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Synthesis of fused pyran-carbahexopyranoses as glycosidase inhibitors

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ABSTRACT

Synthesis of polyhydroxylated oxabicyclo[4,4,0]decanes, which constitute a new family of annulated carbasugars, has been accomplished in a stereoselective manner by employing readily available 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glycopyranoses.

1. Introduction

Carbasugars, also called as pseudosugars **1**[1,2] (Fig. 1), have structural similarities with monosaccharides except that the ring oxygen is replaced by a methylene group. Carbasugars, especially pseudo-β-fructopyranoses, have been found to be useful as artificial sweeteners,[1–3] and they also occur in nature as part of the structure of antibiotics validamycins.[1a,e,f] More importantly, they act as glycosidase inhibitors,[1a,4] molecules of high current interest[5] both from synthetic and medicinal points of view. For example, acarbose,[5] a tetrasaccharide and an α-glucosidase inhibitor that is being used as an antidiabetic drug, contains a carba-amino sugar moiety as its integral and active part. More recently,[6] the synthetic carbasugar derivative oseltamivir, popularly known as Tamiflu, is being used as a drug against influenza. Because of these important developments, it is desirable to synthesize derivatives of carbasugars for improved/or selective activity as glycosidase inhibitors. Efforts in this direction are already underway,[1,4] including the recent notable reports by Shing et al.[7] on the synthesis of carbasugar derivatives as potent glycosidase inhibitors.

In continuation of our ongoing program[8] on synthesizing new glycosidase inhibitors, we report in this paper the synthesis of a new class of fused pyran-carbahexopyranoses (**2**, Fig. 1) as glycosidase inhibitors. These compounds can be considered as a hybrid[9] of a normal sugar **A** (Fig. 1) and a carbasugar derivative **B**.[10] The three fused pyran-carbahexopyranoses **17**, **19** and **29** have been synthesized from oxiranes **7** (Scheme 1) and **22** (Scheme 2) and they show moderate inhibitions of glycosidases.

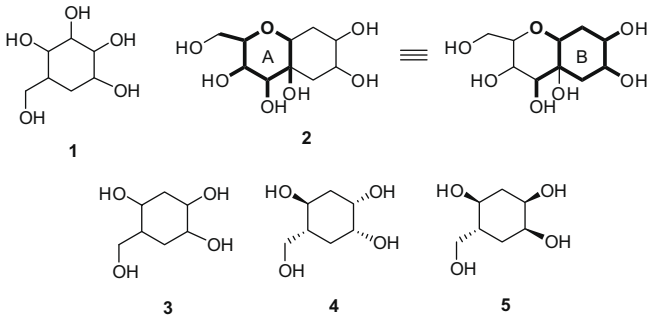

Figure 1.

2. Results and discussion

Our synthesis emanated from 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glucopyranose (**7**), which can be easily obtained from tri-*O*-benzyl-glucal **6,** by reaction with in situ generated dimethyldioxirane (DMDO) using a known procedure developed by Dondoni et al.[11] A regio- and stereospecific ring opening of oxirane **7** with allyl magnesium chloride in THF at 0 °C gave an alcohol **8** as a single diastereomer.[12] Alcohol **8** was oxidized with DMSO–Ac_2O to afford ketone **9**,[13] which was subjected to a Grignard reaction with allyl magnesium bromide in THF affording a separable mixture of tertiary alcohols **10** and **11** (9:1 ratio, 65%) in favor of the D-*manno* configured isomer **10**. The major diene **10** has the allyl group at C-2 equatorially oriented and it is trans to the anomeric allyl group, as expected,[14] and it is characterized by ^{1}H NMR and nOe spectral analysis. Its ^{1}H NMR spectrum showed a clean doublet at δ 3.55 with J = 9.0 Hz indicating that proton H-4 couples only with H-5

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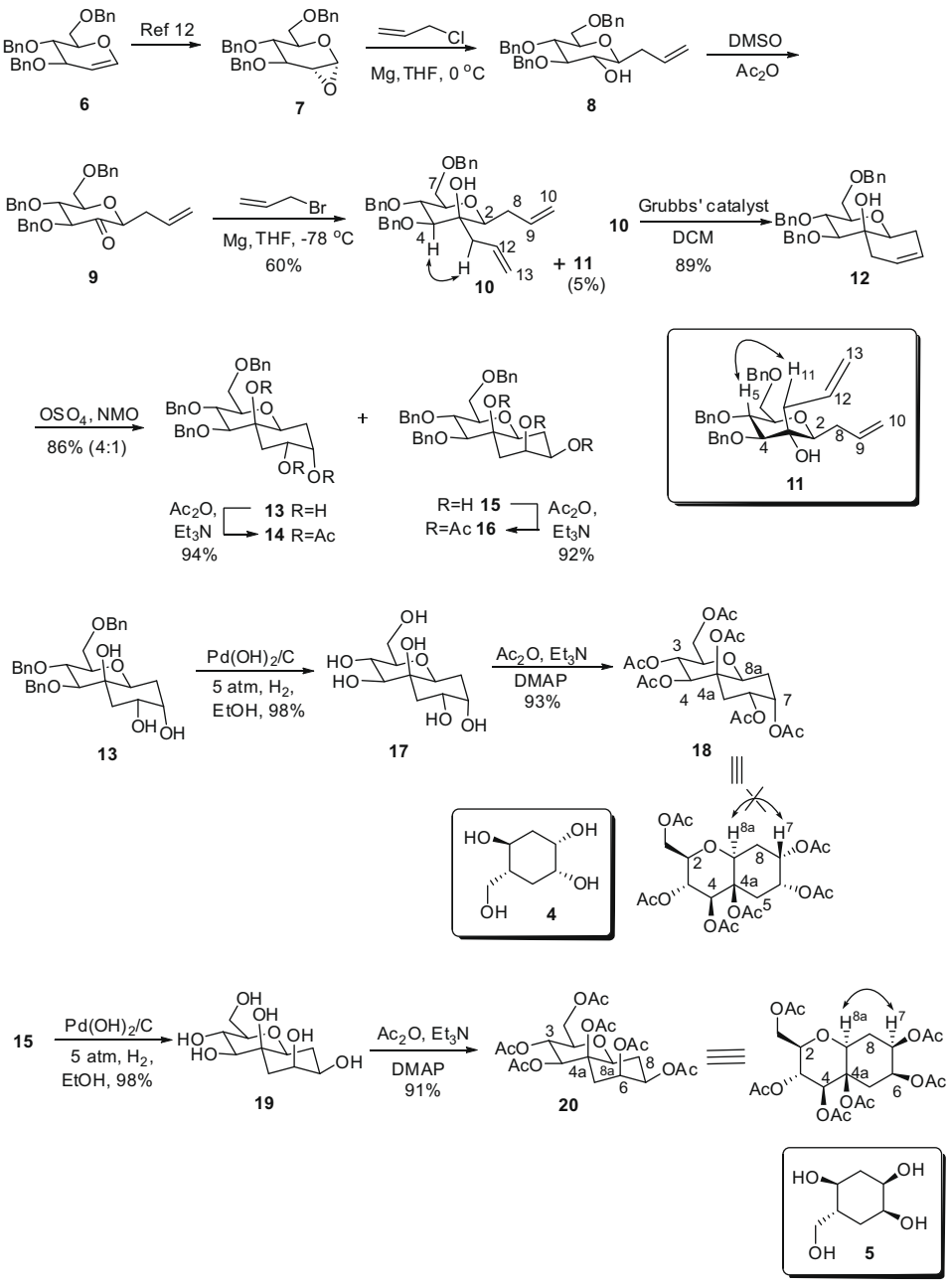
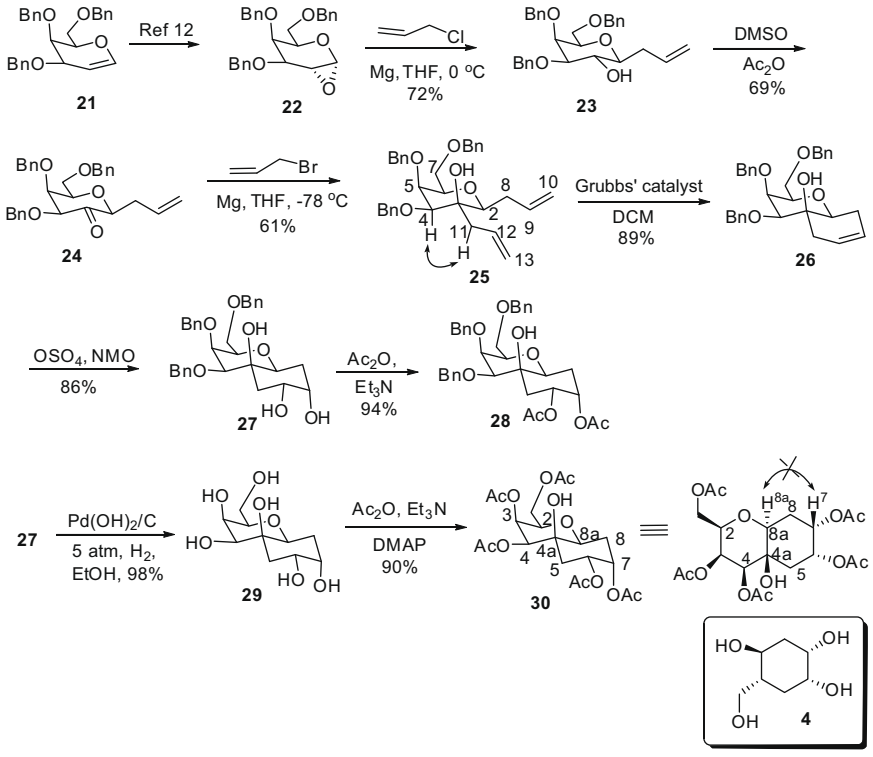


Scheme 1.

and thus must be *trans* diaxial to each other. Proton H-11 appeared as a doublet of doublets at δ 2.67 with J = 14.1, 7.3 Hz, and proton H-12 appeared as a multiplet at δ 5.66–5.55. In an nOe experiment, when the signal for proton H-11 was irradiated, the signal for H-4 was enhanced along with the signals for H-11′and H-12 suggesting that the C-2 allyl group is in the equatorial position. When H-12 proton was irradiated, signals corresponding to H-4 and H-2 were enhanced along with the signals for H-11 and H-13, which further confirmed that the C-2 allyl group of the major compound **10** is in equatorial position.

Likewise, the structure of the minor compound **11** was established on the basis of its spectral data (cf. Supplementary data) including COSY and nOe experiments. All protons were identified based on the ^{1}H NMR and COSY spectral data. As expected, its ^{1}H NMR spectrum showed a doublet for proton H-4 at δ 3.54 with J = 9.7 Hz indicating that H-4, being coupled only with H-5, must be *trans* diaxial to each other. Proton H-5 appeared at δ 3.64 as a doublet of doublets with J = 9.7, 10.8 Hz, and the allylic proton H-11 of C-2 allyl group appeared at δ 2.64-2.62 as a multiplet. In an nOe experiment, when the signal for proton H-11 was irradiated the signal for H-5 was enhanced, and there was no enhancement of signals corresponding to H-4 and H-2 suggesting that C-2 allyl group is in axial position. The signal corresponding to H-2 appeared at δ 3.27 as a doublet of doublet with J = 9.0, 2.2 Hz. Irradiation of the H-2 proton signal resulted in the enhancement of signals corresponding to H-4 and H-6, but there was no enhancement of signals corresponding to H-11 and H-12. This further confirmed that the C-2 allyl group of the minor compound **11** is in axial position.

Ring closing metathesis of diene **10** using the first-generation Grubbs' catalyst (1 mol %)[15] at ambient temperature afforded the expected cyclized product **12** in 89% yield (Scheme 1). The pres-



Scheme 2.

ence of only two olefinic protons at δ 5.68 as a broad singlet for two protons in its ^{1}H NMR spectrum confirmed the formation of the expected cyclized product. Dihydroxylation of **12** was performed using a catalytic amount of OsO_4 in the presence of *N*-methylmorpholine-*N*-oxide (NMO), which afforded a diastereomeric mixture of triols **13** and **15** in 4:1 ratio in 86% yield. These triols were characterized as their triacetates **14** and **16**, respectively. The absolute stereochemistry of the newly generated stereocenters C-6 and C-7 of compounds **13** and **15** was confirmed from the nOe experiments of the hexaacetates **18** and **20**, respectively, which were obtained later.

Bicyclic triols **13** and **15** were subjected to debenzylation on treatment with 20% $Pd(OH)_2$–C in methanol at 5 atm H_2 to give the hybrid molecules **17** and **19**, both in 98% yield. The annulated carbasugars **17** and **19** were further characterized as their peracetates **18** and **20**, which were obtained in 93% and 91% yields, respectively. The stereochemistry of the major isomer **18** was deduced from the absence of nOe correlation between protons H-7 and H-8a showing the *anti*-relationship between them, which further suggested that dihydroxylation of the olefin **12** had taken place selectively at the lower face of the double bond present in the carbasugar moiety. Interestingly, the proton H-8a appeared as a broad singlet at δ 4.48, although it should have appeared as a doublet of doublet with a coupling constant typical for a diaxial and axial–equatorial coupling if the ring was in chair conformation. Clearly, the conformation is distorted, and does not permit such couplings. At this stage, however, the identity of conformation is unclear. The stereochemistry of the minor isomer **20** was confirmed from the observed nOe correlation between protons H-7 and H-8a. Compound **17** represents a hybrid of D-mannose and 3-deoxy-β-D-*manno*-carbasugar analog **4**[11] (Fig. 1 and Scheme 1), the diastereomeric bicyclic carbasugar **19** represents a hybrid of D-mannose and 3-deoxy-α-D-*gluco* derivative **5**[11] as shown in Scheme 1.

Likewise, compound **29** (Scheme 2) was synthesized from 3,4,6-tri-*O*-benzyl-D-galactal **21,** and it represents a hybrid of D-talose with 3-deoxy-β-D-manno-carbasugar analog **4**. The synthetic pathway follows the same sequence as was used for the synthesis of hybrids **17** and **19** from 3,4,6-tri-*O*-benzyl-D-galactal **6**. Thus, oxirane **23** upon reaction with allyl magnesium chloride led to the formation of the known[16] olefinic alcohol **23** in 72% yield. Oxidation of the alcohol **23** with DMSO–Ac_2O led to the formation of the ulose **24**, which upon treatment with allyl magnesium bromide in THF at −78 °C formed alcohol **25** as a single diastereomer, which could be isolated in 61% yield after chromatography. The assigned structure of the tertiary alcohol **25** (D-*talo* configured) was confirmed by ^{1}H NMR and nOe spectral analysis (Scheme 2). Chemical shifts of protons were identified based on the ^{1}H NMR and COSY spectral data. The ^{1}H NMR spectrum of compound **25** showed a clean doublet at δ 3.34 with J = 2.6 Hz indicating that H-4 that can have coupling with only H-5 must have axial, equatorial relationship between them. In an nOe experiment, when the signal for proton H-4 was irradiated the signals for H-2, H-11 and H-12 were enhanced along with those for H-6 and H-13 confirming that C-2 allyl group is in equatorial position. Diene **25** was then dihydroxylated using OsO_4/NMO which gave a single diastereomer **27**, which was characterized as the diacetate **28**, obtained in 94% yield. The stereochemistry of the newly generated stereocenters was, however, established by nOe analysis of the pentaacetate, which was obtained later. Debenzylation of **28** with $Pd(OH)_2$–C and hydrogen gave the desired target molecule **29** in 98% yield, which was characterized from its spectral data (see experimental section). Peracetylation of hybrid **29** under standard acetylation conditions afforded the pentaacetate **30** in 90% yield instead of the expected hexaacetate, as confirmed from its mass spectrum, in addition to other spectral data, which showed HRMS $[M+H]^+$ peak at 461.1659 (calculated 461.1654). This may be attributed to the fact that the tertiary alcohol was not acetylated due to developing 1,3-diaxial steric hindrance in the galactal ring. The stereochemistry of compound **30** was deduced from the absence of an nOe correlation between protons H-7 and H-8a showing an *anti*-relationship between them. These data further suggested that dihydroxylation

Table 1
IC_{50} (mM) values for compounds **17**, **19**, and **29**[a]

Enzyme	17	19	29
α-Glucosidase (yeast)	NI	NI	NI
β-Glucosidase (almonds)	NI	NI	NI
α-Galactosidase (coffee beans)	NI	NI	1.68 mM
β-Galactosidase (bovine)	NI	0.73 mM	1.20 mM
α-Mannosidase (Jack beans)	NI	NI	NI

[a] Inhibition studies were carried out at millimolar concentration, optimal pH of the enzymes, and at 37 °C. NI: no inhibition at 5 mM concentration of the inhibitor.

of olefin **26** had taken place only at the α-face of the double bond present in the carbasugar part as shown in Scheme 2.

2.1. Enzyme inhibition studies

In summary, we have synthesized three new polyhydroxylated oxabicyclo[4,4,0]decanes **17**, **19**, and **29**, which represent hybrids of D-mannose and D-talose with 3-deoxy-carbasugar analogs (**4** and **5**). These compounds are found to be moderate glycosidase inhibitors. It is possible to improve the inhibition activity by appropriately changing the structural features of these molecules.

Preliminary screening of the three annulated carbasugars **17**, **19**, and **29** was carried out against five common glycosidases: α-glucosidase (EC 3.2.1.20), β-glucosidase (EC 3.2.1.21), α-galactosidase (EC 3.2.1.22), β-galactosidase (EC 3.2.1.23), and α-mannosidase (EC 3.2.1.24), which accept the corresponding *p*-nitrophenyl glycosides as their substrates.[17] Hybrid **17** exhibited no significant inhibition against these enzymes even at 5 mM concentration. However, annulated carbasugar **19** showed moderate inhibition only against β-galactosidase at a concentration of 0.73 mM (Table 1). Compound **29** showed less inhibition against α-galactosidase at a concentration of 1.68 mM and against β-galactosidase at a concentration of 1.20 mM as shown in Table 1. This suggests further screening to be carried out against a wider range of glycosidases to assess the potential of these compounds.

3. Experimental

3.1. General methods

IR spectra were recorded with an FTIR as a thin film or by using KBr pellets, and are expressed in cm^{-1}. ^1H (400 or 500 MHz) and ^{13}C (100 or 125 MHz) NMR spectra were recorded using $CDCl_3$ as a solvent. The stereochemistry of the compounds was assigned with the help of nOe experiments. Chemical shifts are reported in ppm downfield to tetramethylsilane. Coupling constants are reported and expressed in Hertz; splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublets), ddd (doublet of a doublet of doublets), and m (multiplet). Elemental analyses were carried out on a Thermoquest CE-instruments EA-1110 C, H, N, S analyzer. Rotation values were recorded on Autopol II automatic polarimeter at the wavelength of sodium D-line (589 nm) at 25 °C. All reactions were carried out using freshly distilled and dry solvents. The visualization of spots on TLC plates was effected by exposure to iodine or by spraying with 10% H_2SO_4 and charring. Column chromatography was performed over silica gel (100–200 Mesh) using hexane and ethyl acetate as eluent. The mass spectra were recorded on a Micromass Quattro II Triple Quadrupole Mass Spectrometer.

3.2. General procedure (A): allylation of 2-uloses with Grignard reagents

To a stirred mixture of THF (5 mL), Mg (58.3 mg, 2.4 m atom) and a catalytic amount of I_2 at 0 °C was added allyl bromide (0.1 mL, 1.2 mmol). After disappearance of the color of iodine, the solution was further stirred for 30 min at ambient temperature to give a solution of allylmagnesium bromide in THF. This freshly prepared reagent was added to a solution of ketone (472 mg, 1 mmol) in THF (5 mL) at −78 °C and stirred at the same temperature for 1 h. The reaction mixture was quenched by the addition of a satd aq soln of NH_4Cl (15 mL). The aq layer was extracted with ether (2 × 15 mL), and the combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$, and concentrated in vacuo, and the crude product was purified by silica gel chromatography.

3.3. General procedure (B): ring closing metathesis reaction

To a stirred solution of diene (514 mg, 1 mmol) in dry CH_2Cl_2 at room temperature was added Grubbs' first-generation catalyst (6 mg, 1 mol %). The mixture was stirred for 5 h and after completion of the reaction (TLC monitoring), the solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography to give the desired cyclized compound.

3.4. General procedure (C): dihydroxylation using OsO_4–NMO

To a stirred solution of olefin (486 mg, 1 mmol) in a mixture of acetone, water, and *t*-BuOH (1:1:0.4, 5 mL) at room temperature were added NMO·H_2O (162 mg, 1.2 mmol) and a catalytic amount of OsO_4 (10 μL of 2% *t*-BuOH solution). The reaction mixture was stirred for 24 h, and then it was treated with $Na_2S_2O_5$ (228 mg, 1.2 mmol). The reaction mixture was stirred for further 1 h and extracted with EtOAc (2 × 15 mL). The combined organic extracts were washed with 1 N HCl (10 mL), water, and finally with brine, and the organic layer dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a residue that was purified by column chromatography to obtain the dihydroxylated product.

3.5. General procedure (D): deprotection of benzyl groups

The cyclized product (260 mg, 0.5 mmol) was dissolved in 10 mL of MeOH, 20% $Pd(OH)_2$–C (100 mg) was added, and this mixture was shaken under 5 atm H_2 for 30–35 h at room temperature. The catalyst was filtered through Celite, and the mixture was concentrated in vacuo to obtain the target hybrid molecules.

3.6. General procedure (E): acetylation of alcohols

An alcohol was subjected to acetylation with excess of triethylamine, Ac_2O (1:1, 2 mL), and a catalytic amount of *N*,*N*-dimethyl-4-aminopyridine (DMAP) at room temperature for 10 h. Removal of the solvent under reduced pressure gave a residue that was purified by column chromatography to obtain an acetylated product.

3.7. Allylation of compound 9

2-Ulose **9** (472 mg, 1 mmol) was allylated with allylmagnesium bromide using the general procedure A to give **10** (308 mg, 60%) and **11** (26 mg, 5%) as a separable mixture of diastereomers (9:1).

3.7.1. (2*S*,3*R*,4*S*,5*R*,6*R*)-2,3-Diallyl-4,5-bis(benzyloxy)-6-(benzyloxymethyl) tetra-hydro-2*H*-pyran-3-ol (10)

(Yield: 60%). R_f = 0.6 (hexane–EtOAc 9:1). Colorless oil, α_D^{28} −36.3 (*c* 0.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3550, 3062, 3028, 2868, 1638, 1110, 1049, 913, 753, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.17 (m, 15H, Ar-H), 6.00–5.90 (m, 1H, H-9), 5.66–5.55 (m, 1H, H-12), 5.14–4.96 (m, 4H, H-10, H-10′, H-13, H-13′), 4.99 (d, 1H, *J* = 10.9 Hz, –OCH_2Ph), 4.76 (d, 1H, *J* = 10.7 Hz, –OCH_2Ph), 4.74 (d, 1H, *J* = 10.7 Hz, –OCH_2Ph), 4.66–4.55 (m, 3H, –OCH_2Ph), 3.87 (dd, 1H, *J* = 9.5, 9.0 Hz, H-5), 3.76 (dd, 1H, *J* = 11.0, 1.9 Hz, H-7), 3.70 (dd, 1H, *J* = 11.0, 4.8 Hz, H-7′), 3.55 (d, 1H, *J* = 9.0 Hz, H-4), 3.37

(ddd, 1H, J = 9.5, 4.6, 1.7 Hz, H-6), 3.32 (dd, 1H, J = 9.7, 2.6 Hz, H-2), 2.67 (dd, 1H, J = 14.1, 7.3 Hz, H-11), 2.52–2.32 (m, 2H, H-8, H-8′), 2.26 (dd, 1H, J = 14.1, 7.3 Hz, H-11′); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 138.1, 138.0, 135.8, 132.1, 128.4–127.4 (m), 119.0, 116.2, 82.4, 79.6, 79.4, 77.8, 76.1, 75.3, 74.8, 73.4, 69.1, 39.2, 32.4. ESMS: m/z 537 $[M+Na]^+$. Anal. Calcd for $C_{33}H_{38}O_5$: C, 77.01; H, 7.44. Found: C, 77.03; H, 7.42.

3.7.2. (2*S*,3*S*,4*S*,5*R*,6*R*)-2,3-Diallyl-4,5-bis(benzyloxy)-6-(benzyloxymethyl)tetra-hydro-2*H*-pyran-3-ol (11)

(Yield: 5%). R_f = 0.55 (hexane–EtOAc 9:1). Colorless oil. α_D^{28} −18.3 (c 0.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3552, 3064, 3029, 2920, 2860, 1640, 1496, 1108, 1049, 913, 753, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.13 (m, 15H, Ar-H), 6.12–6.01 (m, 1H, H-12), 5.96–5.83 (m, 1H, H-9), 5.17–5.01 (m, 4H, H-10, H-10′, H-13, H-13′), 4.90 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.79 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.77 (d, 1H, J = 10.9 Hz, –OCH_2Ph), 4.64 (d, 1H, J = 12.0 Hz, –OCH_2Ph), 4.54 (d, 1H, J = 12.0 Hz, –OCH_2Ph), 4.49 (d, 1H, J = 10.9 Hz, –OCH_2Ph), 3.79–3.63 (m, 2H, H-7, H-7′), 3.64 (dd, 1H, J = 9.7, 10.8 Hz, H-5), 3.54 (d, 1H, J = 9.7 Hz, H-4), 3.50–3.48 (m, 1H, H-6), 3.27 (dd, 1H, J = 9.0, 2.2 Hz, H-2), 2.64–2.62 (m, 1H, H-11), 2.44–2.40 (m, 1H, H-8, H-11′), 2.29–2.21 (m, 1H, H-8′); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 138.2, 138.0, 135.9, 134.7, 128.4–127.6 (m), 118.9, 116.3, 90.1, 86.6, 82.8, 80.5, 80.2, 80.0, 79.3, 69.1, 68.6, 34.6, 33.4. ESMS: m/z 537 $[M+Na]^+$. Anal. Calcd for $C_{33}H_{38}O_5$: C, 77.01; H, 7.44. Found: C, 77.05; H, 7.42.

3.8. (2*R*,3*R*,4*S*,4a*R*,8a*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-3,4,4a,5,8,8a-hexahydro-2*H*-chromen-4a-ol (12)

Diene **10** (514 mg, 1 mmol) was subjected to ring closing metathesis using the general procedure B to give **12** (436 mg, 89%) as a colorless thick liquid. R_f = 0.5 (hexane–EtOAc 9:1). α_D^{28} +22.3 (c 0.5, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 3062, 2903, 2861, 1604, 1495, 1453, 1417, 1209, 1109, 1027, 736, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.13 (m, 15H, Ar-H), 5.68 (br s, 2H, H-6, H-7), 4.91 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.87 (d, 1H, J = 11.4 Hz, –OCH_2Ph), 4.80 (d, 1H, J = 10.7 Hz, –OCH_2Ph), 4.59 (d, 1H, J = 12.2 Hz, –OCH_2Ph), 4.51 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.48 (d, 1H, J = 10.2 Hz, OCH_2Ph), 3.72–3.60 (m, 4H, H-9, H-9′, H-3, H-4), 3.53–3.50 (m, 1H, H-2), 3.38 (d, 1H, J = 4.3 Hz, H-8a), 2.54–2.39 (m, 2H, H-8, H-8′), 2.30–2.20 (m, 2H, H-5, H-5′), 1.85 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 138.2, 138.1, 128.5-127.5 (m), 123.7, 122.1, 88.6, 79.8, 78.0, 75.5, 75.4, 75.0, 73.3, 72.1, 69.2, 29.4, 27.7. ESMS: m/z 509 $[M+Na]^+$. Anal. Calcd for $C_{31}H_{34}O_5$: C, 76.52; H, 7.04. Found: C, 76.50; H, 7.05.

3.9. Dihydroxylation of compound 12

Olefin **12** (486 mg, 1 mmol) was subjected to dihydroxylation using the general procedure C to give **13** (358 mg, 69%) and **15** (88 mg, 17%) as a separable mixture of diastereomers (4:1), which were further subjected to acetylation using the general procedure E to give **14** (Yield: 94%) and **16** (Yield: 92%), respectively.

3.9.1. (2*R*,3*R*,4*S*,4a*R*,6*R*,7*S*,8a*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)octahydro-2*H*-chromene-4a,6,7-triyl triacetate (14)

(Yield: 94%). R_f = 0.4 (hexane–EtOAc 4:1). White solid. α_D^{28} +24.5 (c 0.8, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3030, 2923, 2854, 1738, 1648, 1496, 1453, 1400, 1237, 1135, 1098, 1048, 1028, 798, 738, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.12 (m, 15H, Ar-H), 5.36 (d, 1H, J = 3.1 Hz, H-6), 5.24 (td, 1H, J = 12.7, 3.9 Hz, H-7), 4.76–4.64 (m, 5H, –OCH_2Ph, H-3, H-4), 4.59 (d, 1H, J = 12.7 Hz, –OCH_2Ph), 4.54 (d, 1H, J = 12.4 Hz, –OCH_2Ph), 4.49 (d, 1H, J = 10.7 Hz, –OCH_2Ph), 3.66–3.55 (m, 4H, H-9, H-9′, H-8a, H-2), 2.62–2.57 (m, 1H, H-5′), 2.55 (dd, 1H, J = 1.2, 1.0 Hz, H-8), 2.35 (dd, 1H, J = 8.0, 1.0 Hz, H-5), 2.09 (s, 3H, –COCH_3), 1.99 (s, 3H, –COCH_3), 1.99–1.95 (m, 1H, H-8′), 1.91 (s, 3H, –COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 170.0, 169.9, 138.4, 138.1, 137.9, 128.3–127.5 (m), 82.7, 82.3, 79.3, 77.9, 75.1, 74.9, 73.3, 72.9, 68.8, 67.4, 67.3, 29.6, 26.6, 22.4, 21.2, 21.0. ESMS: m/z 669 $[M+Na]^+$. Anal. Calcd for $C_{37}H_{42}O_{10}$: C, 68.71; H, 6.55. Found: C, 68.69; H, 6.58.

3.9.2. (2*R*,3*R*,4*S*,4a*R*,6*S*,7*R*,8a*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)octahydro-2*H*-chromene-4a,6,7-triyl triacetate (16)

(Yield: 92%). R_f = 0.38 (hexane–EtOAc, 4:1). Colorless oil. α_D^{28} −9.2 (c 0.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2924, 2854, 1737, 1648, 1496, 1453, 1400, 1235, 1141, 1109, 1046, 1027, 738, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.14 (m, 15H, Ar-H), 5.16–5.15 (m, 2H, H-6, H-7), 4.82–4.75 (m, 3H, –OCH_2Ph, H-3, H-4), 4.66 (d, 1H, J = 11.0 Hz, –OCH_2Ph), 4.62 (d, 1H, J = 11.5 Hz, –OCH_2Ph), 4.56–4.45 (m, 3H, –OCH_2Ph), 3.75–3.68 (m, 3H, H-8a, H-9, H-9′), 3.48 (br d, 1H, J = 10.0 Hz, H-2), 2.35–2.20 (m, 3H, H-8, H-5, H-5′), 2.03 (s, 3H, –COCH_3), 1.94 (s, 3H, –COCH_3), 1.92 (s, 3H, –COCH_3), 1.74 (br d, 1H, J = 16.0 Hz, H-8′); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 170.5, 170.2, 138.5, 138.1, 128.5–127.8 (m), 85.9, 81.7, 79.4, 78.1, 75.1, 75.0, 73.5, 70.4, 69.2, 68.2, 67.4, 28.7, 21.1, 22.3, 21.2, 21.1. ESMS: m/z 669 $[M+Na]^+$. Anal. Calcd for $C_{37}H_{42}O_{10}$: C, 68.71; H, 6.55. Found: C, 68.70; H, 6.54.

3.10. (2*R*,3*S*,4*S*,4a*S*,6*R*,7*S*,8a*S*)-2-(Hydroxymethyl)octahydro-2*H*-chromene-3,4,4a,6,7-pentaol (17)

Compound **13** (260 mg, 0.5 mmol) was subjected to global deprotection using the general procedure D to give **17** (124 mg, 98%) as a thick liquid. R_f = 0.45 (MeOH–EtOAc 1:9). α_D^{28} −16.4 (c 0.2, H_2O). ^{1}H NMR (400 MHz, D_2O): δ 3.92 (br s, 1H, J = 3.9 Hz), 3.79 (br d, 1H, J = 11.9 Hz), 3.68 (d, 1H, J = 11.9 Hz), 3.51 (dd, 1H, J = 11.7, 5.1 Hz), 3.41 (br s, 1H), 3.24–3.18 (m, 3H), 1.97–1.84 (m, 2H), 1.73 (dd, 1H, J = 8.5, 4.8 Hz), 1.58 (br d, 1H, J = 13.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 81.1, 80.1, 79.2, 73.8, 70.0, 69.2, 67.4, 61.8, 30.2, 28.7. HRMS calcd for $C_{10}H_{17}O_7$ $[M-H]^-$ 249.0974, found 249.0975.

3.11. (2*R*,3*S*,4*S*,4a*S*,6*S*,7*R*,8a*S*)-2-(Hydroxymethyl)octahydro-2*H*-chromene-3,4,4a,6,7-pentaol (19)

Compound **15** (60 mg, 0.12 mmol) was subjected to global deprotection using the general procedure D to give **19** (28 mg, 98%) as a thick liquid. R_f = 0.43 (MeOH–EtOAc 1:9). α_D^{28} −13.6 (c 1.0, H_2O). ^{1}H NMR (400 MHz, D_2O): δ 3.77–3.76 (m, 2H), 3.70 (dd, 1H, J = 12.4, 2.2 Hz), 3.54 (dd, 1H, J = 12.4, 5.8 Hz), 3.37–3.28 (m, 3H), 3.40 (dd, 1H, J = 7.3, 6.3 Hz), 1.92–1.91 (m, 2H), 1.70 (dd, 1H, J = 10.6, 4.4 Hz), 1.54 (t, 1H, J = 12.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 83.2, 82.3, 78.9, 76.8, 71.3, 70.8, 69.6, 63.3, 32.5, 30.1. HRMS calcd for $C_{10}H_{17}O_7$ $[M-H]^-$ 249.0974, found 249.0972.

3.12. (2*R*,3*R*,4*S*,4a*R*,6*R*,7*S*,8a*S*)-2-(Acetoxymethyl)octahydro-2H-chromene-3,4,4a,6,7-pentayl pentaacetate (18)

Compound **17** (50 mg, 0.2 mmol) was acetylated using the general procedure E to give **18** (93 mg, 93%) as a colorless oil. R_f = 0.5 (hexane–EtOAc 1:1). α_D^{28} −91.6 (c 1.0, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2853, 1743, 1369, 1235, 1144, 1038, 680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.69 (d, 1H, J = 9.5 Hz, H-4), 5.40–5.41 (m, 1H, H-6), 5.18 (td, 1H, J = 8.2, 4.1, H-7), 5.02 (dd, 1H, J = 10.5, 9.5 Hz, H-3), 4.48 (br s, 1H, H-8a), 4.17–4.08 (m, 2H, H-9, H-9′), 3.70 (ddd, 1H, J = 10.5, 2.6, 2.2 Hz, H-2), 2.88 (br d, 1H, J = 15.8 Hz, H-5), 2.22–2.19 (m, 1H, H-8), 2.09–1.98 (m, 2H, H-8′,

H-5′), 2.10 (s, 3H, –COCH_3), 2.07 (s, 3H, –COCH_3), 2.05 (s, 3H, –COCH_3), 2.01 (s, 3H, –COCH_3), 2.00 (s, 3H, –COCH_3), 1.99 (s, 3H, –COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 170.6, 170.3, 170.2, 169.7, 83.2, 76.2, 72.5, 71.2, 68.1, 67.7, 67.2, 62.5, 28.3, 26.9, 22.2, 21.1, 20.8, 20.7, 20.6. HRMS calcd for $C_{22}H_{31}O_{13}$ $[M+H]^+$ 503.1759, found 503.1765.

3.13. (2*R*,3*R*,4*S*,4a*R*,6*S*,7*R*,8a*S*)-2-(Acetoxymethyl)octahydro-2*H*-chromene-3,4,4a,6,7-pentayl pentaacetate (20)

Compound **19** (30 mg, 0.12 mmol) was acetylated using the general procedure E to give **20** (61 mg, 91%) as a colorless oil. R_f = 0.5 (hexane–EtOAc 1:1). α_D^{28} −70.3 (*c* 1.0, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2924, 2853, 1744, 1430, 1370, 1253, 1037 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39–5.37 (m, 1H, H-3), 5.27–5.25 (m, 1H, H-6), 4.83 (td, 1H, *J* = 4.9, 8.5 Hz, H-7), 4.78 (d, 1H, *J* = 12.2 Hz, H-4), 4.16–4.13 (m, 2H, H-9, H-9′), 3.96–3.93 (m, 1H, H-2), 3.43 (dd, 1H, *J* = 11.9, 3.8 Hz, H-8a), 2.45–2.31 (m, 2H, H-8, H-5), 1.99–1.95 (m, 1H, H-8′), 1.36 (brd, 1H, *J* = 13.7 Hz, H-5′), 2.08 (s, 3H, –COCH_3), 2.07 (s, 3H, –COCH_3), 2.05 (s, 3H, –COCH_3), 2.04 (s, 3H, –COCH_3), 2.03 (s, 3H, –COCH_3), 2.00 (s, 3H, –COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.5, 170.2, 170.0, 169.6, 83.1, 77.3, 76.1, 72.4, 71.1, 68.0, 67.5, 67.1, 62.4, 28.2, 26.8, 22.1, 21.0, 20.7, 20.6. HRMS calcd for $C_{22}H_{31}O_{13}$ $[M+H]^+$ 503.1759, found 503.1764.

3.14. (2*S*,3*S*,4*R*,5*S*,6*R*)-2-Allyl-4,5-bis(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-3-ol (23)

To a solution of epoxide **22** (864 mg, 2 mmol) in THF (30 mL) was added allylmagnesium chloride (2 mL of 2.0 M solution in THF, 4 mmol) dropwise at 0 °C, and then the reaction mixture was allowed to stir at ambient temperature. After 30 min, the reaction mixture was quenched by the addition of a satd aq soln of NH_4Cl (25 mL), and the aq phase was extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (15 mL), dried over Na_2SO_4, and concentrated in vacuo, and the crude product was purified by silica gel chromatography to give **23** (Yield: 685 mg, 72%) as a white solid. R_f = 0.5 (hexane–EtOAc 9:1). α_D^{28} −39.4 (*c* 0.8, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2854, 1737, 1601, 1453, 1101, 1020, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.25 (m, 15H, Ar-H), 5.95–5.88 (m, 1H, H-9), 5.10 (d, 1H, *J* = 17.0 Hz, H-10), 5.03 (d, 1H, *J* = 10.2 Hz, H-10′), 4.84 (d, 1H, *J* = 11.7 Hz, –OCH_2Ph), 4.74 (d, 1H, *J* = 11.9 Hz, –OCH_2Ph), 4.62 (d, 1H, *J* = 11.7 Hz, –OCH_2Ph), 4.54–4.44 (m, 3H, –OCH_2Ph), 4.02 (s, 1H, H-4), 3.80 (dd, 1H, *J* = 9.5, 8.0 Hz, H-5), 3.59 (br s, 3H, H-3, H-7, H-7′), 3.38 (dd, 1H, *J* = 7.0, 2.4 Hz, H-6), 3.24 (dd, 1H, *J* = 8.5, 5.8 Hz, H-2), 2.60–2.59 (m, 1H, H-8), 2.34–2.29 (m, 2H, H-8′, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 138.0, 137.8, 135.0, 128.6–127.5 (m), 116.6, 84.2, 79.6, 74.3, 73.6, 72.7, 71.6, 70.4, 68.9, 36.3. ESMS: *m*/*z* 497 $[M+Na]^+$. Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 76.93; H, 7.24.

3.15. (2*S*,4*S*,5*S*,6*R*)-2-Allyl-4,5-bis(benzyloxy)-6-(benzyloxymethyl)dihydro-2*H*-pyran-3(4H)-one (24)

A solution of alcohol **23** (474 mg, 1 mmol) in a mixture of DMSO–Ac_2O (2:1 24 mL) was stirred for 5 h under N_2 atmosphere. The reaction mixture was quenched by the addition of ice-cold water (100 mL), and the aq phase was extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (15 mL), dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography to give **24** (Yield: 327 mg, 69%) as a white solid. R_f = 0.6 (hexane–EtOAc 9:1). α_D^{28} −40.2 (*c* 0.8, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2854, 1729, 1601, 1382, 1095, 1021, 698, 465 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.21 (m, 15H, Ar-H), 5.84–5.77 (m, 1H, H-9), 5.08 (d, 1H, *J* = 17.3 Hz, H-10), 5.01 (d, 1H, *J* = 10.2 Hz, H-10′), 4.92 (d, 1H, *J* = 12.2 Hz, –OCH_2Ph), 4.90 (d, 1H, *J* = 11.7 Hz, –OCH_2Ph), 4.59 (d, 1H, *J* = 11.9 Hz, –OCH_2Ph), 4.50 (d, 1H, *J* = 12.2 Hz, –OCH_2Ph), 4.41 (d, 1H, *J* = 11.9 Hz, –OCH_2Ph), 4.36 (d, 1H, *J* = 11.7 Hz, –OCH_2Ph), 4.27 (d, 1H, *J* = 2.4 Hz, H-4), 4.15 (d, 1H, *J* = 2.4 Hz, H-2), 3.92 (dd, 1H, *J* = 6.1, 5.8 Hz, H-5), 3.81 (dd, 1H, *J* = 7.0, 4.8 Hz, H-6), 3.57-3.47 (m, 2H, H-7, H-7′), 2.61–2.36 (m, 2H, H-8, H-8′); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 138.6, 138.0, 137.8, 135.0, 128.5–126.9 (m), 116.8, 83.7, 80.9, 79.1, 74.4, 73.5, 71.9, 69.9, 68.6, 33.0. ESMS: *m*/*z* 495 $[M+Na]^+$. Anal. Calcd for $C_{30}H_{32}O_5$: C, 76.25; H, 6.83. Found: C, 76.23; H, 6.85.

3.16. (2*S*,3*R*,4*S*,5*S*,6*R*)-2,3-Diallyl-4,5-bis(benzyloxy)-6-(benzyloxymethyl)tetra-hydro-2*H*-pyran-3-ol (25)

2-Ulose **24** (472 mg, 1 mmol) was allylated with allylmagnesium bromide using the general procedure A to give **25** (313 mg, 61%) as a colorless oil. R_f = 0.45 (hexane–EtOAc 9:1). α_D^{28} −21.9 (*c* 1.0, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2869, 1601, 1495, 1452, 1272, 1095, 1026, 917, 738, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.22 (m, 15H, Ar-H), 5.85–5.83 (m, 1H, H-9), 5.36–5.32 (m, 1H, H-12), 5.04–4.93 (m, 4H, H-10, H-10′, H-13, H-13′), 4.88 (d, 1H, *J* = 10.8 Hz, –OCH_2Ph), 4.74 (d, 1H, *J* = 11.4 Hz, –OCH_2Ph), 4.50–4.46 (m, 3H, –OCH_2Ph), 4.42 (d, 1H, *J* = 11.7 Hz, –OCH_2Ph), 4.09 (br s, 1H, H-5), 3.63–3.56 (m, 2H, H-7, H-7′), 3.47 (dd, 1H, *J* = 6.8, 5.6 Hz, H-6), 3.34 (d, 1H, *J* = 2.6 Hz, H-4), 3.20 (dd, 1H, *J* = 10.0, 2.4 Hz, H-2), 2.84 (dd, 1H, *J* = 14.0, 7.7 Hz, H-11), 2.45–2.41 (m, 1H, H-8), 2.29–2.27 (m, 1H, H-8′), 2.10 (dd, 1H, *J* = 14.1, 7.5 Hz, H-11′); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 137.6, 137.6, 136.1, 132.7, 128.5-127.8 (m), 118.5, 115.9, 81.7, 77.5, 75.6, 75.2, 73.7, 73.6, 73.5, 71.2, 68.7, 37.4, 32.4; ESMS: *m*/*z* 537 $[M+Na]^+$. Anal. Calcd for $C_{33}H_{38}O_5$: C, 77.01; H, 7.44. Found: C, 77.05; H, 7.42.

3.17. (2*R*,3*S*,4*S*,4a*R*,8a*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-3,4,4a,5,8,8a-hexahydro-2*H*-chromen-4a-ol (26)

Diene **25** (514 mg, 1 mmol) was subjected to ring closing metathesis using the general procedure B to give **26** (432 mg, 89%) as a colorless thick liquid. R_f = 0.4 (hexane–EtOAc 9:1). α_D^{28} +26.8 (*c* 0.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3063, 2904, 2865, 1605, 1455, 1207, 1106, 1023, 739, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.19 (m, 15H, Ar-H), 5.49–5.44 (m, 2H, H-6, H-7), 4.93 (d, 1H, *J* = 11.0 Hz, –OCH_2Ph), 4.74 (d, 1H, *J* = 12.2 Hz, –OCH_2Ph), 4.51 (d, 1H, *J* = 11.0 Hz, –OCH_2Ph), 4.03 (m, 1H, H-3), 3.55–3.53 (m, 3H, H-4, H-9, H-9′), 3.35 (dd, 1H, *J* = 10.2, 6.0 Hz, H-2), 3.14 (d, 1H, *J* = 2.4 Hz, H-8a), 2.56 (dd, 1H, *J* = 17.8, 3.9 Hz, H-8), 2.35–2.29 (m, 1H, H-5′), 2.15-2.10 (m, 1H, H-5), 1.70 (br d, 1H, *J* = 17.8 Hz, H-8′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.8, 137.6, 128.4–127.8 (m), 123.8, 123.3, 80.9, 78.2, 78.1, 75.1, 73.5, 71.6, 71.4, 71.2, 68.8, 35.1, 27.3. ESMS: *m*/*z* 509 $[M+Na]^+$. Anal. Calcd for $C_{31}H_{34}O_5$: C, 76.52; H, 7.04. Found: C, 76.50; H, 7.01.

3.18. (2*R*,3*S*,4*S*,4a*R*,6*R*,7*S*,8a*S*)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-4a-hydroxy-octahydro-2*H*-chromene-6,7-diyl diacetate (28)

Olefin **26** (486 mg, 1 mmol) was subjected to dihydroxylation using the general procedure C to give **27** (447 mg, 86%), which was further subjected to acetylation using the general procedure E to give **28** (Yield: 484 mg, 94%) as a white solid. R_f = 0.5 (hexane–EtOAc 4:1). α_D^{28} +96.3 (*c* 0.8, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3087, 3062, 2927, 1743, 1496, 1264, 1100, 1028, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39–7.24 (m, 15H, Ar-H), 5.41 (br s, 1H, H-6), 5.23–5.20 (m, 1H, H-7), 4.94 (d, 1H, *J* = 11.0 Hz, –OCH_2Ph),

4.75 (d, 1H, J = 11.9 Hz, –OCH_2Ph), 4.58 (d, 1H, J = 11.9 Hz, –OCH_2Ph), 4.53 (d, 1H, J = 11.0 Hz, –OCH_2Ph), 4.54 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.52 (d, 1H, J = 11.7 Hz, –OCH_2Ph), 4.34 (d, 1H, J = 2.1 Hz, H-4), 4.05 (d, 1H, J = 2.6 Hz, H-3), 3.61–3.56 (m, 3H, H-9, H-9′, OH), 3.44 (dd, 1H, J = 11.7, 4.4 Hz, H-2), 3.27 (d, 1H, J = 2.6 Hz, H-8a), 2.36 (dd, 1H, J = 11.4, 4.4 Hz, H-5′), 2.18–2.14 (m, 1H, H-8′), 1.88–1.85 (m, 1H, H-5), 2.06 (s, 3H, –COCH_3), 1.96 (s, 3H, –COCH_3), 1.46–1.44 (m, 1H, H-8); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 169.8, 137.6, 137.4, 137.3, 128.5–127.9 (m), 80.0, 77.9, 76.3, 75.2, 73.7, 73.6, 72.8, 71.8, 69.1, 68.7, 68.2, 32.1, 29.4, 21.1, 20.9. ESMS: m/z 627 $[M+Na]^+$. Anal. Calcd for $C_{35}H_{40}O_9$: C, 69.52; H, 6.67. Found: C, 69.56; H, 6.65.

3.19. (2*R*,3*R*,4*S*,4a*S*,6*R*,7*S*,8a*S*)-2-(Hydroxymethyl)octahydro-2*H*-chromene-3,4,4a,6,7-pentaol (29)

Compound **27** (520 mg, 1 mmol) was subjected to global deprotection using the general procedure D to give **29** (249 mg, 98%) as a thick liquid. R_f = 0.5 (MeOH–EtOAc 1:4). α_D^{28} −19.2 (c 0.2, H_2O). ^{1}H NMR (400 MHz, D_2O): δ 3.94 (br s, 1H, J = 3.9 Hz), 3.77–3.74 (m, 2H), 3.63 (dd, 1H, J = 11.5, 4.0 Hz), 3.61 (d, 1H, J = 5.0 Hz), 3.57–3.44 (m, 2H), 3.41 (d, 1H, J = 2.5 Hz), 3.35 (d, 1H, J = 2.5 Hz), 1.95 (dd, 1H, J = 13.0, 4.0 Hz), 1.88–1.85 (m, 2H), 1.40 (dd, 1H, J = 13.0, 12.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.0, 75.0, 73.8, 71.6, 69.6, 68.8, 66.7, 61.4, 30.0, 30.7. HRMS calcd for $C_{10}H_{17}O_7$ $[M-H]^-$ 249.0974, found 249.0974.

3.20. (2*R*,3*S*,4*S*,4a*R*,6*R*,7*S*,8a*S*)-2-(Acetoxymethyl)-4a-hydroxyoctahydro-2*H*-chromene-3,4,6,7-tetrayl tetraacetate (30)

Compound **29** (50 mg, 0.2 mmol) was acetylated using the general procedure E to give **30** (82 mg, 90%) as a colorless oil. R_f = 0.5 (hexane–EtOAc, 1:1). α_D^{28} +6.2 (c 1.0, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 2926, 2851, 1746, 1237, 1141, 1039, 680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.43 (m, 1H, H-7), 5.39 (d, 1H, J = 2.9 Hz, H-3), 5.19–5.17 (m, 1H, H-6), 4.19 (d, 1H, J = 3.5 Hz, H-4), 4.13–4.11 (m, 2H, H-9, H-9′), 3.96 (dd, 1H, J = 6.6, 2.9 Hz, H-2), 3.67 (dd, 1H, J = 11.9, 4.8 Hz, H-8a), 2.90 (br s, 1H, OH), 2.16–2.15 (m, 1H, H-8), 2.11–2.07 (m, 2H, H-8′, H-5), 1.65–1.62 (m, 1H, H-5′), 2.16 (s, 3H, –COCH_3), 2.11 (s, 3H, –COCH_3), 2.09 (s, 3H, –COCH_3), 2.05 (s, 3H, –COCH_3), 1.97 (s, 3H, –COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.4, 170.0, 169.9, 169.3, 76.2, 75.3, 72.1, 71.1, 68.6, 67.7, 67.6, 61.6, 31.3, 29.2, 21.0, 20.8, 20.7, 20.6, 20.5. HRMS calcd for $C_{20}H_{29}O_{12}$ $[M+H]^+$ 461.1654, found 461.1659.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.01.017.

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