Stereoselective Synthesis of Diverse α-Hydroxy-β-amino Acids and It's Application for Synthesis of Dipeptide Expecting as a Protease Inhibitor

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Few α-hydroxy-β-amino acids were synthesized *via* various nucleophilic addition of the epoxide and followed by stereoselective nucleophilic substitution reaction and eliminative cleavage of the acetal selectively in diacetal compound. One of the synthesized α-hydroxy-β-amino acid reacted with L-leucine methylester to give corresponding dipeptide in good yields.

Key Words: α-Hydroxy-β-amino acids, Nucleophilic addition, Epoxide ring opening, Eliminative cleavage

Introduction

Amino alcohols especially vicinal *syn*- and *anti*-hydroxy amino units are an important class of compounds. Because of these units are constituents of many natural products such as paclitaxel (taxol), KRI 1230 and KRI 1314. In recent years, *syn*-α-hydroxy-β-amino acids like cyclohexylnorstatine **1** have received considerable interest from a pharmaceutical point of view.[1] Because of cyclohexylnorstatine is the C-terminal residue of KRI 1314 **2**, a tripeptide with potent rennin inhibitory activity (Fig. 1).[2,3]

Many methods have already been developed for the synthesis of these α-hydroxy-β-amino acid units.[4] Most of the early studies used chiral natural products as starting materials were limited in their flexibility of structural modification. In connection with these points, we noticed that a nucleophilic addition of epoxide is very useful methodology for synthesis of various α-hydroxy-β-amino acids.[5]

In this paper, we wish to report synthetic routes for α-hydroxy-β-amino acid derivatives *via* the various nucleophilic addition of epoxide and followed by regio- and stereoselective nucleophilic substitution reaction and eliminative cleavage of the acetal selectively in diacetal compounds (Fig. 2).

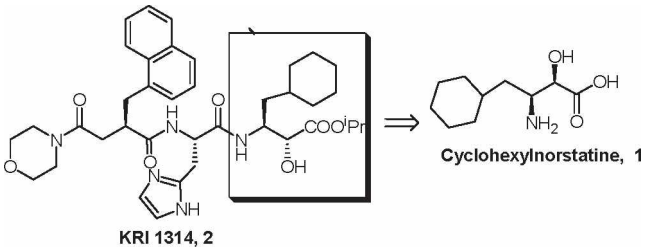


Figure 1. Cyclohexylnorstatine 1 is one of the part of the KRI 1314 which is potent rennin inhibitor.

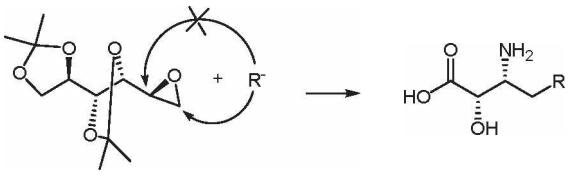
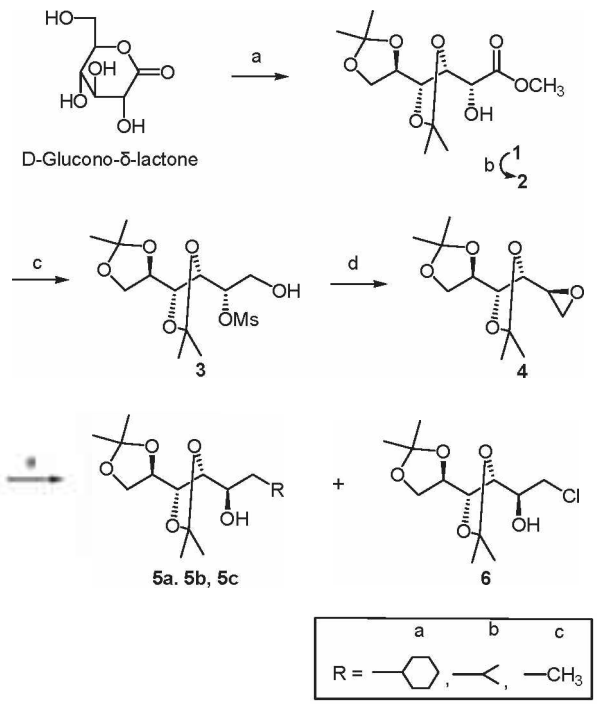


Figure 2. Regioselective epoxide ring opening reaction for synthesis of diverse α-hydroxy-β-amino acids.



Scheme 1. Reagents and conditions; a) 2,2-Dimethoxypropane, MeOH, Acetone, TsOH, H_2O, rt, 97%. b) MsCl, Et_3N, CH_2Cl_2, 0 °C, rt, 98%. c) $NaBH_4$, THF, 0 °C, 95%. d) NaOMe, MeOH, rt, 87%. e) RMgX, CuI, THF, -10 °C to rt, 80%.

Results and Discussion

The compound **1** prepared easily by the usual method[6] from *D*-glucono-δ-lactone. After mesylation and ester reduction of **1**, treated with NaOMe to afford epoxide **4** in quantitative yield (Scheme 1).

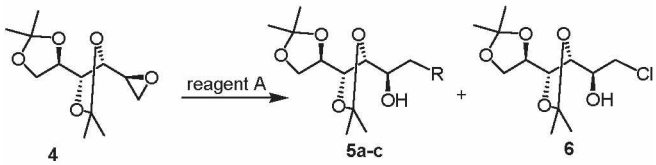
To open epoxide ring of **4**, we reacted various nucleophiles such as alkyl lithiums, Grignard reagents and Gilman reagents. Treatment of epoxide **4** with alkyl lithium reagents (methyl lithium, isopropyl lithium and cyclohexyl lithium) gave many undesired product as mixture of stereoselectively and regioselectively uncontroled product. On the other hand, treatment of **4** with Grignard reagents (methyl, isopropyl and cyclohexyl Grignard reagents) gave unexpected the halogen attacked compound (**6**, X = Cl) as major product instead of desired **5a-c**. After several unsuccessful trials, the ring opening reaction of epoxide **4** using Grignard reagents in presence of copper(I) iodide gave alcohol **5** as major product (Table 1). According to these results, we thought the copper(I) iodide is useful for the regioselective ring opening of **4**. Under the these consideration, we reacted **4** with cuprates (Gilman reagent) to give desired product **5a-c** in reasonable yield.[7]

The alcohol **5** was converted to azido compound **8** through mesylation and S_N2 intramolecular displacement by sodium azide. The azido compound **8** was hydrogenated with H_2 in the presence of 10% Pd/C followed by protection of amino group with 9-phenyl-9-fluorenyl (Pf) bromide to give **10** in good yield (Scheme 2).[8] At this stage, we introduced the Pf group as a protection of amino group because there are remains many steps should be proceed under the strong acid conditions.

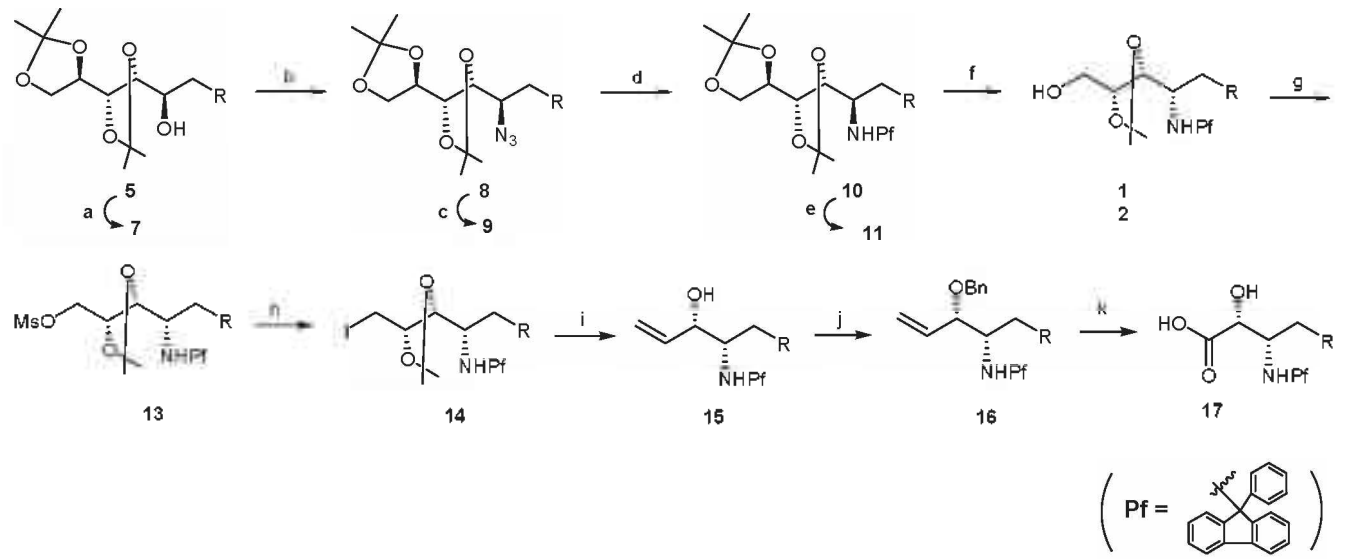
The selective cleavage of terminal isopropylidene group of **10** was proceed in 70% acetic acid condition to give **11** in good yield.[9] The diol **11** was converted to alcohol **12** by using $NaIO_4$ and $NaBH_4$. The alcohol **12** was mesylated and followed by substitution with lithium iodide to give **14**. The isopropylidene iodide **14** was treated with *n*-BuLi to give allylic alcohol **15** through simultaneous elimination reaction. Allylic alcohol **15** was protected with benzyl bromide and followed by dihydroxylation of alkene with OsO_4 to give corresponding diol.[10] The obtained diol compound oxidizied with $NaIO_4$ to give aldelyde and followed by oxidation with $KMnO_4$ resulted to desired α-hydroxy-β-amino carboxylic acid **17** in good yield. The **17a** has different stereochemistry with cyclohexylnorstatine (**1**) but it has the same skeleton and functional groups and **17b** has the same skeleton and functional groups with (2*S*, 3*R*)-3-amino-2-hydroxy-5-methylhexanoic acid which is the *N*-terminal amino acid of amastatin[11] that a tripeptide which has been found to inhibit leucine aminopeptidase and aminopeptidase A.[12]

Among of **17a**, **17b** and **17c**, compound **17a** reacted with L-leucine methylester under the presence of DCC, HOBT and Et_3N in THF to give desired dipeptide **18** in good yield. Hydrolysis of **18** by LiOH in mixed solvent (THF : H_2O = 2 :

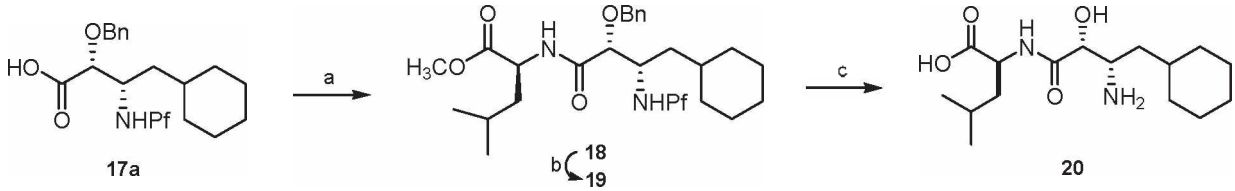
Table 1. Ring Opening Reaction of Epoxide **4** by Various Nucleophiles.



R	X	A	Product
Cyclohexyl	Cl	RMgX	**5a**:**6** = 5:5
	Cl	RMgX, CuI	**5a**:**6** = 7:3
		RLi, CuI	**5a**
Isopropyl	Cl	RMgX	**5b**:**6** = 6:4
	Cl	RMgX, CuI	**5b**:**6** = 7:3
		RLi, CuI	**5b**
Methyl	Cl	RMgX	**6**
	Cl	RMgX, CuI	**5c**:**6** = 8:2
		RLi, CuI	**5c**



Scheme 2. Reagents and conditions; a) Ms-Cl, Et_3N, CH_2Cl_2, 0°C, 98%. b) NaN_3, DMF, 80°C, 87%. c) 10% Pd/C, H_2, MeOH, rt, 95%. d) Pf-Br, $Pb(NO_3)_2$, CH_2Cl_2, rt, 87%. e) 70% Acetic Acid, CH_2Cl_2, rt, 90%. f) $NaIO_4$, $NaBH_4$, H_2O/EtOH(1/2), rt, 95%. g) Ms-Cl, Et_3N, CH_2Cl_2, rt, 98%. h) LiI, DMF, 80 °C, 80%. i) *n*-BuLi, THF, -40 °C, 90%. j) NaH, Benzylbromide, THF, rt, 90%. k) 60% NMO, OsO_4, Acetone, $NaIO_4$, EtOH/H_2O(1/1), K_2CO_3, $KMnO_4$, THF/H_2O(1/1), rt, 75%.



Scheme 3. Reagents and conditions; a) TsOH, L-leu-OCH_3, HOBT, DCC, Et_3N, THF, 0°C, 75 %. b) LiOH, THF/H_2O(2/1), 0°C. c) 10% Pd/C, H_2, MeOH, 70-80°C, 83%.

1) to give acid **19** in quantitative yield. The obtained **19** was deprotected with H_2-Pd/C in MeOH at 70-80 °C to give desired peptide **20** with 83% yield (Scheme 3).

In conclusion, we reported the result of regioselective reaction of epoxide ring opening by nucleophiles attack. According to survey, regioselective ring opening of epoxide was completed more easily under the conditions of Gilman reagents than Grignard reagents. And also, we synthesized dipeptide **20** which expecting as a protease inhibitor.

Experiments

General. All solvents were purified before use with standard drying procedures, unless otherwise specified. Reactions were monitored by TLC using Merck silica gel 60 F-254 plates with UV indicator or/and visualized with phosphomolybdic acid (10% solution in EtOH). All the organic layers were dried over Na_2SO_4 before concentration in vacuo. Column chromatography was carried out using 230-400 mesh silica gel. Elemental analysis or C, H and N are in agreement with the theoretical data, except for compounds containing halogens, where combustion analysis could not be performed. Melting points were measured on Thomas-Hoover melting point apparatus but the temperatures were not corrected. ^{1}H- and ^{13}C-NMR experiments were conducted on Bruker AW-500 spectrometer. Optical rotation were measured on a Jasco DIP-1000 polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} degcm^2g^{-1}.

Preparation of methyl 3,4;5,6-di-*O*-isopropylidene-2-*O*-methanesulfonyl-*D*-gluconate (1) and methyl 3,4;5,6-di-*O*-isopropylidene-2-*O*-methanesulfonyl-*D*-gluconate (2) were prepared according to ref.[13] and physical and spectral dates were correlated well with previously reported.

Methyl 3,4;5,6-di-*O*-isopropylidene-2-*O*-methanesulfonyl-*D*-glucitol (3). To a solution of compound **2** (2.22 g, 6.03 mmol) in MeOH (30 mL) was added portionwise $NaBH_4$ (0.68 g, 18.1 mmol) at 0 °C for 3 min and stirred for 11 h and then quenched with water (5 mL). The reaction mixture was extracted with EtOAc (3×30 mL) and the organic layers were evaporated in vacuo. The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 9:1, v/v) to afford pure **3** (2.03 g, 98%) as an oil. $[\alpha]_D$ = -6.3 (*c* 2.20, $CHCl_3$); IR (KRS-5) 3490, 2980, 2970, 2900, 1370, 1360, 1300, 1290, 1280, 1100, 990 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.39 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 2.64-2.67 (t, -OH, *J* = 6.7 Hz), 3.14 (s, 3H), 3.92-3.97 (m, 4H), 4.04-4.07 (m, 1H), 4.18-4.24 (m, 2H), 4.82 (q, 1H, *J* = 4.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.6, 110.3, 81.9, 79.9, 77.8, 76.8, 68.1, 63.0, 38.9, 30.9, 27.2, 26.6, 26.3, 25.2. Anal. Calcd for $C_{13}H_{24}O_8S_1$: C, 45.87; H, 7.11. Found : C, 45. 86 H, 7.10.

1,2-Anhydro-1,2-epoxy-3,4;5,6-*O*-diisopropylidene-*D*-glucose (4). To a stirred solution of compound **3** (4.4 g, 12.9 mmol) in MeOH (50 mL) was added portionwise Na metal (0.45 g, 19.4 mmol) at 0 °C. After stirring 2 h at rt., water (10 mL) was slowly added and extracted with EtOAc (3×40 mL). The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 5:1, v/v) to afford pure **3** (2.76 g, 87%) as an oil. $[\alpha]_D$ = -4.3 (*c* 2.00, $CHCl_3$); IR (KRS-5) 2980, 2970, 2970, 2350, 1370, 1310, 1290, 1100, 920 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 3H), 1.42 (s, 3H), 1.43 (s, 3H), 1.45 (s, 3H), 2.84-2.85 (m, 2H), 3.22 (dd, 1H, *J* = 3.5, 6.8 Hz), 3.85 (t, 1H, *J* = 7.29 Hz), 3.98 (dd, 1H, *J* = 4.9, 8.1 Hz), 4.07-4.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.4, 110.1, 79.2, 79.1, 77.1, 67.8, 52.3, 44.6, 31.3, 27.4, 27.1, 27.0, 25.6. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.98; H, 8.24.

General preparation of epoxy 5a, 5b and 5c : Representative procedure for the preparation of 1-deoxy-1-cyclohexyl-3,4;5,6-*O*-diisopropylidene-*D*-mannose (5a). To a solution of dried CuI (1.37 g, 7.2 mmol, 99.99%) in ether (20 mL) was slowly added dropwise for 5 min cyclohexylmagnesium chloride (4 mL, 8.0 mmol) at -20 °C. After stirring for 5 min, compound **4** (0.488 g, 2.00 mmol) dissolved in ether (10 mL) added for 5 min *via* cannula and stirred for 30 min. To the reaction mixture added saturated NH_4Cl solution (5 mL) and stirred additional 20 min. The reaction quenched with water (30 mL) and extracted with EtOAc (30 mL×3). The organic layer washed with water (30 mL×2) and brine and dried with anhydrous $MgSO_4$. Filtration and removal of the solvent gave a dark yellow oil which was further purified by flash column chromatography (hexane/EtOAc, 10/1, v/v) to afford pure **5a** (1.67 g, 70%) as white solid.

mp 42-44 °C. $[\alpha]_D$ = -3.6 (*c* 3.00, $CHCl_3$); IR (KBr) 3470, 2980, 2950, 2920, 2890, 2850, 1440, 1350, 1240, 1220, 1140, 1070, 860 cm^{-1}; ^{1}H NMR (500MHz, $CDCl_3$) δ 0.85-0.88 (m, 1H), 0.98-1.03 (m, 1H), 1.14-1.19 (m, 1H), 1.23-1.30 (m, 1H), 1.36 (s, 6H), 1.37 (s, 3H), 1.39-1.42 (m, 1H), 1.44 (s, 3H), 1.50-1.59 (m, 2H), 1.63-1.71 (m, 5H), 1.84-1.89 (m, 1H), 3.11 (s, -OH), 3.71-3.76 (m, 3H), 3.98 (dd, 1H, *J* = 5.7, 8.44 Hz), 4.14-4.07 (m, 1H), 4.20 (dd, 1H, *J* = 5.92, 8.7 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 110.2, 109.1, 84.1, 80.8, 77.3, 76.7, 69.7, 68.1, 34.7, 33.6, 32.5, 26.9, 27.0, 26.7, 26.5, 26.5, 26.2, 25.2. Anal. Calcd for $C_{18}H_{32}O_5$: C, 65.82; H, 9.82. Found: C, 65.80; H, 9.81.

1-Deoxy-1-isopropyl-3,4;5,6-*O*-diisopropylidene-*D*-man-

nose (5b). According to the general procedure with isopropylmagnesium chloride (9 mL, 18.1 mmol) and compound **4** (2.95 g, 12.1 mmol) in THF afforded pure compound **5b** (2.81 g, 80%) as a colorless oil. $[\alpha]_D$ = -3.0 (*c* 3.00, $CHCl_3$); IR (KRS-5) 3470, 2980, 2950, 2930, 2900, 2870, 1450, 1370, 1240, 1210, 1150, 1070, 850 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (dd, 6H, *J* = 6.6, 15.2 Hz), 1.34 (s, 3H), 1.36 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 1.42-1.47 (m, 2H), 1.81-1.90 (m, 1H), 3.16 (s, -OH), 3.71-3.75 (m, 3H), 3.97-4.00 (dd, 1H, *J* = 5.6, 8.5 Hz), 4.05-4.06 (m, 1H), 4.19 (dd, 1H, *J* = 6.1, 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.5, 109.5, 84.4, 81.1, 77.0, 70.6, 68.4, 43.0, 27.3, 27.2, 26.8, 25.6, 24.5, 24.3, 21.9. Anal. Calcd for $C_{15}H_{28}O_5$: C, 62.47; H, 9.79. Found: C, 62.45; H, 9.78.

1-Deoxy-1-methyl-3,4;5,6-*O*-diisopropylidene-*D*-mannose (5c). According to the general procedure with methylmagnesium bromide (5.18 mL, 15.5 mmol) and compound **4** (2.53 g, 10.4 mmol) in Et_2O afforded pure compound **5c** (2.95 g, 80%) as a colorless oil. $[\alpha]_D$ = -2.23 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3480, 2980, 2930, 2880, 1370, 1240, 1210, 1150, 1060, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, 3H, *J* =7.3 Hz), 1.23 (s, 3H), 1.24 (s, 3H), 1.24 (s, 3H), 1.25 (s, 3H), 1.51-1.69 (m, 2H), 1.73-1.80 (m, 1H), 3.39 (m, -OH), 3.54-3.58 (m, 1H), 3.70-3.74 (m, 2H), 4.01 (dd, 1H, *J* = 3.0, 5.5 Hz), 4.05-4.09 (m, 1H), 4.20 (dd, 1H, *J* = 6.0, 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.20, 109.12, 83.12, 81.11, 76.58, 73.35, 68.07, 26.91, 26.80, 26.44, 26.40, 25.18, 9.41. Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.99; H, 9.28.

General preparation of 7a, 7b and 7c: Representative procedure for the preparation of 1-cyclohexyl-1-deoxy-3,4;5,6-*O*-diisopropylidene-2-*O*-methansulfonyl-*D*-mannose (7a). To a solution of **5a** (2.0 g, 6.09 mmol) in CH_2Cl_2 (20 mL) was added dropwise Et_3N (0.2 g, 1.83 mmol) for 5 min at 0 °C. After stirring for 5 min, MsCl (0.76 g, 6.70 mmol) was slowly added to the mixture. The reaction mixture stirred for 30 min at rt. and then was quenched with saturated aqueous $NaHCO_3$ (20 mL). The reaction mixture extracted with EtOAc (3×30 mL) and the organic layers were evaporated in vacuo. The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 10:1, v/v) to afford pure **7a** (2.43 g, 98%) as an oil. **7a**: $[\alpha]_D$ = -5.69 (*c* 3.00, $CHCl_3$); IR (KRS-5) 2980, 2930, 2880, 1450, 1340, 1210, 1160, 1060, 910, 840 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.81-0.88 (m, 1H), 0.97-1.04 (m, 1H), 1.12-1.32 (m, 4H), 1.34 (s, 3H), 1.37 (s, 3H), 1.41 (s, 3H), 1.41 (s, 3H), 1.45-1.56 (m, 2H), 1.64-1.87 (m, 6H), 3.06 (s, 3H), 3.74-3.80 (m, 1H), 3.93 (dd, 1H, *J* = 5.6, 8.6 Hz), 4.03-4.07 (m, 1H), 4.14-4.30 (m, 1H), 4.33-4.38 (m, 1H), 5.01-5.04 (m, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 110.0, 109.9, 81.7, 79.5, 78.0, 77.1, 68.0, 38.8, 37.3, 33.8, 33.3, 32.4, 27.1, 25.0, 26.7, 26.4, 26.1, 25.9, 25.2. Anal. Calcd for $C_{19}H_{34}O_7S$: C, 56.13; H, 8.43. Found: C, 56.12; H, 8.43.

7b: Yield : 99 %; $[\alpha]_D$ = +13.62 (*c* 4.00, $CHCl_3$); IR (KRS-5) 2980, 2870, 1360, 1460, 1210, 1170, 1070, 980, 920 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (dd, 6H, *J* = 6.4, 11.8 Hz), 1.35 (s, 3H), 1.38 (s, 3H), 1.42 (s, 3H), 1.42 (s, 3H), 1.14-1.49 (m, 1H), 1.80-1.85 (m, 2H), 3.08 (s, 3H), 3.76-3.78 (dd, 1H, *J* = 7.3, 8.5 Hz), 3.95 (dd, 1H, *J* = 5.4, 8.6 Hz), 4.04-4.08 (m, 1H), 4.17 (dd, 1H, *J* = 6.2, 8.6 Hz), 4.25(dd, 1H, *J* = 2.4, 7.2 Hz), 4.99-5.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.0, 110.0, 81.7, 80.1, 78.0, 77.1, 68.0, 38.8, 38.8, 27.0, 27.0, 26.7, 25.2, 24.0, 23.2, 21.6. Anal. Calcd for $C_{16}H_{30}O_7S$: C, 52.44; H, 8.25. Found: C, 52.45; H, 8.26.

7c: Yield : 98 %; $[\alpha]_D$ = -5.65 (c 2.00, $CHCl_3$); IR (KRS-5) 2990, 2940, 2890, 1460, 1360, 1240, 1220, 1180, 1070, 930, 850 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, 3H, *J* = 7.8 Hz), 1.31 (s, 3H), 1.34 (s, 3H), 1.38 (s, 6H), 1.75-1.89 (m, 3H), 3.04 (s, 3H), 3.83 (dd, 1H, *J* =7.0, 8.0 Hz), 3.91 (dd, 1H, *J* = 5.5, 8.5 Hz), 4.02-4.06 (m, 1H), 4.11 (dd, 1H, *J* = 6.0, 8.5 Hz), 4.17 (dd, 1H, *J* = 3.5, 7.0 Hz), 4.76-4.79 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$); δ 110.4, 110.2, 84.0, 81.1, 78.6, 77.4, 68.0, 39.0, 27.5, 27.5, 26.9, 25.6, 23.7, 10.1. Anal. Calcd for $C_{14}H_{26}O_7S$: C, 49.69; H, 7.74. Found: C, 48.70; H, 7.76.

General preparation of 8a, 8b and 8c : Representative procedure for the preparation of 2-azido-1-cyclohexyl-1,2-dideoxy-3,4;5,6-O-diisopropylidene-D-glucose (8a). To a solution of **7a** (2.0 g, 6.39 mmol) in *N,N*-dimethyl formamide (20 mL) was added NaN_3 (3.20 g, 32 mmol, 5 times excess) at rt. The reaction mixture stirred for 10 h at 80 °C and then cooled down rt. and quenched with water (30 mL). The reaction mixture extracted with EtOAc (3×30 mL) and the organic layers were evaporated in vacuo. The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 10:1, v/v) to afford pure **8a** (1.97 g, 87%) as an oil. $[\alpha]_D$ = -6.69 (c 2.00, $CHCl_3$); IR (KRS-5) 2990, 2920, 2850, 2360, 2110 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.89- 0.92 (m, 1H), 0.97-1.00 (m, 1H), 1.15-1.20 (m, 1H), 1.23-1.31 (m, 2H), 1.32 (s, 3H), 1.37 (s, 3H), 1.39 (s, 3H), 1.47 (s, 3H), 1.48-1.52 (m, 2H), 1.66-1.85 (m, 6H), 3.28-3.32 (m, 1H), 3.91-4.03 (m, 4H), 3.13 (dd, 1H, *J* = 5.64, 8.33 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 110.1, 109.8, 83.3, 78.0, 77.4, 67.9, 58.2, 38.5, 34.5, 33.8, 32.5, 27.2, 26.7, 26.5, 26.3, 26.1, 25.3. Anal. Calcd for $C_{18}H_{31}N_3O_4$: C, 61.17; H, 8.84. Found: C, 61.18; H, 8.85.

8b: Yield : 88 %; $[\alpha]_D$ = -25.49 (c 4.00, $CHCl_3$); IR (KRS-5) 2990, 2960, 2940, 2870, 2110, 1470, 1370, 1250, 1220, 1070, 850 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.96 (d, 3H, *J* = 6.5 Hz), 0.99 (d, 3H, *J* = 6.44 Hz), 1.32 (s, 3H), 1.37 (s, 3H), 1.39 (s, 3H) 1.47 (s, 3H), 1.47-1.49 (m, 1H), 1.82-1.87 (m, 2H), 3.28-3.28 (m, 4H), 4.13 (dd, 1H, *J* = 5.5, 8.2 Hz); ^{13}C NMR (500MHz, $CDCl_3$) δ 110.1, 109.8, 83.1, 78.0, 77.5, 68.0, 58.9, 39.8, 27.2, 26.7, 26.7, 25.3, 25.1, 23.0, 21.8. Anal. Calcd for $C_{15}H_{27}N_3O_4$: C, 57.4; H, 8.68. Found: C, 57.48; H, 8.67.

8c: Yield : 85 %; $[\alpha]_D$ = -11.34 (c 3.00, $CHCl_3$); IR (KRS-5) 2990, 2930, 2880, 2100, 1380, 1250, 1220, 1070, 850 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 1.09 (t, 3H, *J* = 7.4 Hz), 1.33 (s, 3H), 1.37 (s, 3H), 1.40 (s, 3H), 1.46 (s, 3H), 1.74-1.79 (m, 1H), 1.86-1.92 (m, 1H), 3.13-3.14 (m, 1H), 3.95-4.12 (m, 4H), 4.13-4.15 (dd, 1H, *J* = 5.7, 8.3 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 110.0, 109.8, 82.5, 82.0, 79.0, 78.0, 77.4, 68.0, 67.6, 65.6, 62.6, 27.5, 27.2, 26.8, 26.7, 26.5, 25.3, 24.4, 23.3, 11.1, 11.0. Anal. Calcd for $C_{13}H_{23}N_3O_4$: C, 54.72; H, 8.12. Found: C, 54.73; H, 8.13.

General preparation of 9a, 9b and 9c : Representative procedure for the preparation of 2-amino-1,2-dideoxy-1-cyclohexyl-3,4;5,6-O-diiso-propylidene-*D*-glucose (9a). To a solution of

8a (1.4 g, 4.25 mmol) in MeOH (20 mL) was added catalytic amount of 10% Pd/C and the reaction mixture stirred for 30 h at rt. Reaction mixture filtered by glass funnel which was padded with celite. The solvent was evaporated in vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 1:2, v/v) to afford pure **9a** (1.32 g, 95%) as an oil. **9a**: $[\alpha]_D$ = -13.26 (c 2.00, $CHCl_3$); IR (KRS-5) 3390, 3330, 2990, 2920, 2850, 1370, 1240, 1210, 1070, 850 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.83-0.86 (m, 1H), 0.95-0.97 (m, 1H) 1.14-1.19 (m, 1H), 1.23-1.29 (m, 5H), 1.34-1.40 (m, 1H), 1.34 (s, 3H), 1.36 (s, 3H), 1.40 (s, 3H), 1.41 (s, 3H), 1.46-1.52 (m, 1H), 1.64-1.71 (m, 4H), 1.77-1.89 (m, 1H), 2.90-2.94 (m, 1H), 3.80 (dd, 1H, J = 3.85, 6.79 Hz), 3.85 (dd, 1H, J = 6.8, 8.0 Hz), 3.96 (dd, 1H, J = 5.1, 8.4 Hz), 4.03-4.07 (m, 1H), 4.13 (dd, 1H, J = 6.16, 8.38 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 109.6, 109.2, 84.4, 78.4, 77.4, 67.8, 49.3, 43.2, 34.4, 34.2, 32.6, 27.5, 27.4, 26.7, 26.7, 26.4, 26.2, 25.3. Anal. Calcd for $C_{18}H_{33}NO_4$: C, 66.05; H, 10.09; N, 4.28. Found: C, 66.04; H, 10.07; N, 4.25.

9b: $[\alpha]_D$ = -19.4 (c 2.00, $CHCl_3$); IR (KRS-5) 3480, 3400, 3060, 2960, 2930, 2850, 2340, 1710, 1610, 1450, 1300, 920, 730 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.90 (d, 3H, J = 6.54 Hz), 0.94 (d, 3H, J = 6.62 Hz), 1.29-1.40 (m, 5H), 1.34 (s, 3H), 1.36 (s, 3H), 1.40 (s, 6H), 1.77-1.83 (m, 1H), 2.88-2.91 (m, 1H), 3.82 (dd, 1H, J = 3.5, 6.9 Hz), 3.88 (dd, 1H, J = 6.9, 7.9 Hz), 3.96 (dd, 1H, J = 5.05, 8.4 Hz), 4.03-4.07 (m, 1H), 4.13 (dd, 1H, J = 6.1, 8.4 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 109.6, 109.2, 84.1, 78.3, 77.4, 67.8, 49.9, 44.8, 27.4, 27.3, 26.7, 25.3, 24.7, 23.5, 21.8. Anal. Calcd for $C_{15}H_{29}NO_4$: C, 62.72; H, 10.10; N, 4.87. Found: C, 62.71; H, 10.08; N, 4.85.

9c: $[\alpha]_D$ = +8.28 (c 2.00, $CHCl_3$); IR (KRS-5) 3380, 3390, 2980, 2930, 2880, 2360, 1460, 1380, 1250, 1220, 1160, 1070, 850 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 1.00 (t, 3H, J = 7.4 Hz), 1.27 (s, 2H), 1.34 (s, 3H), 1.36 (s, 3H), 1.40 (s, 3H), 1.34-1.39 (m, 1H), 1.58-1.63 (m, 1H), 2.70-2.73 (m, 1H), 3.85-3.91 (m, 2H), 3.96 (dd, 1H, J = 5.20, 8.35 Hz), 4.03-4.07 (m, 1H), 4.13 (dd, 1H, J = 6.2, 8.3 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 110.0, 109.4, 83.9, 78.6, 68.1, 53.7, 31.2, 28.7, 27.7, 27.6, 27.0, 25.7, 11.2. Anal. Calcd for $C_{13}H_{25}NO_4$: C, 60.23; H, 9.65; N, 5.41. Found: C, 60.22; H, 9.66; N, 5.44.

General preparation of 10a, 10b and 10c : Representative procedure for the preparation of 1-cyclohexyl-1,2-dideoxy-3,4;5,6-*O*-diisopropylidene-2-[(9-phenylfluoren-9-yl)amino)-*D*-glucose (10a). To a solution of **9a** (0.9 g, 3.05 mmol) in CH_2Cl_2 (10 mL) was added $Pb(NO_3)_2$ (0.94 g, 4.58 mmol), 9-bromo-9-phenylfluorene (1.47 g, 4.58 mmol) and Et_3N (0.93 g, 9.16 mmol) at rt. The reaction mixture stirred for 30 min at rt. and quenched with water (30 mL). The reaction mixture extracted with CH_2Cl_2 (3 × 20 mL) and the organic layers were evaporated in vacuo. The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 10:1, v/v) to afford pure **10a** (1.51 g, 87%) as an oil.

10a: $[\alpha]_D$ = +7.44 (c 2.00, $CHCl_3$); IR (KRS-5) 3430, 3330, 3060, 2990, 2920, 2850, 1720, 1450, 1370, 1250, 1210, 1060, 850 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.28-0.33 (m, 1H), 0.39-0.45 (m, 1H), 0.88-1.17 (m, 7H), 1.19-1.24 (m, 5H), 1.25 (s, 3H), 1.13 (s, 3H), 1.14-1.44 (m, 4H), 1.50-1.55 (m, 3H), 2.34-2.45 (m, 1H), 2.63 (d, 1H, J = 8.7 Hz), 3.64-3.69 (m, 2H), 3.90-4.03 (m, 3H), 7.07-7.21 (m, 5H), 7.28-7.39 (m, 4H), 7.43-7.45 (m, 2H), 7.67 (d, 2H, J = 7.5 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 151.0, 150.5, 145.9, 140.6, 140.5, 128.1, 128.1, 127.7, 127.5, 126.9, 126.5, 126.3, 126.1, 125.9, 125.8, 120.0, 119.8, 109.3, 108.4, 80.9, 77.3, 76.8, 72.4, 67.5, 49.3, 41.5, 33.7, 33.3, 32.8, 30.9, 27.3, 26.8, 26.6, 26.4, 26.2, 26.1, 25.3, 13.8. Anal. Calcd for $C_{36}H_{45}NO_4$: C, 77.80; H, 8.16; N, 2.52. Found: C, 77.83; H, 8.13; N, 2.55.

10b: Yield : 85%; $[\alpha]_D$ = +3.84 (c 2.00, $CHCl_3$); IR (KRS-5) 3330, 3060, 2980, 2930, 2870, 1740, 1450, 1380, 1250, 1210, 1160, 1070, 850, 740 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.38 (d, 3H, J = 6.5 Hz), 0.45 (d, 3H, J = 6.5 Hz), 0.83-0.87 (m, 1H), 1.17-1.24 (m, 1H), 1.22 (s, 3H), 1.26 (s, 3H), 1.30 (s, 3H), 1.34-1.44 (m, 1H), 1.46 (s, 3H), 2.32 (s, 1H), 2.56 (s, 1H), 3.67-3.71 (m, 1H), 3.88-3.92 (m, 1H), 4.01-4.03 (m, 1H), 7.16-7.35 (m, 9H), 7.45 (d, 2H, J = 7.0 Hz), 7.66 (d, 2H, J = 7.4 Hz); ^{13}C NMR (125MHz, $CDCl_3$) δ 151.2, 150.4, 146.0, 140.6, 140.5, 128.5, 128.2, 128.1, 127.7, 127.6, 126.9, 126.3, 125.9, 125.4, 120.1, 119.9, 119.8, 109.3, 108.5, 80.9, 77.5, 77.0, 72.4, 67.5, 50.2, 43.1, 27.3, 26.8, 26.4, 25.3, 24.4, 22.9, 21.7. Anal. Calcd for $C_{33}H_{41}NO_4$: C, 76.86; H, 8.01; N, 2.72 . Found: C, 76.83; H, 8.03; N, 2.75.

10c: Yield : 89%; $[\alpha]_D$ = +8.52 (c 2.00, $CHCl_3$); IR (KRS-5) 3420, 3330, 3040, 2987, 2920, 2850, 1715, 1440, 1350, 1250, 1210, 1060, 870 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.64 (t, 3H, J = 7.4 Hz), 1.03-1.07 (m, 1H), 1.14-1.17 (m, 1H), 1.19 (s, 3H), 1.27 (s, 3H), 1.32 (s, 3H), 1.39 (s, 3H), 2.25 (s, 1H), 2.27 (s, 1H), 3.68 (dd, 1H, J = 2.7, 7.4 Hz), 3.75 (dd, 1H, J = 6.9, 8.1 Hz), 3.89-3.93 (m, 1H), 3.95-3.98 (m, 1H), 4.01-4.04 (m, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 148.5, 148.4, 143.3, 141.6, 140.2, 129.0, 128.9, 128.8, 128.1, 128.0, 127.6, 126.2, 125.9, 125.3, 120.5, 120.2, 107.7, 81.5, 76.1, 73.0, 72.0, 64.4, 54.1, 26.8, 26.3, 23.3, 11.5. Anal. Calcd for $C_{31}H_{37}NO_4$: C, 76.36 H, 7.65; N, 2.87. Found: C, 76.37; H, 7.63; N, 2.87.

General preparation of 11a, 11b and 11c : Representative procedure for the preparation of 1-cyclohexyl-1,2-dideoxy-3,4-*O*-isopropylidene-2-[(9-phenylfluoren-9-yl)amino]-*D*-lyxitol (11a). To a solution of **10a** (1.17 g, 2.11 mmol) in CH_2Cl_2 (5 mL) was added acetic acid (70%, 35 mL) at rt. The reaction mixture stirred for 24 h at rt. and then added water (30 mL). The reaction mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 10:1, v/v) to afford pure **11a** (0.98 g, 90%) as an oil.

11a: $[\alpha]_D$ = +29.26 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3440, 3290, 3060, 2980, 2930, 2850, 1720, 1450, 1370, 1250, 1070, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.38-0.41 (m, 1H), 0.75-0.78 (m, 1H), 0.88-0.92 (m, 1H), 0.94 (s, 3H), 0.97-1.03 (m, 2H), 1.04-1.16 (m, 3H), 1.21 (s, 3H), 1.24-1.27 (m, 1H), 1.36-1.40 (m, 1H), 1.42-1.46 (m, 2H), 1.55-1.63 (m, 2H), 2.03 (s, 1H), 2.54-2.57 (m, 1H), 3.12 (dd, 1H, J = 3.2, 11.7 Hz), 3.47-3.50 (m, 1H), 3.67-3.74 (m, 2H), 3.35 (dd, 1H, J = 4.0, 11.2 Hz), 7.19-7.30 (m, 7H), 7.31-7.36 (m, 2H), 7.39-7.42 (m, 1H), 7.46 (d, 1H, J = 7.5 Hz), 7.74 (d, 1H, J = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 148.5, 143.2, 141.6, 140.1,

129.0, 128.9, 128.8, 128.2, 128.1, 127.6, 126.3, 125.9, 124.9, 120.5, 120.2, 107.7, 81.4, 76.0, 73.1, 72.2, 64.8, 60.4, 49.1, 38.9, 34.5, 33.1, 32.2, 26.8, 26.4, 26.3, 25.9, 14.2. Anal. Calcd for $C_{33}H_{41}NO_4$: C, 76.86 H, 8.01; N, 2.72. Found: C, 76.84; H, 8.00; N, 2.70.

11b: Yield : 91%; $[\alpha]_D$ = +24.52 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3410, 3290, 3060, 2980, 2950, 2930, 2870, 2780, 2250, 1450, 1370, 1240, 1070, 910, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.33 (d, 1H, *J* = 6.3 Hz), 0.73 (d, 1H, *J* = 6.5 Hz), 0.96 (s, 3H), 1.09-1.19 (m, 2H), 1.23-1.27 (m, 4H), 1.33-1.39 (m, 1H), 1.46-1.49 (m, 1H), 2.03 (s, 1H), 2.50-2.53 (m, 1H), 3.18 (dd, 1H, *J* = 3.2, 8.5 Hz), 3.48-3.52 (m, 1H), 3.70-3.75 (m, 1H), 3.85 (dd, 1H, *J* = 4.0, 11.2 Hz), 7.11-7.31 (m, 8H), 7.34-7.36 (m, 2H), 7.39-7.42 (m, 1H), 7.45-7.49 (m, 1H), 7.70-7.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 148.5, 143.2, 141.6, 140.2, 129.0, 128.9, 128.7, 128.3, 128.0, 127.6, 126.4, 125.9, 125.0, 120.5, 120.2, 107.7, 81.5, 76.0, 73.0, 72.3, 64.8, 50.0, 40.6, 26.8, 26.3, 24.0, 23.7, 21.6. Anal. Calcd for $C_{30}H_{37}NO_4$: C, 75.76; H, 7.84; N, 2.94. Found: C, 75.73; H, 7.83; N, 2.95.

11c: Yield : 89%; $[\alpha]_D$ = +25.22 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3430, 3310, 3060, 2980, 2930, 2870, 1730, 1600, 1450, 1380, 1250, 1070 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.73 (t, 3H, *J* = 7.5 Hz), 0.96 (s, 3H), 1.21-1.27 (m, 2H), 1.22 (s, 3H), 1.66 -1.71 (m, 1H), 2.03 (s, 1H), 2.37 - 2.40 (m, 1H), 3.15 (dd, 1H, *J* = 3.3, 8.6 Hz), 3.48-3.50 (m, 1H), 3.69-3.73 (m, 2H), 3.85 (dd, 1H, *J* = 3.9, 11.1 Hz), 7.19- 7.31 (m, 7H), 7.33-7.36 (m, 1H), 7.39-7.42 (m, 1H), 7.47 (d, 1H, *J* = 7.6 Hz), 7.71 (dd, 2H, *J* = 7.5, 17.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 148.4, 143.3, 141.6, 140.2, 129.0, 128.9, 128.8, 128.1, 128.0, 127.6, 126.2, 125.9, 125.3, 120.3, 120.2, 107.7, 81.5, 76.1, 73.0, 72.0, 64.4, 54.1, 26.8, 26.3, 23.3, 11.5. Anal. Calcd for $C_{28}H_{33}NO_4$: C, 75.14; H, 7.43; N, 3.13. Found: C, 75.12; H, 7.41; N, 3.10.

General preparation of 12a, 12b and 12c : Representative procedure for the preparation of 1-cyclohexyl-1,2-dideoxy-3,4-O-isopropylidene-2-[(9-phenylfluoren-9-yl)amino]-D-xylitol (12a). To a solution of **11a** (0.79 g, 1.53 mmol) in H_2O/EtOH = (1:2, 30 mL) was added $NaIO_4$ (0.49g, 2.27 mmol) at rt. The reaction mixture stirred for 2 h at rt. and then added $NaBH_4$ (7.45mg, 1.97 mmol) and stirred for 15 min. EtOH in the reaction bottle was evaporated and the reaction mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried with Na_2SO_4 and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 3:1, v/v) to afford pure **12a** (0.67 g, 90%) as an oil.

12a: $[\alpha]_D$ = +18.51 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3440, 3060, 3030, 2990, 2980, 2850, 1590, 1370, 1220, 1150, 1050, 930, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.38-0.45 (m, 1H), 0.60-.68 (m, 1H), 0.79-0.90 (m, 2H), 0.96-1.03 (m, 2H) 1.04 (s, 3H), 1.00-1.12 (m, 3H), 1.24-1.29 (m, 1H), 1.28 (s, 3H), 1.30-1.58 (m, 2H), 1.55-1.61 (m, 1H), 2.30 (s, 1H), 2.46-2.48 (m, 1H), 3.15 (dd, 1H, *J* = 3.1, 8.6 Hz), 3.48 (dd, 1H, *J* = 8.3, 10.7 Hz), 3.71-3.74 (m, 1H), 3.94-3.98 (m, 1H), 7.22-7.48 (m, 11H), 7.68-7.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 148.9, 143.8, 141.5, 140.1, 128.8, 128.7, 128.6, 128.1, 127.9, 127.5, 126.3, 126.0, 125.1, 120.4, 120.2, 107.6, 81.5, 75.7, 73.0, 63.0, 49.0, 39.5, 34.0, 33.3, 32.6, 27.0, 26.5, 26.4, 26.3, 25.9. Anal. Calcd for $C_{32}H_{39}NO_3$: C, 79.14 H, 8.09 N, 2.88. Found: C, 79.12 H, 8.07 N, 2.85.

12b: Yield : 79%; $[\alpha]_D$ = +20.32 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3460, 3290, 3060, 2980, 2950, 2870, 1450, 1370, 1240, 1170, 1070, 910, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.43 (d, 3H, *J* = 6.1 Hz), 0.62 (d, 3H, *J* = 6.3 Hz), 1.07-1.11 (m, 1H), 1.17 (s, 3H), 1.37 (s, 3H), 1.39-1.49 (m, 2H), 2.42 -2.45 (m, 1H), 3.29 (dd, 1H, *J* = 2.9, 8.6 Hz), 3.54 (dd, 1H, *J* = 7.6, 10.9 Hz), 3.70 (dd, 1H, *J* = 4.2, 10.9 Hz), 4.04-4.09 (m, 1H), 7.23-7.45 (m, 11H), 7.72-7.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 148.9, 144.0, 141.4, 140.2, 128.8, 128.7, 128.5, 128.1, 127.8, 127.4, 126.2, 126.0, 125.2, 120.3, 120.1, 107.6, 81.0, 75.9, 72.9, 62.8, 49.6, 41.3, 27.0, 26.6, 24.1, 22.9, 22.1. Anal. Calcd for $C_{29}H_{35}NO_3$: C, 78.17 H, 7.92 N, 3.14. Found: C, 78.13 H, 7.93 N, 3.15.

12c: Yield : 78%; $[\alpha]_D$ = +35.28 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3460, 3340, 3230, 3060, 2980, 2930, 2870, 1740, 1450, 1370, 1240, 1170, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.66 (t, 3H, *J* = 7.5 Hz), 1.11 (s, 3H), 1.12-1.16 (m, 1H), 1.32 (s, 3H), 1.44-1.50 (m, 1H), 2.26-2.28 (m, 1H), 2.29 (s, 1H), 3.29 (dd, 1H, *J* = 3.38, 8.58 Hz), 3.51 (dd, 1H, *J* = 7.14, 11.0 Hz), 3.63 (dd, 1H, *J* = 4.2, 10.9 Hz), 3.97-4.01 (m, 1H), 7.17-7.25 (m, 6H), 7.30-7.37 (m, 5H), 7.66-7.70 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 149.0, 144.2, 141.1, 140.2, 128.7, 128.6, 128.5, 127.8, 127.4, 126.1, 126.0, 125.4, 120.2, 120.1, 107.7, 80.8, 76.3, 72.9, 62.7, 53.9, 27.0, 26.6, 24.3, 10.9. Anal. Calcd for $C_{27}H_{31}NO_3$: C, 77.67 H, 7.48 N, 3.35. Found: C, 77.63; H, 7.49 N, 3.35.

General preparation of 13a, 13b and 13c : Representative procedure for the preparation of 1-cyclohexyl-1,2-dideoxy-3,4-*O*-isopropylidene-5-*O*-mesyl-2-[(9-phenylfluoren-9-yl)amino]-*D*-xylitol (13a). To a solution of **12a** (0.73 g, 1.51 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (0.32 mL, 2.27 mmol) at 0 °C. The reaction mixture stirred for 20 min and added MsCl (0.15 mL, 1.97 mmol) and stirred for 30 min. The reaction quenched by addition of $NaHCO_3$ solution (10%, 10 mL) and the reaction mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (CH_2Cl_2) to afford pure **13a** (0.84 g, 99%) as an oil.

13a: $[\alpha]_D$ = +11.15 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3350, 2990, 2920, 2850, 1740, 1450, 1360, 1250, 1250, 1180, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.22-0.26 (m, 1H), 0.43-0.47 (m, 1H), 0.82-0.88 (m, 2H), 0.93-0.98 (m, 3H), 0.99-1.05 (m, 1H), 1.13-1.15 (m, 1H), 1.22-1.27 (m, 5H), 1.42-1.49 (m, 5H), 1.99 (s, 1H), 2.22 (s, 1H), 3.50 (dd, 1H, *J* = 2.3, 8.4 Hz), 4.01 (dd, 1H, *J* = 6.3, 11.1 Hz), 4.35 (dd, 1H, *J* = 2.7, 11.1 Hz), 4.42 - 4.46 (m, 1H), 7.18-7.32 (m, 8H), 7.37-7.42 (m, 3H), 7.66-7.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 149.1, 145.0, 141.1, 140.2, 128.6, 128.4, 127.9, 127.7, 127.2, 126.2, 125.7, 125.5, 120.2, 119.9, 109.0, 78.4, 74.6, 72.6, 69.8, 48.3, 41.0, 37.7, 33.8, 33.6, 32.5, 27.3, 26.8, 26.4, 26.0, 25.9, 14.2. Anal. Calcd for $C_{33}H_{41}NO_5S$: C, 70.31 H, 7.33 N, 2.48. Found: C, 70.33; H, 7.35 N, 2.45.

13b: Yield : 98%; $[\alpha]_D$ = +14.27 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3330, 3060, 2980, 2950, 2870, 1450, 1360, 1180, 960, 740

cm^{-1}; ^{1}H NMR(500 MHz, $CDCl_3$) δ 0.27 (d, 3H, J = 6.5 Hz), 0.47 (d, 3H, J = 6.5 Hz), 0.74-0.80 (m, 1H), 1.18-1.33 (m, 3H), 1.30 (s, 3H), 1.50 (s, 3H), 2.02 (s, 1H), 2.15 (s, 1H), 3.01 (s, 3H), 3.55 (dd, 1H, J = 2.1, 8.5 Hz), 3.94 (dd, 1H, J = 5.9, 11.2 Hz), 4.28 (dd, 1H, J = 2.8, 11.2 Hz), 4.46-4.49 (m, 1H), 7.19-7.31 (m, 8H), 7.36-7.42 (m, 3H), 7.66-7.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 149.1, 145.1, 141.0, 140.3, 128.6, 128.4, 127.8, 127.2, 126.1, 125.7, 125.6, 120.1, 119.9, 109.0, 78.2, 74.5, 72.6, 69.4, 49.1, 42.6, 37.7, 27.4, 26.8, 24.4, 23.2, 21.3. Anal. Calcd for $C_{30}H_{37}NO_5S$: C, 68.81; H, 7.21; N, 7.12. Found: C, 68.83; H, 7.25; N, 7.15.

13c: Yield : 95%; $[\alpha]_D$ = +48.88 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3340, 2980, 2940, 1730, 1450, 1360, 1250, 1180, 970, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.54 (t, 3H, J = 7.4 Hz), 1.14-1.16 (m, 1H), 1.12-1.18 (m, 1H), 1.30 (s, 3H), 1.47 (s, 3H), 2.03 (m, 1H), 2.21 (s, 1H), 3.02 (s, 3H), 3.61 (dd, 1H, J = 2.84, 8.42 Hz), 3.96 (dd, 1H, J = 5.85, 11.2 Hz), 4.29 (dd, 1H, J = 2.6, 11.3 Hz), 4.37-4.41 (m, 1H), 7.19-7.27 (m, 7H), 7.30-7.33 (m, 1H), 7.35-7.38 (m, 1H), 7.41-7.42 (m, 2H), 7.68 (dd, 2H, J = 7.7, 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 149.1, 145.3, 140.6, 140.3, 128.5, 128.4, 127.8, 127.7, 127.2, 126.1, 125.6, 125.4, 120.1, 119.9, 109.1,78.3, 75.0, 72.5, 69.3, 53.0, 37.7, 27.3, 26.8, 26.1, 14.2, 10.3. Anal. Calcd for $C_{28}H_{33}NO_5S$: C, 67.85; H, 6.71; N, 2.83. Found: C, 67.83; H, 6.75; N, 2.85.

General preparation of 14a, 14b and 14c : Representative procedure for the preparation of 1-cyclohexyl-1,2,5-tridideoxy-3,4-O-isopropylidene-5-iodo-2-[(9-phenylfluoren-9-yl)amino]- *D*-lyxose (14a). To a solution of **13a** (1.2 g, 2.13 mmol) in DMF (20 mL) was added LiI (0.31g, 2.33 mmol) at rt. The reaction mixture stirred for 36 h at 75 °C and cooled down to rt with cold water. To the reaction mixture added saturated $NaHCO_3$ solution (10 mL) and stirred for 5 min and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 3:1, v/v) to afford pure **14a** (1.01 g, 80%) as an oil.

14a: $[\alpha]_D$ = +14.56 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3330, 3040, 2930, 2850, 1450, 980, 870, 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40-1.66 (m, 10H), 1.33 (s, 3H), 1.39 (s, 3H), 1.42-1.47 (m, 1H), 1.82-1.87 (m, 2H), 2.22-2.43 (bs, NH), 2.92-3.01 (m, 1H), 3.23 (dd, 2H, J = 2.8 Hz), 3.31-3.34 (m, 1H), 3.38-3.41 (m, 1H), 7.16-7.30 (m, 8H), 7.35-7.40 (m, 3H), 7.63-7.69 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150 5, 148 7, 144.4, 142.0, 141.1, 127.7, 127.3, 126.6, 126.3, 126.0, 125.4, 124.8, 124.3, 119.5, 118.7, 107.4, 81.4, 74.7, 71.4, 59.3, 48.2, 44.5, 26.6, 26.1, 22.5, 22.3, 22.1, 22.0, 15.1, 6.0.

14b: Yield : 85%; $[\alpha]_D$ = +21.34 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3330, 3060, 2950, 2870, 1450, 1370, 1240, 1170, 1120, 1040, 890, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.21 (d, 3H, J = 6.5 Hz), 0.51 (d, 3H, J = 6.5 Hz), 0.67-0.72 (m, 1H), 0.86-0.90 (m, 1H), 1.39 (s, 3H), 1.55 (s, 3H), 2.06 (s, 1H), 2.16 (s, 1H), 2.88 (dd, 1H, J = 5.9, 10.6 Hz), 3.08 (dd, 1H, J = 4.5, 10.6 Hz), 3.49 (dd, 1H, J = 1.5, 7.8 Hz), 4.17-4.21 (m, 1H), 7.18-7.29 (m, 8H), 7.30-7.31 (m, 1H), 7.36-7.40 (m, 1H), 7.42-7.44 (m, 2H), 7.66-7.71 (m, 2H); ^{13}C NMR(125 MHz, $CDCl_3$) δ 151.3, 149.3, 145.4, 141.0, 140.3, 128.5, 128.3, 127.9, 127.7, 127.2, 126.2, 125.8, 125.7, 120.0, 119.9, 108.5, 82.5, 75.5, 72.5, 60.4, 49.4, 43.2, 27.6, 27.4, 24.6, 23.6, 21.0, 14.2, 6.8.

14c: Yield : 81%; $[\alpha]_D$ = +11.56 (*c* 2.00, $CHCl_3$); IR (KRS-5) 3430, 3060, 2980, 2930, 2870, 1450, 1370, 1240, 1030, 730 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.53 (t, 3H, J = 7.4 Hz), 0.92-0.97 (m, 1H), 1.05-1.11 (m, 1H), 1.39 (s, 3H), 1.51 (s, 3H), 2.02 (s, 1H), 2.25 (s, 1H), 2.92 (dd, 1H, J = 6.0, 10.6 Hz), 3.12 (dd, 1H, J = 4.0, 10.6 Hz), 3.53 (dd, 1H, J = 2.4, 7.8 Hz), 4.08-4.11 (m, 1H), 7.16-7.25 (m, 5H), 7.27-7.30 (m, 2H), 7.30-.32 (m, 1H), 7.35-7.38 (m, 1H), 7.42-7.44 (m, 2H), 7.67-7.70 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 149.2, 145.5, 140.5, 140.3, 128.4, 128.3, 128.0, 127.9, 127.7, 127.1, 126.2, 125.7, 125.4, 120.0, 119.9, 119.6, 108.6, 82.6, 76.0, 72.4, 53.0, 27.6, 27.4, 26.7, 10.2, 6.9.

General preparation of 15a, 15b and 15c : Representative procedure for the preparation of (3*S*,4*S*)-4-(9-phenyl-9H-fluoren-9-ylamino)-5-cyclohexylpent-1-en-3-ol (15a). To a solution of **14a** (1.36 g, 4.11 mmol) in THF (15 mL) was added *n*-BuLi (1.6 M in hexane, 7.69 mL, 12.3 mmol) at 0 °C. The reaction mixture stirred for 20 min and quenched by addition of saturated NH_4Cl solution (10 mL) and the reaction mixture extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 7:1, v/v) to afford pure **15a** (1.57 g, 90%) as an oil.

15a: IR (KRS-5) 3450, 3390, 3310, 3060, 2920, 2850, 1450, 1070, 930, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.27-0.29 (m, 1H), 0.46-0.51 (m, 1H), 0.82-0.90 (m, 6H), 1.15-0.31 (m, 2H), 1.42-1.50 (m, 3H), 2.13-2.17 (m, 1H), 2.58 (s, 2H), 3.62-3.64 (m, 1H), 4.99-5.01 (m, 1H), 5.12-5.16 (m, 1H), 5.48-5.55 (m, 1H), 7.17-7.40 (m, 11H), 7.65-7.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.4, 149.0, 145.3, 141.0, 140.2, 139.6, 128.4, 128.3, 127.8, 127.2, 126.4, 126.1, 125.4, 120.0, 119.9, 115.4, 74.1, 72.6, 54.2, 41.6, 34.0, 33.6, 32.8, 26.4, 26.2, 26.1, 14.1.

15b: IR (KRS-5) 3570, 3420, 3310, 3060, 2950, 2870, 1450, 1280, 1030, 920, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.31 (d, 3H, J = 6.2 Hz), 0.51 (d, 3H, J = 6.2 Hz) 0.80-0.90 (m, 2H), 1.20-1.36 (m, 2H), 2.09-2.12 (m, 1H), 2.40 (s, 1H), 3.63-3.65 (m, 1H), 4.98 (d, 1H, J = 10.5 Hz), 5.12 (d, 1H, J = 17.2 Hz), 5.46-5.51 (m, 1H), 7.19-7.40 (m, 11H), 7.66-7.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 140.0, 128.4, 127.8, 127.7, 127.2, 126.4, 126.0, 125.5, 120.0, 119.8, 115.3, 74.0, 54.8, 43.2, 24.5, 23.1, 21.6.

15c: IR (KRS-5) 3600, 3410, 3340, 3060, 2960, 2930, 2870, 1450, 1380, 1280 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56-0.59 (t, 3H, J = 7.4 Hz), 0.84-0.96 (m, 2H), 0.99-1.09 (m, 1H), 1.25 (s, 1H), 2.01- 2.12 (m, 1H), 3.71-3.73 (m, 1H), 5.01-5.03 (m, 1H), 5.14-5.18 (m, 1H), 5.43-5.50 (m, 1H), 7.18- 7.46 (m, 11H), 7.68 (dd, 2H, J = 7.5, 13.9 Hz)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 141.5, 140.6, 136.9, 129.4, 128.6, 128.2, 127.7, 126.3, 125.8, 118.2, 79.1, 67.8, 56.3, 24.6, 9.6.

General preparation of 16a, 16b and 16c : Representative procedure for the preparation of (3*S*,4*S*)-3-benzyloxy-5-cyclohexyl-4-(9-phenyl-9H-fluoren-9-ylamino)-1-penten (17a). To a solution of **15a** (1.20 g, 3.54 mmol) in THF (15 mL) was added slowly NaH (0.15 g, 6.37 mmol) at 0 °C. The reaction

mixture stirred for 10 min. and added benzylbromide (0.72 g, 4.25mmol) and stirred for 30 h at rt. The reaction quenched by addition of saturated $NaHCO_3$ solution (15 mL) and the reaction mixture extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 10:1, v/v) to afford pure **16a** (1.64 g, 90%) as an oil.

16a: IR (KRS-5) 3330, 3060, 3030, 2920, 2850, 2360, 1450, 1110, 1070, 740, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.40-0.43 (m, 1H), 0.54-0.59 (m, 1H), 0.83-0.88 (m, 2H), 0.99-1.08 (m, 3H), 1.25 - 1.30 (m, 3H), 1.43-1.45 (m, 1H), 1.51-1.53 (m, 2H), 1.98 (s, 1H), 2.39-2.44 (m, 1H), 3.28-3.29 (m, 1H), 3.90 (d, 1H, J = 12.3 Hz), 4.04 (d, 1H, J = 12.3 Hz), 5.15-5.23 (m, 2H), 5.90-5.97 (m, 1H), 7.03-7.07 (m, 2H), 7.13-7.28 (m, 11H), 7.32-7.35 (m 1H), 7.43-7.45 (m, 2H), 7.57-7.59 (m, 1H), 7.67 (d, 1H, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.4, 150.3, 145.8, 140.8, 139.1, 136.1, 128.4, 128.2, 128.1, 128.0, 127.8, 127.4, 127.2, 127.1, 126.3, 126.2, 125.6, 120.0, 119.7, 81.9, 72.8, 70.1, 52.0, 39.8, 34.0, 33.5, 32.9, 26.6, 26.4, 26.2.

16b: IR (KRS-5) 3330, 3060, 3030, 3000, 2870, 1450, 1360, 1110, 1070, 1030, 740, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.40 (d, 3H, J = 6.5 Hz), 0.54 (d, 3H, J = 6.5 Hz), 0.79-0 93 (m, 1H), 1.20- 1.30 (m, 2H), 1.41-1.48 (m, 1H), 2.38-2.41 (m, 1H), 3.30-3.32 (m, 1H), 3.91 (d, 1H, J = 12.3 Hz), 4.06 (d, 1H, J = 12.3 Hz), 5.13-5.22 (m, 2H), 5.89-5.96 (m, 1H), 6.98-7.07 (m, 2H), 7.19-7.27 (m, 8H), 7.34-7.36 (m, 4H), 7.43-7.45 (m, 2H), 7.58-7.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 139.1, 136.1, 128.4, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.4, 127.2, 127.1, 127.0, 126.3, 126.1, 125.7, 119.8, 119.7, 117.1, 82.1, 72.8, 72.2, 70.2, 53.0, 41.4, 24.1, 23.0, 22.2.

16c: IR (KRS-5) 3330, 3060, 3030, 2960, 2930, 2870, 1490, 1450, 1230, 1070, 930 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.62 (t, 3H, J = 7.4 Hz), 0.90-0.99 (m, 1H), 1.14-1.22 (m, 1H), 2.28-2.32 (m, 2H), 3.39-3.41 (m, 1H), 4.03 (d, 1H, J = 12.2 Hz), 4.27 (d, 1H, J = 12.2 Hz), 5.14-5.24 (m, 2H), 5.73-5.80 (m, 1H), 7.04-7.36 (m, 14H), 7.41-7.46 (m, 2H), 7.61-7.66 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150 5, 150.3, 146.1, 140.5, 140.2, 138.9, 136.0, 128.4, 128.2, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 127.3, 127.2, 127.0, 126.2, 126.0, 125.8, 119.7, 118.0, 82.3, 72.9, 72.2, 70.2, 57.0, 23.8, 10.0.

General preparation of 17a, 17b and 17c : Representative procedure for the preparation of (2*R*,3*R*)-2-benzyloxy-4-cyclohexyl-3-(9-phenyl-9H-fluoren-9-ylamino)-1-pentanoic acid (17a). To a solution of **16a** (1.00 g, 1.95 mmol) in acetone (20 mL) was added NMO (0.66 g, 6.23 mmol) and catalytic amount of OsO_4 at 0 °C. The reaction mixture stirred for 12 h, and added water (30 mL) and stirred for 10 min at rt. The reaction mixture extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude product dissolved in EtOH/H_2O (1:1, 20 mL) and added $NaIO_4$ (0.54 g, 2.53 mmol) at rt. and stirred for 1h. The solvent was evaporated under vacuo and the crude mixture dissolved in THF/H_2O (1:1, 20 mL) and added K_2CO_3 (0.54 g, 0.39 mmol) and stirred for 5h. at rt. The reaction mixture extracted with EtOAc (3 × 30 mL) and combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 1:2, v/v) to afford pure **17a** (0.78 g, 75 %) as an oil.

17a: IR (KRS-5) 3380, 3030, 2950, 2920, 2840, 1710, 1640, 1430, 1270, 1210, 710, 670 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34-1.36 (m, 2H), 1.40-1.44 (m, 11H), 2.01-2.10 (bs, NH), 3.25-3.34 (m, 1H), 3.94 (d, 1H, J = 12.4 Hz), 7.06-7.07 (m, 3H), 7.14-7.19 (m, 5H), 7.34-7.55 (m, 2H), 7.60-7.89 (m, 8H), 11.0 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 143.2, 142.5, 141.9, 140.3, 137.5, 137.2, 136.4, 136.2, 129.0, 129.2, 128.9, 128.7, 128.4, 128.1, 127.9, 127.6, 127.5, 127.3, 126.5, 126.3, 89.6, 73.9, 67.0, 45.1, 35.4, 32.0, 31.4, 28.1, 27.5, 25.1, 24.6.

17b: IR (KRS-5) 3390, 3060, 2960, 2920, 2850, 1720, 1650, 1450, 1270, 1110, 740, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.35 (d, 3H, J = 6.4 Hz), 0.68 (d, 3H, J = 6.4 Hz), 0.96-1.01 (m, 1H), 1.24- 1.27 (m, 1H), 1.33-1.40 (m, 1H), 1.42-1.48 (m, 1H), 2.54-2.59 (m, 1H), 3.15 (d, 1H, J = 4.2 Hz), 4.01 (d, 1H, J = 12.4 Hz), 4.45 (d, 1H, J = 12.4 Hz), 6.98-7.05 (m, 2H), 7.12-7.16 (m, 1H), 7.22- 7.37 (m, 12H), 7.44-7.55 (m, 2H), 7.73-7.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172 0, 147.9, 147.0, 142.6, 141.2, 139.7, 137.5, 129.4, 129.2, 128.9, 128.5, 128.4, 128.3, 128.0, 127.6, 127.4, 125.7, 125.6, 124.8, 120.5, 120.3, 72.5, 72.4, 52.0, 39.3, 23.9, 23.2, 21.6.

17c: IR (KRS-5) 3330, 3060, 2960, 2930, 2870, 1730, 1600, 1450, 1210, 1120 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.70 (t, 3H, J = 7.4 Hz), 1.08-1.17 (m, 1H), 1.24-1.27 (m, 1H), 1.63-1.71 (m, 1H), 2.39-2.43 (m, 1H), 3.17 (d, 1H, J = 4.3 Hz), 4.00 (d, 1H, J = 12.3 Hz), 4.51 (d, 1H, J = 12.3 Hz), 7.01-7.04 (m, 2H), 7.08-7.16 (m, 1H), 7.21-7.29 (m, 5H), 7.31-7.36 (m, 2H), 7.44-7.47 (m, 1H), 7.53 (d, 1H, J = 7.5 Hz), 7.72 (d, 1H, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 147.6, 147.0, 142.7, 141.3, 139.6, 137.5, 129.4, 129.3, 129.0, 128.4, 128.3, 128.0, 127.6, 127.5, 125.7, 125.4, 124.9, 120.5, 120.3, 72.8, 72.5, 55.7, 22.8, 10.5.

Methyl *N*-[(2*S*,3*S*)-2-benzyloxy-4-cyclohexyl-3-(9-phenyl-9H-fluoren-9-ylamino)butanoyl-L-leucinate (18). To a mixed solution of **17** (0.57 g, 1.08 mmol), L-leu-OCH_3 (0.41 g, 3.24 mmol) and HOBT in THF (10 mL) with catalytic amount of *p*-TsOH was added dropwise DCC (0.16 g, 1.19 mmol) in THF (4 mL) at 0 °C. The reaction mixture stirred for 5 min and added Et_3N (0.22 mL, 1.60 mmol) and stirred for 5 h at rt. The reaction mixture filtered with celite sintered glass filter. The organic layer treated with saturated $NaHCO_3$ and extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo. The crude mixture was purified by flash column chromatography (hexane/EtOAc, 5:1, v/v) to afford pure **18** (0.53 g, 75 %) as an oil.

IR (KRS-5) 3480, 3310, 3060, 2960, 2870, 2120, 1740, 1660, 1450, 1210, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.79 (t, 3H, J = 7.4 Hz), 0.88 (d, 6H, J = 6.4 Hz), 1.06-1.11 (m, 1H), 1.25-1.29 (m, 1H), 1.35-1.38 (m, 1H), 1.40-1.49 (m, 2H), 1.57-1.61 (m, 1H) 2.29-2.34 (m, 1H), 2.31-2.32 (m, 1H), 3.25 (d, 1H, J = 9.5 Hz), 3.42 (d, 1H, J = 3.5 Hz), 3.70 (s, 3H), 3.81 (d, 1H, J = 11.9 Hz), 3.92 (d, 1H, J = 11.9 Hz), 4.51-4.56 (m, 1H), 6.96-6.99 (m, 3H), 7.13-7.18 (m, 4H), 7.19-7.25 (m, 3H), 7.29-7.33 (m, 3H), 7.41-7.44 (m, 3H), 7.64-7.67 (m, 2H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 173.0, 171.7, 151.4, 150.1, 145.7, 140.5, 140.2, 137.6, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 126.9, 126.3, 126.2, 119.7, 119.6, 80.2, 72.7, 72.4, 56.0, 55.8, 52.2, 50.0, 41.4, 35.0, 25.5, 24.9, 24.8, 24.7, 24.2, 22.8, 22.0, 11.4.

***N*-[(2*S*,3*S*)-3-Amino-2-hydroxy-4-cyclohexylbutanoyl]-L-leucine (20).** To a solution of **18** (0.80 g, 1.22 mmol) in THF/H_2O (2:1, 20 mL) was LiOH (0.05 mg, 2.4 mmol) at 0 °C. The reaction mixture stirred for 3 h at rt. and added 3% HCl (15 mL). The reaction mixture extracted with *i*-PrOH/CH_2Cl_2 (1:3, 40 mL) and the combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated under vacuo to give crude product **19**. The crude product **19** was hydrogenated with 10% Pd/C (0.09 g) in MeOH (15 mL) at 70 °C for 10 h. The reaction mixture was filtered through celite and evaporated under vacuo to give crude solid product. The filterate and solid were subjected to ion-exchange chromatography (Dowex 50W-X8, eluting 3 N NH_3 in H_2O) to afford pure **20** (0.32 g, 83 %) as a solid. mp 201-203 °C; $[\alpha]_D$ = -13.6 (*c* 1.50, 1N HCl); IR (KRS-5) 3400, 3360, 3350, 2970, 2820, 1720, 1670, 1470, 1200, 670 cm^{-1}; ^1H NMR (500 MHz, D_2O) δ 0.90 (d, 6H, *J* = 6.4 Hz), 1.25-1.47 (m, 13H), 1.74(m, 2H), 1.85(m, 1H), 2.90 (m, 1H), 4.39 (d, 1H, *J* = 8.9 Hz), 4.42 (d, 1H, *J* = 13.5 Hz) ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 172.7, 73.1, 53.5, 52.4, 41.2, 35.9, 33.5, 33.2, 31.4, 29.6, 28.9, 25.8, 23.6, 23.3, 22.1. Anal. Calcd for $C_{16}H_{30}N_2O_4$: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.15; H, 9.65; N, 8.89.

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