (154 mg, 0.28 mmol) in 71% yield as a colorless viscous oil; TLC, Rf 0.35 (20%, EtOAc/hexane); [α]D26 -14.7° (c 0.92, CHCl3); IR (KBr): 3441, 2932, 2857, 2361, 2335, 1714, 1504, 1472, 1366, 1255, 1168, 1084, 835, 777, 670 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 5.39-5.26 (bs, 1H), 4.28-4.18 (m, 2H), 4.10-4.03 (m, 1H), 3.82
(dd, J = 4.3, 10.7 Hz, 1H), 3.78-3.74 (m, 3H), 3.70 (dd, J = 4.3, 10.7 Hz, 1H), 1.44 (s, 12H), 1.33 (s, 3H), 0.90 (s, 18H), 0.17 (s, 3H), 0.15 (s, 3H), 0.07 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 108.0, 79.7, 76.8, 72.4, 64.5, 63.9, 52.8, 28.3, 27.0, 25.9, 25.1, 18.3, 18.2, -4.1, -4.5, -5.4, -5.5; MS (LC-MSD): m/z 550 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C26H35NO3NaSi2 572.3414. Found 572.3407.

Note: Signal for carbonyl carbon and –O–CMe3 quaternary not picked up in 13C NMR.

**Compound 45**: To a stirred solution of alcohol 44 (154 mg, 0.28 mmol) in dichloromethane (1.5 mL), was added 2,2–dimethoxypropane (0.17 mL, 1.4 mmol) and CSA (4 mg, 0.014 mmol) successively and the reaction mixture stirred at RT for 6 hr. Et3N (3 µL, 0.02 mmol) was then added and the reaction mixture was concentrated under reduced pressure. The crude residue was purified by column chromatography using 5% EtOAc/hexane (v/v) as the eluent to furnish the N,O-acetoneide 45 (146 mg, 0.25 mmol) in 89% yield, as a viscous oil. TLC, Rf 0.8 (20% EtOAc/hexane); [α]D27 –40.4° (c 0.97, CHCl3); IR (KBr): 2933, 2859, 1697, 1472, 1389, 1257, 1076, 942, 835, 777, 667 cm\(^{-1}\); 1H NMR (300 MHz, CDCl3): δ 4.61-4.46 (m, 1H), 4.29 (t, J = 6.0 Hz, 1H), 4.22-4.14 (m, 1H), 4.14-4.02 (m, 1H), 3.91-3.74 (m, 2H), 3.66 (dd, J = 4.3, 10.2 Hz, 1H), 1.49 (s, 12H), 1.43 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.13 (s, 6H), 0.07 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 107.6, 107.5, 94.0, 93.1, 79.8, 76.8, 75.5, 72.4, 65.1, 64.6, 58.1, 57.6, 29.7, 28.6, 28.5, 26.4, 26.3, 26.1, 25.8, 25.5, 25.0, 24.8, 23.5, 18.5, 18.2, -4.1, -4.3, -4.4, -5.4; MS (LC-MSD): m/z 612 [M+Na]+; HRMS (ESI): m/z [M+Na]+ Calcd for C26H35NO3NaSi2 612.3727. Found 612.3715.

Note: Signal for carbonyl carbon and –O–CMe3 quaternary not picked up in 13C NMR.

**Compound 46**: To a solution of N,O-acetoneide 45 (146 mg, 0.25 mmol) in THF (5 mL) in a Nalgene tube was added freshly prepared buffered pyridinium hydrofluoride (3.8 mL, stock solution prepared from 2.0 g of Aldrich pyridinium hydrofluoride, 4 mL of pyridine and 16 mL of THF). After 6 hr, another 0.7 mL portion of the stock solution was added. After 8 hr total, the reaction mixture was poured into 110 mL of saturated aqueous NaHCO3 and extracted with CH2Cl2 (3 × 75 mL). The combined organic extracts were washed with saturated brine and dried over anhydrous Na2SO4. Evaporation of the solvent afforded the crude residue which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to furnish alcohol 46 (102 mg, 0.21 mmol) in 86% yield, as a viscous liquid; TLC, Rf 0.45 (20% EtOAc/hexane); [α]D28 –34.6° (c 1.64, CHCl3); IR (KBr): 3475, 2941, 2860, 2361, 2335, 1695, 1466, 1390, 1366, 1256, 1073, 773, 670 cm\(^{-1}\); 1H NMR (300 MHz, CDCl3): δ 4.71-4.56 (m, 1H), 4.34-4.23 (m, 2H), 4.16 (d, J = 9.1 Hz, 1H), 3.98-3.86 (m, 2H), 3.75 (d, J = 4.5 Hz, 2H), 1.50 (s, 3H), 1.47 (s, 12H), 1.42 (s, 3H), 1.35 (s, 3H), 0.91 (s, 9H), 0.14 (s, 6H); 13C NMR (75 MHz, CDCl3): δ 152.4, 107.8, 93.4, 80.1, 78.1, 75.9, 71.3, 65.1, 64.3, 57.7, 28.6, 28.4, 26.4, 26.2, 26.02, 24.8, 18.3, -4.1, -4.3; MS (LC-MSD): m/z 498 [M+Na]+; HRMS (ESI): m/z [M+Na]+ Calcd for C25H34NO3NaSi 498.2863. Found 498.2875.

**Compound 47**: Dess–Martin periodinane (120 mg, 0.27 mmol) and sodium bicarbonate (26 mg, 0.3 mmol) were added to the solution of alcohol 46 (102 mg, 0.21 mmol) in dichloromethane (1.5 mL) at 0°C and the mixture stirred for 30 min at the same temperature. The reaction mixture was diluted with dichloromethane (10 mL), the precipitate filtered through a plug of Celite and the filtrate washed with aqueous saturated NaHCO3 solution (3 mL), water (3 mL), saturated brine (3 mL), dried over anhydrous Na2SO4 and concentrated. The residue was purified by column chromatography using 5% EtOAc/hexane (v/v) to afford aldehyde 47 (94 mg, 0.19 mmol) in 93% yield, as a viscous oil; TLC, Rf 0.55 (20% EtOAc/hexane); [α]D27 –40° (c 1.64, CHCl3); IR (KBr): 3293, 2855, 1698, 1462, 1390, 1255, 1166, 1096, 863, 751, 696 cm\(^{-1}\); 1H NMR (200 MHz, CDCl3): δ 9.66 (s, 1H), 4.49-4.38 (m, 3H), 4.18-4.13 (m, 1H), 3.91-3.81 (m, 2H), 1.50 (s, 3H), 1.47 (s, 12H), 1.42 (s, 3H), 1.35 (s, 3H), 0.91 (s, 9H), 0.14 (s, 6H); MS (LC-MSD): m/z 452 [M+Na]+; HRMS (ESI): m/z [M+Na]+ Calcd for C28H43NO3NaSi 452.2706. Found 452.2700.

**Compound 51**: DDQ (136 mg, 0.6 mmol) was added portion-wise over a period of 10 min to a solution of acetonide 32 (267 mg, 0.5 mmol) in a mixture of dichloromethane/water (19:1, 3 mL) cooled at 0°C. The reaction mixture was stirred at the same temperature for 30 min and then diluted with dichloromethane (10 mL). The precipitated solid was filtered and the filtrate was washed successively with saturated aqueous NaHCO3 solution (2 × 3 mL), water (3 mL), saturated brine (3 mL) and dried over anhydrous Na2SO4. Evaporation of the solvent in vacuo afforded a crude product which was purified by column chromatography using 25% EtOAc/hexane (v/v) as the eluent to yield the alcohol 51 (176 mg,
0.42 mmol) in 85% yield as a viscous oil; TLC, Rf 0.4 (50% EtOAc/hexane); [α]D25 +12° (c 0.2, CHCl3); IR (KBr): 3344, 2927, 2956, 1786, 1729, 1447, 1407, 1299, 1144, 1084, 752, 688 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ 7.66-7.60 (m, 2H); 7.57-7.48 (m, 3H), 4.55-4.47 (m, 1H), 4.39 (t, J = 6.0 Hz, 1H), 3.68 (dd, J = 6.8, 12.1 Hz, 1H); 3.55 (dd, J = 6.0, 12.1 Hz, 1H), 3.08 (dd, J = 8.3, 13.6 Hz, 1H), 2.99 (dd, J = 3.0, 13.6 Hz, 1H), 1.45 (s, 3H), 1.38 (s, 3H), 0.89 (m, 9H), 0.16 (s, 3H), 0.11 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 144.1, 131.3, 129.4, 124.0, 108.3, 78.5, 77.2, 66.5, 62.5, 61.4, 60.4, 27.9, 25.7, 25.6, 18.0, -4.2, -4.6; MS (EI): m/z 437 [M+Na]+; HRMS (EI); m/z [M+Na]+ Calcd for C20H32N2O2NaSSi 437.1793. Found 437.1803.

**Compound 52:** To a stirred solution of oxaryl chloride (55 μL, 0.63 mmol) in anhydrous dichloromethane (3 mL) cooled at −78°C was added dropwise a solution of DMSO (63 μL, 0.84 mmol) in anhydrous dichloromethane (1 mL) and the reaction mixture stirred at the same temperature for 15 min. A solution of alcohol 51 (176 mg, 0.42 mmol) in anhydrous dichloromethane (1 mL) was added dropwise to the above mixture and stirring continued at −60°C for 45 min. Disopropylethyl amine (0.36 mL, 2.1 mmol) was added and the reaction mixture allowed to warm to −10°C. Water (2 mL) was added, the two layers were separated and the aqueous layer was extracted with dichloromethane (2 × 3 mL). The combined organic layers were washed with an 1N aqueous HCl solution (3 mL), water (3 mL), saturated brine (2 mL) and dried over anhydrous Na2SO4. Evaporation of the solvent in vacuo afforded the crude product which was purified by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to furnish oximeether 53 (129 mg, 0.25 mmol) in 73% yield as a viscous oil; TLC, Rf 0.45 (30% EtOAc/hexane); [α]D25 -3.6° (c 0.6, CHCl3); IR (KBr): 2929, 2860, 1732, 1575, 1447, 1035, 1219, 1147, 1081, 772, 686 cm⁻¹; 1H NMR (200 MHz, CDCl3): δ 7.68-7.57 (m, 2H), 7.55-7.45 (m, 3H), 7.41-7.31 (m, 5H), 5.09 (s, 2H), 4.59 (t, J = 6.6 Hz, 1H), 4.43 (dd, J = 3.7, 7.3 Hz, 1H), 4.38-4.29 (m, 1H), 2.99-2.92 (m, 2H), 1.44 (s, 3H), 1.40 (s, 3H), 0.88 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 149.5, 144.3, 135.8, 131.1, 129.4, 128.5, 128.3, 128.0, 123.9, 110.3, 80.2, 76.3, 74.2, 67.3, 62.0, 26.8, 26.6, 25.0, 18.0, -4.5; MS (EI): m/z 540 [M+Na]+; HRMS (EI): m/z [M+Na]+ Calcd for C23H34NO4NaSSi 540.2215. Found 540.2204.

**Compound 54:** To a stirred solution of oximeether 53 (129 mg, 0.25 mmol) and NaI (113 mg, 0.75 mmol) in acetone (1.3 mL) cooled at 0°C was added TFAA (52 μL, 0.37 mmol) dropwise. The reaction mixture was stirred for 3 hr at 0°C and then quenched by adding a saturated aqueous NaHCO3 solution (1 mL). Acetone was evaporated under reduced pressure and the aqueous phase was extracted with dichloromethane (3 × 3 mL). The combined organic extracts were successively washed with saturated aqueous NaHCO3 solution (2 mL), water (2 mL), saturated brine (2 mL) and dried over anhydrous Na2SO4. Evaporation of the solvent under reduced pressure afforded a crude product which was purified by column chromatography using 4% EtOAc/hexane (v/v) as the eluent to afford the sulfide 54 (96 mg, 0.19 mmol) in 77% yield as a colorless viscous oil; TLC, Rf 0.75 (20% EtOAc/hexane); 1H NMR (300 MHz, CDCl3): δ 7.43 (d, J = 8.5 Hz, 1H), 7.38-7.22 (m, 10H), 5.07 (s, 2H), 4.55 (dd, J = 6.2, 8.3 Hz, 1H), 4.42 (dd, J = 4.5, 6.2 Hz, 1H), 4.15-4.06 (m, 1H), 3.05 (dd, J = 7.2, 13.8 Hz, 1H), 2.94 (dd, J = 4.7, 13.8 Hz, 1H), 1.47 (s, 3H), 1.32 (s, 3H), 0.92 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); MS (EI): m/z 502 [M+H]+; HRMS (ESI): m/z [M+H]+ Calcd for C24H32N2O4NaSSi 524.2266. Found 524.2283.

**Compound 56:** To a solution of di-MOM derivative 11 (1.16 g, 2 mmol) in anhydrous CH2Cl2 (15 mL) cooled at 0°C was added Et3N (0.84 mL, 6 mmol) followed by TFAA (0.84 mL, 6 mmol) under an atmosphere of nitrogen and stirred for 15 min. Then a 5% aqueous NaHCO3 solution (15 mL) was added to the above reaction mixture at 0°C and stirred for a
The reaction mixture was then extracted into CH₂Cl₂ (3 × 25 mL). The combined organic layers were washed successively with water (2 × 15 mL), saturated brine (15 mL) and dried over anhydrous Na₂SO₄. The solvent was evaporated in vacuo and the residue was purified by column chromatography using 7% EtOAc/hexane (v/v) as the eluent to afford aldehyde 56 (726 mg, 1.54 mmol) in 77% yield as a viscous oil; TLC, Rf 0.65 (40% EtOAc/hexane); [α]D²⁰ +10.4° (c 1.6, CHCl₃); IR (KBr): 2934, 2858, 1612, 1511, 1466, 1362, 1256, 1104, 1033, 835, 775 cm⁻¹; ¹H NMR (200 MHz, CDCl₃): δ 9.46 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 4.68-4.58 (m, 4H), 4.51 (d, J = 6.6 Hz, 1H), 4.44 (d, J = 2.2 Hz, 1H), 2.45-2.40 (m, 1H), 4.13 (dd, J = 2.2, 8.1 Hz, 1H), 3.78 (s, 3H), 3.64 (dd, J = 2.2, 10.3 Hz, 1H), 3.55 (dd, J = 2.9, 10.3 Hz, 1H), 3.32 (s, 3H), 3.28 (s, 3H), 0.92 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 200.2, 159.2, 130.1, 129.5, 113.7, 97.0, 96.7, 78.8, 77.9, 75.2, 73.1, 68.8, 56.2, 55.8, 55.2, 25.7, 18.2, -4.8, -5.1; MS (ESI): m/z 490 [M+NH₄⁺]; HRMS (ESI): m/z [M+Na⁺] Calcd for C₃₃H₆₀O₆NaSi 495.2390. Found 495.2419.

**Compound 57:** To a mixture of aldehyde 56 (726 mg, 1.54 mmol) and dimethyl disulfide (0.16 mL, 1.85 mmol) was added commercial tributylphosphine (0.46 mL, 1.85 mmol) at 0°C, by means of syringe under nitrogen atmosphere. Evolution of heat gave an indication of the reaction progress. The reaction mixture was gradually brought to ambient temperature and stirred overnight in order to confirm the complete consumption of the starting material, which was difficult to ascertain by TLC due to the low polarity difference and high MeSSMe concentration. The volatiles were removed under reduced pressure and the residue was subjected to column chromatography using 1% EtOAc/benzene (v/v) as the eluent to yield the alcohol 57 (584 mg, 1.06 mmol) in 86% yield as a viscous oil; TLC, Rf 0.25 (20% EtOAc/hexane); [α]D²⁰ +3° (c 0.5, CHCl₃); IR (KBr): 3466, 2928, 2855, 1628, 1739, 1466, 1253, 1151, 1104, 1030, 837, 778 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 4.73 (d, J = 8.1 Hz, 1H), 4.71 (d, J = 6.6 Hz, 1H), 4.70 (d, J = 6.6 Hz, 1H), 4.68 (d, J = 8.1 Hz, 1H), 4.19-4.14 (m, 1H), 3.97-3.91 (m, 1H), 3.90-3.85 (m, 2H), 3.82-3.73 (m, 1H), 3.70-3.63 (m, 1H), 3.43 (s, 3H), 3.41 (s, 3H), 2.12 (s, 3H), 2.11 (s, 3H), 0.94 (s, 9H), 0.18 (s, 3H), 0.13 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 97.0, 96.8, 79.8, 78.4, 75.8, 62.2, 58.3, 56.2, 55.7, 26.2, 18.6, 14.4, 13.1, -4.1, -4.3; MS (ESI): m/z 448 [M+NH₄⁺]; HRMS (ESI): m/z [M+Na⁺] Calcd for C₃₃H₆₀O₆NaSi 453.1800. Found 453.1790.

**Compound 58:** To a stirred solution of alcohol 58 (370 mg, 0.86 mmol) in anhydrous dichloromethane and DMSO (2:1, 12 mL) were added tetrylamine (0.34 mL, 4.3 mmol) and SO₂py (540 mg, 3.44 mmol) at ambient temperature. The resulting mixture was stirred for 3 hr before it was quenched with water (40 mL). Two layers were separated and the aqueous phase was extracted with ethyl acetate (4 × 70 mL). The combined organic layers were washed with saturated brine (50 mL) and dried over anhydrous Na₂SO₄. Evaporation under reduced pressure afforded a crude product which was purified by column chromatography using 6% EtOAc/hexane (v/v) as the eluent to afford the aldehyde 59 (316 mg, 0.74 mmol) in 86% yield as a viscous liquid; TLC, Rf 0.4 (20% EtOAc/hexane); [α]D²⁰ +12° (c 2, CHCl₃); IR (KBr): 2929, 2856, 1735, 1468, 1253, 1108, 1028, 838, 778 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.65 (s, 1H), 4.78-4.65 (m, 4H), 4.39-4.34 (m, 1H), 4.34-4.29 (m, 1H), 26.3, 18.6, 14.7, 14.0, -0.41, -0.42; MS (ESI): m/z 573 [M+Na⁺]; HRMS (ESI): m/z [M+Na⁺] Calcd for C₃₃H₆₀O₆NaSi₂ 573.2351. Found 573.2361.

**Compound 59:** To a mixture of compound 59 (370 mg, 0.86 mmol) in anhydrous dichloromethane and DMSO (2:1, 12 mL) were added tetrylamine (0.34 mL, 4.3 mmol) and SO₂py (540 mg, 3.44 mmol) at ambient temperature. The resulting mixture was stirred for 3 hr before it was quenched with water (40 mL). Two layers were separated and the aqueous phase was extracted with ethyl acetate (4 × 70 mL). The combined organic layers were washed with saturated brine (50 mL) and dried over anhydrous Na₂SO₄. Evaporation under reduced pressure afforded a crude product which was purified by column chromatography using 6% EtOAc/hexane (v/v) as the eluent to afford the aldehyde 59 (316 mg, 0.74 mmol) in 86% yield as a viscous liquid; TLC, Rf 0.4 (20% EtOAc/hexane); [α]D²⁰ +12° (c 2, CHCl₃); IR (KBr): 2929, 2856, 1735, 1468, 1253, 1108, 1028, 838, 778 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.65 (s, 1H), 4.78-4.65 (m, 4H), 4.39-4.34 (m, 1H), 4.34-4.29 (m, 1H), 26.3, 18.6, 14.7, 14.0, -0.41, -0.42; MS (ESI): m/z 573 [M+Na⁺]; HRMS (ESI): m/z [M+Na⁺] Calcd for C₃₃H₆₀O₆NaSi₂ 573.2351. Found 573.2361.
washed successively with saturated aqueous NaHCO
diluted with DCE (15 mL). The organic layer was
starting aldehyde. The solution was cooled and further
examination revealed complete consumption of the
hydrochloride (142 mg, 0.89 mmol), pyridine (0.4
(500 MHz, CDCl
TLC, R
(291 mg, 0.54 mmol) in 74% yield as a viscous oil;
(128 mg, 0.37 mmol) as the eluent to furnish oximeether derivative
by column chromatography using 4% EtOAc/hexane
vacuo furnished the crude product which was purified by
column chromatography using 8% EtOAc/hexane (v/v) as the eluent to furnish an inseparable mixture of
cyclised product 61 and 62 (181 mg, 0.37 mmol) in 68% yield as a viscous oil in a 6:4 ratio respectively;
TLC, Rf 0.25 (20% EtOAc/hexane); IR (KBr): 3447, 2928, 2854, 1633, 1465, 1363, 1252, 1151, 1038, 836, 775, 697 cm
MS (ESI): m/z 488 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C

Compound 60: To a solution of the crude aldehyde 59 (316 mg, 0.74 mmol) in dichloroethane (DCE) (5 mL) was added N-benzyl hydroxylamine hydrochloride (142 mg, 0.89 mmol), pyridine (0.4 mL) and few drops of water. The reaction mixture was then heated to reflux for 8 hr when TLC examination revealed complete consumption of the starting aldehyde. The solution was cooled and further diluted with DCE (15 mL). The organic layer was washed successively with saturated aqueous NaHCO₃ solution (5 mL), saturated brine (5 mL) and dried over anhydrous Na₂SO₄. Evaporation of the solvent in vacuo afforded the crude product which was purified by column chromatography using 4% EtOAc/hexane (v/v) as the eluent to furnish oximeether derivative 60 (291 mg, 0.54 mmol) in 74% yield as a viscous oil; TLC, Rf 0.5 (20% EtOAc/hexane); [δ(30)D-27° (c 0.6, CHCl₃); IR (KBr): 2928, 2854, 1633, 1465, 1364, 1253, 1211, 1152, 1102, 1028, 838, 778, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.39 (d, J = 7.8 Hz, 1H), 7.35-7.25 (m, 5H), 5.11 (d, J = 11.7 Hz, 1H), 5.08 (d, J = 11.7 Hz, 1H), 4.76 (d, J = 6.8 Hz, 1H), 4.74 (d, J = 6.8 Hz, 1H), 4.62 (d, J = 6.8 Hz, 1H), 4.52 (dd, J = 3.9, 7.8 Hz, 1H), 4.15 (dd, J = 3.9, 4.9 Hz, 1H), 3.97 (d, J = 4.9 Hz, 1H), 3.87 (t, J = 4.9 Hz, 1H), 3.37 (s, 3H), 3.33 (s, 3H), 2.15 (s, 3H), 2.09 (s, 3H), 0.93 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 148.2, 137.6, 128.2, 127.8, 97.5, 94.1, 79.7, 76.0, 74.9, 73.0, 58.5, 56.3, 55.6, 26.4, 18.6, 14.6, 14.5, -4.0, -4.2; MS (ESI): m/z 534 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C₂₆H₃₇NO₆NaSi₂ 556.2189. Found 556.2178.

Compound 60 and 62: To a solution of the radical precursor 60 (291 mg, 0.54 mmol) in deoxygenated toluene (50 mL) at reflux was added a solution of tributyltin hydride (0.58 mL, 2.16 mmol) and AIBN (9 mg, 0.05 mmol) in toluene (5 mL) via syringe pump over a period of 6 hr. The reaction mixture was refluxed for another 1 hr, then cooled and concentrated under reduced pressure. The residue was dissolved in diethyl ether (25 mL) and stirred overnight with a 20% aqueous KF solution (10 mL). The organic phase was separated and dried over anhydrous Na₂SO₄. Evaporation of the solvent in vacuo afforded the crude product which was purified by column chromatography using 8% EtOAc/hexane (v/v) as the eluent to furnish an inseparable mixture of cyclised product 61 and 62 (181 mg, 0.37 mmol) in 68% yield as a viscous oil in a 6:4 ratio respectively; TLC, Rf 0.25 (20% EtOAc/hexane); IR (KBr): 3447, 2928, 2854, 1633, 1465, 1363, 1252, 1151, 1038, 836, 775, 697 cm⁻¹; MS (ESI): m/z 488 [M+H]+; HRMS (ESI): m/z [M+Na]+ Calcd for C₂₆H₃₇NO₆NaSi₂ 556.2189. Found 556.2178.

Conclusion
In summary the sulfinyl group has been utilized as a pendant nucleophile to prepare a bromohydrin stereoselectively. The sulfinyl group was further used to open an epoxide regioselectively. The tert-butyl sulfanamide group was effectively utilized to introduce the amino stereogenic center. Though the synthesis of LCB was unsuccessful, the study was useful from a pedagogical view. It became clear that Pummerer reaction cannot be effected in the presence of free N-H. Though it was not possible to prepare mannostatin analogs by generating a sulfinyl carbanion, radical chemistry proved useful.

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References
14. The structure of diol 10 was assigned based on precedent and confirmed by X-ray crystallographic study of compound 42.
24. The structure of sulfanamide 16 was not rigorously established. The assignment of syn relative configuration for the amino alcohol moiety in 16 was supported by the structure of major sulfanamide 42, that was proven unambiguously by X-ray.
26. The triol was isolated as mixture of isomers diastereomeric at sulfur formed probably as a consequence of not using anhydrous methanol for deprotecting MOM groups.
38. The outcome was no different using α-chloro sulfoxide.