



Cite this: *Org. Biomol. Chem.*, 2015, **13**, 8512

## Divergent synthesis of various iminocyclitols from D-ribose†

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A very efficient route to the diastereoselective synthesis of polyhydroxy pyrrolidines, piperidines and azepanes from an aldehyde derivative of ribose is reported. Asymmetric  $\alpha$ -amination of aldehydes using proline catalysed hydrazination is the key step in the synthesis. The method utilizes the stereocenters present in ribose and the extra carbon atoms present in the target molecules are incorporated using Wittig reactions. The incorporation of the amino group is carried out asymmetrically to account for additional stereocenters. This synthetic route to iminocyclitols has the potential to be extended for the synthesis of a large class of such compounds starting from other sugar derived aldehydes.

Received 22nd May 2015,  
Accepted 30th June 2015

DOI: 10.1039/c5ob01042j

www.rsc.org/obc

### Introduction

Iminocyclitols are sugar analogues with a secondary or tertiary amino group replacing the oxygen atom in the ring. These compounds, consisting of a 5, 6 or 7 membered polyhydroxy N-heterocyclic frameworks are generally referred to as iminosugars or azasugars (Fig. 1). They are potential inhibitors of various carbohydrate processing enzymes<sup>1</sup> and are key to the development of therapeutics for a wide range of diseases such as diabetes, cancer and viral infections including AIDS.<sup>2</sup> 2,5-

Dihydroxymethyl-3,4-dihydropyrrolidine (DMDP, **1a**) along with its isomers are first among the pyrrolidine class of iminosugars to be isolated from natural sources. They are known to inhibit both  $\alpha$ - and  $\beta$ -glycosidases.<sup>3</sup> 1- and 2-deoxynojirimycin derivatives **2a**, **2b**, **3a** and **3b** are among the 6-membered iminosugars, which exhibit inhibitory activity towards  $\alpha$ -glucosidases and ceramide glucosyltransferases (CGT).<sup>4</sup> Compounds **4a** and **4b** are polyhydroxyazepane derivatives and are examples of 7-membered iminocyclitols, which have received relatively less attention in terms of synthesis and evaluation of inhibitory activity.<sup>5</sup> Stereoselective routes to the synthesis of these compounds are of great interest and significance due to their potential in therapeutics.

Incorporation of an amino group stereoselectively into a cyclic or linear polyhydroxy system is the important step in most of the reported syntheses of these compounds. The incorporation of the amino group is achieved by nucleophilic displacement of a leaving group with azide anions or with alkyl amines.<sup>6–11</sup> These routes are generally limited to the possibility of synthesizing only one diastereomer of the molecule from a starting compound. It will therefore, be useful to have strategies, where at least two diastereomers of the target molecules can be synthesized from the same intermediate by switching a chiral catalyst to generate new stereocentres with control. The incorporation of additional carbon atoms into a synthetic intermediate is achieved either by Wittig reaction or using organometallic reagents in general. Generation of new stereocentres during or after the incorporation of additional carbon atoms on a synthetic intermediate is often done through the asymmetric induction offered by the existing stereocentres within the intermediate.

We report here a divergent method for the synthesis of various iminocyclitols starting from ribose. The method opens

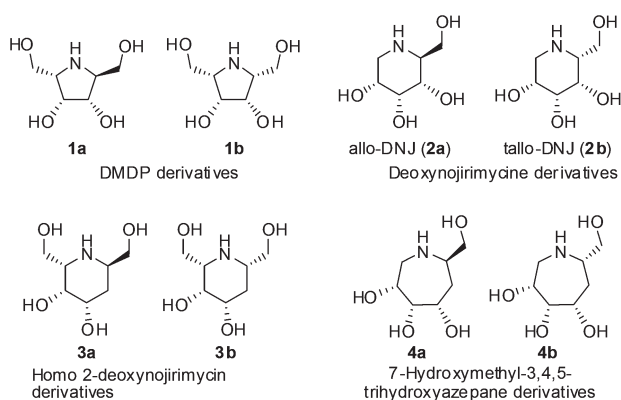


Fig. 1 Iminosugars synthesized in this report.

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† Electronic supplementary information (ESI) available: Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra of all the compounds, 2D NMR spectra of the final compounds and HPLC data. See DOI: 10.1039/c5ob01042j

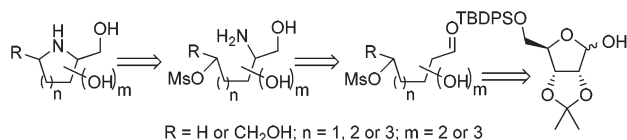


up the possibility of synthesizing target molecules with higher number of carbon atoms and stereocentres than the starting material used. Wittig reactions were used to incorporate additional carbon atoms and organocatalytic asymmetric amination of aldehydes<sup>12</sup> was used for the generation of new chiral centres functionalized with nitrogen atoms. The use of *L*- and *D*-proline separately as catalysts offers the possibility to generate two different diastereomers with high selectivity.<sup>13</sup> Although, proline catalysed asymmetric amination has been used widely in synthesis<sup>13d,e,14</sup> it has not been explored to the same extent in carbohydrate chemistry.<sup>13a,15</sup>

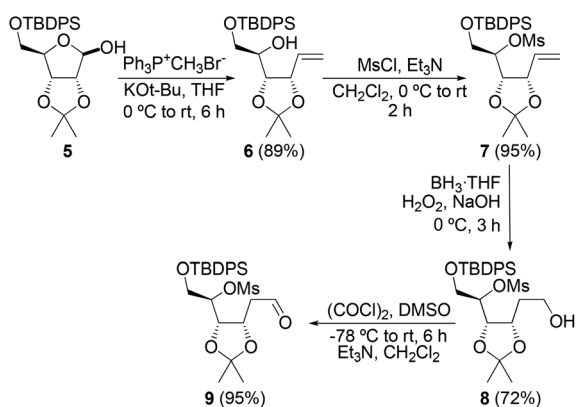
## Results and discussion

Our strategy towards the synthesis of these molecules is based on the synthesis of an amino alcohol derivative with a suitably positioned leaving group (mesylate). These amino alcohols are prepared by proline catalysed asymmetric amination of aldehydes derived from ribose. A nucleophilic substitution of the mesylate group by the free amino group leading to the formation of 5, 6 or 7 membered rings was expected (Scheme 1).

The syntheses of the 5-membered iminocyclitols **1a** and **1b** were achieved from the aldehyde **9**, synthesized from the commercially available ribose derivative **5** (Scheme 2). Wittig reaction of **5** using methyltriphenylphosphonium bromide yielded the alkene **6**.<sup>16</sup> The secondary hydroxyl group in **6** was converted to a mesylate to get **7** in very high yield. Hydroboration/oxidation of **7** gave the primary alcohol **8**, which on Swern oxidation yielded the aldehyde **9** (Scheme 2).



**Scheme 1** Retrosynthetic strategy for 5, 6 and 7 membered iminosugars.



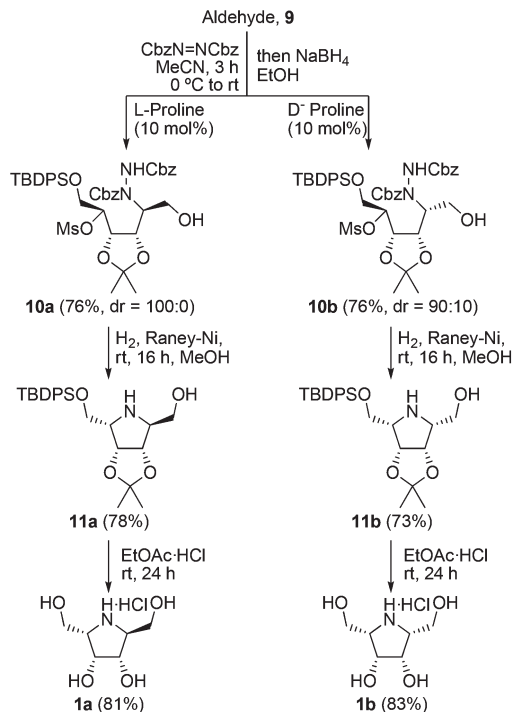
**Scheme 2** Synthesis of aldehyde **9**.

The aldehyde **9** was treated with dibenzyl azodicarboxylate in the presence of both *L*- and *D*-proline (0.1 equiv.) in separate reactions to get the hydrazino aldehydes, which were reduced to the corresponding primary alcohols **10a** and **10b** in one-pot. The diastereomeric ratios of these compounds were estimated using chiral HPLC and were established by comparing the chromatograms with that of a 1 : 1 mixture of the diastereomers obtained through reactions catalyzed by *DL*-proline.<sup>17</sup> The asymmetric  $\alpha$ -hydrazination reaction follows a very ordered transition state, which is similar to the one proposed by List and Jorgensen.<sup>12</sup> The orientation of the carboxylic acid function of proline decides the outcome of the reaction and thus the stereochemistry of the products. While *L*-proline prefers the attack on the *Re*-face, the reaction using *D*-proline proceeds on the *Si*-face.<sup>12</sup> While asymmetric hydrazination catalyzed by *L*-proline gave **10a** as a single diastereomer, the reaction catalyzed by *D*-proline yielded **10b** and **10a** in a 90 : 10 ratio. The lower selectivity achieved in one of these  $\alpha$ -functionalization reactions is expected and is accounted for based on the influence of the stereochemistry of the  $\beta$ -carbon. Such differences in selectivity during asymmetric hydrazination using *L*- and *D*-proline on the same substrate can be more prominent depending on the nature of the substrate.<sup>13b,e</sup> Similar observations in the case of proline catalysed aldol reactions have extensively been studied.<sup>7k</sup>

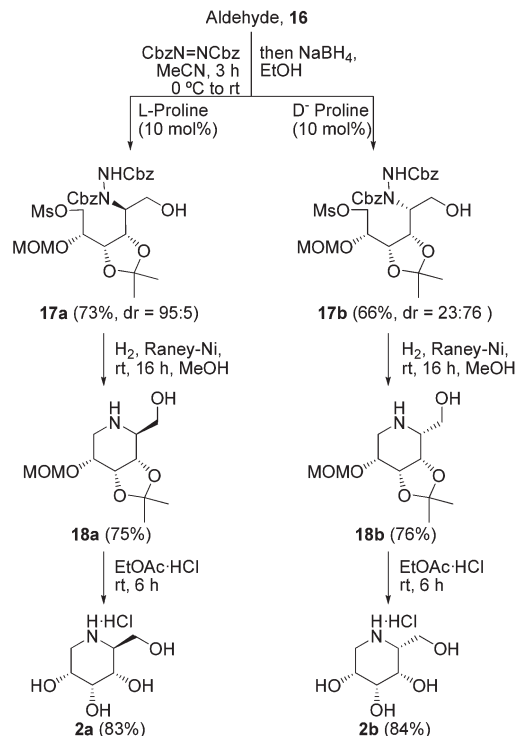
Hydrogenolysis of the hydrazino groups in **10a** and **10b** using freshly prepared RANEY® Ni and H<sub>2</sub> yielded the corresponding amino compounds, which underwent immediate cyclization by displacing the mesylate to give the pyrrolidine derivatives **11a** and **11b** in 78% and 73% yields respectively. The targeted iminocyclitols **1a** and **1b** were obtained in overall yields of 27% and 21%, respectively by acidolysis of the protecting groups using 4 N HCl in EtOAc (Scheme 3). The absolute stereochemistry of **1a** was established by detailed NMR analysis of a dibenzyl derivative prepared from **11a**.<sup>18</sup> Compound **1b** was a *meso* derivative with no optical activity. The spectral data for **1a** and **1b** were compared with those available in the literature and found to be matching.<sup>6c</sup>

The deoxyojirimycin derivatives **2a** and **2b** were synthesized using a similar strategy as the one used for the synthesis of **1a** and **1b** through **9**. An aldehyde derivative **16** was prepared from **6** by using a different strategy for protecting and activating the hydroxyl groups. Accordingly, the secondary hydroxyl group in **6** was protected using MOMCl to get **12** in 89% yield. The TBDPS group in **12** was removed with TBAF to get the primary alcohol **13**, which was treated with MsCl to get **14**. Hydroboration/oxidation of **14** gave the primary alcohol **15**, which on Swern oxidation yielded the required aldehyde **16** (Scheme 4). Following the strategy used for the synthesis of **1a** and **1b** from **9**, **2a** and **2b** were synthesized from **16** with overall yields of 19% and 17%, respectively (Scheme 5). The diastereoselectivity of the *L*-proline catalyzed reaction was very high (95 : 5) in favour of **17a**. However, the corresponding *D*-proline catalyzed reaction was only moderately selective. It has to be noted that the *DL*-proline catalyzed reaction on **16** proceeded to give **17a** and **17b** as a 60 : 40 mixture. Although **17a**

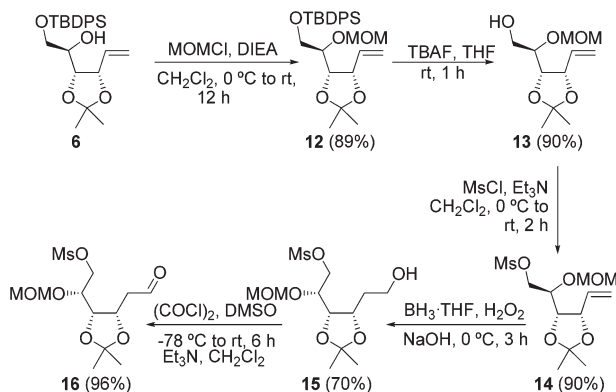




**Scheme 3** Synthesis of 2,5-dihydroxymethyl-3,4-dihydropyrrolidine derivatives **1a** and **1b**.



**Scheme 5** Synthesis of deoxynojirimycin derivatives **2a** and **2b**.



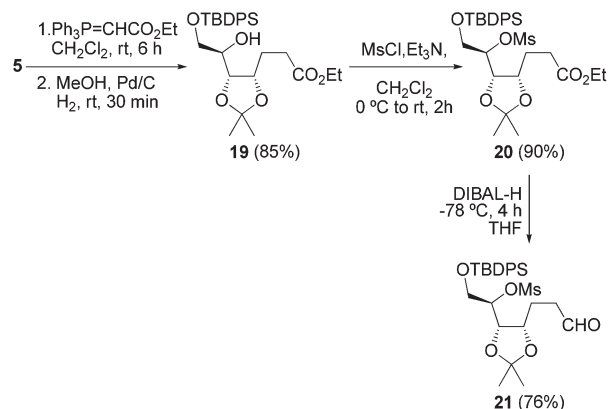
**Scheme 4** Synthesis of aldehyde **16**.

and **17b** are not separable by column chromatography, the iminocyclitol derivatives **18a** and **18b** are separated easily. If **2a** and **2b** are required to be synthesized, use of DL-proline as a catalyst and separation of **18a** and **18b** are preferred. The stereochemistry of **2a** and **2b** was confirmed using NMR studies<sup>18</sup> and the spectral data were also found to match with those reported in the literature.<sup>7i,10d</sup>

The homonojirimycin derivatives **3a** and **3b** and the 7-hydroxymethyl-3,4,5-trihydroxyazepane derivatives **4a** and **4b** were synthesized by increasing the number of carbon atoms in the ribose derivative **5** by two through a Wittig reaction using the stabilized ylide,  $\text{Ph}_3\text{P}=\text{CHCOOEt}$ . The  $\alpha,\beta$ -unsaturated

ester obtained was reduced using Pd/C and  $\text{H}_2$  to get the hydroxy ester **19** in 85% yield (Scheme 6). The secondary hydroxyl group was converted to a mesylate using MsCl in the presence of triethylamine to get **20**. The ester group in **20** was reduced using DIBAL-H to get the aldehyde **21** required for the preparation of **3a** and **3b** (Scheme 6).

Hydrazination of **21** under similar conditions used for the synthesis of **10** from **9**, using both L- and D-proline yielded **22a** and **22b** in good yields. Unlike the  $\alpha$ -functionalization of **9** and **16**, the reaction of the aldehyde **21** proceeded with very high diastereoselectivity with L- and D-proline. The absence of inherent chirality on the  $\beta$ -carbon atom allows the asymmetric

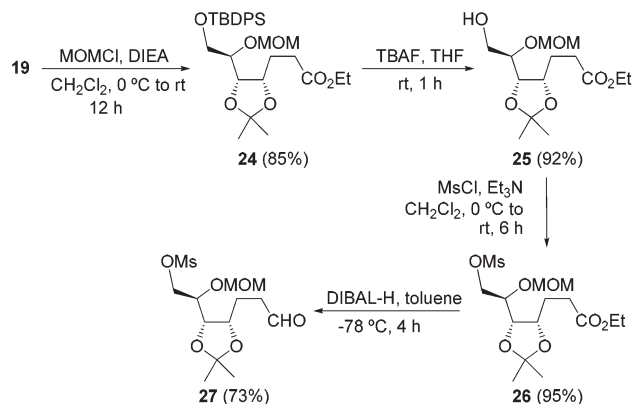


**Scheme 6** Synthesis of aldehyde **21**.

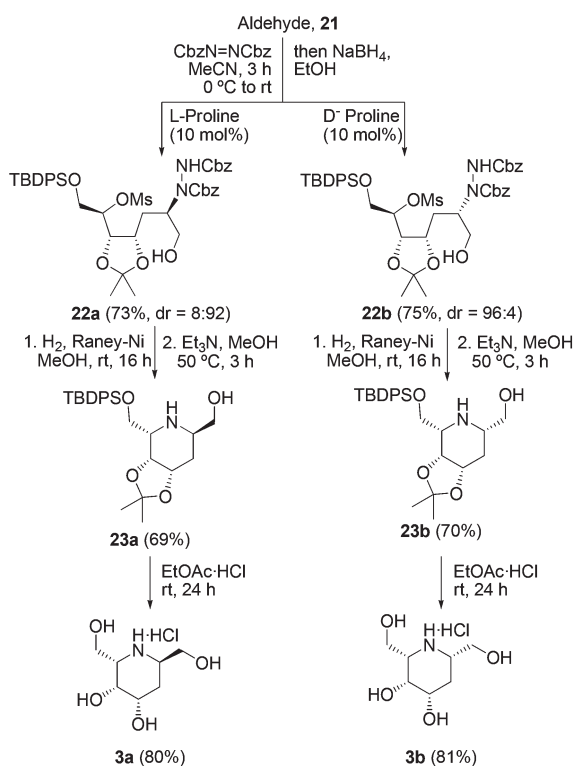


induction to be controlled entirely by proline. The amine generated by hydrogenolysis of **22** with RANEY® Ni did not undergo cyclization *in situ* unlike the reaction of **17**. The crude reaction mixture had to be heated in the presence of triethylamine to displace the mesylate and get the piperidine derivatives **23a** and **23b**. It may be assumed that the secondary mesylate was difficult to be displaced in the presence of an adjacent O-TBDPS group. The homojirimycin derivatives **3a** and **3b** were obtained by acidolysis of **23a** and **23b**, respectively using 4 N HCl in EtOAc (Scheme 7). Detailed NMR analysis of the benzyl derivatives of **3a** and **3b** prepared by the dibenzylation of **23** confirmed their structures to be as given in Scheme 7.<sup>18</sup>

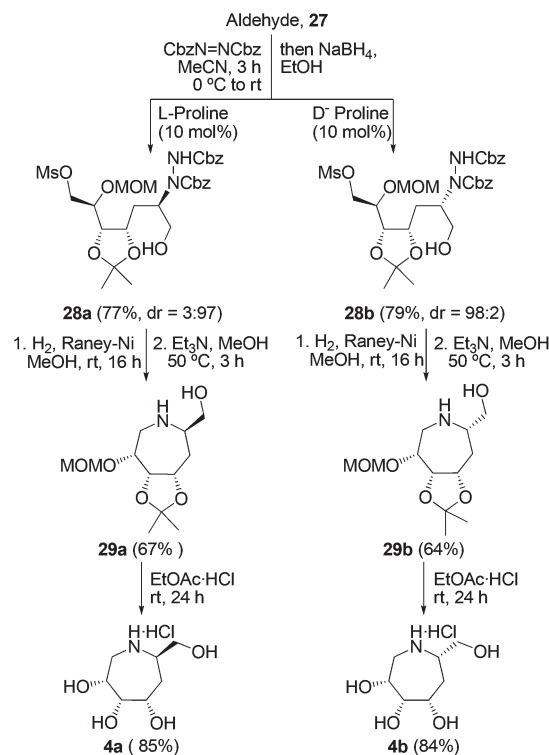
The aldehyde **27** required for the preparation of **4a** and **4b** was prepared from **19** by using a different protection and activation strategy for the hydroxyl groups. Similar to the preparation of aldehyde **16**, the primary hydroxyl group was converted to a mesylate and the adjacent secondary hydroxyl group was protected as a MOM derivative to get **27** (Scheme 8). Asymmetric hydrazination of **27** using L- and D-proline proceeded in good yield and high diastereoselectivity, as in the case of **22a** and **22b**, to give **28a** and **28b**, respectively (Scheme 9).<sup>17</sup> Hydrogenolysis followed by cyclization using triethylamine yielded the azepane derivatives **29a** and **29b** from **28a** and **28b**, respectively. Acidolysis of **29a** and **29b** gave the target molecules **4a** and **4b** in overall yields of 20% and 19% (Scheme 9). Dibenzylation derivatives made from **29** were analyzed using NMR spectroscopy to confirm the stereochemistry of **4a** and **4b**.<sup>18</sup>



Scheme 8 Synthesis of aldehyde **27**.



Scheme 7 Synthesis of homojirimycin derivatives **3a** and **3b**.



Scheme 9 Synthesis of 7-hydroxymethyl-3,4,5-trihydroxyazepanes **4a** and **4b**.

## Conclusions

We have developed a divergent strategy for synthesizing various iminocyclitols from ribose and have successfully applied this in the synthesis of 5, 6 and 7 membered imino-sugars. The absolute configuration of the stereocenter bearing the imino group is switched by changing the catalyst from L-proline to D-proline. While most of these reactions proceeded with very high diastereoselectivity, induction by the adjacent chiral centres reduced the diastereoselectivity achieved in the





reactions catalyzed by D-proline in two of the examples. In comparison with other methods available for the synthesis of similar compounds, the current strategy allows the preparation of target molecules with increased number of carbon atoms and stereocenters to that of the starting compounds. The method reported here has the potential to be a very useful strategy for making a large number of iminocyclitols by varying the sugar unit used as the starting compound. It provides a general method for the synthesis of imino and azasugars from a lower sugar homolog.

## Experimental section

### General experimental methods

All the commercially available reagents were used directly without any further purification. All the reactions were carried out under an inert atmosphere unless otherwise mentioned. Acetonitrile was distilled initially from phosphorus pentoxide and subsequently from calcium hydride; DCM was distilled from calcium hydride. Yields reported are for purified compounds using column chromatography. All the reactions were monitored by analytical thin layer chromatography carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and ninhydrin, 5% H<sub>2</sub>SO<sub>4</sub> as a staining agent. Merck silica gel (particle size 60–120 and 100–200 mesh) was used for column chromatography. All proton NMR spectra were recorded at either 400 or 500 MHz using a Jeol spectrometer and <sup>13</sup>C NMR spectra were recorded at 100 or 125 MHz. <sup>1</sup>H NMR splitting pattern was designated as singlet (s), doublet (d), doublet of doublets (dd), triplet (t), multiplet (m), and broad singlet (bs). IR spectra were recorded as a thin film for liquids and as KBr pellets for solids. High-resolution mass spectra were recorded using a Waters Q/ToF Premier micromass HAB 213 spectrometer with an ESI source. Optical rotation was measured using a 5.0 ml cell with a 10 dm path length and is reported as [ $\alpha$ ]<sub>D</sub><sup>25</sup> (c in g per 100 mL solvent). The diastereoselectivity was determined by chiral HPLC analysis using a Daicel chiralpack OD-H column with a 254 nm UV detector and by using a mixture of isopropanol and *n*-hexane as the eluent at 25 °C.

**Procedure for the synthesis of 6 from 5.** Potassium *t*-butoxide (0.8 g, 7.8 mmol, 3.9 equiv.) was added to the stirred solution of methyl triphenylphosphonium bromide (2.8 g, 8 mmol, 4 equiv.) in THF (30 mL) at 0 °C and the stirring was continued at this temperature for 30 min; after 30 min the aldehyde (5) (0.85 g, 2 mmol, 1 equiv.) in THF (10 mL) was added to the reaction mixture dropwise and further stirred at room temperature for 5 h. After the complete disappearance of 5 on TLC, the reaction mixture was quenched with saturated ammonium chloride (10 mL). The organic layer was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated, and purified by column chromatography.

**Compound 6.** Column chromatography (petroleum ether/EtOAc, 9 : 1); oily liquid (0.76 g, 1.78 mmol, 89%); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -7.23

(c 1.3, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.69–7.66 (m, 4H), 7.45–7.37 (m, 6H), 6.01 (ddd, *J* = 16.6, 10.3, 6.3 Hz, 1H), 5.40 (d, *J* = 17.1 Hz, 1H), 5.27 (d, *J* = 10.3 Hz, 1H), 4.69 (t, *J* = 6.5 Hz, 1H), 4.15 (dd, *J* = 8.6, 6.3 Hz, 1H), 3.86 (dd, *J* = 10.3, 2.9 Hz, 1H), 3.82–3.78 (m, 1H), 3.71 (bs, 1H), 2.55 (bs, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 1.07 (s, 9H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  135.6, 134.1, 129.9, 127.8, 117.7, 108.7, 78.9, 77.5, 69.9, 65.3, 27.8, 26.9, 25.5, 19.4 ppm; IR  $\nu_{\max}$  (thin film): 3460, 2030, 1585 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>25</sub>H<sub>34</sub>NaO<sub>4</sub>Si 449.2124; found 449.2128.

**Procedure for mesylation of 6 to get 7.** Triethylamine (0.6 mL, 4.4 mmol, 2.2 equiv.) followed by mesyl chloride (0.17 mL, 2.2 mmol, 1.1 equiv.) were added to a stirred solution of 6 (0.85 g, 2 mmol, 1 equiv.) in dichloromethane (10 mL) at 0 °C, and stirred the reaction mixture for 2 h at room temperature. After the complete disappearance of 6 on TLC, the reaction mixture was quenched with water. The organic layer was extracted with dichloromethane (2 × 10 mL), and the combined organic phases were washed with water (1 × 20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated, and purified by column chromatography.

The same procedure was used for the preparation of 14, 20 and 26.

**Compound 7.** Column chromatography (petroleum ether/EtOAc, 8 : 2); oily liquid (0.96 g, 1.9 mmol, 95%); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -0.45 (c 0.20, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.68–7.64 (m, 4H), 7.45–7.37 (m, 6H), 5.79 (ddd, *J* = 17.1, 8.6, 6.8 Hz, 1H), 5.35 (d, *J* = 18.6 Hz, 1H), 5.28–5.25 (m, 1H), 4.74–4.71 (m, 1H), 4.68 (t, *J* = 6.8 Hz, 1H), 4.51–4.48 (m, 1H), 3.98–3.95 (m, 1H), 3.92–3.88 (m, 1H), 3.02 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H), 1.07 (s, 9H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  135.7, 132.8, 132.7, 132.4, 130.1, 130.0, 127.9, 127.8, 119.5, 109.0, 81.9, 78.0, 76.3, 63.0, 39.3, 27.0, 26.8, 25.0, 19.2 ppm; IR  $\nu_{\max}$  (thin film): 3072, 1589 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>26</sub>H<sub>36</sub>NaO<sub>6</sub>SSi 527.1900; found 527.1897.

**Compound 14.** Column chromatography (petroleum ether/EtOAc, 6 : 4); oily liquid (0.56 g, 1.8 mmol, 90%); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +9.34 (c 0.4, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  5.91–5.84 (m, 1H), 5.41 (d, *J* = 17.2 Hz, 1H), 5.26 (d, *J* = 10.3 Hz, 1H), 4.71 (t, *J* = 6.5 Hz, 1H), 4.66 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.53 (dd, *J* = 10.9, 2.3 Hz, 1H), 4.34 (dd, *J* = 10.8, 4.0 Hz, 1H), 4.26 (dd, *J* = 7.7, 6.5 Hz, 1H), 3.68–3.69 (m, 1H), 3.39 (s, 3H), 3.02 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  133.1, 118.0, 108.9, 97.3, 78.0, 76.1, 75.2, 70.0, 56.3, 37.3, 27.6, 25.2 ppm; IR  $\nu_{\max}$  (thin film): 2988, 1643, 1546 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>12</sub>H<sub>22</sub>NaO<sub>7</sub>S 333.0984; found 333.0987.

**Compound 20.** Column chromatography (petroleum ether/EtOAc, 9 : 1); oily liquid (1.04 g, 1.8 mmol, 90%); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -1.08 (c 0.74, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.70–7.68 (m, 4H), 7.44–7.37 (m, 6H), 4.76 (m, 1H), 4.39 (t, *J* = 6.6 Hz, 1H), 4.22–4.18 (m, 1H), 4.13 (q, *J* = 7.4 Hz, 2H), 3.99–3.98 (m, 2H), 3.06 (s, 3H), 2.52–2.38 (m, 2H), 2.03–1.96 (m, 1H), 1.77–1.69 (m, 1H), 1.29 (s, 3H), 1.26–1.23 (m, 6H), 1.07 (s, 9H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  173.1, 135.7, 132.8, 130.0, 129.9, 127.9, 127.8, 108.5, 80.6, 76.2, 75.0, 63.4, 60.4, 39.4,



30.9, 27.6, 26.8, 25.5, 24.9, 19.3, 14.3 ppm; IR  $\nu_{\max}$  (thin film): 3072, 1737, 1589  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{29}\text{H}_{42}\text{NaO}_8\text{SSi}$  601.2267; found 601.2270.

**Compound 26.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.73 g, 1.9 mmol, 95%);  $[\alpha]_{\text{D}}^{25} = -1.1$  ( $c$  0.35,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.76 (d,  $J = 6.8$  Hz, 1H), 4.70 (d,  $J = 6.8$  Hz, 1H), 4.58 (d,  $J = 11$  Hz, 1H), 4.35 (dd,  $J = 10.9, 3.4$  Hz, 1H), 4.21–4.17 (m, 1H), 4.17–4.13 (m, 1H), 4.11 (q,  $J = 6.8$  Hz, 2H), 3.79 (d,  $J = 7.9$  Hz, 1H), 3.40 (s, 3H), 3.03 (s, 3H), 2.56–2.50 (m, 1H), 2.44–2.37 (m, 1H), 1.99–1.92 (m, 1H), 1.80–1.72 (m, 1H), 1.38 (s, 3H), 1.30 (s, 3H), 1.23 (t,  $J = 6.9$  Hz, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.2, 108.4, 96.7, 76.5, 75.2, 74.4, 69.7, 60.4, 56.4, 37.3, 31.1, 28.0, 25.6, 24.9, 14.2 ppm; IR  $\nu_{\max}$  (thin film): 1734  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{15}\text{H}_{28}\text{NaO}_9\text{S}$  407.1352; found 407.1351.

**Procedure for hydroboration followed by oxidation of 7 to get 8.** Borane (1 M solution in THF – 4 mL, 4 mmol, 2 equiv.) was added to the stirred solution of 7 (1.00 g, 2 mmol, 1 equiv.) in THF at 0 °C under a nitrogen atmosphere, and stirred for 2 h. After the disappearance of 7 on TLC, 2 N NaOH (8 mL, 16 mmol) and then 30%  $\text{H}_2\text{O}_2$  (8 mL) were added and stirring was continued for further 30 min at 0 °C. The reaction was quenched with saturated ammonium chloride, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2  $\times$  25 mL). The combined organic phases were dried over  $\text{Na}_2\text{SO}_4$ , filtered, concentrated, and purified by column chromatography.

The same procedure was used for the preparation of 15 from 14.

**Compound 8.** Column chromatography (petroleum ether/EtOAc, 7 : 3); oily liquid (0.75 g, 1.44 mmol, 72%);  $[\alpha]_{\text{D}}^{25} = -0.877$  ( $c$  0.23,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.69–7.66 (m, 4H), 7.43–7.37 (m, 6H), 4.77–4.75 (m, 1H), 4.40–4.35 (m, 2H), 4.02–3.95 (m, 2H), 3.79–3.73 (m, 2H), 3.03 (s, 3H), 1.88–1.69 (m, 2H), 1.30 (s, 3H), 1.37 (s, 3H), 1.08 (s, 9H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  135.7, 132.7, 130.1, 130.0, 127.9, 127.8, 108.6, 81.1, 76.2, 75.2, 63.3, 61.0, 39.5, 32.3, 27.5, 26.9, 25.4, 19.3 ppm; IR  $\nu_{\max}$  (thin film): 3486, 3080, 1546  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{26}\text{H}_{38}\text{NaO}_7\text{SSi}$  545.2005; found 545.2009.

**Compound 15.** Column chromatography (petroleum ether/EtOAc, 4 : 6); oily liquid (0.46 g, 1.4 mmol, 70%);  $[\alpha]_{\text{D}}^{25} = -3.16$  ( $c$  0.32,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.74 (d,  $J = 6.8$  Hz, 1H), 4.69 (d,  $J = 6.8$  Hz, 1H), 4.58 (dd,  $J = 10.9, 1.7$  Hz, 1H), 4.39–4.30 (m, 2H), 4.17–4.14 (m, 1H), 3.83–3.77 (m, 3H), 3.39 (s, 3H), 3.03 (s, 3H), 1.85–1.77 (m, 2H), 1.40 (s, 3H), 1.32 (s, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  108.6, 96.7, 76.3, 75.3, 74.6, 69.7, 61.0, 56.4, 37.3, 31.6, 27.9, 25.5 ppm; IR  $\nu_{\max}$  (thin film): 3460, 2938, 1455  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{24}\text{O}_8\text{S}$  329.1270; found 329.1273.

**Procedure for oxidation of 8 to get 9.** Anhydrous dimethyl sulfoxide (0.34 mL, 4.8 mmol, 2.4 equiv.) was added dropwise to a stirred solution of oxalyl chloride (0.19 mL, 2.3 mmol, 1.15 equiv.) in dry dichloromethane (5 mL) at –78 °C under a nitrogen atmosphere and stirring was continued for 15 min.

Alcohol (1.04 g, 2 mmol, 1 equiv.) 8 in dichloromethane (1 mL) was added to the reaction mixture followed by dropwise addition of triethyl amine (1.4 mL, 10 mmol, 5 equiv.), and stirring was continued at the same temperature for 1 h. The reaction mixture was allowed to attain room temperature and was stirred for 2 h at this temperature. The reaction mixture was diluted with dichloromethane (10 mL) and quenched by the addition of water. The aqueous layer was acidified with 2 N HCl, and extracted with dichloromethane (2  $\times$  15 mL). The organic phases were combined and were washed sequentially with 1% HCl and saturated NaCl, followed by 5%  $\text{NaHCO}_3$ . The aqueous layer was extracted with dichloromethane (10 mL), the combined organic phases were washed with brine, dried using  $\text{Na}_2\text{SO}_4$ , filtered, concentrated and purified by column chromatography.

The same procedure was used for the preparation of 16 from 15.

**Compound 9.** Column chromatography (petroleum ether/EtOAc, 9 : 1); oily liquid (0.98 g, 1.9 mmol, 95%);  $[\alpha]_{\text{D}}^{25} = +9.3$  ( $c$  0.8,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.73 (s, 1H), 7.69–7.64 (m, 4H), 7.44–7.37 (m, 6H), 4.75–4.66 (m, 2H), 4.42–4.39 (m, 1H), 4.00–3.95 (m, 2H), 3.02 (s, 3H), 2.88–2.70 (m, 2H), 1.32 (s, 3H), 1.26 (s, 3H), 1.04 (s, 9H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  199.5, 135.7, 132.6, 130.2, 130.0, 128.0, 127.9, 108.8, 80.2, 74.1, 71.8, 63.2, 43.8, 39.5, 27.6, 26.9, 25.4, 19.2 ppm; IR  $\nu_{\max}$  (thin film): 2740, 1728, 1589  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{NH}_4]^+$  calcd for  $\text{C}_{26}\text{H}_{40}\text{NO}_7\text{SSi}$  538.2295; found 538.2299.

**Compound 16.** Column chromatography (petroleum ether/EtOAc, 7 : 3); oily liquid (0.62 g, 1.92 mmol, 96%);  $[\alpha]_{\text{D}}^{25} = +13.1$  ( $c$  0.32,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.77 (s, 1H), 4.76–4.72 (m, 2H), 4.67 (d,  $J = 6.8$  Hz, 1H), 4.59 (dd,  $J = 8.7$  Hz, 1H), 4.34 (dd,  $J = 10.9, 3.2$  Hz, 1H), 4.21 (dd,  $J = 5.9, 5.5$  Hz, 1H), 3.71 (d,  $J = 8.7$  Hz, 1H), 3.39 (s, 3H), 3.03 (s, 3H), 2.80–2.03 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  199.7, 108.9, 96.5, 74.6, 74.4, 72.1, 69.1, 56.4, 43.8, 37.4, 27.9, 25.4 ppm; IR  $\nu_{\max}$  (thin film): 2937, 2726, 1727, 1455  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{23}\text{O}_8\text{S}$  327.1114; found 327.1118.

**Procedure for asymmetric  $\alpha$ -hydrazination of 9 to get 10.** The aldehyde 9 (1.04 g, 2 mmol, 1 equiv.) in dry acetonitrile (15 mL) was treated with dibenzylazodicarboxylate (0.59 g, 2 mmol, 1 equiv.) and proline (either D or L, 0.02 g, 10 mol%) at 0 °C. The mixture was stirred for 2 h and the temperature was raised to 20 °C over a period of 1 h. The mixture was stirred until the solution turned colorless from yellow (1 to 2 h) and was cooled to 0 °C and then treated with sodium borohydride (0.05 g) in ethanol (15 mL). The stirring was continued for 5 min and the reaction was quenched with saturated ammonium chloride solution (20 mL). The organic layer was extracted with ethyl acetate (3  $\times$  30 mL) and the combined organic phases were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, concentrated, and purified by column chromatography.

*Note:* The hydrazine derivatives give complex NMR spectra at room temperature due to the existence of rotamers.



The same procedure was used for the preparation of **17**, **22** and **28**.

**Compound 10a.** Column chromatography (petroleum ether/EtOAc, 8 : 2); oily liquid (1.25 g, 1.52 mmol, 76%);  $[\alpha]_{\text{D}}^{25} = +2.80$  (*c* 0.25, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.74–7.62 (m, 4H), 7.46–7.26 (m, 16H), 5.19–5.09 (m, 3H), 4.84–4.67 (m, 2H), 4.52–4.27 (m, 4H), 4.03–3.91 (m, 2H), 3.80 (d, *J* = 12 Hz, 1H), 3.57–3.55 (m, 1H), 2.81 (s, 3H), 1.27 (s, 3H), 1.23 (s, 3H), 1.10 (s, 9H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.5, 155.9, 141.0, 135.8, 135.6, 135.1, 132.5, 132.3, 130.3, 130.1, 128.7, 128.6, 128.5, 128.2, 128.1, 127.9, 127.6, 127.0, 109.5, 82.7, 76.7, 73.5, 68.6, 65.3, 62.9, 60.4, 57.6, 38.5, 26.9, 26.5, 25.2 ppm; IR  $\nu_{\text{max}}$  (thin film): 3464, 3378, 1717, 1588 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>42</sub>H<sub>52</sub>N<sub>2</sub>O<sub>11</sub>SSi 843.2959; found 843.2962.

**Compound 10b.** Column chromatography (petroleum ether/EtOAc, 8 : 2); oily liquid (1.13 g, 1.38 mmol, 69%);  $[\alpha]_{\text{D}}^{25} = +4.6$  (*c* 0.46, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.72–7.64 (m, 4H), 7.42–7.24 (m, 16H), 6.74 (bs, 1H), 5.30–5.05 (m, 4H), 4.86–4.36 (m, 2H), 4.20–3.90 (m, 4H), 3.73–3.55 (m, 2H), 3.16–3.03 (m, 3H), 2.66 (bs, 1H), 1.19–1.06 (m, 15H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.2, 158.5, 157.2, 156.0, 135.8, 135.6, 135.1, 133.1, 132.9, 132.8, 130.3, 130.1, 129.9, 129.8, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 108.4, 108.2, 79.6, 78.5, 74.2, 73.2, 73.6, 73.4, 69.6, 68.8, 68.4, 68.2, 67.8, 64.4, 62.9, 62.6, 60.0, 59.8, 58.7, 53.5, 39.4, 39.1, 26.9, 26.8, 25.4, 25.3, 19.4, 19.3 ppm; IR  $\nu_{\text{max}}$  (thin film): 3464, 3378, 1717, 1588 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>42</sub>H<sub>52</sub>N<sub>2</sub>O<sub>11</sub>SSi 843.2959; found 843.2962.

**Compound 17a.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.91 g, 1.46 mmol, 73%);  $[\alpha]_{\text{D}}^{25} = -22.85$  (*c* 0.14, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.39–7.13 (m, 10H), 5.33–5.05 (m, 4H), 4.53–4.16 (m, 8H), 3.94–3.84 (m, 1H), 3.61 (bs, 1H), 3.28 (s, 3H), 2.99–2.93 (d, 3H), 1.42 (s, 3H), 1.29 (s, 3H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.2, 158.8, 155.8, 155.6, 135.5, 135.4, 135.1, 128.9, 128.7, 128.6, 128.3, 108.8, 96.9, 75.3, 74.7, 74.4, 74.2, 69.9, 69.4, 68.9, 68.6, 60.4, 58.6, 57.6, 56.3, 56.2, 37.1, 27.6, 25.6 ppm; IR  $\nu_{\text{max}}$  (thin film): 3422, 1704, 1720, 1650, 1596 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + NH<sub>4</sub>]<sup>+</sup> calcd for C<sub>28</sub>H<sub>42</sub>N<sub>3</sub>O<sub>12</sub>S 644.2489; found 644.2494.

**Compound 17b.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.82 g, 1.32 mmol, 66%);  $[\alpha]_{\text{D}}^{25} = +18.33$  (*c* 0.12, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.37–7.19 (m, 10H), 6.61 (bs, 1H), 5.33–5.06 (m, 4H), 4.68–4.63 (m, 1H), 4.59–4.39 (m, 2H), 4.30–4.26 (m, 2H), 4.02–3.89 (m, 2H), 3.74–3.47 (m, 3H), 3.32–3.28 (m, 3H), 3.03–2.99 (d, 3H), 1.29 (s, 3H), 1.27 (s, 3H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.1, 158.3, 157.4, 156.4, 135.7, 135.5, 135.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 127.7, 108.8, 108.3, 108.2, 96.9, 96.6, 75.3, 74.9, 74.7, 74.3, 74.2, 74.0, 68.9, 68.7, 68.6, 68.4, 60.1, 59.9, 59.0, 57.7, 56.8, 56.6, 56.3, 56.2, 37.2, 29.7, 29.6, 27.7, 27.6 ppm; IR  $\nu_{\text{max}}$  (thin film): 3422, 1704, 1720, 1650, 1596 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + NH<sub>4</sub>]<sup>+</sup> calcd for C<sub>28</sub>H<sub>42</sub>N<sub>3</sub>O<sub>12</sub>S 644.2489; found 644.2494.

**Compound 22a.** Column chromatography (petroleum ether/EtOAc, 7 : 3); oily liquid (1.21 g, 1.46 mmol, 73%);  $[\alpha]_{\text{D}}^{25} = -16.3$

(*c* 0.8, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.69–7.63 (m, 4H), 7.42–7.30 (m, 16H), 6.49–6.44 (m, 1H), 5.25–5.12 (m, 4H), 4.69–4.62 (m, 1H), 4.30–4.19 (m, 2H), 4.14–4.03 (m, 1H), 3.69–3.84 (m, 2H), 1.30 (s, 3H), 3.55–3.39 (m, 2H), 3.04–2.97 (m, 3H), 1.70–1.45 (m, 1H), 1.09–1.02 (m, 14H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.0, 158.3, 156.9, 156.6, 135.9, 135.7, 135.2, 132.6, 130.1, 130.0, 128.7, 128.6, 128.5, 128.2, 127.9, 127.8, 127.7, 127.6, 108.7, 108.5, 81.0, 80.8, 75.5, 75.4, 75.2, 68.6, 68.4, 68.1, 63.5, 63.3, 61.8, 61.6, 59.9, 58.7, 39.6, 39.5, 39.4, 27.2, 27.1, 26.9, 24.8, 24.6, 19.3 ppm; IR  $\nu_{\text{max}}$  (thin film): 3473, 1721, 1588 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>43</sub>H<sub>54</sub>N<sub>2</sub>NaO<sub>11</sub>SSi 857.3115; found 857.3115.

**Compound 22b.** Column chromatography (petroleum ether/EtOAc, 7 : 3); oily liquid (1.25 g, 1.5 mmol, 75%);  $[\alpha]_{\text{D}}^{25} = +23.5$  (*c* 1.6, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.68–7.65 (m, 4H), 7.44–7.30 (m, 16H), 7.11–7.03 (m, 1H), 5.22–5.12 (m, 4H), 4.70–4.64 (m, 1H), 4.29–4.20 (m, 2H), 4.14–4.05 (m, 1H), 3.96–3.88 (m, 2H), 3.50–3.42 (m, 2H), 3.01–2.97 (m, 3H), 1.76–1.47 (m, 2H), 1.32–1.23 (m, 6H), 1.06 (s, 9H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.1, 158.7, 156.9, 156.2, 136.0, 135.7, 135.6, 135.5, 135.3, 132.7, 132.6, 130.2, 130.0, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 109.1, 108.7, 108.5, 81.0, 80.8, 80.6, 80.2, 75.5, 75.4, 75.2, 74.3, 74.1, 73.6, 68.6, 68.4, 68.3, 68.2, 68.1, 67.9, 63.7, 63.6, 63.5, 63.3, 62.3, 62.2, 39.6, 39.4, 28.2, 28.1, 27.1, 26.9, 25.9, 25.8, 24.8, 24.6, 19.3 ppm; IR  $\nu_{\text{max}}$  (thin film): 3317, 1722, 1586 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd for C<sub>43</sub>H<sub>55</sub>N<sub>2</sub>O<sub>11</sub>SSi 835.3296; found 835.3292.

**Compound 28a.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.98 g, 1.53 mmol, 77%);  $[\alpha]_{\text{D}}^{25} = -33.93$  (*c* 0.28, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.37–7.26 (m, 10H), 6.60 (bs, 1H), 5.26–5.10 (m, 4H), 4.74–4.70 (m, 1H), 4.65–4.48 (m, 3H), 4.34–4.28 (m, 2H), 4.16–4.00 (m, 2H), 3.69–3.67 (m, 1H), 3.66–3.41 (m, 1H), 3.36 (s, 3H), 3.00 (s, 3H), 1.89–1.79 (m, 1H), 1.50–1.46 (m, 1H), 1.34–1.30 (m, 3H), 1.10–1.09 (m, 3H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.0, 158.4, 156.9, 156.8, 135.9, 135.6, 135.3, 128.7, 128.6, 128.5, 128.4, 128.2, 127.6, 108.6, 108.5, 96.5, 75.8, 75.5, 75.3, 74.5, 69.2, 68.6, 68.5, 68.4, 68.1, 61.9, 61.8, 59.8, 58.6, 65.5, 37.4, 29.7, 27.7, 26.9, 24.9, 24.8 ppm; IR  $\nu_{\text{max}}$  (thin film): 3463, 1719 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd for C<sub>29</sub>H<sub>41</sub>N<sub>2</sub>O<sub>12</sub>S 641.2380; found 641.2388.

**Compound 28b.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (1.00 g, 1.56 mmol, 79%);  $[\alpha]_{\text{D}}^{25} = +22.1$  (*c* 0.16, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.88–7.27 (m, 10H), 6.63–6.59 (m, 1H), 5.27–5.10 (m, 4H), 4.74–4.71 (m, 1H), 4.66–4.62 (m, 1H), 4.55–4.49 (m, 1H), 4.35–4.28 (m, 2H), 4.16–4.04 (m, 2H), 3.70–3.66 (m, 1H), 3.52–3.41 (m, 2H), 3.38–3.35 (m, 3H), 3.01–3.00 (m, 3H), 1.90–1.79 (m, 1H), 1.55–1.47 (m, 1H), 1.34–1.31 (m, 3H), 1.11–1.10 (m, 1H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.3, 158.6, 157.2, 157.0, 136.1, 135.9, 135.5, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 127.8, 108.8, 108.7, 96.8, 76.0, 75.7, 75.6, 74.8, 69.4, 68.9, 68.8, 68.6, 68.4, 62.2, 62.1, 60.1, 58.9, 56.8, 37.6, 27.9, 25.1 ppm; IR  $\nu_{\text{max}}$  (thin film): 3463, 1719 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd for C<sub>29</sub>H<sub>41</sub>N<sub>2</sub>O<sub>12</sub>S 641.2380; found 641.2388.





**Procedure for the hydrogenolysis of compound 10 to get 11.** Freshly prepared RANEY® nickel (around 0.80 g, pre-washed with absolute ethanol) was added to the stirred solution of **10** (2 mmol) in dry methanol (15 mL) followed by 40 drops of acetic acid. The reaction mixture was hydrogenated at atmospheric pressure for 16 h at room temperature. After the complete disappearance of the starting material on TLC, the reaction mixture was passed over Celite and concentrated, and purified by column chromatography.

The same procedure was used for the preparation of **18** from **17**. Compounds **23** and **29** were also prepared using a similar procedure, however refluxing with triethylamine (2 equiv.) was required for the desired cyclization to occur.

**Compound 11a.** Column chromatography (petroleum ether/EtOAc, 4 : 6); oily liquid (0.69 g, 1.56 mmol, 78%);  $[\alpha]_{\text{D}}^{25} = +12.3$  (c 0.31, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.68–7.66 (m, 4H, Ar–H), 7.40–7.32 (m, 6H, Ar–H), 4.75–4.71 (m, 1H, C<sub>3</sub>H), 4.59–4.52 (m, 1H, C<sub>2</sub>H), 3.99–3.54 (m, 6H, C<sub>1</sub>H, C<sub>4</sub>H, C<sub>5</sub>H, C<sub>6</sub>H), 1.44 (s, 3H, C<sub>7</sub>H), 1.25 (s, 3H, C<sub>8</sub>H), 1.02 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C–Si) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 135.7 (C–Ar), 133.0 (C–Ar), 132.9 (C–Ar), 129.8 (C–Ar), 127.8 (C–Ar), 127.7 (C–Ar), 112.3 (C-9), 81.8 (C-3), 79.4 (C-2), 66.3 (C-5), 62.8 (C-6), 60.2 (C-1), 60.0 (C-4), 26.8 ((CH<sub>3</sub>)<sub>3</sub>C–Si), 26.2 (C-8), 24.3 (C-7), 19.2 (C–Si) ppm; IR  $\nu_{\text{max}}$  (thin film): 3407, 3470, 1669 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>36</sub>NO<sub>4</sub>Si 442.2414; found 442.2417.

**Compound 11b.** Chromatography (petroleum ether/EtOAc, 4 : 6); oily liquid (0.65 g, 1.46 mmol, 73%);  $[\alpha]_{\text{D}}^{25} = +10.5$  (c 0.2, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.71–7.67 (m, 4H, Ar–H), 7.43–7.33 (m, 6H, Ar–H), 4.67–4.64 (m, 2H, C<sub>2</sub>H, C<sub>3</sub>H), 3.98–3.83 (m, 4H, C<sub>5</sub>H, C<sub>6</sub>H), 3.11–3.08 (m, 1H, C<sub>1</sub>H), 2.96–2.93 (m, 1H, C<sub>4</sub>H), 1.41 (s, 3H, C<sub>7</sub>H), 1.27 (s, 3H, C<sub>8</sub>H), 1.04 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C–Si) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 135.7 (C–Ar), 135.6 (C–Ar), 133.6 (C–Ar), 133.4 (C–Ar), 129.7 (C–Ar), 127.7 (C–Ar), 127.6 (C–Ar), 111.4 (C-9), 82.3 (C-3), 81.2 (C-2), 63.6 (C-5), 62.7 (C-6), 61.7 (C-1), 60.9 (C-4), 26.9 ((CH<sub>3</sub>)<sub>3</sub>C–Si), 25.6 (C-8), 23.9 (C-7), 19.3 (C–Si) ppm; IR  $\nu_{\text{max}}$  (thin film): 3407, 3470, 1669 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>36</sub>NO<sub>4</sub>Si 441.2414; found 442.2416.

**Compound 18a.** Column chromatography (DCM/MeOH, 95 : 5); oily liquid (0.37 g, 1.5 mmol, 75%);  $[\alpha]_{\text{D}}^{25} = -16.25$  (c 0.24, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 4.76 (s, 2H, –O–CH<sub>2</sub>–O–), 4.46 (dd,  $J = 4, 3.4$  Hz, 1H, C<sub>3</sub>H), 3.92–3.87 (m, 3H, C<sub>2</sub>H, C<sub>4</sub>H), 3.57 (dd,  $J = 10.9, 6.3$  Hz, 1H, C<sub>5</sub>H), 3.40 (s, 3H, –OCH<sub>3</sub>), 3.15 (dd,  $J = 11.4, 5.1$  Hz, 1H, C<sub>1</sub>H), 2.89 (dd,  $J = 11.4, 11.4$  Hz, 1H, C<sub>1</sub>H), 2.76 (bs, 1H, –OH), 1.53 (s, 3H, C<sub>8</sub>H), 1.38 (s, 3H, C<sub>7</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 110.2 (C-9), 96.5 (–O–CH<sub>2</sub>–O–), 74.5 (C-2), 74.0 (C-3), 72.5 (C-4), 62.7 (C-6), 58.9 (–OCH<sub>3</sub>), 55.7 (C-5), 44.2 (C-1), 28.3 (C-8), 26.4 (C-7) ppm; IR  $\nu_{\text{max}}$  (thin film): 3486 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>22</sub>NO<sub>5</sub> 248.1498; found 248.1499.

**Compound 18b.** Column chromatography (DCM/MeOH, 95 : 5); oily liquid (0.37 g, 1.52 mmol, 76%);  $[\alpha]_{\text{D}}^{25} = -12.1$  (c 0.22, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 4.66 (d,  $J = 6.9$  Hz, 1H, –O–CH<sub>2</sub>–O–), 4.60 (d,  $J = 6.8$  Hz, 1H, –O–CH<sub>2</sub>–O–),

4.57 (dd,  $J = 8.0, 2.8$  Hz, 1H, C<sub>3</sub>H), 4.42 (dd,  $J = 7.4, 3.4$  Hz, 1H, C<sub>2</sub>H), 3.80 (dd,  $J = 9.7, 6.9$  Hz, 1H, C<sub>4</sub>H), 3.76–3.71 (m, 2H, C<sub>6</sub>H), 3.33 (s, 3H, –OCH<sub>3</sub>), 2.98 (dd,  $J = 10.9, 10.8$  Hz, 1H, C<sub>5</sub>H), 2.92–2.89 (m, 1H, C<sub>1</sub>H), 2.44 (dd,  $J = 15.0, 5.0$  Hz, 1H, C<sub>1</sub>H), 1.56 (s, 3H, C<sub>7</sub>H), 1.37 (s, 3H, C<sub>8</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 109.1 (C-9), 95.2 (–O–CH<sub>2</sub>–O–), 75.4 (C-2), 72.9 (C-3), 69.3 (C-4), 59.2 (C-6), 57.5 (–OCH<sub>3</sub>), 55.5 (C-5), 46.3 (C-1), 26.2 (C-8), 24.4 (C-8) ppm; IR  $\nu_{\text{max}}$  (thin film): 3486 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>22</sub>NO<sub>5</sub> 248.1498; found 248.1499.

**Compound 23a.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.63 g, 1.38 mmol, 69%);  $[\alpha]_{\text{D}}^{25} = +12.6$  (c 0.1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.70–7.67 (m, 4H, Ar–H), 7.43–7.35 (m, 6H, Ar–H), 4.52–4.49 (m, 1H, C<sub>3</sub>H), 4.36–4.34 (m, 1H, C<sub>2</sub>H), 3.65–3.63 (m, 2H, C<sub>7</sub>H), 3.41–3.36 (m, 1H, C<sub>1</sub>H), 3.19–3.13 (m, 2H, C<sub>6</sub>H), 2.77–2.74 (m, 1H, C<sub>5</sub>H), 1.84–1.79 (m, 2H, C<sub>4</sub>H), 1.44 (s, 3H, C<sub>10</sub>H), 1.35 (s, 3H, C<sub>11</sub>H), 1.05 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C–Si) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 135.7 (C–Ar), 135.6 (C–Ar), 133.7 (C–Ar), 133.5 (C–Ar), 129.8 (C–Ar), 129.7 (C–Ar), 127.7 (C–Ar), 127.6 (C–Ar), 127.4 (C–Ar), 107.8 (C-12), 71.9 (C-3), 71.7 (C-2), 64.8 (C-7), 63.9 (C-6), 52.0 (C-1), 47.9 (C-5), 29.2 (C-4), 26.9 (C-12), 26.3 ((CH<sub>3</sub>)<sub>3</sub>C–Si), 26.0 (C-11), 19.3 (C–Si) ppm; IR  $\nu_{\text{max}}$  (thin film): 3408, 3071, 1670 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>38</sub>NO<sub>4</sub>Si 456.2570; found 456.2572.

**Compound 23b.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.63 g, 1.4 mmol, 70%);  $[\alpha]_{\text{D}}^{25} = +14.8$  (c 0.6, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.68–7.65 (m, 4H, Ar–H), 7.41–7.33 (m, 6H, Ar–H), 4.50–4.48 (m, 1H, C<sub>3</sub>H), 4.35–4.33 (m, 1H, C<sub>2</sub>H), 3.64–3.60 (m, 2H, C<sub>7</sub>H), 3.41–3.36 (m, 1H, C<sub>1</sub>H), 3.18–3.12 (m, 2H, C<sub>6</sub>H), 2.76–2.74 (m, 1H, C<sub>5</sub>H), 2.02–1.99 (m, 1H, C<sub>4</sub>H), 1.81–1.77 (m, 1H, C<sub>4</sub>H), 1.42 (s, 3H, C<sub>10</sub>H), 1.34–1.28 (s, 3H, C<sub>11</sub>H), 1.03 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C–Si) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 134.2 (C–Ar), 134.1 (C–Ar), 132.1 (C–Ar), 131.9 (C–Ar), 128.2 (C–Ar), 126.2 (C–Ar), 126.1 (C–Ar), 106.3 (C-12), 70.3 (C-3), 70.1 (C-2), 63.1 (C-7), 62.2 (C-6), 50.5 (C-1), 46.4 (C-5), 30.5 (C-4), 28.2 (C-12), 27.9 ((CH<sub>3</sub>)<sub>3</sub>C–Si), 25.3 (C-11), 20.0 (C–Si) ppm; IR  $\nu_{\text{max}}$  (thin film): 3408, 3071, 1670 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>38</sub>NO<sub>4</sub>Si 456.2570; found 456.2572.

**Compound 29a.** Column chromatography (DCM/MeOH, 95 : 0.5); oily liquid (0.35 g, 1.34 mmol, 67%);  $[\alpha]_{\text{D}}^{25} = -10.37$  (c 0.27, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 4.82 (d,  $J = 6.9$  Hz, 1H, –O–CH<sub>2</sub>–O–), 4.71 (d,  $J = 6.8$  Hz, 1H, –O–CH<sub>2</sub>–O–), 4.56 (d,  $J = 8.5$  Hz, 1H, C<sub>4</sub>H), 4.48–4.45 (m, 1H, C<sub>3</sub>H), 4.20–4.18 (m, 1H, C<sub>5</sub>H), 3.77 (dd,  $J = 11.4, 2.8$  Hz, 1H, C<sub>7</sub>H), 3.62 (dd,  $J = 10.9, 8.6$  Hz, 1H, C<sub>7</sub>H), 3.39 (s, 3H, (–OCH<sub>3</sub>)), 3.38–3.30 (m, 3H, C<sub>1</sub>H, C<sub>6</sub>H), 2.07–1.94 (m, 2H, C<sub>2</sub>H), 1.54 (s, 3H, C<sub>10</sub>H), 1.37 (s, 3H, C<sub>11</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 108.3 (C-12), 96.0 (–O–CH<sub>2</sub>–O–), 78.4 (C-4), 74.0 (C-3), 71.8 (C-5), 64.0 (C-7), 55.9 (–OCH<sub>3</sub>), 55.2 (C-1), 45.1 (C-6), 32.5 (C-2), 25.7 (C-11), 23.5 (C-10) ppm; IR  $\nu_{\text{max}}$  (thin film): 3439 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>24</sub>NO<sub>5</sub> 262.1654; found 262.1651.

**Compound 29b.** Column chromatography (DCM/MeOH, 95 : 5); oily liquid (0.33 g, 1.28 mmol, 64%);  $[\alpha]_{\text{D}}^{25} = +18.6$





(*c* 0.22, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 4.84 (d, *J* = 6.8 Hz, 1H, -O-CH<sub>2</sub>-O-), 4.71 (d, *J* = 6.3 Hz, 1H, -O-CH<sub>2</sub>-O-), 4.41 (q, *J* = 8.0 Hz, 1H, C<sub>4</sub>H), 4.19 (dd, *J* = 8.0, 2.8 Hz, 1H, C<sub>3</sub>H), 3.91 (dd, *J* = 5.7, 2.2 Hz, 1H, C<sub>5</sub>H), 3.51 (dd, *J* = 10.3, 4.5 Hz, 1H, C<sub>1</sub>H), 3.38 (s, 3H, (-OCH<sub>3</sub>)), 3.32–3.23 (m, 2H, C<sub>7</sub>H), 2.64 (d, *J* = 14.8 Hz, 1H, C<sub>6</sub>H), 2.56–2.52 (m, 1H, C<sub>6</sub>H), 1.91–1.88 (m, 2H, C<sub>2</sub>H), 1.47 (s, 3H, C<sub>10</sub>H), 1.33 (s, 3H, C<sub>11</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 109.8 (C-12), 97.5 (-O-CH<sub>2</sub>-O-), 80.6 (C-4), 76.3 (C-3), 76.1 (C-5), 65.7 (C-7), 56.3 (-OCH<sub>3</sub>), 55.7 (C-1), 48.3 (C-6), 35.8 (C-2), 26.6 (C-11), 24.0 (C-10), ppm; IR ν<sub>max</sub> (thin film): 3401 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>24</sub>NO<sub>5</sub> 262.1654; found 262.1655.

**Procedure for acidolysis of 11 to get 1.** 4 N HCl in ethyl acetate (4 mL) was added to the cyclic amino alcohol **11a** or **11b** (0.44 g, 1 mmol, 1 equiv.), and stirred for 24 h at room temperature. After the disappearance of the starting material on TLC, the ethyl acetate was decanted carefully and the white solid was washed with fresh ethyl acetate (3 × 5 mL) and concentrated.

The same procedure was used for the preparation of **2**, **3** and **4** from **18**, **23** and **29**, respectively.

**Compound 1a.** White solid; (0.161 g, 0.81 mmol, 81%); [α]<sub>D</sub><sup>25</sup> = -23.1 (*c* 0.4, H<sub>2</sub>O) [lit.<sup>6b</sup> [α]<sub>D</sub><sup>25</sup> -25.5 (*c* 0.90, H<sub>2</sub>O)]; mp 122–125 °C; <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O): δ 4.25–4.23 (m, 1H, C<sub>3</sub>H), 4.17 (dd, *J* = 9.1, 4.0 Hz, 1H, C<sub>4</sub>H), 3.91–3.85 (m, 2H, C<sub>6</sub>H), 3.82–3.73 (m, 2H, C<sub>7</sub>H), 3.68–3.65 (m, 1H, C<sub>2</sub>H), 3.56–3.53 (m, 1H, C<sub>5</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, D<sub>2</sub>O): δ 71.2 (C-3), 70.1 (C-4), 62.2 (C-7), 61.8 (C-6), 58.2 (C-2), 57.5 (C-5) ppm; IR ν<sub>max</sub> (KBr): 3356 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>4</sub> 164.0923; found 164.0923.

**Compound 1b.** White solid (0.165 g, 0.83 mmol, 83%); [α]<sub>D</sub><sup>25</sup> = 0.00 (*c* 0.39, MeOH); mp 138–139 °C; <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O): δ 4.34–4.28 (m, 2H, C<sub>3</sub>H), 3.92–3.86 (m, 4H, C<sub>4</sub>H), 3.61–3.56 (m, 2H, C<sub>2</sub>H) ppm; <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O): δ 70.2 (C-3), 61.9 (C-4), 57.9 (C-2) ppm; IR ν<sub>max</sub> (KBr): 3356 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>4</sub> 164.0923; found 164.0923.

**Compound 2a.** White solid (0.08 g, 0.41 mmol, 83%); [α]<sub>D</sub><sup>25</sup> = -35.2 (*c* 0.43, MeOH) [lit.<sup>7i</sup> [α]<sub>D</sub><sup>25</sup> -37.7 (*c* 1.00, MeOH)]; mp 152–153 °C; <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O): δ 4.01 (bs, 1H, C<sub>3</sub>H), 3.86–3.85 (m, 1H, C<sub>4</sub>H), 3.77–3.69 (m, 3H, C<sub>5</sub>H, C<sub>7</sub>H), 3.19–3.11 (m, 1H, C<sub>2</sub>H), 3.12–3.10 (m, 1H, C<sub>6</sub>H), 2.98–2.96 (m, 1H, C<sub>6</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, D<sub>2</sub>O): δ 69.9 (C-3), 65.4 (C-4), 64.6 (C-5), 57.7 (C-7), 54.7 (C-2), 41.6 (C-6) ppm; IR ν<sub>max</sub> (KBr): 3436 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>4</sub> 164.0923; found 164.0923.

**Compound 2b.** White solid (0.08 g, 0.42 mmol, 84%); [α]<sub>D</sub><sup>25</sup> = -23.4 (*c* 0.4, MeOH), [lit.<sup>10d</sup> [α]<sub>D</sub><sup>25</sup> -21.7 (*c* 0.8, MeOH)]; mp 153–155 °C; <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O): δ 4.10–4.09 (m, 1H, C<sub>3</sub>H), 4.02–4.01 (m, 1H, C<sub>4</sub>H), 3.74 (m, 2H, C<sub>5</sub>H, C<sub>2</sub>H), 3.71 (t, *J* = 3.2 Hz, 1H, C<sub>7</sub>H), 3.37 (dd, *J* = 13.7, 3.0 Hz, 1H, C<sub>7</sub>H), 3.26 (dt, *J* = 1.3, 6.8 Hz, 1H, C<sub>6</sub>H), 3.13 (dd, *J* = 13.7, 1.8 Hz, 1H, C<sub>6</sub>H) ppm; <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O): δ 69.8 (C-3), 65.2 (C-4), 64.5 (C-5), 57.5 (C-7), 54.6 (C-2), 41.4 (C-6) ppm; IR ν<sub>max</sub> (KBr): 3436 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>4</sub> 164.0923; found 164.0924.

**Compound 3a.** White solid (0.10 g, 0.5 mmol, 80%); [α]<sub>D</sub><sup>25</sup> = +3.8 (*c* 0.22, MeOH); mp 162–163 °C; <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD): δ 3.94–3.90 (m, 2H, C<sub>3</sub>H, C<sub>4</sub>H), 3.88–3.83 (m, 2H, C<sub>8</sub>H), 3.81–3.74 (m, 2H, C<sub>7</sub>H), 3.60–3.55 (m, 1H, C<sub>6</sub>H), 3.46–3.43 (m, 1H, C<sub>2</sub>H), 2.13–2.05 (m, 2H, C<sub>5</sub>H) ppm; <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD): δ 66.4 (C-3), 64.9 (C-4), 58.8 (C-7), 58.7 (C-8), 56.2 (C-2), 52.7 (C-6), 26.7 (C-5) ppm; IR ν<sub>max</sub> (KBr): 3353 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>7</sub>H<sub>16</sub>NO<sub>4</sub> 178.1079; found 178.1080.

**Compound 3b.** In a similar manner as described for the molecule **1a**, white solid (0.10 g, 0.5 mmol, 81%); [α]<sub>D</sub><sup>25</sup> = +6.3 (*c* 0.18, MeOH); mp 158–159 °C; <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O): δ 3.95 (bs, 1H, C<sub>3</sub>H), 3.91 (dd, *J* = 6.3, 3.4 Hz, 1H, C<sub>4</sub>H), 3.87 (dd, *J* = 5.9, 3.2 Hz, 1H, C<sub>7</sub>H), 3.80–3.78 (m, 2H, C<sub>8</sub>H), 3.72 (dd, *J* = 16, 4.5 Hz, 1H, C<sub>7</sub>H), 3.65–3.59 (m, 1H, C<sub>6</sub>H), 3.40 (dt, *J* = 8.5, 2.3 Hz, 1H, C<sub>2</sub>H), 1.78–1.73 (m, 2H, C<sub>4</sub>H) ppm; <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O): δ 66.0 (C-3), 64.5 (C-4), 58.9 (C-7), 58.1 (C-8), 55.3 (C-2), 52.8 (C-6), 25.5 (C-5) ppm; IR ν<sub>max</sub> (KBr): 3456 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>7</sub>H<sub>16</sub>NO<sub>4</sub> 178.1079; found 178.1078.

**Compound 4a.** White solid (0.10 g, 0.5 mmol, 85%); [α]<sub>D</sub><sup>25</sup> = -9.6 (*c* 0.64, H<sub>2</sub>O); mp 145–146 °C; <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O): δ 4.10–4.06 (m, 2H, C<sub>4</sub>H, C<sub>5</sub>H), 3.73–3.62 (m, 3H, C<sub>8</sub>H, C<sub>6</sub>H), 3.49 (dd, *J* = 12.3, 8.2 Hz, 1H, C<sub>2</sub>H), 3.21–3.17 (m, 2H, C<sub>7</sub>H), 1.99 (ddd, 15.6, 7.8, 4.3 Hz, 1H, C<sub>3</sub>H), 1.72 (dd, 15.5, 10.5 Hz, 1H, C<sub>3</sub>H) ppm; <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O): δ 74.1 (C-4), 68.8 (C-5), 67.8 (C-6), 61.4 (C-8), 54.4 (C-2), 43.3 (C-7), 28.1 (C-3) ppm; IR ν<sub>max</sub> (KBr): 3436 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>7</sub>H<sub>16</sub>NO<sub>4</sub> 178.1079; found 178.1080.

**Compound 4b.** White solid (0.10 g, 0.5 mmol, 84%); [α]<sub>D</sub><sup>25</sup> = +6.0 (*c* 0.82, H<sub>2</sub>O); mp 149–150 °C; <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O): δ 4.10 (dd, *J* = 8.6, 3.2 Hz, 1H, C<sub>4</sub>H), 4.00 (bs, 1H, C<sub>5</sub>H), 3.90 (dt, 10.9, 2.9 Hz, 1H, C<sub>6</sub>H), 3.69 (dd, *J* = 12.3, 4.1 Hz, 1H, C<sub>8</sub>H), 3.49 (dd, *J* = 11.8, 8.2 Hz, 1H, C<sub>8</sub>H), 3.37–3.28 (m, 2H, C<sub>7</sub>H, C<sub>2</sub>H), 3.17 (dd, 13.7, 4.1 Hz, 1H, C<sub>7</sub>H), 1.98–1.88 (m, 1H, C<sub>3</sub>H), 1.75–1.71 (m, 1H, C<sub>3</sub>H) ppm; <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O): δ 75.4 (C-4), 69.5 (C-5), 65.7 (C-6), 62.1 (C-8), 55.7 (C-2), 44.5 (C-7), 29.4 (C-3) ppm; IR ν<sub>max</sub> (KBr): 3456 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* [(M + H) - (HCl)]<sup>+</sup> calcd for C<sub>7</sub>H<sub>16</sub>NO<sub>4</sub> 178.1079; found 178.1080.

**Procedure for MOM protection of 6 to get 12.** Hünig's base, DIPEA (3.49 mL, 20 mmol, 10 equiv.) followed by MOM chloride (0.60 mL, 8 mmol, 4 equiv.) were added to the stirred solution of compound **6** (0.8 g, 2 mmol, 1 equiv.) in dichloromethane at 0 °C, and stirred for 12 h at room temperature. After the complete disappearance of the starting material on TLC, the reaction mixture was quenched with water. The organic layer was extracted with dichloromethane (2 × 10 mL), and the combined organic phases were washed with 4% HCl (2 × 20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated, and purified by column chromatography.

The same procedure was used for the preparation of **24** from **19**.

**Compound 12.** Column chromatography (petroleum ether/EtOAc, 9 : 1); oily liquid (0.84 g, 1.78 mmol, 89%); [α]<sub>D</sub><sup>25</sup> = -9.4 (*c* 0.32, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.72–7.36



(m, 10H), 5.86–5.83 (m, 1H), 5.32 (d,  $J = 17.1$  Hz, 1H), 5.20 (d,  $J = 10.4$  Hz, 1H), 4.76 (d,  $J = 6.7$  Hz, 1H), 4.68 (d,  $J = 6.7$  Hz, 1H), 4.66 (d,  $J = 6.7$  Hz, 1H), 4.45 (t,  $J = 7.0$  Hz, 1H), 3.92 (dd,  $J = 11.0, 2.45$  Hz, 1H), 3.87 (dd,  $J = 11.0, 4.25$  Hz, 1H), 3.71–3.61 (m, 1H), 3.34 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.07 (s, 9H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  135.8, 135.7, 134.3, 133.6, 133.4, 129.7, 129.6, 127.7, 127.6, 117.9, 108.4, 96.9, 78.7, 77.4, 76.5, 64.0, 56.0, 27.7, 26.9, 25.3, 19.3 ppm; IR  $\nu_{\text{max}}$  (thin film): 3072, 3049, 1589, 1472  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{27}\text{H}_{38}\text{NaO}_5\text{Si}$  493.2386; found 493.2381.

**Compound 24.** Column chromatography (petroleum ether/EtOAc, 9.5 : 0.5); oily liquid (0.92 g, 1.7 mmol, 85%);  $[\alpha]_{\text{D}}^{25} = -8.6$  (c 0.18,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.71–7.68 (m, 4H), 7.41–7.35 (m, 6H), 4.85 (d,  $J = 6.9$  Hz, 1H), 4.69 (d,  $J = 6.9$  Hz, 1H), 4.30 (t,  $J = 7.1$  Hz, 1H), 4.19–4.15 (m, 1H), 4.12 (q,  $J = 7.4$  Hz, 2H), 3.98–3.94 (m, 1H), 3.87–3.83 (m, 1H), 3.72–3.70 (m, 1H), 3.36 (s, 3H), 2.56–2.49 (m, 1H), 2.42–2.36 (m, 1H), 2.01–1.94 (m, 1H), 1.79–1.70 (m, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 1.24 (t,  $J = 7.4$  Hz, 3H), 1.03 (s, 9H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.5, 135.8, 135.7, 133.5, 133.4, 129.7, 129.6, 127.7, 127.6, 108.0, 96.2, 76.8, 76.4, 75.7, 63.9, 60.3, 56.2, 31.1, 28.1, 26.9, 25.8, 25.4, 19.3, 14.1 ppm; IR  $\nu_{\text{max}}$  (thin film): 3049, 1735, 1587  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{30}\text{H}_{44}\text{NaO}_7\text{Si}$  567.2754; found 567.2751.

**Procedure for TBDPS deprotection of 12 to get 13.** TBAF (1 M solution in THF 2.4 mL, 2.4 mmol, 1.2 equiv.) was added to the stirred solution of compound 12 (0.94 g, 2 mmol, 1 equiv.) in THF at room temperature and stirred for 1 h. After the disappearance of the starting material on TLC, the reaction was quenched with saturated ammonium chloride solution (10 mL). The organic layer was extracted with ethyl acetate (2  $\times$  20 mL) and the combined organic phases were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, concentrated, and purified by column chromatography.

The same procedure was used for the preparation of 25 from 24.

**Compound 13.** Column chromatography (petroleum ether/EtOAc, 6 : 4); oily liquid (0.42 g, 1.8 mmol, 90%);  $[\alpha]_{\text{D}}^{25} = +7.33$  (c 2.4,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.89–5.82 (m, 1H), 5.35 (d,  $J = 17.1$  Hz, 1H), 5.22 (d,  $J = 10.4$  Hz, 1H), 4.65 (t,  $J = 6.7$  Hz, 1H), 4.60 (q,  $J = 6.7$  Hz, 1H), 4.12 (t,  $J = 7.3$  Hz, 1H), 3.83 (d,  $J = 10.4$  Hz, 1H), 3.62 (q,  $J = 6.4$  Hz, 1H), 3.51 (t,  $J = 6.4$  Hz, 1H), 3.40 (s, 3H), 3.70–3.33 (m, 1H), 1.45 (s, 3H), 1.34 (s, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  133.8, 117.7, 108.9, 97.7, 81.4, 78.7, 77.1, 63.9, 56.0, 27.7, 25.3 ppm; IR  $\nu_{\text{max}}$  (thin film): 3460, 1590  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{11}\text{H}_{20}\text{NaO}_5$  255.1208; found 255.1201.

**Compound 25.** Column chromatography (petroleum ether/EtOAc, 1 : 1); oily liquid (0.56 g, 1.84 mmol, 92%);  $[\alpha]_{\text{D}}^{25} = +13.1$  (c 0.42,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.72 (d,  $J = 6.8$  Hz, 1H), 4.68 (d,  $J = 6.8$  Hz, 1H), 4.17–4.14 (m, 1H), 4.11 (q,  $J = 6.8$  Hz, 2H), 4.03 (dd,  $J = 8.0, 5.7$  Hz, 1H), 3.86 (dd,  $J = 11.5, 2.8$  Hz, 1H), 3.66–3.58 (m, 2H), 3.41 (s, 3H), 2.55–2.49 (m, 1H), 2.42–2.36 (m, 1H), 1.92–1.86 (m, 1H), 1.79–1.71 (m, 1H), 1.38 (s, 3H), 1.29 (s, 3H), 1.23 (t,  $J = 7.4$  Hz, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.4, 108.3, 97.1, 80.3, 76.7,

76.3, 63.8, 60.4, 56.1, 31.1, 28.0, 25.6, 25.2, 14.2 ppm; IR  $\nu_{\text{max}}$  (thin film): 3472, 1735  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{14}\text{H}_{26}\text{NaO}_7$  329.1576; found 329.1571.

## Acknowledgements

The authors thank Department of Science and Technology, Ministry of Science and Technology for financial support (grant number: SR/FT/CS-12/2011) and R. P. thanks University Grants Commission for a senior research fellowship and V. K. J. thanks CSIR India for a JRF.

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- 17 The diastereomeric ratio of these compounds was estimated using chiral HPLC and was established by comparing the chromatograms with that of a 1 : 1 mixture of the diastereomers obtained through reactions catalyzed by DL-proline (given in the ESI†).
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