DOI: 10.1002/ejoc.200800770

Synthesis of Hybrids of D-Glucose and D-Galactose with Pyrrolidine-Based Iminosugars as Glycosidase Inhibitors

Venkata Ramana Doddi,[a] Hari Prasad Kokatla,[a] A. P. John Pal,[a] Ranjan K. Basak,[a] and Yashwant D. Vankar*[a]

Keywords: Glycosidase inhibitors / Iminosugars / Azasugars / Oxidative cyclization

Sugar–iminosugar hybrid molecules made up of D-glucose and D-galactose with pyrrolidine-based iminosugars, viz. 1,4-dideoxy-1,4-imino-L-xylitol and 1,4-dideoxy-1,4-imino-L-lyxitol, are synthesized from glycal epoxides and found to be moderate glycosidase inhibitors.

Introduction

Naturally occurring iminosugars (also known as azasugars) or their synthetic analogues are classified as glycomimetics due to their structural resemblance to sugars and many of them act as good glycosidase inhibitors.[1] These inhibitors have found applications as antineoplastic,[2] antidiabetic[3] and antiviral agents.[4] Among these, polyhydroxylated piperidine and pyrrolidine alkaloids and their synthetic analogues are more important.[5,6] MDL 73945 (**1**) (Figure 1), a disaccharide mimetic possessing piperidine based iminosugar and a sugar entity within the molecule, is known to show promising antidiabetic activity.[7] Pyrrolidine-derived iminosugars are also known[5] to exhibit powerful glycosidase inhibition activity though the stereochemical similarity between these iminosugars and the appropriate hexoses or enzyme-bound intermediates derived from it is not apparent. 1,4-Dideoxy-1,4-imino-D-arabinitol **2** is a potent α-glucosidase inhibitor[8] and 1,4-dideoxy-1,4-imino-D-lyxitol **3** is an α-galactosidase inhibitor.[9]

Recently, design and synthesis of hybrid molecules have gained importance as they could be useful in improving or altering the properties of pharmaceutically important molecules.[10] As part of our ongoing programme towards the design and synthesis and biological evaluation of iminosugars[11a,11b] including hybrid sugars[11c–11f] as glycosidase inhibitors, in this paper we wish to report the synthesis and biological evaluation of the hybrid molecules **6**–**9** derived through domain integration of pyrrolidine-based iminosugars: 1,4-dideoxy-1,4-imino-L-xylitol **4**,[12] 1,4-dideoxy-1,4-imino-L-lyxitol **5**,[13] and sugar entities.

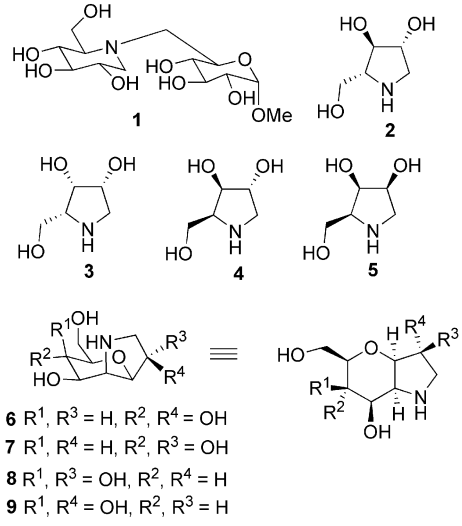


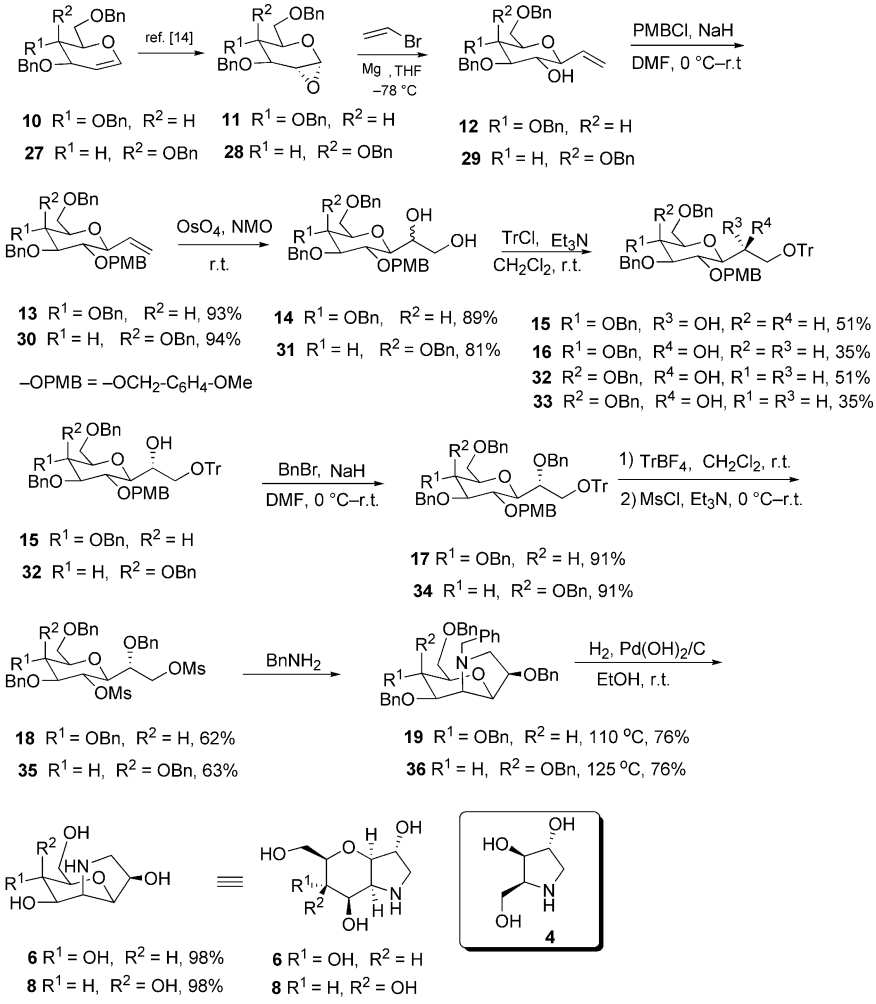
Figure 1. Piperidine- and pyrrolidine-based iminosugars.

Results and Discussions

Thus, the synthesis emanated from 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glucopyranose **11** which can be easily obtained from tri-*O*-benzylglucal (**10**), by reaction with in situ generated DMDO from a known procedure developed by Dondoni et al.[14] (Scheme 1). A regiospecific and stereospecific ring opening of oxirane **11** with vinylmagnesium bromide[15] in THF at –78 °C gave an alcohol **12** as a single diastereomer and it was protected as its *p*-methoxybenzyl ether (–O-PMB) **13** by treating with *p*-methoxybenzyl chlo-

[a] Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India
Fax: +91-512-259-0007
E-mail: vankar@iitk.ac.in

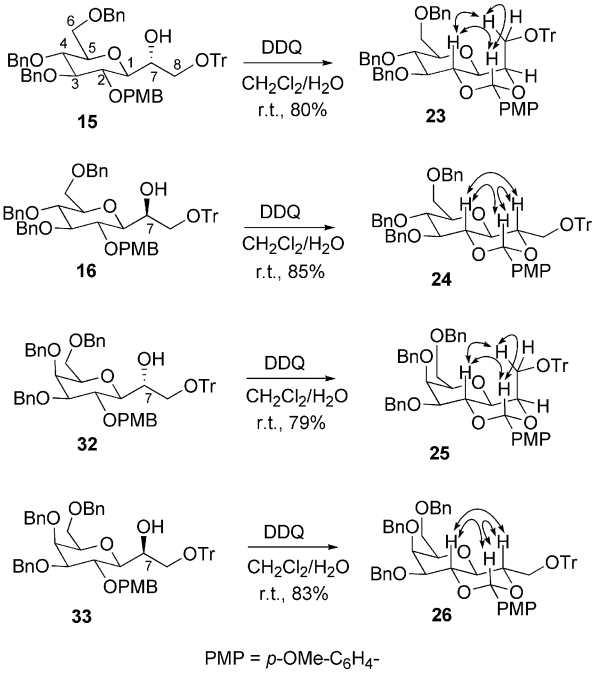
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.



Scheme 1.

ride and NaH as a base. Dihydroxylation of olefin **13** with OsO_4 and NMO furnished a mixture of the corresponding diastereomeric diols **14** in 3:2 ratio as an inseparable mixture. However, protection of the primary hydroxyl group with a trityl group permitted the separation of the diastereomeric secondary alcohols **15** and **16** by SiO_2 column chromatography. The stereochemical outcome of this dihydroxylation follows Kishi's empirical rule.[16] These secondary alcohols **15** and **16** were converted uneventfully to the cyclized compounds **23** and **24**, respectively, by oxidative ring closure using DDQ[17] (see Scheme 2). The nOe correlations at this stage, served to confirm the configuration at C-7 in compounds **15** and **16** and the equatorial nature of the *p*-methoxyphenyl group in the two acetals **23** and **24** as well.

Protection of the secondary hydroxyl group in **15** with benzyl group gave the differentially protected compound **17**. We aimed at the deprotection of both O-PMB ether and trityl group in a single step using trifluoroacetic acid as both the groups are acid labile, however, the reaction yielded a complex mixture of products. Treatment of **17** with $TrBF_4$ in CH_2Cl_2,[18] a recently developed methodology from our group for the deprotection of anomeric –OMe group, at ambient temperature gave a polar product which, without further purification, was subjected to mesylation to obtain mesylate **18**. Presence of two singlet peaks at δ = 2.90 and 2.85 ppm for –OMs group and absence of OMe at δ = 3.74 ppm as well as decrement of protons in the aromatic region of the ^{1}H NMR spectrum of compound **18** confirmed its structure. This served as an evidence for the deprotection of trityl group with $TrBF_4$ under dilute conditions.[18] Treatment of the dimesylate derivative **18** with neat benzylamine at 110 °C gave the pyrrolidine derivative **19** by sequential intermolecular and intramolecular nucleophilic substitutions. The ^{1}H NMR spectrum showed the complete disappearance of mesylate peaks and increment in the phenylic protons which confirmed the formation of pyrrolidine system **19**. This was further confirmed from its mass spectrum which showed HRMS $[M + H]^+$ peak at 656.3376 (calculated 656.3371).[19] Pyrrolidine derivative **19** on treatment with 20% $Pd(OH)_2/C$ in methanol at 5 atm H_2 gave the hybrid molecule **6** in 96% yield. Bicyclic pyrrolidine **6** represents a hybrid of D-glucose and pyrrolidine azasugar **4** as shown in Scheme 1. Likewise, the bicyclic pyrrolidine **7** was synthesized from the compound **16** using the same synthetic sequence and reaction conditions as shown in

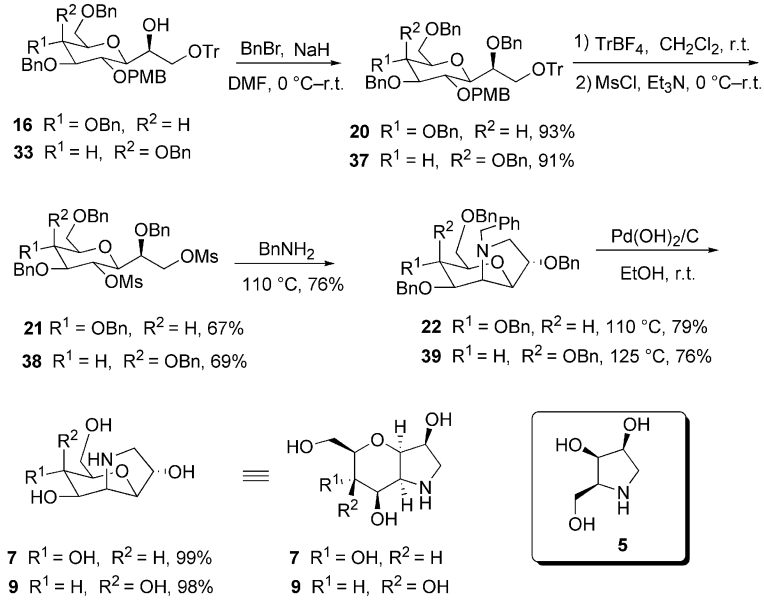


Scheme 2. Diagnostic nOe correlations for compounds **23**, **24**, **25** and **26**.

Scheme 3. Bicyclic pyrrolidine **7** represents a hybrid of D-glucose and pyrrolidine azasugar **5** (Scheme 3).

Compounds **8** (Scheme 1) and **9** (Scheme 3) synthesized from 3,4,6-tri-*O*-benzyl-D-galactal **27** are hybrids of D-galactose with pyrrolidine-based iminosugars: 1,4-dideoxy-1,4-imino-L-xylitol **4** and 1,4-dideoxy-1,4-imino-L-lyxitol **5**, respectively. The synthetic pathway follows the same sequence as used for the synthesis of hybrids **6** and **7** from 3,4,6-tri-*O*-benzyl-D-glucal **10**. The nOe correlations of compounds **25** and **26** indicated in Scheme 2 served to confirm both the configuration at C-7 in compounds **32** and **33**, as well as the equatorial nature of the *p*-methoxyphenyl group in the two acetals **25** and **26**. Dimesylate derivatives **35** and **38** were subjected to cyclization with neat benzylamine at 125 °C, a temperature comparatively higher than that required for glucal series, gave the pyrrolidine derivatives **36** and **39** by intermolecular followed by intramolecular nucleophilic substitution reactions. Further, cyclization of dimesylates **35** and **38** via consecutive nucleophilic substitution reactions was comparatively slow due to the developing 1,3-diaxial interaction in the galactal ring when it underwent intramolecular nucleophilic substitution reaction.

Enzyme inhibition activity of these hybrid molecules has been studied with only three glycosidases.[20] Thus, the 1,4-dideoxy-1,4-imino-L-xylitol **4** inhibits almond emulsion β-glucosidase at a concentration of 7.3 mM.[12a] Interestingly, in our studies with the same glucosidase, no inhibition was shown for hybrid molecules **6** and **8** of D-glucose and D-galactose with 1,4-dideoxy-1,4-imino-L-xylitol **4** even at 5 mM concentrations. However, **6** showed inhibition of α-galactosidase (coffee beans) at low concentration (0.88 mM) and moderate inhibition of β-galactosidase (bovine) at c = 2.56 mM. The hybrid **8** of D-galactose with 1,4-dideoxy-1,4-imino-L-xylitol **4** showed moderate inhibition of α-glucosidase (yeast) at 4.8 mM concentration and also β-galactosidase (bovine) at c = 1.8 mM. Likewise, the hybrid **7** of D-glucose with 1,4-dideoxy-1,4-imino-L-lyxitol **5** showed only moderate inhibition of α-galactosidase (coffee beans) at c = 1.24 mM. Hybrid molecule **9** showed inhibition against α-galactosidase (coffee beans), and β-galactosidase (bovine) at 1.0 mM and 2.56 mM, respectively (see Table 1). These studies indicate that the hybrid molecules **6**, **7**, **8** and **9** are indeed moderate inhibitors of glycosidases. Interestingly, hybrids **6**, **7** and **9** specifically inhibit galactosidases only. Hybrid **8** only inhibits α-glucosidase along with β-galactos-



Scheme 3.

idase. Clearly, there is a change in terms of specificity as well as the inhibition constant values as a result of the combination of the structural features as aimed in the present studies. This further suggests that structural variations of these hybrid molecules could promote better and specific glycosidase inhibition. We are currently investigating this possibility and will report our results in due course.

Table 1. IC_{50} (mM) values for compounds **6**, **7**, **8** and **9**.[a]

Enzyme	**6**	**7**	**8**	**9**
α-Glucosidase (yeast)	n.i.	n.i.	4.8 mM	n.i.
β-Glucosidase (almonds)	n.i.	n.i.	n.i.	n.i.
α-Galactosidase (coffee beans)	0.8 mM	1.24 mM	n.i.	1.0 mM
β-Galactosidase (bovine)	2.5 mM	n.i.	1.8 mM	2.5 mM
α-Mannosidase (Jack beans)	n.i.	n.i.	n.i.	n.i.

[a] Inhibition studies were carried out at millimolar concentration, optimal pH of the enzymes, and 37 °C; no inhibition (n.i.) at 5 mM concentration of the inhibitor.

Conclusion

In summary, we have synthesized four new hybrids of D-glucose and D-galactose with pyrrolidine-based imino sugars: 1,4-dideoxy-1,4-imino-L-xylitol and 1,4-dideoxy-1,4-imino-L-lyxitol and evaluated against a variety of enzymes that puts them shown them into a class of glycosidase inhibitors. Although the enzyme inhibition activity is moderate, it may be possible to improve the same by appropriately changing the structural features of these molecules. Work in this direction is being pursued. To the best of our knowledge a one pot deprotection of –O-PMB ether and trityl ether with $TrBF_4$, as observed by us in the present study, is not known in the literature.

Experimental Section

General Procedure (A). Benzylation of Alcohols: 60% suspension of NaH in paraffin oil (4.347 mmol) was added in small portions to a stirred solution of an alcohol (2.173 mmol) in DMF (10 mL) at 0 °C. After 30 min benzyl chloride or *p*-methoxybenzyl chloride (2.607 mmol) was added dropwise at 0 °C and the reaction mixture stirred for 4 h at room temperature. Excess of NaH was quenched by pouring the reaction mixture in ice and then extracted with diethyl ether (30 mL) followed by washing with water (3 × 10 mL). The orgnic layer was dried with $MgSO_4$ and concentrated in vacuo and the crude product purified by column chromatography to get benzylated products.

General Procedure (B). Dihydroxylation Using OsO_4-NMO: To a stirred solution of olefin (1 mmol) in acetone/water/*tert*-butyl alcohol (1:1: 0.4, 5 mL) at room temperature, were added NMO·H_2O (1.3 mmol) and OsO_4 (0.004 equiv.). The reaction mixture was stirred for 24–48 h (monitored by TLC) and it was treated with $Na_2S_2O_5$ (1.3 mmol). The reaction mixture was stirred for further 1 h and extracted with EtOAc (2 × 50 mL). The organic layer was washed with 1 N HCl, water and finally with brine, dried with $MgSO_4$ and concentrated in vacuo. Purification was done by silica gel column chromatography to give diols.

General Procedure (C). Tritylation of Primary Alcohols: To a solution of mixture of diols (1 mmol) in CH_2Cl_2 (5 mL) were added trityl chloride (1.1 mmol), Et_3N (2 mmol). The reaction mixture was stirred for 8 h and then the usual work-up with water and CH_2Cl_2 gave a crude product which was purified by flash chromatography to give the pure tritylated compounds.

General Procedure (D). One-Pot Deprotection of *p*-Methoxybenzyl Ether and Trityl Ether Followed by Dimesylation of Diol: To a solution of the protected compound (1 mmol) in dry CH_2Cl_2 (20 mL) was added trityl tetrafluoroborate (1 mmol) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 20–30 min. After completion of the reaction (TLC monitoring), the reaction mixture was quenched with excess of sodium hydrogen carbonate. The organic phase was washed with water, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure to obtain a crude diol. To the stirred solution of a crude diol in CH_2Cl_2 (8 mL) at 0 °C was added Et_3N (3 mmol), followed by MsCl (2.1 mmol) and catalytic amount of DMAP. After 2 h, 5 mL of aqueous solution of $NaHCO_3$ was added and the organic layer was washed with water (2 × 5 mL), followed by brine (5 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification was done by silica gel column chromatography to give the dimesylates.

General Procedure (E). Cyclization of Dimesylates with Benzylamine: The dimesylate (0.5 mmol) was dissolved in benzylamine (5 mL) and stirred for 18 h at 110–125 °C. To the reaction mixture, 10 mL of 1 N HCl was added and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (10 mL), dried with $MgSO_4$, concentrated in vacuo and the crude produt purified by silica gel column chromatography.

General Procedure (F). Deprotection of Benzyl Groups: The cyclized product (0.3 mmol) was dissolved in 5 mL of MeOH and 20% $Pd(OH)_2$/C (300 mg) was added to it. The reaction mixture was stirred under 5 atm H_2 pressure for 30–35 h at room temperature. The catalyst was filtered off through Celite, and concentrated in vacuo to obtain hybrid molecules.

General Procedure (G). Oxidative Cylization with DDQ: A solution of alcohol (0.2 mmol) in CH_2Cl_2/water (9:1, 5 mL) was treated with DDQ (0.2 mmol) at room temperature and stirred for 10–15 min. The reaction mixture was diluted with CH_2Cl_2 and washed with a saturated solution of $NaHCO_3$, water and brine. The organic layer was dried with Na_2SO_4, concentrated and purified by column chromatography to give the cyclized product.

(2*R*,3*R*,4*R*,5*S*,6*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)-6-vinyltetrahydro-2*H*-pyran (13): Alcohol **12** (2 g, 4.34 mmol) was benzylated with PMBCl using the general procedure (A) to give **13** (2.1 g, 93%) as colorless oil. R_f = 0.6 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +65.2 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3063, 3030, 2917, 1612, 1248, 1073, 753, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.22 (m, 15 H), 7.11 (d, *J* = 7.3 Hz, 2 H), 6.84 (d, *J* = 7.3 Hz, 2 H), 6.14 (ddd, *J* = 17.6, 11.0, 5.1 Hz, 1 H), 5.47 (dd, *J* = 17.6, 1.7 Hz, 1 H), 5.42 (dd, *J* = 11.0, 1.7 Hz, 1 H), 4.92 (d, *J* = 12.3 Hz, 1 H), 4.80 (d, *J* = 10.7 Hz, 1 H), 4.77 (d, *J* = 10.7 Hz, 1 H), 4.62–4.53 (m, 3 H), 4.48 (d, *J* = 12.0 Hz, 1 H), 4.44 (d, *J* = 12.0 Hz, 1 H), 3.79 (s, 3 H), 3.78–3.59 (m, 7 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.2, 138.0, 131.9, 130.2, 129.4, 128.3–127.5 (m), 119.7, 113.7, 82.7, 79.6, 78.2, 75.4, 75.0, 74.0, 73.4, 72.5, 71.9, 69.0, 55.2 ppm. ESMS: *m*/*z* 603 $[M + Na]^+$. $C_{37}H_{40}O_6$ (580.28): calcd. C 76.53, H 6.94, O 16.53; found C 76.51, H 6.92.

1-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]ethane-1,2-diol (14):

Olefin **13** (580 mg) was dihydroxylated using the general procedure (B) to give diastereomeric mixture (3:2) **14** (546 mg) as a colorless thick liquid in 89% yield. R_f = 0.4 (hexane/EtOAc, 3:2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3401, 3063, 2924, 1605, 1453, 1090, 736, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.13 (m, 17 H, both isomers), 6.84 (d, J = 8.8 Hz, 2 H, major), 6.83 (d, J = 8.8 Hz, 2 H, minor), 4.86–4.65 (m, 4 H, both isomers), 4.18–4.16 (m, 2 H, both isomers), 3.92–3.81 (m, 2 H, both isomers), 3.88 (s, 3 H, both isomers), 3.88–3.65 (m, 3 H, both isomers), 3.62–3.50 (m, 2 H, both isomers), 2.45 (br. s, 1 H, both isomers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 138.3, 138.0, 129.9–127.7 (m), 114.1, 113.9, 81.4, 78.9, 78.7, 77.4, 77.5, 74.7, 74.8, 74.4, 74.0, 73.8, 73.4, 72.3, 72.4, 70.1, 69.4, 69.0, 64.3, 64.4, 55.2 ppm. ESMS: m/z 637 $[M + Na]^+$. $C_{37}H_{42}O_8$ (614.28): calcd. C 72.29, H 6.89, O 20.82; found C 72.20, H 6.87.

Diol 14 (614 mg) was tritylated using the general procedure (C) to give **15** (441 mg) and **16** (295 mg) in a ratio (3:2) (86%).

(*R*)-1-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]-2-(trityloxy)-ethanol (15): (441 mg, 51%) White solid. R_f = 0.5 (hexane/EtOAc, 4:1). $[\alpha]_D^{28}$ = +32.0 (c = 0.8, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 2855, 1611, 1513, 1492, 1249, 1087, 742, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.13 (m, 32 H), 6.82 (d, J = 6.8 Hz, 2 H), 4.79 (d, J = 11.5 Hz, 1 H), 4.72 (d, J = 11.2 Hz, 1 H), 4.71 (d, J = 10.9 Hz, 1 H), 4.65 (d, J = 11.2 Hz, 1 H), 4.56 (d, J = 11.2 Hz, 1 H), 4.47 (d, J = 12.3 Hz, 1 H), 4.44 (d, J = 10.9 Hz, 1 H), 4.34 (d, J = 12.3 Hz, 1 H), 4.32–4.31 (m, 1 H), 3.95 (dd, J = 8.9, 4.9 Hz, 1 H), 3.91–3.84 (m, 2 H), 3.79 (s, 3 H), 3.64 (dd, J = 8.9, 7.5 Hz, 1 H), 3.49–3.43 (m, 2 H), 3.31 (dd, J = 9.8, 3.2 Hz, 1 H), 3.27–3.20 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 144.1, 138.4, 138.2, 137.7, 130.0–127.0 (m), 114.0, 86.6, 81.5, 79.0, 74.8, 74.4, 73.9, 73.5, 71.9, 69.7, 68.3, 65.1, 55.3, 29.8 ppm. ESMS: m/z 879 $[M + Na]^+$. $C_{56}H_{56}O_8$ (856.40): calcd. C 78.48, H 6.59, O 14.93; found C 78.32, H 6.60.

(*S*)-1-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]-2-(trityloxy)-ethanol (16): (295 mg, 35%) White solid. R_f = 0.49 (hexane/EtOAc, 4:1). $[\alpha]_D^{28}$ = +76.0 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 2855, 1611, 1513, 1492, 1249, 1087, 742, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.10 (m, 32 H), 6.76 (d, J = 8.3 Hz, 2 H), 4.83 (d, J = 11.2 Hz, 1 H), 4.72 (d, J = 10.9 Hz, 1 H), 4.71 (d, J = 10.9 Hz, 1 H), 4.52 (d, J = 11.5 Hz, 1 H), 4.50 (d, J = 11.5 Hz, 1 H), 4.43 (d, J = 11.2 Hz, 1 H), 4.38 (d, J = 12.6 Hz, 1 H), 4.34 (d, J = 12.6 Hz, 1 H), 4.21–4.20 (m, 1 H), 4.13 (dd, J = 8.1, 8.0 Hz, 1 H), 4.00 (br. d, J = 8.9 Hz, 1 H), 3.80–3.76 (m, 1 H), 3.76 (s, 3 H), 3.69 (dd, J = 8.1, 6.3 Hz, 1 H), 3.56–3.51 (m, 2 H), 3.45 (br. d, J = 10.1 Hz, 1 H), 3.36 (dd, J = 9.2, 3.5 Hz, 1 H), 3.27 (dd, J = 9.2, 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.3, 143.9, 138.8, 138.4, 138.1, 130.1–127.0 (m), 113.8, 86.8, 82.2, 78.7, 74.9, 74.5, 74.3, 73.3, 72.9, 70.6, 68.8, 64.9, 55.3, 29.8 ppm. ESMS: m/z 879 $[M + Na]^+$. $C_{56}H_{56}O_8$ (856.40): calcd. C 78.48, H 6.59, O 14.93; found C 78.52, H 6.52.

(2*R*,3*R*,4*S*,5*R*,6*S*)-3,4-Bis(benzyloxy)-6-[(*R*)-1-(benzyloxy)-2-(trityloxy)ethyl]-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran (17): Alcohol **15** (856 mg) was benzylated with BnCl using the general procedure (A) to give **17** (890 mg, 91%) as colorless oil. R_f = 0.6 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = –10.6 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3061, 2924, 2855, 1611, 1513, 1493, 1451, 1092, 1029, 736, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.44 (m, 6 H), 7.29–7.18 (m, 29 H), 7.10 (d, J = 8.5 Hz, 2 H), 6.71 (d, J = 8.5 Hz, 2 H), 4.78 (d, J = 11.4 Hz, 1 H), 4.60 (d, J = 11.4 Hz, 1 H), 4.58 (d, J = 12.4 Hz, 1 H), 4.55 (d, J = 12.4 Hz, 1 H), 4.51 (d, J = 11.7 Hz, 1 H), 4.46 (d, J = 11.4 Hz, 1 H), 4.44 (d, J = 11.4 Hz, 1 H), 4.40 (d, J = 11.7 Hz, 1 H), 4.38 (d, J = 12.0 Hz, 1 H), 4.29 (d, J = 12.0 Hz, 1 H), 4.11 (dd, J = 8.8, 3.4 Hz, 1 H), 4.02 (m, 1 H), 3.91 (t, J = 5.1 Hz, 1 H), 3.85–3.81 (m, 2 H), 3.74 (s, 3 H), 3.65 (m, 1 H), 3.54 (d, J = 2.9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 144.1, 138.8, 138.4, 168.3, 130.4–126.8 (m), 113.6, 86.7, 78.1, 78.0, 75.9, 75.8, 73.7, 73.2, 72.9, 72.4, 71.9, 70.9, 69.2, 64.3, 55.2 ppm. ESMS: m/z 969 $[M + Na]^+$. $C_{63}H_{62}O_8$ (946.45): calcd. C 79.89, H 6.60, O 13.51; found C 79.90, H 6.54.

(*R*)-2-(Benzyloxy)-2-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-(benzyloxymethyl)-3-(methylsulfonyloxy)tetrahydro-2*H*-pyran-2-yl]-ethyl Methanesulfonate (18): Compound **17** (946 mg) was converted to give dimesylate **18** (462 mg, 62%, two steps) as a colorless oil using the general procedure (D). R_f = 0.5 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = +6.2 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3063, 3030, 2924, 1603, 1496, 1093, 1028, 741, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, J = 7.0 Hz, 2 H), 7.36–7.19 (m, 18 H), 5.01 (br. s, 1 H), 4.91 (d, J = 10.2 Hz, 1 H), 4.69–4.61 (m, 3 H), 4.54–4.45 (m, 5 H), 4.39 (dd, J = 11.0, 3.4 Hz, 1 H), 4.16 (d, J = 3.68 Hz, 1 H), 4.12 (dd, J = 6.8, 3.4 Hz, 1 H), 4.08 (d, J = 7.0 Hz, 1 H), 3.94 (br. d, J = 9.0 Hz, 1 H), 3.76 (dd, J = 10.0, 6.3 Hz, 1 H), 3.64 (dd, J = 10.2, 5.8 Hz, 1 H), 3.55 (dd, J = 6.8, 3.4 Hz, 1 H), 2.90 (s, 3 H), 2.85 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 137.5, 137.3, 137.1, 128.7–127.8 (m), 75.0, 74.6, 74.1, 73.4, 73.3, 72.9, 72.7, 72.6, 72.3, 67.8, 67.1, 39.2, 37.3 ppm. ESMS: m/z 763 $[M + Na]^+$. $C_{38}H_{44}O_{11}S_2$ (740.23): calcd. C 61.60, H 5.99, O 23.75, S 8.66; found C 61.51, H 6.00.

(3*R*,3a*R*,5*R*,6*S*,7*R*,7a*S*)-1-Benzyl-3,6,7-tris(benzyloxy)-5-(benzyloxymethyl)octahydropyrano[3,2-*b*]pyrrole (19): Dimesylate **18** (370 mg) was subjected to cylization using the general procedure (E) to give **19** (248 mg, 76%) as a thick liquid. R_f = 0.4 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = –19.5 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3062, 2923, 1602, 1495, 1096, 1027, 735, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.21 (m, 25 H), 5.04 (d, J = 2.9 Hz, 1 H), 4.78 (d, J = 11.4 Hz, 1 H), 4.67–4.52 (m, 6 H), 4.40 (d, J = 11.7 Hz, 1 H), 4.21–4.20 (m, 1 H), 4.15–4.16 (m, 1 H), 3.97 (dd, J = 7.8, 4.6 Hz, 1 H), 3.86 (dd, J = 7.0, 5.3 Hz, 1 H), 3.81 (dd, J = 10.7, 5.3 Hz, 1 H), 3.77–3.71 (m, 4 H), 2.91 (dd, J = 8.0, 12.4 Hz, 1 H), 2.84 (dd, J = 12.4, 4.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 128.4–127.5 (m), 126.8, 97.3, 78.1, 74.5, 74.2, 73.4, 73.1, 71.2, 71.1, 70.5, 68.4, 53.5, 51.9, 29.6 ppm. HRMS calcd. for $C_{43}H_{46}NO_5$ $[M+ H]^+$ 656.3371, found 656.3373.

(3*R*,3a*R*,5*R*,6*S*,7*R*,7a*S*)-5-(Hydroxymethyl)octahydropyrano[3,2-*b*]-pyrrole-3,6,7-triol (6): Compound **19** (196 mg) was subjected to global deprotection using the general procedure (F) to give **6** (60 mg, 98%) as a thick liquid. R_f = 0.3 (MeOH/EtOAc, 1:4). $[\alpha]_D^{28}$ = –13.4 (c = 1.0, H_2O). ^1H NMR (400 MHz, D_2O): δ = 3.75–3.59 (m, 2 H), 4.78 (d, J = 11.4 Hz, 1 H), 3.18–2.92 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.8, 77.2, 73.1, 69.2, 62.5, 50.8, 44.5, 35.5 ppm. ESMS: m/z 206 $[M + H]^+$. $C_8H_{15}NO_5$ (205.10): calcd. C 46.82, H 7.37, N 6.83, O 38.98; found C 46.84, H 7.39, N 6.84.

(2*R*,3*R*,4*S*,5*R*,6*S*)-3,4-Bis(benzyloxy)-6-[(*S*)-1-(benzyloxy)-2-(trityloxy)ethyl]-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran (20): Alcohol **16** (856 mg) was benzylated with BnCl using the general procedure (A) to give **20** (879 mg, 93%) as white solid. R_f = 0.55 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +16.9 (c = 0.8, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 2854, 1612, 1513, 1450, 1248, 1072, 742, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.40 (m, 6 H), 7.26–7.19 (m, 29 H), 7.11 (d, J = 7.8 Hz, 2 H), 6.84 (d, J = 7.8 Hz, 2 H), 4.75 (d, J = 10.7 Hz, 1 H), 4.70 (d, J = 11.0 Hz,

1 H), 4.64–4.46 (m, 6 H), 4.41–4.36 (m, 2 H), 4.27 (dd, *J* = 8.5, 8.7 Hz, 1 H), 4.11 (dd, *J* = 6.8, 3.2 Hz, 1 H), 4.05 (br. d, *J* = 9.5 Hz, 1 H), 3.95–3.94 (m, 1 H), 3.79–3.75 (m, 1 H), 3.78 (s, 3 H), 3.58 (d, *J* = 8.5 Hz, 1 H), 3.53 (dd, *J* = 8.8, 6.8 Hz, 1 H), 3.50–3.43 (m, 1 H), 3.36 (br. d, *J* = 6.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 138.9, 138.6, 130.7, 129.3–126.9 (m), 113.8, 87.2, 82.0, 79.5, 79.4, 78.2, 74.8, 74.6, 73.8, 73.7, 73.3, 73.2, 69.2, 55.2 ppm. ESMS: *m*/*z* 969 [M + Na]$^+$. $C_{63}H_{62}O_8$ (946.45): calcd. C 79.89, H 6.60, O 13.51; found C 79.93, H 6.54.

(*S*)-2-(Benzyloxy)-2-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-(benzyloxymethyl)-3-(methylsulfonyloxy)tetrahydro-2*H*-pyran-2-yl]-ethyl Methanesulfonate (21): Compound **20** (946 mg) was converted to give dimesylate **21** (495 mg, 67%, two steps) as a colorless oil using the general procedure (D). R_f = 0.5 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = +54.8 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3063, 3030, 2924, 1603, 1496, 1093, 1028, 741, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.12 (m, 20 H), 4.81 (d, *J* = 11.2 Hz, 1 H), 4.71 (d, *J* = 11.2 Hz, 1 H), 4.67 (d, *J* = 11.7 Hz, 1 H), 4.66 (d, *J* = 10.7 Hz, 1 H), 4.62 (d, *J* = 11.7 Hz, 1 H), 4.56 (d, *J* = 11.9 Hz, 1 H), 4.48 (d, *J* = 10.5 Hz, 1 H), 4.46 (d, *J* = 11.9 Hz, 1 H), 4.45 (d, *J* = 10.9 Hz, 1 H), 4.40 (dd, *J* = 4.1, 5.8 Hz, 1 H), 4.36 (dd, *J* = 10.5, 4.4 Hz, 1 H), 4.33 (dd, *J* = 6.5, 2.2 Hz, 1 H), 4.31 (dd, *J* = 7.3, 4.1 Hz, 1 H), 4.23–4.15 (m, 1 H), 3.69 (dd, *J* = 10.7, 2.2 Hz, 1 H), 3.71–3.55 (m, 3 H), 2.90 (s, 3 H), 2.80 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 137.7, 137.1, 128.5–127.2 (m), 80.2, 78.9, 78.4, 75.3, 75.1, 74.9, 74.6, 74.3, 73.5, 67.8, 66.9, 37.5, 37.0 ppm. ESMS: *m*/*z* 763 [M + Na]$^+$. $C_{38}H_{44}O_{11}S_2$ (740.23): calcd. C 61.60, H 5.99, O 23.75, S 8.66; found C 61.66, H 6.12.

(3*S*,3a*R*,5*R*,6*S*,7*R*,7a*S*)-1-Benzyl-3,6,7-tris(benzyloxy)-5-(benzyloxymethyl)octahydropyrano[3,2-*b*]pyrrole (22): Dimesylate **21** (370 mg) was subjected to cylization using the general procedure (E) to give **22** (154 mg, 79%) as colorless oil. R_f = 0.4 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = –28.6 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2922, 2853, 1594, 1493, 1094, 736, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.25 (m, 25 H), 5.05 (d, *J* = 2.7 Hz, 1 H), 4.82 (d, *J* = 11.2 Hz, 1 H), 4.67 (d, *J* = 11.2 Hz, 1 H), 4.65–4.51 (m, 7 H), 4.41 (d, *J* = 11.7 Hz, 1 H), 4.24 (dd, *J* = 5.8, 2.6 Hz, 1 H), 4.02–3.96 (m, 1 H), 3.92–3.75 (m, 4 H), 2.92 (dd, *J* = 12.4, 8.0 Hz, 1 H), 2.84 (dd, *J* = 12.4, 3.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 138.2, 128.3–127.6 (m), 126.9, 97.7, 77.8, 76.0, 74.4, 73.5, 73.4, 71.1, 70.4, 68.3, 53.4, 51.9, 29.6 ppm. HRMS calcd. for $C_{43}H_{46}NO_5$ [M + H]$^+$ 656.3371, found 656.3376.

(3*S*,3a*R*,5*R*,6*S*,7*R*,7a*S*)-5-(Hydroxymethyl)octahydropyrano-[3,2-*b*]pyrrole-3,6,7-triol (7): Compound **22** (196 mg) was subjected to global deprotection using the general procedure (F) to give **7** (60 mg, 99%) as a thick liquid. R_f = 0.3 (MeOH/EtOAc, 1:4). $[\alpha]_D^{28}$ = –15.9 (*c* = 1.0, H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 3.78–3.70 (m, 2 H), 3.58–3.54 (m, 2 H), 3.45 (dd, *J* = 11.5, 7.5 Hz, 1 H), 3.19–3.17 (m, 2 H), 3.11 (dd, *J* = 9.5, 9.0 Hz, 1 H), 3.00–2.97 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.8, 77.2, 73.1, 69.2, 62.5, 50.8, 44.5, 35.5 ppm. ESMS: *m*/*z* 206 [M + H]$^+$. $C_8H_{15}NO_5$ (205.10): calcd. C 46.82, H 7.37, N 6.83, O 38.98; found C 46.85, H 7.38, N 6.82.

(2*R*,3*S*,4*R*,5*S*,6*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)-6-vinyltetrahydro-2*H*-pyran (30): Alcohol **29** (2 g) was benzylated with PMBCl using the general procedure (A) to give **30** (2.37 g, 94%) as colorless oil. R_f = 0.55 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +66.3 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2923, 1612, 1513, 1094, 1028, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 17 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 6.03 (ddd, *J* = 15.4, 10.7, 4.4 Hz, 1 H), 5.40 (dt, *J* = 15.4, 1.9 Hz, 1 H), 5.31 (ddd, *J* = 10.7, 1.9, 1.7 Hz, 1 H), 4.84 (d, *J* = 11.4 Hz, 1 H), 4.69 (s, 2 H), 4.63–4.53 (m, 4 H), 4.51 (d, *J* = 11.9 Hz, 1 H), 4.44 (d, *J* = 11.9 Hz, 1 H), 4.04–3.99 (m, 2 H), 3.95 (dd, *J* = 2.7, 2.4 Hz, 1 H), 3.79 (s, 3 H), 3.68–3.65 (m, 1 H), 3.61 (dd, *J* = 8.8, 2.7 Hz, 1 H), 3.55 (dd, *J* = 10.0, 3.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 138.7, 138.6, 138.2, 132.7, 130.6, 129.4, 128.3–127.3 (m), 118.0, 113.7, 78.8, 76.5, 75.0, 73.9, 73.3, 73.2, 72.9, 71.9, 68.4, 55.2 ppm. ESMS: *m*/*z* 603 [M + Na]$^+$. $C_{37}H_{40}O_6$ (580.28): calcd. C 76.53, H 6.94, O 16.53; found C 76.52, H 6.96.

1-[(2*S*,3*R*,4*S*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]ethane-1,2-diol (31): Olefin **30** (580 mg) was dihydroxylated using the general procedure (E) to give **31** (497 g, 81%) as a colorless thick liqid. Diastereomeric mixture (3:2). R_f = 0.4 (hexane/EtOAc, 3:2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3401, 3063, 2924, 1605, 1453, 1090, 736, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 15 H, both isomers), 7.15 (d, *J* = 8.2 Hz, 2 H, major), 7.09 (d, *J* = 8.5 Hz, 2 H, minor), 6.88 (d, *J* = 8.5 Hz, 2 H, minor), 7.09 (d, *J* = 8.2 Hz, 2 H, major), 4.67–4.44 (m, 8 H, both isomers), 4.21–4.19 (m, 2 H, both isomers), 3.97–3.96 (m, 1 H, both isomers), 3.87–3.76 (m, 5 H, both isomers), 3.77 (s, 3 H, both isomers), 3.66–3.63 (m, 1 H, both isomers), 3.58–3.54 (m, 1 H, both isomers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) major: δ = 159.5, 138.2, 138.1, 137.9, 129.8–127.6 (m), 113.9, 74.9, 74.5, 73.7, 73.1, 73.0, 72.1, 69.5, 69.1, 66.3, 64.7, 55.2 ppm. ESMS: *m*/*z* 637 [M + Na]$^+$. $C_{37}H_{42}O_8$ (614.28): calcd. C 72.29, H 6.89, O 20.82; found C 72.20, H 6.86.

Diols **31** (614 mg) was tritylated using the general procedure (C) to give **32** (440 mg, 51%) and **33** (296 mg, 35%).

(*R*)-1-[(2*S*,3*R*,4*S*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]-2-(trityloxy)-ethanol (32): (440 mg, 51%) White solid. R_f = 0.5 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +38.5 (*c* = 0.8, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 2855, 1610, 1513, 1492, 1248, 1091, 1032, 741, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.24 (m, 32 H), 7.13 (d, *J* = 8.5 Hz, 2 H), 4.63 (d, *J* = 12.2 Hz, 1 H), 4.57–4.16 (m, 4 H), 4.38 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 11.9 Hz, 1 H), 4.19 (d, *J* = 4.8 Hz, 1 H), 4.11 (dd, *J* = 7.0, 6.6 Hz, 1 H), 3.97 (br. d, *J* = 2.9 Hz, 1 H), 3.89–3.79 (m, 3 H), 3.79 (s, 3 H), 3.70 (br. d, *J* = 2.9 Hz, 1 H), 3.67 (d, *J* = 7.0 Hz, 1 H), 3.35 (dd, *J* = 6.6, 3.6 Hz, 1 H), 3.25 (dd, *J* = 6.6, 3.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 130.1–126.8 (m), 113.9, 86.7, 75.1, 74.7, 73.5, 72.8, 72.2, 71.8, 69.3, 68.7, 66.2, 65.4, 64.7, 55.2 ppm. ESMS: *m*/*z* 879 [M + Na]$^+$. $C_{56}H_{56}O_8$ (856.40): calcd. C 78.48, H 6.59, O 14.93; found C 78.51, H 6.57.

(*S*)-1-[(2*S*,3*R*,4*S*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran-2-yl]-2-(trityloxy)ethanol (33): (296 mg, 35%) Colorless oil. R_f = 0.49 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +97.6 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3060, 3030, 2925, 7611, 1513, 1248, 1091, 1030, 736, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.15 (m, 30 H), 6.93 (d, *J* = 8.5 Hz, 2 H), 6.75 (d, *J* = 8.5 Hz, 2 H), 4.59–4.48 (m, 6 H), 4.16 (br. s, 1 H), 4.16–3.95 (m, 6 H), 3.77 (s, 3 H), 3.74 (dd, *J* = 5.1, 2.9 Hz, 1 H), 3.70 (dd, *J* = 11.2, 3.4 Hz, 1 H), 3.05 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 144.0, 138.6, 138.4, 129.9–126.9 (m), 113.8, 86.5, 74.7, 73.7, 73.2, 72.9, 72.6, 72.2, 71.0, 69.4, 66.5, 64.2, 55.2 ppm. ESMS: *m*/*z* 879 [M + Na]$^+$. $C_{56}H_{56}O_8$ (856.40): calcd. C 78.48, H 6.59, O 14.93; found C 78.47, H 6.60.

(2*R*,3*S*,4*S*,5*R*,6*S*)-3,4-Bis(benzyloxy)-6-[(*R*)-1-(benzyloxy)-2-(trityloxy)ethyl]-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran (34): Alcohol **32** (856 mg) was benzylated with BnCl using the general procedure (A) to give **34** (860 mg, 91%) as a white solid. R_f = 0.6 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +55.2 (*c* = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3060, 3029, 2924, 2855, 1609, 1512, 1073, 738,

699, 633 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.13 (m, 35 H), 7.01 (d, J = 8.5 Hz, 2 H), 6.75 (d, J = 8.5 Hz, 2 H), 4.78 (d, J = 11.4 Hz, 2 H), 4.69 (d, J = 5.6 Hz, 1 H), 4.60 (d, J = 11.9 Hz, 1 H), 4.50 (d, J = 12.9 Hz, 1 H), 4.43 (d, J = 10.0 Hz, 1 H), 4.40 (d, J = 11.9 Hz, 1 H), 4.35 (d, J = 11.9 Hz, 1 H), 4.27–4.25 (m, 1 H), 4.24 (d, J = 11.2 Hz, 1 H), 4.19 (d, J = 11.9 Hz, 1 H), 4.12 (d, J = 11.9 Hz, 1 H), 4.09 (d, J = 9.2 Hz, 1 H), 4.00–3.95 (m, 2 H), 3.90 (dd, J = 8.3, 5.4 Hz, 1 H), 3.82–3.75 (m, 2 H), 3.75 (s, 3 H), 3.72 (br. s, 1 H), 3.63 (br. d, J = 10.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 144.3, 138.9, 138.7, 138.6, 138.4, 130.4, 129.4–126.7 (m), 113.7, 86.5, 75.2, 74.9, 73.8, 73.4, 73.0, 72.7, 72.2, 71.4, 67.2, 66.4, 65.4, 64.0, 55.2 ppm. ESMS: m/z 969 [M + Na]$^+$. $C_{63}H_{62}O_8$ (946.44): calcd. C 79.89, H 6.60, O 13.51; found C 79.92, H 6.58.

(*R*)-2-(Benzyloxy)-2-[(2*S*,3*R*,4*S*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-(benzyloxymethyl)-3-(methylsulfonyloxy)tetrahydro-2*H*-pyran-2-yl]ethyl Methanesulfonate (35): Compound **34** (946 mg) was converted to give dimesylate **35** (466 mg, 63%, two steps) as a colorless oil using the general procedure (D). R_f = 0.5 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = +14.28 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 2855, 1599, 1495, 1455, 1176, 1093, 998, 740, 699, 525 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.24 (m, 20 H), 4.98 (d, J = 4.1 Hz, 1 H), 4.97–4.48 (m, 9 H), 4.33–4.31 (m, 1 H), 4.28 (dd, J = 11.0, 3.6 Hz, 1 H), 4.12–4.07 (m, 3 H), 3.93 (dd, J = 6.0, 2.9 Hz, 1 H), 3.78–3.73 (m, 2 H), 2.82 (s, 3 H), 2.79 (s, 3 H) ppm. ESMS: m/z 763 [M + Na]$^+$. $C_{38}H_{44}O_{11}S_2$ (740.23): calcd. C 61.60, H 5.99, O 23.75, S 8.66; found C 61.51, H 6.02.

(3*R*,3a*R*,5*R*,6*R*,7*R*,7a*S*)-1-Benzyl-3,6,7-tris(benzyloxy)-5-(benzyloxymethyl)octahydropyrano[3,2-*b*]pyrrole (36): Dimesylate **35** (370 mg) was subjected to cylization using the general procedure (E) to give **36** (248 mg, 76%) as colorless oil. R_f = 0.4 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = –12.83 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2923, 2853, 1668, 1602, 1495, 1094, 1027, 753, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.21 (m, 25 H), 4.97 (br. s, 1 H), 4.89 (d, J = 11.4 Hz, 1 H), 4.65–4.58 (m, 3 H), 4.49 (m, 7 H), 4.43 (d, J = 12.4 Hz, 1 H), 4.34 (d, J = 11.7 Hz, 1 H), 4.23–4.20 (m, 2 H), 3.99–3.98 (m, 1 H), 3.91–3.90 (m, 1 H), 3.77–3.75 (m, 2 H), 3.72 (s, 2 H), 2.91 (dd, J = 12.2, 8.0 Hz, 1 H), 2.78 (dd, J = 12.2, 4.1 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 140.0, 138.5, 138.2, 137.9, 128.3–126.8 (m), 98.2, 77.8, 75.7, 73.4, 73.2, 71.4, 70.9, 70.7, 68.0, 53.4, 51.6, 29.6 ppm. HRMS calcd. for $C_{43}H_{46}NO_5$ [M+ H]$^+$ 656.3371, found 656.3379.

(3*R*,3a*R*,5*R*,6*R*,7*R*,7a*S*)-5-(Hydroxymethyl)octahydropyrano[3,2-*b*]-pyrrole-3,6,7-triol (8): Compound **36** (196 mg) was subjected to global deprotection using the general procedure (F) to give **8** (59 mg, 98%) as a thick liquid. R_f = 0.3 (MeOH/EtOAc, 1:4). $[\alpha]_D^{28}$ = –10.2 (c = 0.8, H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 3.75–3.74 (m, 2 H), 3.67–3.64 (m, 2 H), 3.61 (dd, J = 8.5, 3.0 Hz, 1 H), 3.55 (dd, J = 11.5, 3.0 Hz, 1 H), 3.41 (m, 2 H), 2.97–2.88 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.6, 76.7, 70.3, 68.7, 67.5, 61.9, 42.1, 29.0 ppm. ESMS: m/z 206 [M + H]$^+$. $C_8H_{15}NO_5$ (205.10): calcd. C 46.82, H 7.37, N 6.83, O 38.98; found C 46.83, H 7.39, N 6.84.

(2*R*,3*S*,4*S*,5*R*,6*S*)-3,4-Bis(benzyloxy)-6-[(*S*)-1-(benzyloxy)-2-(trityloxy)ethyl]-2-(benzyloxymethyl)-5-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran (37): Alcohol **33** (856 mg) was benzylated with BnCl using the general procedure (A) to give **37** (860 mg, 91%) as colorless oil. R_f = 0.55 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +106.9 (c = 1.2, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3060, 2925, 2855, 1611, 1091, 753, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.16 (m, 35 H), 7.02 (d, J = 8.2 Hz, 2 H), 6.78 (d, J = 8.2 Hz, 2 H), 4.69–4.58 (m, 4 H), 4.53–4.44 (m, 6 H), 4.33 (dd, J = 4.8, 2.5 Hz, 1 H), 4.28–4.26 (m, 2 H), 4.09–4.10 (m, 1 H), 3.94 (br. d, J = 4.8 Hz, 1 H), 3.87–3.83 (m, 2 H), 3.60 (dd, J = 6.1, 5.4 Hz, 1 H), 3.46 (dd, J = 9.6, 5.4 Hz, 1 H), 3.16 (dd, J = 9.6, 2.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 144.3, 144.1, 139.2, 139.0, 138.8, 138.6, 130.7–126.7 (m), 113.7, 86.6, 80.1, 76.3, 74.6, 74.4, 73.9, 73.1, 73.0, 72.9, 72.6, 69.0, 63.3, 55.2 ppm. ESMS: m/z 969 [M + Na]$^+$. $C_{63}H_{62}O_8$ (946.44): calcd. C 79.89, H 6.60, O 13.51; found C 79.96, H 6.61.

(*S*)-2-(Benzyloxy)-2-[(2*S*,3*R*,4*S*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-(benzyloxymethyl)-3-(methylsulfonyloxy)tetrahydro-2*H*-pyran-2-yl]ethyl Methanesulfonate (38): Compound **37** (946 mg) was converted to give dimesylate **38** (510 mg, 69%, two steps) as a colorless oil using the general procedure (D). R_f = 0.5 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = +27.8 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 3030, 2924, 2854, 1595, 1453, 1174, 1097, 1050, 964, 739, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.18 (m, 20 H), 5.05 (dd, J = 8.7, 7.3 Hz, 1 H), 4.80 (d, J = 11.4 Hz, 1 H), 4.75 (d, J = 10.7 Hz, 1 H), 4.54 (d, J = 10.7 Hz, 1 H), 4.50 (d, J = 11.4 Hz, 1 H), 4.49 (d, J = 11.7 Hz, 1 H), 4.45 (d, J = 11.7 Hz, 1 H), 4.38–4.34 (m, 6 H), 4.25 (dd, J = 9.2, 2.6 Hz, 1 H), 4.15 (t, J = 6.1 Hz, 1 H), 3.56 (dd, J = 9.0, 7.3 Hz, 1 H), 3.36 (dd, J = 9.2, 5.1 Hz, 1 H), 2.93 (s, 3 H), 2.91 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 137.6, 137.2, 128.5–127.6 (m), 78.0, 77.3, 75.0, 74.4, 73.9, 73.5, 72.5, 69.0, 68.3, 37.6, 37.0 ppm. ESMS: m/z 763 [M + Na]$^+$. $C_{38}H_{44}O_{11}S_2$ (740.23): calcd. C 61.60, H 5.99, O 23.75, S 8.66; found C 61.68, H 6.02.

(3*S*,3a*R*,5*R*,6*R*,7*R*,7a*S*)-1-Benzyl-3,6,7-tris(benzyloxy)-5-(benzyloxymethyl)octahydropyrano[3,2-*b*]pyrrole (39): Dimesylate **38** (370 mg) was subjected to cylization using the general procedure (E) to give **39** (248 mg, 76%) as colorless oil. R_f = 0.4 (hexane/EtOAc, 7:3). $[\alpha]_D^{28}$ = +26.3 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2922, 2853, 1597, 1492, 1093, 1024, 734, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.15 (m, 25 H), 4.98 (br. s, 1 H), 4.88 (d, J = 11.4 Hz, 1 H), 4.65–4.37 (m, 8 H), 4.23 (br. s, 1 H), 4.12 (m, 1 H), 3.99 (br. s, 1 H), 3.93 (dd, J = 6.3, 6.6 Hz, 1 H), 3.71–3.69 (m, 2 H), 3.66–3.61 (m, 2 H), 2.79 (d, J = 6.6 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 138.5, 138.4, 138.2, 138.0, 128.3–126.7 (m), 99.0, 78.7, 75.5, 73.5, 73.4, 72.0, 70.9, 70.6, 67.9, 53.1, 50.9, 29.6 ppm. HRMS calcd. for $C_{43}H_{46}NO_5$ [M+ H]$^+$ 656.3371, found 656.3379.

(3*S*,3a*R*,5*R*,6*R*,7*R*,7a*S*)-5-(Hydroxymethyl)octahydropyrano[3,2-*b*]-pyrrole-3,6,7-triol (9): Compound **39** (196 mg) was subjected to global deprotection using the general procedure (F) to give **9** (59 mg, 98%) as a thick liquid. R_f = 0.3 (MeOH/EtOAc, 1:4). $[\alpha]_D^{28}$ = –16.3 (c = 0.8, H_2O). ^{1}H NMR (400 MHz, D_2O): δ = 3.85–3.81 (m, 1 H), 3.73–3.70 (m, 2 H), 3.64 (br. s, 1 H), 3.61–3.52 (m, 2 H), 3.39–3.35 (m, 1 H), 3.29 (dd, J = 12.5, 3.0 Hz, 1 H), 3.15–3.05 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.9, 77.1, 68.6, 67.4, 67.2, 61.9, 53.9, 29.3 ppm. ESMS: m/z 206 [M + H]$^+$. $C_8H_{15}NO_5$ (205.10): calcd. C 46.82, H 7.37, N 6.83, O 38.98; found C 46.85, H 7.38, N 6.82.

(2*S*,4*R*,4a*S*,6*R*,7*R*,8*S*,8a*R*)-7,8-Bis(benzyloxy)-6-(benzyloxymethyl)-2-(4-methoxy-phenyl)-4-(trityloxymethyl)hexahydro-pyrano-[3,2-*d*][1,3]dioxine (23): Alcohol **15** (100 mg) was subjected to oxidative cyclization using the general procedure (G) to give **23** (80 mg, 80%) as colorless oil. R_f = 0.55 (hexane/EtOAc, 9:1). $[\alpha]_D^{28}$ = +36.5 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2920, 1597, 1099, 1023, 736, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.14 (m, 32 H, Ar-H), 6.89 (d, J = 8.7 Hz, 2 H, Ar-H), 5.95 (s, 1 H, 9-H), 4.74 (d, J = 11.2 Hz, 1 H, -OCH_2Ph), 4.69 (d, J = 11.4 Hz, 1 H, -OCH_2Ph), 4.62 (d, J = 11.4 Hz, 1 H, -OCH_2Ph), 4.53 (d, J = 12.2 Hz, 1 H, -OCH_2Ph), 4.49 (d, J = 11.9 Hz, 1 H, -OCH_2Ph),

4.39 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.28 (dd, J = 9.2, 11.1 Hz, 1 H, 2-H), 4.20 (br. d, J = 5.6 Hz, 1 H, 7-H), 4.03 (dd, J = 5.4, 2.9 Hz, 1 H, 5-H), 3.92 (dd, J = 9.2, 2.9 Hz, 1 H, 1-H), 3.89 (dd, J = 7.0, 11.1 Hz, 1 H, 3-H), 3.83 (dd, J = 7.0, 5.4 Hz, 1 H, 4-H), 3.81 (s, 3 H, -OCH_3), 3.66–3.59 (m, 2 H, 6-H, 6′-H), 3.46–3.38 (m, 2 H, 8-H, 8′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.9, 143.6, 138.3, 138.2, 138.1, 131.0, 128.7–126.9 (m), 113.5, 96.2, 81.4, 75.6, 74.6, 73.4, 73.3, 72.4, 69.6, 66.9, 63.5, 55.2, 29.6 ppm. ESMS: m/z 877 $[M + Na]^+$. $C_{56}H_{54}O_8$ (854.38): calcd. C 78.66, H 6.37, O 14.97; found C 78.63, H 6.39.

(2*S*,4*S*,4a*S*,6*R*,7*R*,8*S*,8a*R*)-7,8-Bis(benzyloxy)-6-(benzyloxymethyl)-2-(4-methoxyphenyl)-4-(trityloxymethyl)hexahydro-pyrano[3,2-*d*]-[1,3]dioxine (24): Alcohol **16** (100 mg) was subjected to oxidative cyclization using the general procedure (G) to give **24** (85 mg, 85%) as a white solid. R_f = 0.53 (hexane/EtOAc, 9:1). $[a]_D^{28}$ = +15.3 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2912, 1595, 1093, 1021, 739, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.14 (m, 32 H, Ar-H), 6.86 (d, J = 8.7 Hz, 2 H, Ar-H), 5.56 (s, 1 H, 9-H), 4.73 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.69 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.67 (d, J = 11.7 Hz, 1 H, -OCH_2Ph), 4.49 (d, J = 11.4 Hz, 1 H, -OCH_2Ph), 4.35 (d, J = 11.4 Hz, 1 H, -OCH_2Ph), 4.24 (d, J = 11.7 Hz, 1 H, -OCH_2Ph), 4.12 (dd, J = 11.4, 8.8 Hz, 1 H, 2-H), 4.05–4.04 (m, 2 H, 5-H, 7-H), 3.93–3.82 (m, 3 H, 4-H, 3-H, 1-H), 3.79 (s, 3 H, -OCH_3), 3.64 (dd, J = 10.4, 3.4 Hz, 1 H, 6-H), 3.58 (dd, J = 10.4, 3.2 Hz, 1 H, 6-H), 3.51 (dd, J = 9.7, 6.6 Hz, 1 H, 8-H), 3.34 (dd, J = 9.7, 5.3 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.0, 138.4, 138.2, 128.0–126.8 (m), 113.5, 100.2, 86.6, 77.8, 74.4, 73.3, 72.1, 69.9, 29.6 ppm. ESMS: m/z 877 $[M + Na]^+$. $C_{56}H_{54}O_8$ (854.38): calcd. C 78.66, H 6.37, O 14.97; found C 78.69, H 6.38.

(2*S*,4*R*,4a*S*,6*R*,7*S*,8*S*,8a*R*)-7,8-Bis(benzyloxy)-6-(benzyloxymethyl)-2-(4-methoxyphenyl)-4-(trityloxymethyl)hexahydro-pyrano[3,2-*d*]-[1,3]dioxine (25): Alcohol **32** (100 mg) was subjected to oxidative cyclization using the general procedure (G) to give **25** (79 mg, 79%) as colorless oil. R_f = 0.5 (hexane/EtOAc, 9:1). $[a]_D^{28}$ = +10.6 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2912, 1611, 1101, 1006, 737, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.18 (m, 32 H, Ar-H), 6.89 (d, J = 8.3 Hz, 2 H, Ar-H), 5.84 (s, 1 H, 9-H), 4.65 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.63 (d, J = 11.7 Hz, 1 H, -OCH_2Ph), 4.58 (d, J = 11.7 Hz, 1 H, -OCH_2Ph), 4.57 (d, J = 11.0 Hz, 1 H, -OCH_2Ph), 4.56 (d, J = 11.0 Hz, 1 H, -OCH_2Ph), 4.49 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.42–4.39 (m, 1 H, 5-H), 4.26–4.23 (m, 2 H, 2-H, 7-H), 4.11 (dd, J = 5.8, 2.7 Hz, 1 H, 4-H), 4.00 (dd, J = 11.7, 8.5 Hz, 1 H, 6-H), 3.85 (dd, J = 6.6, 3.4 Hz, 1 H, 3-H), 3.80 (s, 3 H, -OCH_3), 3.82–3.75 (m, 2 H, 6-H, 1-H), 3.47–3.42 (m, 2 H, 8-H, 8′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 143.6, 138.5, 130.9, 128.7–127.1 (m), 113.5, 96.4, 87.2, 75.8, 75.3, 74.0, 73.9, 73.1, 72.1, 66.0, 63.1, 62.9, 55.3 ppm. ESMS: m/z 877 $[M + Na]^+$. $C_{56}H_{54}O_8$ (854.38): calcd. C 78.66, H 6.37, O 14.97; found C 78.68, H 6.33.

(2*S*,4*S*,4a*S*,6*R*,7*S*,8*S*,8a*R*)-7,8-Bis(benzyloxy)-6-(benzyloxymethyl)-2-(4-methoxyphenyl)-4-(trityloxymethyl)hexahydro-pyrano[3,2-*d*]-[1,3]dioxine (26): Alcohol **33** (100 mg) was subjected to oxidative cyclization using the general procedure (G) to give **26** (83 mg, 83%) as colorless oil. R_f = 0.56 (hexane/EtOAc, 9:1). $[a]_D^{28}$ = +45.3 (c = 1.0, CH_2Cl_2). IR (CH_2Cl_2): $\tilde{\nu}_{max}$ = 2924, 1600, 1091, 1017, 736, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.07 (m, 32 H, Ar-H), 6.88 (d, J = 8.8 Hz, 2 H, Ar-H), 5.54 (s, 1 H, 9-H), 4.96 (d, J = 11.4 Hz, 1 H, -OCH_2Ph), 4.62 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.61 (d, J = 11.7 Hz, 1 H, -OCH_2Ph), 4.59 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.41 (dd, J = 8.0, 5.8 Hz, 1 H, 4-H), 4.35 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.28 (d, J = 11.9 Hz, 1 H, -OCH_2Ph), 4.12–4.06 (m, 2 H, 5-H, 2-H), 4.03–4.02 (m, 1 H, 7-H), 3.97 (dd, J = 8.0, 11.7 Hz, 1 H, 3-H), 3.90 (dd, J = 3.2, 2.9 Hz, 1 H, 8-H), 3.83–3.78 (m, 2 H, 8-H, 1-H), 3.80 (s, 3 H, -OCH_3), 3.55 (dd, J = 9.5, 6.8 Hz, 1 H, 6-H), 3.26 (dd, J = 9.5, 5.3 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 144.0, 138.6, 138.4, 138.3, 130.4, 128.8–126.8 (m), 113.5, 110.5, 86.6, 78.1, 75.8, 75.3, 74.0, 73.4, 73.0, 71.9, 66.0, 63.3, 61.1, 55.3 ppm. ESMS: m/z 877 $[M + Na]^+$. $C_{56}H_{54}O_8$ (854.38): calcd. C 78.66, H 6.37, O 14.97; found C 78.67, H 6.36.

Supporting Information (see also the footnote on the first page of this article): Copies of spectra for all new compounds viz. **6**, **7**, **8**, **9**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**.

Acknowledgments

We thank the Department of Science and Technology, New Delhi, for financial support to one of us (Y. D. V.) in the form of a Ramanna Fellowship (Grant No. SR/S1/RFOC-04/2006). V. R. D., H. P. K., and R. K. B. thank the Council of Scientific and Industrial Research, New Delhi and A. P. J. P thanks the University Grants Commission, New Delhi for senior research fellowships.

[1] a) G. W. J. Fleet, A. Karpus, R. A. Dwek, L. E. Fellows, A. S. Tyms, S. Petursson, S. K. Namgoong, N. G. Ramsden, P. W. Smith, J. C. Son, F. X. Wilson, D. R. Witty, G. S. Jacob, T. W. Rademacher, *FEBS Lett.* **1988**, *237*, 128–132; b) A. D. Elbein, *Ann. Rev. Biochem.* **1987**, *56*, 497–534; c) K. M. Robinson, B. L. Rhinehart, J. B. Ducep, C. Danzin, *Drugs of the Future* **1992**, *17*, 705–720; d) B. Winchester, G. W. J. Fleet, *Glycobiology* **1992**, *2*, 199–210; e) P. Compain, O. R. Martin, *Iminosugars: From Synthesis to Therapeutic Applications*, Wiley-VCH, Weinheim, **2007**.

[2] a) M. J. Hummphries, K. Matsumoto, S. L. White, K. Olden, *Cancer Res.* **1986**, *46*, 5215–5222; b) M. A. Spearman, J. C. Jamieson, J. A. Wright, *Exp. Cell Res.* **1987**, *168*, 116–126.

[3] a) Y. Ichikawa, Y. Igarashi, M. Ichikawa, Y. Suhara, *J. Am. Chem. Soc.* **1998**, *120*, 3007–3018; b) P. B. Anzeveno, L. J. Creemer, J. K. Daniel, C. H. King, P. S. Liu, *J. Org. Chem.* **1989**, *54*, 2539–2542; c) J. L. Treadway, P. Mendys, D. J. Hoover, *Expert. Opin. Invest. Drugs* **2001**, *10*, 439–454; d) G. S. Jacob, *Curr. Opin. Struct. Biol.* **1995**, *5*, 605–611.

[4] a) G. W. J. Fleet, D. R. Witty, *Tetrahedron: Asymmetry* **1990**, *1*, 119–136; b) J. F. Bickley, T. L. Gilchrist, R. Mendoca, *ARKIVOC* **2002**, 192–204; c) W. McDowell, R. T. Schwarz, *Biochimie* **1988**, *70*, 1535–1549; d) P. Westervelt, H. E. Gendelman, L. Patner, *Proc. Natl. Acad. Sci. USA* **1991**, *88*, 3097–3101; e) G. B. Karlsson, T. D. Butter, R. A. Dwek, F. M. Platt, *J. Biol. Chem.* **1993**, *268*, 570–576.

[5] a) J. M. Otero, R. G. Soengas, J. C. Estevez, R. J. Estevez, D. J. Watkin, E. L. Evinson, R. J. Nash, G. W. J. Fleet, *Org. Lett.* **2007**, *9*, 623–626; b) S. Cren, C. Wilson, N. R. Thomas, *Org. Lett.* **2005**, *7*, 3521–3523; c) M. L. Ulf, D. Rui, H. Olle, *Chem. Commun.* **2005**, *13*, 1773–1774; d) T. Ayad, Y. Génisson, S. Broussy, M. Baltas, L. Gorrichon, *Eur. J. Org. Chem.* **2003**, *15*, 2903–2910; e) A. T. Carmona, J. Fuentes, I. Robina, G. E. Rodriguez, D. Raynald, P. Vogel, A. L. Winters, *J. Org. Chem.* **2003**, *68*, 3874–3883.

[6] a) A. Guaragna, S. D'Errico, D. D'Alonzo, S. Pedatella, G. Palumbo, *Org. Lett.* **2007**, *9*, 3473–3476; b) R. W. Wang, F. L. Quing, *Org. Lett.* **2005**, *7*, 2189–2192; c) N. L. Segraves, P. Crews, *J. Nat. Prod.* **2005**, *68*, 118–121; d) K. M. Goodenough, P. Raubo, J. P. A. Harrity, *Org. Lett.* **2005**, *7*, 2993–2996; e) A. Lemire, A. B. Charette, *Org. Lett.* **2005**, *7*, 2747–2750; f) C. Y. Legault, A. B. Charette, *J. Am. Chem. Soc.* **2005**, *127*, 8966–8967.

[7] K. M. Robinson, M. E. Begovic, B. L. Rhinehart, E. W. Heineke, J. B. Ducep, P. R. Kastner, F. N. Marshall, C. Danzin, *Diabetes* **1991**, *40*, 825–830.
[8] G. W. J. Fleet, P. W. Smith, *Tetrahedron* **1986**, *42*, 5685–5692, and references therein.
[9] a) G. W. J. Fleet, S. J. Nicholas, P. W. Smith, S. E. Evans, L. E. Fellows, R. J. Nash, *Tetrahedron Lett.* **1985**, *26*, 3127–3130, and references cited therein; b) G. N. Austin, P. D. Baird, G. W. J. Fleet, J. M. Peach, P. W. Smith, D. J. Watkin, *Tetrahedron* **1987**, *43*, 3095–3108.
[10] a) B. Meunier, *Acc. Chem. Res.* **2008**, *41*, 69–77; b) L. F. Tietze, H. P. Bell, S. Chadrasekhar, *Angew. Chem. Int. Ed.* **2003**, *42*, 3996–4028; c) G. Mehta, V. Singh, *Chem. Soc. Rev.* **2002**, *31*, 324–334; d) L. Abrous, J. Hynes Jr., S. R. Friedrich, A. B. Smith III, R. Hirschmann, *Org. Lett.* **2001**, *3*, 1089–1092; e) L. Abrous, P. K. Jokiel, S. R. Friedrich, J. Hynes Jr., A. B. Smith III, R. Hirschmann, *J. Org. Chem.* **2004**, *69*, 280–302.
[11] a) S. Rani, A. Agarwal, Y. D. Vankar, *Tetrahedron Lett.* **2003**, *44*, 5001–5004; b) V. R. Doddi, Y. D. Vankar, *Eur. J. Chem.* **2007**, 5583–5589; c) B. G. Reddy, Y. D. Vankar, *Angew. Chem. Int. Ed.* **2005**, *44*, 2001–2004; d) K. Jayakanthan, Y. D. Vankar, *Org. Lett.* **2005**, *7*, 5441–5444; e) K. Jayakanthan, Y. D. Vankar, *Tetrahedron Lett.* **2006**, *47*, 8667–8671; f) A. Kumar, G. K. Rawal, Y. D. Vankar, *Tetrahedron* **2008**, *64*, 2379–2390.
[12] a) J. G. Buchanan, K. W. Lumbard, R. J. Sturgeon, D. K. Thompson, R. H. Wightman, *J. Chem. Soc. Perkin Trans. 1* **1990**, 699–706; b) Q. Meng, M. Hesse, *Helv. Chim. Acta* **1991**, *74*, 445–450; c) J. H. Kim, M. S. Yang, W. S. Lee, K. H. Park, *J. Chem. Soc. Perkin Trans. 1* **1998**, 2877–2880.
[13] a) Y. Huang, D. R. Dalton, P. J. Carroll, *J. Org. Chem.* **1997**, *62*, 372–376; b) D. K. Thompson, C. N. Hubert, R. H. Wightman, *Tetrahedron* **1993**, *49*, 3827–3840; c) S. Takano, M. Moriya, K. Ogasawara, *Tetrahedron: Asymmetry* **1992**, *3*, 681–684.
[14] P. Cheshev, A. Marra, A. Dondoni, *Carbohydr. Res.* **2006**, *341*, 2714–2716.
[15] S. P. Allwein, J. M. Cox, B. E. Howard, H. W. B. Johnson, J. D. Rainier, *Tetrahedron* **2002**, *58*, 1997–2009.
[16] a) J. K. Cha, W. J. Christ, Y. Kishi, *Tetrahedron* **1984**, *40*, 2247–2255; b) J. K. Cha, N. S. Kim, *Chem. Rev.* **1995**, *95*, 1761–1795.
[17] a) Y. Oikawa, T. Yoshioka, O. Yonemitsu, *Tetrahedron Lett.* **1982**, *23*, 889; b) D. Crich, A. Banerjee, *Org. Lett.* **2005**, *7*, 1395–1398.
[18] Recently we have developed a method for the deprotection of anomeric *O*-methyl glycosides using the same reagent system. A. Kumar, V. R. Doddi, Y. D. Vankar, *J. Org. Chem.* **2008**, *73*, 5993–5995.
[19] See Supporting Information.
[20] Y.-T. Li, S.-C. Li, *Methods in Enzymology* (Ed.: V. Ginsberg), Academic Press, **1972**, pp. 702.

Received: August 5, 2008
Published Online: October 22, 2008

