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Graphical Abstract

A Convenient Synthesis of Carbohydrate Derived Furo/Pyrano[2,3-*b*]pyrans from 2-hydroxymethyl Glycals

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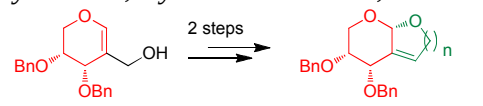

2-hydroxymethyl glycal

n = 1 furo[2,3-*b*]pyrans
n = 2 pyrano[2,3-*b*]pyrans

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ABSTRACT

An efficient method for the stereoselective synthesis of various linearly fused bicyclic acetals using 2-hydroxymethyl glycals, involving Ferrier type rearrangement and ring-closing metathesis as the key steps, is revealed. The methodology was shown to be very general by applying it to various sugar substrates which lead to the formation of various bicyclic furo/pyrano[2,3-*b*]pyran ring systems.

1. Introduction

Linearly fused bicyclic acetals are ubiquitously present as subunits in a number of bio-active natural products.[1] A major portion of these bicyclic acetals exists either as furo[2,3-*b*]pyrans or pyrano[2,3-*b*]pyrans. For instance, Benesudon (antibacterial and cytotoxic with IC_{90} values of 1-2 µg/mL),[2] Euplotin A, B, and C[3] (cytotoxic), Novaxenicin A and B (induces apoptosis),[4] (–)-Penifulvin A and B (potent insecticides),[5] Tetrahydroaplysulfurin-1,[6] Cadlinolides A, B and C,[7] and Neopeapyran[8] possess the furo[2,3-*b*]pyran framework

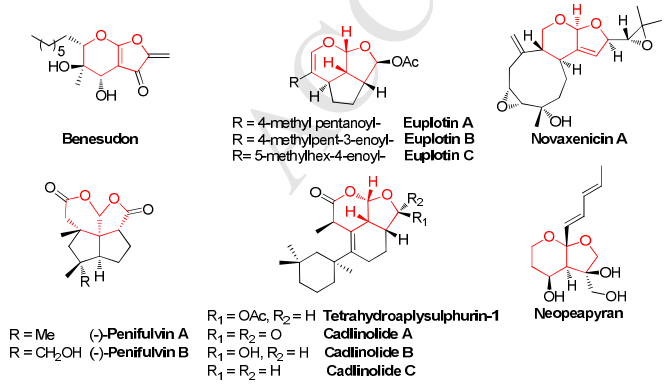

Figure 1: Representative natural products possessing furo[2,3-*b*]pyran framework.

(Figure 1). On the other hand, pyrano[2,3-*b*]pyran containing compound **1** is an important precursor in the total synthesis of ansamycins[9] whereas compound **2** is a natural product produced by a rare bacterial strain *Actinoalloteichus nanshanensis sp. Nov.*[10] The glycofused benzopyran **3** was recently identified as a novel ligand for amyloid β peptidase in the development of novel therapeutics for Alzheimer's disease[11] (Figure 2).

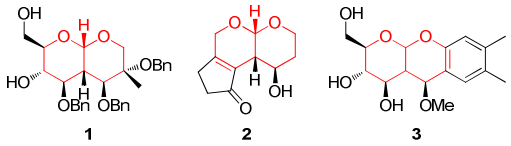

Figure 2: Representative natural and synthetic products containing the pyrano[2,3-*b*]pyran structure.

Very often, the presence of the bicyclic acetal system in bio-active molecules is vital for acquiring the appropriate molecular conformation that helps in eliciting the biological response. In general, the formation of these bicyclic acetal motifs involves the halo etherification of cyclic vinyl ethers, using NBS or NIS and allyl or propargyl alcohol, followed by a radical cyclization to produce the corresponding bicyclic acetals.[12] Various radical initiators like Vitamin B_{12},[13] AIBN,[14] Et_3B,[15] Co(salen),[16] *etc.*, have been studied for the radical cyclization reactions. Carbohydrate derived vinyl ethers, generally called as glycals, have been one of the highly studied precursors in radical cyclization reactions.[17] Apart from these, we previously reported

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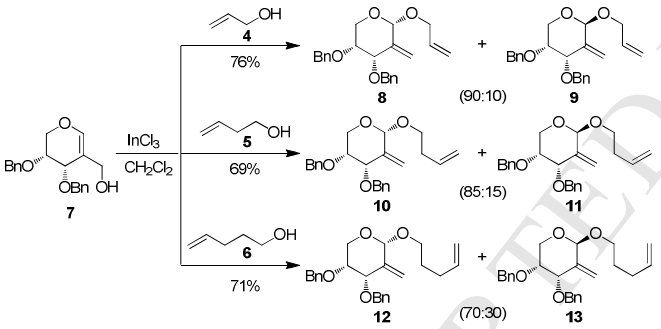
the application of 2-*C*-branched sugars,[18] 3-*C*-branched glycals[19] and 1,2-cyclopropanated sugar derivatives[20] for the stereoselective preparation of a variety of furo/pyrano[2,3-*b*]furans/pyrans. Very recently, Vankar *et al.* reported a distinct method involving Grignard addition of allyl and vinyl magnesium halides on allyl-2-*oxo*-glycosides followed by ring-closing metathesis to produce pyrano[2,3-*b*]pyran/oxepines.[21a] A similar protocol was also described to synthesize 1,2-annulated sugars with β-mannose configuration.[21b] In addition to the above methods, very few approaches were available for the synthesis of furo/pyrano[2,3-*b*]pyran ring systems encompassing acid-catalyzed cyclization of hydroxyacetals,[22] cycloaddition reactions,[23] intramolecular dehydration reactions[24] and ketalization of acyclic dihydroxyaldehydes.[25]

In continuation of our efforts in the synthesis of fused bicyclic acetals,[26] herein we report the application of *C*-2-methylene glycosides in the synthesis of furo/pyrano[2,3-*b*]pyrans in two steps comprising Ferrier type rearrangement and ring closing metathesis.

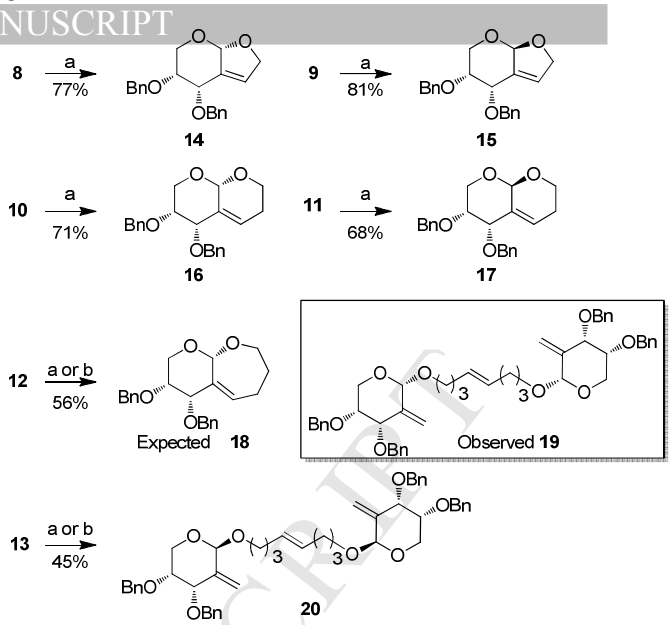
2. Results and Discussion

We intended the synthesis of furo/pyrano[2,3-*b*]pyran systems starting from *C*-2-methylene *O*-alkenyl glycosides of various length. Towards this, 2-hydroxymehtyl D-arabinal **7**[27] was treated with allyl alcohol **4** in the presence of catalytic $InCl_3$[28] to provide the *C*-2-methylene α- and β-glycosides **8** and **9**. In a similar way glycosides **10**, **11** and **12**, **13** were synthesized by the Ferrier type rearrangement of **7** with 3-butenyl alcohol **5** and 4-pentenyl alcohol **6**, respectively (Scheme 1).[29]



Scheme 1: Synthesis of D-arabinose derived *C*-2-methylene *O*-glycoside derivatives.

Having a series of D-arabinose derived glycoside dienes **8-13** in hand, we proceeded to synthesize various bicyclic acetals using ring closing metathesis reaction. Thus, allyl arabinopyranosides **8** and **9** upon treatment with Grubb's 2nd generation catalyst (G-II) provided the furo[2,3-*b*]pyran derivatives **14** and **15** as the only products respectively, in good yield (Scheme 2). Similarly, 3-butenyl alcohol derived arabinopyranoside derivatives **10** and **11** upon exposing to G-II provided the corresponding pyrano[2,3-*b*]pyran derivatives **16** and **17** respectively, again as the only products. However, subjecting the 4-pentenyl derived arabinopyranoside **12** to RCM reaction using G-II provided the dimerization product **19** and no detectable amount of the expected pyrano[2,3-*b*]oxepine **18** was observed. Carrying out the reaction using Grubbs 1st generation catalyst (G-I) also did not show any change in the product formation. Subjecting the β-isomer **13** to G-I or G-II mediated RCM reaction also lead to the formation of dimer **20** as the only isolable product (Scheme 2).



Scheme 2: Synthesis of D-arabinose derived furo/pyrano[2,3-*b*]pyran frameworks. Reagents and conditions: (a) G-II (20 mol%), toluene, 80 °C. (b) G-I (20 mol%), toluene, 80 °C.

Encouraged by these observations, we extended the methodology to glucal and galactal derived 2-hydroxymethyl derivatives **21** and **22**[30] respectively. Thus, glucal derived *C*-2 methylene *O*-glycosides **23**,[28] **24** and **25**[31] were prepared from **21**, galactose derived *C*-2-methylene *O*-glycosides **26**,[28] **27** and **28**[31] were obtained from **22** by following the procedure for the preparation of compound **8**. (Table 1). Unlike in the case of 2-hydroxymethyl arabinal derivative **7**, the Ferrier type rearrangement of **21** and **22** with *O*-nucleophilic allyl alcohol **4**, 3-butenyl alcohol **5** and 4-pentenyl alcohol **6** provided the corresponding *C*-2-methylene-α-D-glycosides as the only products. No isolable amounts of the *C*-2-methylene-β-D-glycosides were obtained.

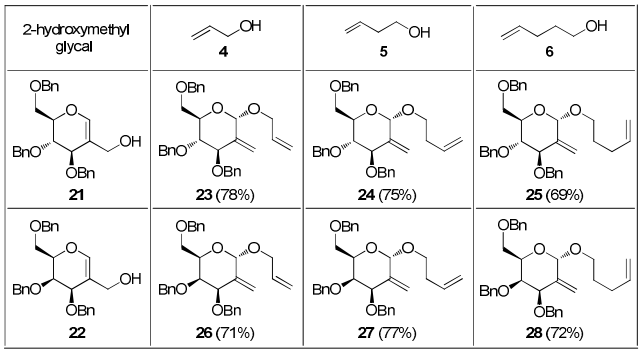
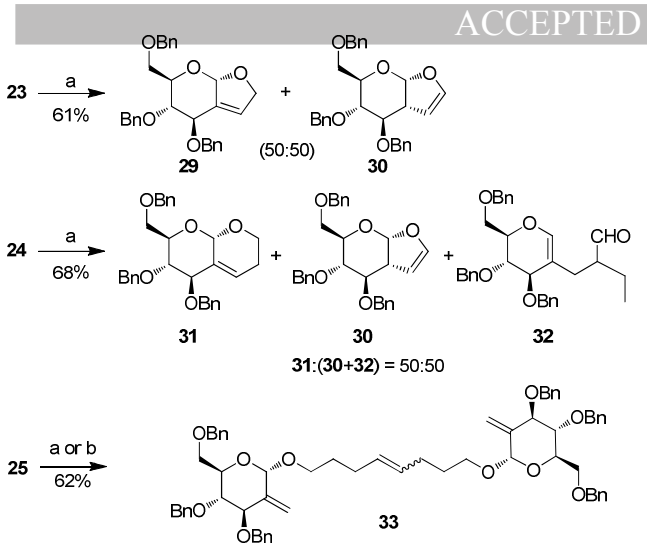


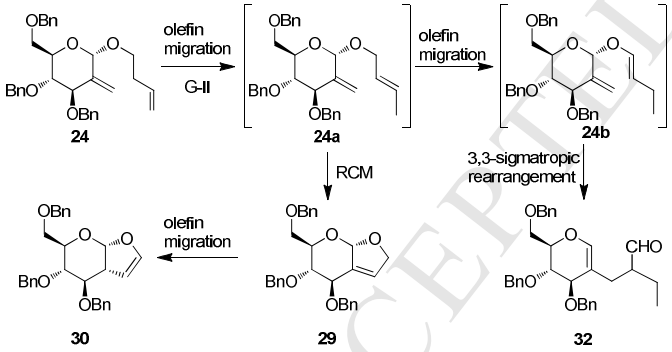
Table 1: Synthesis of D-glucose and D-galactose derived *C*-2-methylene *O*-glycosides.

Subjecting *C*-2-methylene allyl α-D-glucopyranoside **23** to RCM provided the furo[2,3-*b*]pyran **29** along with the olefin migrated furo[2,3-*b*]pyran **30** in 1:1 ratio in 61% yield. On the other hand, *C*-2-methylene 3-butenyl α-D-glucopyranoside **24** upon RCM with G-II provided the expected pyrano[2,3-*b*]pyran derivative **31** in 34% yield along with a mixture of furo[2,3-*b*]pyran **30** and 2-*C*-branched glycal **32** in 34%. Whereas, RCM of compound **25** using G-I or G-II gave the dimer **33** (*cis*, *trans* (0.75:1) mixture) as the only isolable product (Scheme 3).



Scheme 3: Synthesis of D-glucose derived furo/pyrano[2,3-*b*]pyran frameworks. Reagents and conditions: (a) G-II (20 mol%), toluene, 80 °C. (b) G-I (20 mol%), toluene, 80 °C.

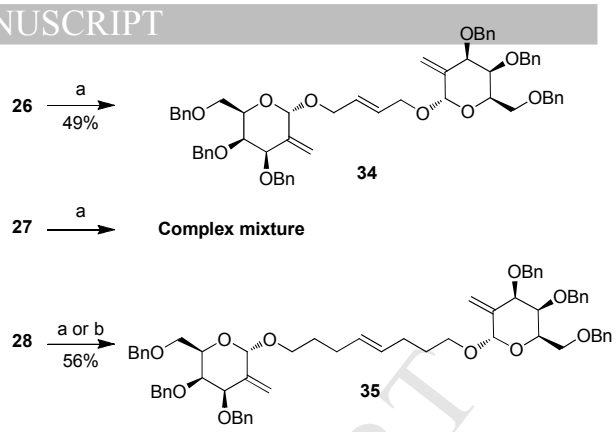
The formation of the unexpected products **30** and **32** from **24** could be explained by considering the following possible intermediates. It has been reported in the literature that terminal olefins undergo olefin migration under the influence of Ru catalysts.[32] Thus, **24** in the presence of Grubs II might undergo olefin migration producing the intermediates **24a** and **24b**. **24a** upon RCM would produce the furo[2,3-*b*]pyran **29** which could undergo further olefin migration leading to the formation of **30**. On the other hand, intermediate **24b** could result in the formation of 2-*C*-branched glycal **32** involving a 3,3-sigmatropic rearrangement (Scheme 4).



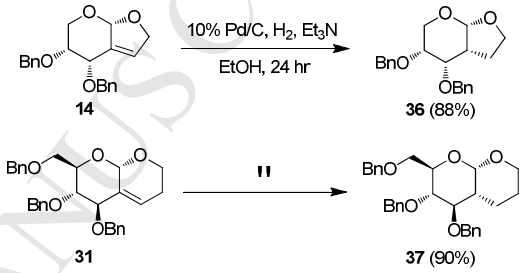
Scheme 4: Possible intermediates in the formation of furo[2,3-*b*]pyran **30** and 2-*C*-branched glycal **32** from **24**.

Unexpectedly, the *C*-2-methylene α-D-galactopyranoside derivatives **26** and **28** upon exposing to G-II provided only the dimerization products **34** and **35**, respectively, whereas the **27** lead to the formation of a complex mixture of products (Scheme 5).

In view of synthesizing fully saturated furo[2,3-*b*]pyran and pyrano[2,3-*b*]pyran derivatives, compounds **14** and **31** were hydrogenated using Pd/C, in EtOH having a trace amount of Et_3N to provide bicyclic acetals **36** and **37**, as single diastereomers in excellent yield (Scheme 6).

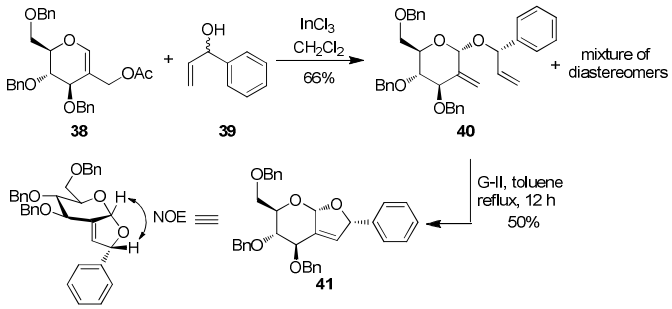


Scheme 5: RCM reaction of galactose derived *C*-2-methylene α-D-galactopyranoside derivatives. Reagents and conditions: (a) G-II (20 mol%), toluene, 80 °C. (b) G-I (20 mol%), toluene, 80 °C.



Scheme 6: Synthesis of fully saturated linearly fused bicycles.

To further extend the scope of the reaction we planned to synthesize substituted furo[2,3-*b*]pyran ring systems. Towards this, 2-acetoxymethyl glucal derivative **38** upon reaction with alcohol **39** in the presence of $InCl_3$ gave the *C*-2-methylene glycoside **40** (as a single diastereomer in 25% isolated yield) along with a mixture of all the diastereomers. Subjecting the glycoside **40** to G-II mediated ring-closing metathesis allowed the isolation of phenyl substituted furo[2,3-*b*]pyran derivative **41** as a single diastereomer (Scheme 7).



Scheme 7: Synthesis of aryl substituted furo[2,3-*b*]pyran framework.

3. Conclusion

In conclusion, various *C*-2-methylene glycosides were synthesized involving Ferrier type rearrangement of 2-hydroxymethyl glycals with different alkenols. The obtained dienes were subjected to RCM reaction to provide a variety of bicyclic acetal systems. These observations revealed that the formation of furo[2,3-*b*]pyran and pyrano[2,3-*b*]pyran systems is reasonably facile in the case of arabinose and glucose derived

dienes. Whereas, the synthesis of pyrano[2,3-*b*]oxepine systems was unsuccessful. Interestingly the galactose derived dienes were highly resistant to undergo RCM indicating the influence of the stereochemistry on pyranose ring. Further application of the developed methodology in the total synthesis of natural products is in progress.

4. Experimental section

General methods: Chemicals and solvents were purchased from the local suppliers and Sigma-Aldrich® chemical company. Solvents were used in the reactions after distilled over the dehydrating agents. All the reactions were carried out under N_2 atmosphere and monitored by the thin layer chromatography (TLC) using silica gel on aluminum plates (GF_{254}) by charring with 5% (v/v) H_2SO_4 in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. Silica-gel (100-200 mesh) was used for column chromatography to purify all the compounds. IR spectra were recorded on JASCO FT/IR-5300. ^{1}H, ^{13}C, DEPT spectra were recorded on Bruker® 400 and 500 Avance MHz spectrometer in $CDCl_3$. ^{1}H NMR chemical shifts were reported in parts per million (ppm) (δ) with TMS as an internal standard (δ 0.00), and ^{13}C NMR were reported in chemical shifts with solvent reference ($CDCl_3$, δ 77.00). High-resolution mass spectra (HRMS) were recorded on Bruker maXis ESI-TOF spectrometer.

4.1. General experimental procedure (A): Synthesis of C-2-methylene-O-glycosides

A solution of 2-hydroxymethyl glycal (1 mmol) in dichloromethane (10 mL) was treated with alkenol (1.2 mmol) in the presence of 5 mol % $InCl_3$. The reaction mixture was stirred at room temperature under nitrogen atmosphere for 2 hr. After completion of the reaction (monitored by TLC), the reaction was quenched with water and extracted with chloroform (3x25 mL). The combined organic layers were washed with brine solution, dried over anhydrous sodium sulfate, filtered and then concentrated under reduced pressure. The crude product thus obtained was further purified by column chromatography using ethyl acetate: hexanes to give the *C*-2-methylene-*O*-glycosides in good to moderate yield.

4.2. General Experimental procedure (B): Synthesis of furo/pyrano[2,3-b]pyrans using ring closing metathesis reaction

To a stirred solution of *C*-2-methylene-*O*-glycoside (0.15 mmol) in anhydrous toluene (40 mL) at 80 °C under argon, Grubb's second generation catalyst 20 mol% was added, and the mixture was stirred at 80 °C for 6-12 hr. The reaction mixture was bought to room temperature and solvent was removed under reduced pressure. The obtained residue was purified by column chromatography on silica gel using ethyl acetate: hexanes as eluent to provide the furo/pyrano[2,3-*b*]pyrans.

*4.3. (2S,4S,5R)-2-(allyloxy)-4,5-bis(benzyloxy)-3-methylene tetrahydro-2H-pyran (**8**) and (2R,4S,5R)-2-(allyloxy)-4,5-bis(benzyloxy)-3-methylenetetrahydro-2H-pyran (**9**)*

Compound **8** and **9** were synthesized from glycal **7** by following the general experimental procedure A. Yield 76% with 90:10 ratio, respectively as a colourless gum. Compound (**8**): R_f = 0.48 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ -57.9 (*c* 1.0, $CHCl_3$); IR (neat): 3081, 3065, 3032, 2924, 2865, 1730, 1649, 1590, 1492, 1449 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.26-7.38 (m, Ar-H, 10H), 5.89-5.97 (m, C2'-H, 1H), 5.37 (d, C3-methylene H_a, 1H, *J* = 1.5 Hz), 5.27-5.31 (m, C3-methylene H_b, C2-H (anomeric), 2H), 5.18-5.21 (m, C3'-$H_{a,b}$, 2H), 4.73 (s, benzyl-CH_2, 2H), 4.67 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.54 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.36-4.37 (m, C4-H, 1H), 4.19-4.23 (m, C1'-H_a, 1H), 4.03-4.07 (m, C1'-H_b 1H), 3.82-3.88 (m, C6-$H_{a,b}$, 2H), 3.76 (m, C5-H, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.7, 138.3, 138.2, 134.0, 128.3, 128.2, 127.8, 127.5, 127.5, 127.3, 117.2, 111.9, 100.1, 76.1, 74.6, 71.4, 70.8, 68.1, 61.8. HRMS (ESI): calcd for $C_{23}H_{26}O_4$+Na 389.1729 found 389.1727. Compound (**9**): R_f = 0.5 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +108.6 (*c* 0.65, $CHCl_3$); IR (neat): 3097, 3059, 3027, 2919, 2870, 1736, 1649, 1600, 1498, 1444 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.26-7.41 (m, Ar-H, 10H), 5.88-5.978 (m, C2'-H, 1H), 5.26-5.36 (m, C3-methylene H_a, C3'-H_a, 2H), 5.16-5.12 (m, C3-methylene H_b, C3'-H_b, 2H), 4.98 (s, C2-H (anomeric), 1H), 4.74 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.63 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.5 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.40 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.22-4.29 (m, C4-H, C6-$H_{a,b}$, 3H), 4.00-4.04 (m, C5-H, 1H), 3.58-3.62 (m, C1'-H_a, 1H), 3.52-3.55 (m, C1'-H_b, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.9, 138.5, 138.1, 134.3, 128.3, 128.2, 128.0, 127.6, 127.6, 127.3, 118.4, 116.5, 98.9, 75.4, 75.2, 70.3, 69.1, 67.9, 57.8. HRMS (ESI): calcd for $C_{23}H_{26}O_4$+Na 389.1729 found 389.1729.

*4.4. (2S,4S,5R)-4,5-bis(benzyloxy)-2-(but-3-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**10**) and (2R,4S,5R)-4,5-bis(benzyloxy)-2-(but-3-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**11**)*

Compound **10** and **11** were synthesized from glycal **7** by following the general experimental procedure A. Yield 69% with 85:15 ratio, respectively as a colourless gum. Compound (**10**): R_f = 0.5 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ -44.5 (*c* 1.0, $CHCl_3$); IR (neat): 2917, 2866, 1723, 1666, 1496, 1453, 1360 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28-7.40 (m, Ar-H, 10H), 5.78-5.88 (m, C3'-H, 1H), 5.37 (s, C3-methylene H_a, 1H), 5.32 (s, C3-methylene H_b, 1H), 5.18 (s, C2-H (anomeric), 1H), 5.12 (d, C4'-H_a,1H, *J* = 17.2 Hz), 5.05 (d, C4'-H_b, 1H, *J* = 10.4 Hz), 4.74 (s, benzyl-CH_2, 2H), 4.68 (d, benzyl-CH,1H, *J* = 12.0 Hz), 4.55 (dd, benzyl-CH, 1H, *J* = 12.0 Hz), 4.35 (s, C4-H, 1H), 3.86 (bs, C6-$H_{a,b}$, 2H), 3.75-3.86 (m, C1'-$H_{a,b}$, 2H), 3.52-3.58 (m, C5-H, 1H), 2.38 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.0, 138.2, 138.2, 134.9, 128.2, 128.2, 127.9, 127.4, 127.4, 127.3, 116.5, 111.8, 100.7, 76.1, 74.6, 71.3, 70.6, 66.8, 61.7, 33.9. HRMS (ESI): calcd for $C_{24}H_{28}O_4$+Na 403.1885 found 403.1886. Compound (**11**): R_f = 0.52 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +76.7 (*c* 1.0, $CHCl_3$); IR (neat): 2986, 2926, 2850, 1495, 1454, 1330 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26-7.42 (m, Ar-H, 10H), 5.82-5.92 (m, C3'-H, 1H), 5.31 (s, C3-methylene H_a, 1H), 5.14 (s, C3-methylene H_b, 1H), 5.03-5.12 (m, C4'-$H_{a,b}$, 2H), 4.95 (s, C2-H (anomeric), 1H), 4.74 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.64 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.54 (d, benzyl-CH, 1H, *J* = 12.6 Hz), 4.39 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.23-4.28 (m, C4-H, C5-H, 2H), 3.78-3.84 (m, C6-H_a, 1H), 3.58-3.63 (m, C6-H_b, 1H), 3.52-3.58 (m, C1'-H_a, 1H), 3.45-3.51 (m, C1'-H_b, 1H), 2.39-2.44 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.0, 138.5, 138.1, 135.3, 128.3, 128.1, 127.9, 127.6, 127.6, 127.3, 118.2, 116.2, 99.8, 75.4, 75.2, 70.3, 69.1, 67.1, 57.7, 34.1. HRMS (ESI): calcd for $C_{24}H_{28}O_4$+Na 403.1885 found 403.1887.

*4.5. (2S,4S,5R)-4,5-bis(benzyloxy)-3-methylene-2-(pent-4-en-1-yloxy)tetrahydro-2H-pyran (**12**) and (2R,4S,5R)-4,5-bis(benzyloxy)-3-methylene-2-(pent-4-en-1-yloxy)tetrahydro-2H-pyran (**13**)*

Compound **12** and **13** were synthesized from glycal **7** by following the general experimental procedure A. Yield 71% with 70:30 ratio, respectively as a colourless gum. Compound (**12**): R_f = 0.52 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ -57.9 (*c* 1.0, $CHCl_3$); IR (neat): 3057, 3030, 2920, 2860, 2350, 1726, 1600, 1490, 1452, 1397 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.26-7.39 (m, Ar-H,

10H), 5.78-5.87 (m, C4'-H, 1H), 5.36 (s, C3-methylene H_a, 1H), 5.31 (s, C3-methylene H_b, 1H), 5.14 (s, C2-H (anomeric), 1H), 4.98-5.08 (m, C5'-$H_{a,b}$, 2H), 4.73 (s, benzyl-CH_2, 2H), 4.68 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.55 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.35 (s, C4-H, 1H), 3.85 (d, C6-$H_{a,b}$, 2H, *J* = 3.0 Hz), 3.77 (d, C5-H, 1H, *J* = 3.0 Hz), 3.76 (dt, C1'-H_a, 1H, *J* = 6.5 Hz, *J* = 9.5 Hz), 3.50 (dt, C1'-H_b, 1H, *J* = 6.5 Hz, *J* = 9.5 Hz), 2.11-2.16 (m, C3'-$H_{a,b}$, 2H) 1.69-1.75 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): *δ* 141.0, 138.3, 138.3, 138.0, 128.2, 128.2, 127.7, 127.4, 127.3, 114.7, 111.7, 100.9, 76.3, 74.8, 71.3, 70.7, 67.1, 61.8, 30.2, 28.7. HRMS (ESI): calcd for $C_{25}H_{30}O_4$+Na 417.2042 found 417.2038. Compound (**13**): R_f = 0.54 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +81.1 (*c* 1.0, $CHCl_3$); IR (neat): 2931, 2865, 1638, 1490, 1452, 1205 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): *δ* 7.26-7.41 (m, Ar-H, 10H), 5.77-5.85 (m, C4'-H, 1H), 5.30 (s, C3-methylene H_a, 1H), 5.11 (s, C3-methylene H_b, 1H), 5.01 (dd, C5'-H_a , 1H, *J* = 1.0 Hz, *J* = 17.0 Hz), 4.95 (dd, C5'-H_b, 1H, *J* = 1.0 Hz, *J* = 10. Hz), 4.93 (s, C2-H (anomeric), 1H), 4.74 (d, 1H, benzyl-CH, *J* = 12.5 Hz), 4.64 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.54 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.40 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.20-4.24 (m, C4-H, C5-H, 2H), 3.75-3.80 (m, C1'-H_a, 1H), 3.59-3.62 (m, C6-H_a,1H), 3.53 (dd, C6-H_b, 1H, *J* = 5.0 Hz, *J* = 11.0 Hz), 3.41-3.45 (m, C1'-H_b,1H), 2.09-2.20 (m, C3'-$H_{a,b}$, 2H), 1.68-1.75 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): *δ* 140.3, 138.6, 138.3, 138.2, 128.3, 128.2, 127.9, 127.6, 127.6, 127.2, 117.9, 114.6, 99.9, 75.7, 75.4, 70.4, 69.2, 67.0, 57.8, 30.3, 20.8. HRMS (ESI): calcd for $C_{25}H_{30}O_4$+Na 417.2042 found 417.2044.

*4.6. (4S,5R,7aS)-4,5-bis(benzyloxy)-4,5,6,7a-tetrahydro-2H-furo[2,3-b]pyran (**14**)*

Compound **14** was synthesized from **8** by following the general experimental procedure B. Yield 77%, as a colourless gum. R_f = 0.48 (30% EtOAc/hexanes). IR (neat): 2908, 2866, 1600, 1473, 1362 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): *δ* 7.28-7.35 (m, Ar-H, 10H), 5.98 (s, C7a-H, 1H), 5.83 (d, C3-H, 1H, *J* = 2.0 Hz), 5.80-5.81 (m, C2-$H_{a,b}$, 2H), 4.74 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.59 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.57 (d, C6-H_a, 1H, *J* = 5.0 Hz), 4.50 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.89 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.02 (t, C5-H, 1H, *J* = 11.0 Hz), 3.85 (dd, C6-H_b, 1H, *J* = 5.0 Hz, *J* = 11.5 Hz), 3.56-3.60 (m, C5-H, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): *δ* 137.8, 137.7, 136.2, 128.4, 128.0, 127.8, 127.8, 127.7, 126.4, 105.0, 76.6, 76.2, 70.9, 70.8, 70.2, 62.3. HRMS (ESI): calcd for $C_{21}H_{24}O_4$+Na 361.1416 found 361.1418.

*4.7. (4S,5R,7aR)-4,5-bis(benzyloxy)-4,5,6,7a-tetrahydro-2H-furo[2,3-b]pyran (**15**)*

Compound **15** was synthesized from **9** by following the general experimental procedure B. Yield 81%, as a colourless gum. R_f = 0.4 (30% EtOAc/hexanes). $[\alpha]_D^{25}$ +27.6 (*c* 0.5, $CHCl_3$); IR (neat): 2923, 2849, 1597, 1501, 1352 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.28-7.41 (m, Ar-H, 10H), 6.12 (s, C7a-H, 1H), 5.53 (d, C3-H, 1H, *J* = 4.4 Hz), 4.94-4.97 (m, C2-H_a, 1H), 4.82 (d, benzyl-CH, 1H, *J* = 12.8 Hz), 4.79 (d, C2-H_b, 1H, *J* = 8.4 Hz), 4.76 (d, benzyl-CH, 1H, *J* = 12.8 Hz), 4.68 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.63 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.22 (s, C4-H, 1H), 4.09 (dd, C6-H_a, 1H, *J* = 1.6 Hz, *J* = 13.2 Hz), 3.74 (s, C5-H, 1H), 3.41 (d, C6-H_b, 1H, *J* = 13.2). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 138.2, 137.8, 136.1, 128.4, 128.3, 128.0, 127.7, 127.6, 127.3, 121.6, 107.3, 76.0, 73.6, 71.3, 70.7, 63.7. HRMS (ESI): calcd for $C_{21}H_{22}O_4$+Na 361.1416 found 361.1419.

*4.8. (3R,4S,8aS)-3,4-bis(benzyloxy)-2,3,4,6,7,8a-hexahydro pyrano[2,3-b]pyran (**16**)*

Compound **16** was synthesized from **10** by following the general experimental procedure B. Yield 71%, as a colourless gum. R_f = 0.5 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ -13.5 (*c* 1.0, $CHCl_3$); IR (neat): 2917, 2863, 1729, 1609, 1501, 1444, 1419, 1387 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.27-7.38 (m, Ar-H, 10H), 5.89 (d, C5-H, 1H, *J* = 4.4 Hz), 5.17 (s, C8a-H, 1H), 4.69 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.55 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.48 (d, benzyl-CH, 1H, *J* = 12.8 Hz), 4.45 (d, benzyl-CH, 1H, *J* = 12.8 Hz), 4.17 (d, C4-H, 1H, *J* = 2.8 Hz), 4.02 (t, C2-H_a, 1H, *J* = 10.8 Hz), 3.89 (dd, C7-H_a, 1H, *J* = 5.2 Hz, *J* = 11.2 Hz), 3.84 (dd, C7-H_b, 1H, *J* = 4.8 Hz, *J* = 11.2 Hz), 3.73-3.79 (dt, C2-H_b, 1H, *J* = 3.2 Hz, *J* = 10.8 Hz), 3.55 (ddd, C3-H, 1H, *J* = 3.2 Hz, *J* = 4.8 Hz, *J* = 10.4 Hz), 2.27-2.40 (m, C6-H_a, 1H), 1.89-1.96 (m, C6-H_b, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 138.0, 132.7, 128.3, 128.3, 127.9, 127.7, 1276, 127.5, 126.2, 92.1, 76.4, 76.0, 70.6, 69.4, 63.3, 59.8, 24.3. HRMS (ESI): calcd for $C_{22}H_{24}O_4$+Na 375.1572 found 375.1571.

*4.9. (3R,4S,8aR)-3,4-bis(benzyloxy)-2,3,4,6,7,8a-hexahydro pyrano[2,3-b]pyran (**17**)*

Compound **17** was synthesized from **11** by following the general experimental procedure B. Yield 68%, as a colourless gum. R_f = 0. 5 (30% EtOAc/hexanes). $[\alpha]_D^{25}$ +60.2 (*c* 1.0, $CHCl_3$); IR (neat): 2922, 2852, 1718, 1496, 1453, 1397, 1353 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.26-7.41 (m, Ar-H, 10H), 6.20 (d, C5-H, 1H, *J* = 6.0 Hz), 4.83 (d, benzyl-CH, 1H, *J* = 12.8 Hz), 4.82 (s, C8a-H, 1H), 4.76 (d, benzyl-CH, 1H, *J* = 11.2 Hz), 4.61 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.56 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.12 (dd, C2-H_a, 1H, *J* = 1.6 Hz, *J* = 13.2 Hz), 4.00 (s, C4-H, 1H), 3.95 (dd, 1H, C7-H_a, *J* = 2.8 Hz, *J* = 10.8 Hz), 3.89 (dd, C7-H_b, 1H, *J* = 4.8 Hz, *J* = 10.8 Hz), 3.69 (s, C3-H, 1H), 3.42 (d, C2-H_b, 1H, *J* = 13.2 Hz), 2.30-2.37 (m, C6-H_a, 1H), 2.04-2.10 (m, C6-H_b, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 138.4, 138.0, 132.1, 128.4, 128.2, 127.8, 127.6, 127.5, 127.2, 119.7, 94.6, 78.1, 73.2, 71.0, 70.9, 64.1, 60.7, 24.2. HRMS (ESI): calcd for $C_{22}H_{24}O_4$+Na 375.1572 found 375.1572.

*4.10. (E)-1,8-bis(((2S,4S,5R)-4,5-bis(benzyloxy)-3-methylenetetrahydro-2H-pyran-2-yl)oxy)oct-4-ene (**19**)*

Compound **19** was synthesized from **12** by following the general experimental procedure B. Yield 56%, as a colourless gum. R_f = 0.4 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ -40.0 (*c* 0.66, $CHCl_3$); IR (neat): 2915, 2843, 1731, 1654, 1446, 1358 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): *δ* 7.29-7.39 (m, Ar-H, 20H), 5.41 (t, C4'-H, 2H, *J* = 3.5 Hz), 5.34 (s, C3-methylene H_a, 2H), 5.30 (s, C3-methylene H_b, 2H), 5.13 (s, C2-H (anomeric), 2H), 4.72 (s, benzyl-CH_2, 4H), 4.67 (d, benzyl-CH, 2H, *J* = 12.0 Hz), 4.54 (d, benzyl-CH, 2H, *J* = 12.0 Hz), 4.33 (s, C4-H, 2H), 3.84 (bs, C6-$H_{a,b}$, 4H), 3.75-3,78 (m, C5-H, 2H), 3.68-3.72 (m, C1'-H_a, 2H), 3.45-3.48 (m, C1'-H_b, 2H), 2.04-2.06 (m, C3'-$H_{a,b}$, 4H), 1.63-1.69 (m, C2'-$H_{a,b}$, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): *δ* 141.1, 138.4, 138.3, 130.0, 128.3, 128.3, 127.8, 127.5, 127.5, 127.4, 111.8, 100.9, 76.3, 74.9, 71.4, 70.7, 67.3, 61.9, 29.6, 29.1. HRMS (ESI): calcd for $C_{48}H_{56}O_8$+Na 783.3873 found 783.3873.

*4.11. (E)-1,8-bis(((2R,4S,5R)-4,5-bis(benzyloxy)-3-methylenetetrahydro-2H-pyran-2-yl)oxy)oct-4-ene (**20**)*

Compound **20** was synthesized from **13** by following the general experimental procedure B. Yield 45%, as a colourless gum. R_f = 0.45 (20% EtOAc/hexanes). IR (neat): 3043, 2921, 2700, 2551, 1651, 1593 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.30-7.42 (m, Ar-H, 20H), 5.37 (t, C4'-H, 2H, *J* = 3.6 Hz), 5.30 (d, C3-methylene CH_a, 2H, *J* = 4.0 Hz), 5.12 (s, C3-methylene CH_b, 2H), 4.92 (s, C2-H (anomeric), 2H), 4.75 (d, benzyl-CH, 2H, *J* = 12.0 Hz), 4.64 (d, benzyl-CH, 2H, *J* = 12.0 Hz), 4.54 (d, benzyl-

CH, 2H, *J* = 12.0 Hz), 4.40 (d, benzyl-CH, 2H, *J* = 12.4 Hz), 4.18-4.24 (m, C4-H, C5-H, 4H), 3.76 (dt, C1'-H_a, 2H, *J* = 6.8 Hz, *J* = 13.2 Hz), 3.58-3.63 (m, C6-H_a, 2H), 3.53 (dd, C6-H_b, 2H, *J* = 4.0 Hz, *J* = 10.0 Hz), 3.41 (dt, C1'-H_b, 2H, *J* = 6.4 Hz, *J* = 12.4 Hz), 2.04-2.13 (m, C3'-$H_{a,b}$, 4H), 1.65-1.70 (m, C2'-$H_{a,b}$, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.2, 138.6, 138.3, 130.0, 128.3, 128.2, 127.9, 127.7, 127.6, 127.3, 118.1, 99.9, 75.6, 75.3, 70.3, 69.1, 67.1, 57.8, 29.5, 29.2. HRMS (ESI): calcd for $C_{48}H_{56}O_8$+Na 783.3873 found 783.3871.

*4.12. (2S,4R,5S,6R)-2-(allyloxy)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-methylenetetrahydro-2H-pyran (**23**)*

Compound **23** was synthesized from glycal **21** by following the general experimental procedure A. Yield 78% as a colourless gum. R_f = 0.45 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +31.4 (*c* 1.0, $CHCl_3$); IR (neat): 2910, 2863, 1647, 1552, 1492, 1448 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.18-7.43 (m, Ar-H, 15H), 5.91-6.01 (m, C2'-H, 1H), 5.31-5.36 (m, C3-methylene CH_a, C3'-H_a, 2H), 5.26 (s, C3-methylene CH_b, 1H), 5.26 (d, C3'-H_b, 1H, *J* = 10.5 Hz), 5.20 (s, C2-H (anomeric), 1H), 4.92 (d, benzyl-CH, 1H, *J* = 10.8 Hz), 4.81 (d, benzyl-CH, 1H, *J* = 11.6 Hz), 4.75 (d, benzyl-CH, 1H, *J* = 11.2 Hz), 4.68 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.54 (d, benzyl-CH, 1H, *J* = 12.4 Hz), 4.53 (d, benzyl-CH, 1H, *J* = 10.4 Hz), 4.51 (dt, C4-H, 1H, *J* = 2.0 Hz, 9.2 Hz), 4.21 (ddt, C1'-H_a, 1H, *J* = 2.8 Hz, *J* = 5.2 Hz, *J* = 13.2 Hz), 4.06 (ddt, C1'-H_b, 1H, *J* = 1.2 Hz, *J* = 4.8 Hz, *J* = 12.8 Hz), 4.02 (ddd, C6-H, 1H, *J* = 2.0 Hz, *J* = 4.0 Hz, *J* = 10.0 Hz), 3.81 (dd, C6-methylene H_b, 1H, *J* = 4.4 Hz, *J* = 10.8 Hz), 3.72 (dd, C6-methylene H_a, 1H, *J* = 2.0 Hz, *J* = 10.4 Hz), 3.66 (dd, C5-H, 1H, *J* = 9.2 Hz, *J* = 9.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.2, 138.2, 138.0, 133.8, 128.3, 128.2, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 117.3, 110.5, 100.4, 81.1, 79.9, 74.9, 73.4, 73.3, 71.5, 68.7, 67.6. HRMS (ESI): calcd. for $C_{31}H_{34}O_5$ +NH_4^+ 504.2750; found 504.2755.

*4.13. (2S,4R,5S,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(but-3-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**24**)*

Compound **24** was synthesized from glycal **21** by following the general experimental procedure A. Yield 75% as a colourless gum. R_f = 0.5 (10%, EtOAc/hexanes). $[\alpha]_D^{25}$ +25.0 (*c* 1.0, $CHCl_3$); IR (neat): 2910, 2863, 1647, 1552, 1492, 1448, 1353 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.20-7.44 (m, Ar-H, 15H), 5.82-5.90 (m, C3'-H, 1H), 5.34 (s, C3-methylene CH_a, 1H), 5.22 (s, C2-H (anomeric), 1H), 5.19 (s, C3-methylene CH_b, 1H), 5.14 (dd, C4'-H_a, 1H, *J* = 1.5 Hz, *J* = 4.5 Hz), 5.08-5.10 (m, C4'-H_b, 1H), 4.92 (d, benzyl-CH, 1H, *J* = 10.5 Hz), 4.82 (d, benzyl-CH, 1H, *J* = 11.5 Hz), 4.76 (d, benzyl-CH, 1H, *J* = 11.5 Hz), 4.68 (d, benzyl-CH, 1H, *J* = 12.5 Hz), 4.55 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.53 (d, benzyl-CH, 1H, *J* = 11.0 Hz), 4.48 (dt, C4-H, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz), 4.00 (ddd, 1H, C6-H, *J* = 2.0 Hz, *J* = 3.5 Hz, *J* = 9.5 Hz), 3.81 (dd, C6-methylene H_a, 1H, *J* = 4.0 Hz, *J* = 10.5 Hz), 3.76 (dt, C1'-H_a, 1H, *J* = 7.5 Hz, *J* = 9.5 Hz), 3.73 (dd, C6-methylene H_b, 1H, *J* = 2.0 Hz, *J* = 12.0 Hz), 3.66 (t, C5-H, 1H, *J* = 9.5 Hz), 3.56 (dt, C1'-H_b, 1H, *J* = 7.0 Hz, *J* = 9.5 Hz), 2.39-2.43 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.0, 138.2, 138.2, 138.0, 134.8, 128.3, 128.3, 128.3, 128.2, 127.9, 127.9, 127.8, 127.6, 116.6, 110.4, 101.2, 81.1, 79.9, 74.9, 73.3, 73.3, 71.5, 68.7, 66.5, 33.9. HRMS (ESI): calcd for $C_{32}H_{36}O_5$+Na 523.2460 found 523.2464.

*4.14. (2S,4R,5S,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(pent-4-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**25**)*

Compound **25** was synthesized from glycal **21** by following the general experimental procedure A. Yield 69% as a colourless gum R_f = 0.52 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +24.4 (*c* 1.0, $CHCl_3$); IR (neat): 3024, 2958, 2926, 2865, 1720, 1638, 1490, 1446, 1358 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26-7.47 (m, Ar-H, 15H), 5.84-5.94 (m, C4'-H, 1H), 5.38 (s, C3-methylene H_a, 1H), 5.25 (s, C3-methylene H_b, 1H), 5.23 (s, C2-H (anomeric), 1H), 5.06-5.16 (m, C5'-$H_{a,b}$, 2H), 4.96 (d, benzyl-CH, 1H, *J* = 10.8 Hz), 4.87 (d, benzyl-CH, 1H, *J* = 11.2 Hz), 4.81 (d, benzyl-CH, 1H, *J* = 11.2 Hz), 4.72 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.58 (d, benzyl-CH_2, 2H, *J* = 11.6 Hz), 4.55 (d, C4-H, 1H, *J* = 6.8 Hz), 4.04-4.06 (m, C6-H, 1H), 3.72-3.89 (m, C6-methylene $H_{a,b}$, C1'-H_a, C5-H, 4H) 3.51-3.56 (m, C1'-H_b, 1H), 2.21 (m, C3'-$H_{a,b}$, 2H), 1.77-1.80 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.4, 138.2, 138.1, 138.0, 137.9, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 127.4, 114.7, 110.2, 101.2, 81.1, 79.9, 74.8, 73.3, 71.4, 68.6, 66.5, 30.2, 28.5. HRMS (ESI): calcd for $C_{33}H_{38}O_5$ +Na 537.2617 found 537.2619.

*4.15. (2S,4R,5R,6R)-2-(allyloxy)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-methylenetetrahydro-2H-pyran (**26**)*

Compound **26** was synthesized from glycal **22** by following the general experimental procedure A. Yield 71% as a colourless gum. R_f = 0.62 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +9.4 (*c* 1.0, $CHCl_3$); IR (neat): 2907, 2863, 1644, 1558, 1533, 1501, 1451, 1416, 1365 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.26-7.43 (m, Ar-H, 15H), 5.93-6.00 (m, C2'-H, 1H), 5.47 (t, C3-methylene H_a, 1H, *J* = 2.0 Hz), 5.29-5.34 (m, C3'-H_a, C3-methylene H_b, C2-H (anomeric), 3H), 5.22 (dd, C3'-H_b, 1H, *J* = 1.5 Hz, *J* = 10.5 Hz), 4.96 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.76 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.70 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.66 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.53 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.49 (d, C4-H, 1H, 2.0 Hz), 4.45 (d, benzyl-CH, 1H, *J* = 11.5 Hz), 4.25 (ddt, C1'-H_a, 1H, *J* = 1.5 Hz, *J* = 5.5 Hz, *J* = 11.5 Hz), 4.20 (t, C6-H, 1H, *J* = 6.5 Hz), 4.09 (ddt, C1'-H_b, 1H, *J* = 1.5 Hz, *J* = 6.0 Hz, *J* = 11.5 Hz), 4.05 (d, C5-H, 1H, *J* = 2.0 Hz), 3.62 (dd, C6-methylene $H_{a,b}$, 2H, *J* = 3.0 Hz, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.7, 138.6, 138.3, 138.0, 134.0, 128.3, 128.2, 128.0, 127.6, 127.5, 127.4, 127.4, 127.0, 117.2, 111.4, 100.6, 78.1, 75.4, 73.9, 73.3, 71.6, 70.7, 69.3, 67.7. HRMS (ESI): calcd for $C_{31}H_{34}O_5$+Na 509.2304 found 509.2304.

*4.16. (2S,4R,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(but-3-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**27**)*

Compound **27** was synthesized from glycal **22** by following the general experimental procedure A. Yield 77% as a colourless gum. R_f = 0.52 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +12.1 (*c* 1.0, $CHCl_3$); IR (neat): 2920, 2866, 1641, 1492, 1451, 1353 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.27-7042 (m, Ar-H, 15H), 5.80-5.88 (m, C3'-H, 1H), 5.45 (s, C3-methylene H_a, 1H), 5.29 (s, C3-methylene H_b,1H), 5.25 (s, C2-H (anomeric), 1H), 5.12 (d, C4'-H_a, 1H, *J* = 17.0 Hz), 5.07 (d, C4'-H_b, 1H, *J* = 10.0 Hz), 4.95 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.76 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.69 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.66 (d, benzyl-CH, 1H, *J* = 12.0 Hz), 4.52 (d, benzyl-CH, 1H, *J* = 11.5 Hz), 4.44-4.46 (m, benzyl-CH, C4-H, 2H), 4.16 (t, C6-H, 1H, 6.0 Hz), 4.02 (bs, C5-H, 1H), 3.73-3.78 (m, C1'-H_a, 1H), 3.54-3.61 (m, C6-methylene $H_{a,b}$, C1'-H_b, 3H), 2.40 (m, C2'-$H_{a,b}$,2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.9, 138.6, 138.4, 138.1, 135.0, 128.3, 128.3, 128.0, 127.6, 127.6, 127.5, 127.4, 127.1, 116.5, 111.2, 101.4, 78.1, 75.5, 74.0, 73.4, 71.6, 70.7, 69.3, 66.5, 33.9. HRMS (ESI): calcd for $C_{32}H_{36}O_5$+Na 523.2460 found 523.2461.

*4.17. (2S,4R,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(pent-4-en-1-yloxy)-3-methylenetetrahydro-2H-pyran (**28**)*

Compound **28** was synthesized from glycal **22** by following the general experimental procedure A. Yield 72% as a colourless gum. R_f = 0.52 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +0.8 (*c* 1.0, $CHCl_3$);

IR (neat): 3057, 3024, 2904, 2356, 1726, 1452, 1353, 1315 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.27-7.40 (m, Ar-H, 15H), 5.79-5.90 (m, C4'-H,1H), 5.45 (s, C3-methylene H_a, 1H), 5.29 (s, C2-H (anomeric), 1H), 5.23 (s, C3-methylene H_b,1H), 4.94-5.08 (m, C5'-$H_{a,b}$, 2H), 4.75 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.69 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.66 (d, benzyl-CH, 1H, J = 11.2 Hz), 4.60 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.52 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.46 (s, C4-H, 1H), 4.44 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.14 (t, C6-H, 1H, J = 8.0 Hz), 4.03 (s, C5-H, 1H), 3.44-3.75 (m, C6-methylene $H_{a,b}$, C1'-$H_{a,b}$, 4H), 2.12-2.17 (m, C3'-$H_{a,b}$, 2H), 1.68-1.77 (m, C2'-$H_{a,b}$, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.1, 138.7, 138.4, 138.1, 138.1, 128.5, 128.4, 128.3, 128.1, 127.8, 127.6, 127.5, 127.2, 114.8, 111.3, 101.6, 78.1, 75.5, 74.0, 73.4, 71.6, 70.7, 69.4, 66.7, 30.4, 28.7. HRMS (ESI): calcd for $C_{33}H_{38}O_5$+Na 537.2617 found 537.2618.

*4.18. (4R,5S,6R,7aS)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-4,5,6,7a-tetrahydro-2H-furo[2,3-b]pyran (**29**) and (3aR,4R,5S,6R,7aS)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-4,5,6,7a-tetrahydro-3aH-furo[2,3-b]pyran (**30**)*

Compound **29** and **30** were synthesized from **23** by following the general experimental procedure B. Yield 61% with 50:50 ratio, respectively as a colourless gum. Compound (**29**): R_f = 0.4 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +77.2 (c 0.45, $CHCl_3$); IR (neat): 3062, 3029, 2862, 1790, 1733, 1670, 1496, 1453, 1362, 1327 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.16-7.41 (m, Ar-H, 15H), 6.23 (d, C7a-H, 1H, J = 1.2 Hz), 6.20-6.22 (m, C3-H, 1H, J = 2.4 Hz), 4.71-4.80 (m, C4-H, 2H), 4.63 (m, benzyl-CH, C4-H, 2H), 4.56 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.54 (d, benzyl-CH, 1H, J = 12.4 Hz), 4.43 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.39-4.42 (m, benzyl-CH_2, 2H), 3.88 (dd, C8-H_a, 1H, J = 1.6 Hz, J = 8.8 Hz), 3.70 (m, C8-H_b, C5-H, 2H), 3.62 (dt, C6-H, 1H, J = 3.6Hz, J = 9.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.2, 137.5, 137.5, 134.4, 130.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.8, 127.4, 104.4, 79.6, 76.0, 74.9, 73.3, 72.2, 71.7, 70.4, 68.3. HRMS (ESI): calcd for $C_{29}H_{30}O_5$+Na 481.1991 found 481.1991. Compound (**30**): R_f = 0.6 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +35.0 (c 1.0, $CHCl_3$); IR (neat): 2917, 2850, 1619, 1596, 1492, 1448, 1362, 1258 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.20-7.39 (m, Ar-H, 15H), 6.53 (t, C2-H, 1H, J = 2.8 Hz), 6.02 (d, C7a-H, 1H, J = 8.4 Hz), 5.00 (t, C3-H, 1H, J = 2.8 Hz), 4.65 (s, benzyl-CH_2, 2H), 4.63 (d, benzyl-CH, 1H, J = 12.4 Hz), 4.62 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.59 (d, benzyl-CH, 1H, 12.0 Hz), 4.46 (d, benzyl-CH, 1H, J = 11.6 Hz), 3.88-3.91 (m, C6-H, 1H), 3.73-3.77 (m, C4-H, C5-H, 2H), 3.69-3.70 (m, C8-$H_{a,b}$, 2H), 3.25 (ddd, C3a-H, 1H, J = 2.4 Hz, J = 4.8 Hz, J = 10.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.1, 138.1, 138.0, 137.9, 128.4, 128.3, 128.2, 127.8, 127.7, 127.7, 127.7, 127.5, 102.3, 102.1, 79.1, 75.5, 73.3, 72.5, 71.7, 71.0, 69.5, 43.7. HRMS (ESI): calcd for $C_{29}H_{30}O_5$+Na 481.1991 found 481.1991.

*4.19. (2R,3S,4R,8aS)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-2,3,4,6,7,8a-hexahydropyrano[2,3-b]pyran (**31**), (**30**) and 2-(((2R,3S,4R)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-3,4-dihydro-2H-pyran-5-yl)methyl)butanal (**32**)*

Compound **31** and **(30+32)** were synthesized from **24** by following the general experimental procedure B. Yield 68% with 50:50 ratio, respectively as a colourless gum. Compound (**31**): R_f = 0.42 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +48.3 (c 0.8, $CHCl_3$); IR (neat): 3024, 2891, 2860, 1723, 1663, 1501, 1453, 1363, 1328 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.15-7.38 (m, Ar-H, 15H), 6.06 (t, C5-H, 1H, J = 3.2 Hz), 5.44 (d, C8a-H, 1H, J = 1.2 Hz), 4.64 (d, benzyl-CH, 1H, J = 12.4 Hz), 4.62 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.57 (d, benzyl-CH, 1H, J = 12.4 Hz), 4.50 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.39 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.36 (d, benzyl-CH, 1H, J = 12.0 Hz), 3.93-3.97 (m, C4-H, C3-H, 2H), 3.78-3.87 (m, C7-H_a, C2-H, C2-methylene H_a, 3H), 3.62-3.72 (m, C7-H_b, C2-methylene H_b, 2H), 2.23-2.32 (m, C6-H_a, 1H), 2.13-2.21 (m, C6-H_b, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.3, 137.9, 137.6, 131.9, 130.1, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.7, 127.4, 92.4, 80.7, 79.5, 74.0, 73.3, 71.4, 69.6, 69.0, 60.6, 25.0. HRMS (ESI): calcd for $C_{30}H_{32}O_5$+Na 495.2147 found 495.2148. Compounds (**30**) and (**32**): Obtained as an inseparable mixture. R_f = 0.62 (20% EtOAc/hexanes). IR (neat): 3066, 3028, 2917, 2866, 1721, 1496, 1453, 1361, 1263 cm^{-1}. Compound **32**: HRMS (ESI): calcd for $C_{32}H_{36}O_5$+Na 523.2460 found 523.2460.

*4.20. (E,Z)-1,8-bis(((2S,4R,5S,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-methylenetetrahydro-2H-pyran-2-yl)oxy)oct-4-ene (**33**).*

Compound **33** (as a *cis, trans* mixture) was synthesized from **25** by following the general experimental procedure B. Yield 62% as a colourless gum. R_f = 0.54 (20% EtOAc/hexanes). IR (neat): 3063, 3030, 2926, 2854, 1956, 1720, 1490, 1452, 1358 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.15-7.39 (m, Ar-H, 30H), 5.42 (t, C4'-H, 1H, J = 3.5 Hz), 5.38 (t, C4'-H, 1H, J = 4.5 Hz), 5.29 (s, C3-methylene H_a, 2H), 5.13 (bs, C3-methylene H_b, C2-H (anomeric), 4H), 4.87 (d, benzyl-CH, 2H, J = 10.5 Hz), 4.78 (d, benzyl-CH, 2H, J = 11.5 Hz), 4.71 (d, benzyl-CH, 2H, J = 11.0 Hz), 4.63 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.51 (d, benzyl-CH, 2H, J = 12.5 Hz), 4.50 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.44 (d, C4-H, 2H, J = 9.0 Hz), 3.92-3.95 (m, C6-H, 2H), 3.74-3.77 (m, C6-methylene H_a, 2H), 3.63-3.69 (m, C6-methylene H_b, C1'-H_a, 4H), 3.61 (t, C5-H, 2H, J = 9.5 Hz), 3.40-3.45 (m, C1'-H_a, 2H), 2.01-2.12 (m, C3'-$H_{a,b}$, 4H), 1.65 (quin, C2'-$H_{a,b}$, 4H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.6, 138.4, 138.4, 138.2, 130.0, 129.5, 128.4, 128.3, 128.3, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 110.2, 101.4, 81.3, 80.1, 74.9, 73.4, 71.6, 68.9, 66.7, 29.4, 29.1. HRMS (ESI): calcd for $C_{64}H_{72}O_{10}$+NH_4^+ 1018.5469 found 1018.5461.

*4.21. (E)-1,4-bis(((2S,4R,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-methylenetetrahydro-2H-pyran-2-yl)oxy)but-2-ene (**34**)*

Compound **34** was synthesized from **26** by following the general experimental procedure B. Yield 49%, as a colourless gum. R_f = 0.4 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +9.5 (c 1.0, $CHCl_3$); IR (neat): 2923, 2857, 1720, 1498, 1451, 1368 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.27-7.39 (m, Ar-H, 30H), 5.82 (t, C2'-H, 2H, J = 2.5 Hz), 5.43 (t, C3-methylen H_a, 2H, J = 1.5 Hz), 5.27 (s, C3-methylen H_b, 2H), 5.24 (s, C2-H (anomeric), 2H), 4.92 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.72 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.65 (d, benzyl-CH, 2H, J = 10.5 Hz), 4.63 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.48 (d, benzyl-CH, 2H, J = 11.5 Hz), 4.44 (d, C4-H, 2H, J = 2.5 Hz), 4.41 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.18 (dd, C1'-H_a, 2H, J = 2.5 Hz, J = 13.0 Hz), 4.10-4.13 (m, C6-H, 2H), 3.99-4.03 (m, C1'-H_b, C5-H, 4H), 3.53-3.59 (m, C6-methylene $H_{a,b}$, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.7, 138.7, 138.4, 138.1, 128.9, 128.4, 128.3, 128.1, 127.7, 127.6, 127.5, 127.4, 127.1, 111.6, 100.8, 78.2, 75.5, 74.0, 73.4, 71.7, 70.8, 69.4, 66.7. HRMS (ESI): calcd for $C_{60}H_{64}O_{10}$+Na 967.4397 found 967.4399.

*4.22. (E)-1,8-bis(((2S,4R,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-methylenetetrahydro-2H-pyran-2-yl)oxy)oct-4-ene (**35**)*

Compound **35** was synthesized from **28** by following the general experimental procedure B. Yield 56%, as a colourless gum. R_f = 0.4 (20% EtOAc/hexanes). $[\alpha]_D^{25}$ +4.1 (c 1.0, $CHCl_3$); IR (neat): 3035, 2865, 1726, 1621, 1457 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz):

δ 7.24-7.38 (m, Ar-H, 30H), 5.36-5.45 (m, C4'-H, C3-methylene H_a, 4H), 5.25 (s, C3-methylene H_b, 2H), 5.18 (s, C2-H (anomeric), 2H), 4.91 (d, benzyl-CH, 2H, J = 12.0 Hz), 4.62-4.73 (m, benzyl-CH, 6H), 4.48 (d, benzyl-CH, 2H, J = 11.5 Hz), 4.39-4.42 (m, benzyl-CH, C4-H, 4H), 4.11 (t, C6-H, 2H, J = 6.0 Hz), 3.99 (s, C5-H, 2H), 3.62-3.67 (m, C1'-H_a, 2H), 3.56 (d, C6-metylene $H_{a,b}$, 4H, J = 6.5 Hz), 3.41-3.49 (m, C1'-H_b, 2H), 2.04-2.06 (m, C3'-$H_{a,b}$, 4H), 1.63-1.66 (m, C2'-$H_{a,b}$, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 141.1, 138.7, 138.4, 138.1, 130.0, 129.7, 129.0, 128.3, 128.3, 128.1, 127.7, 127.6, 127.5, 127.4, 127.1, 111.1, 101.5, 78.2, 75.5, 74.0, 73.4, 71.6, 70.7, 69.4, 66.8, 29.6, 29.1. HRMS (ESI): calcd for $C_{64}H_{72}O_{10}+NH_4^+$ 1018.5469 found 1018.5483.

*4.23. (3aR,4S,5R,7aS)-4,5-bis(benzyloxy)hexahydro-2H-furo[2,3-b]pyran (**36**)*

To a stirred solution of **14** (20 mg, 0.059 mmol) in ethanol (3 mL) was added Et_3N (16 µL, 0.12 mmol), 10% Pd/C (4 mg). The mixture was stirred for 4h under H_2 atmosphere. After completion of the reaction (by TLC) the suspension was filtered through a pad of Celite and concentrated *in vacuo*, the obtained residue was further purified by silica gel column chromatography provided the compound **36** as the single diastereomer in 88% yield. R_f = 0.48 (30% EtOAc/hexanes). $[\alpha]_D^{25}$ -5.2 (*c* 1.0, $CHCl_3$); IR (neat): 2915, 2854, 1731, 1594, 1452, 1364 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28-7.35 (m, Ar-H, 10H), 5.30 (d, C7a-H, 1H, J = 3.0 Hz), 4.72 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.67 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.61 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.54 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.00 (dt, C2-H_a, 1H, J = 7.0 Hz, 5.0 Hz), 3.91 (dd, C6-H_a, 1H, J = 4.5 Hz, J = 8.5 Hz), 3.88 (dt, C2-H_b, 1H, J = 7.0 Hz, J = 5.0 Hz), 3.74-3.79 (m, C5-H, C6-H_b, 2H), 3.69 (dd, C4-H, 1H, J = 2.0 Hz, J = 5.5 Hz), 2.46-2.51 (m, C3a-H, 1H), 1.95-2.02 (m, C3-H_a, 1H), 1.82-1.89 (m, C3-H_b, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.4, 138.3, 128.4, 128.4, 127.9, 127.8, 127.7, 127.6, 100.9, 75.2, 71.7, 71.2, 71.0, 66.4, 62.0, 42.4, 26.3. HRMS (ESI): calcd for $C_{21}H_{24}O_4$+Na 363.1572 found 363.1574.

*4.24. (2R,3S,4R,4aR,8aS)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)octahydropyrano[2,3-b]pyran (**37**)*

To a stirred solution of **31** (25 mg, 0.052 mmol) in ethanol (4 mL) was added Et_3N (16 µL, 0.105 mmol), 10% Pd/C (5 mg). The mixture was stirred for 6h under H_2 atmosphere. After completion of the reaction (by TLC) the suspension was filtered through a pad of Celite and concentrated *in vacuo*, the obtained residue was further purified by silica-gel column chromatography provided the compound **37** as the single diastereomer in 90% yield. R_f = 0.5 (30% EtOAc/hexanes). $[\alpha]_D^{25}$ +38.8 (*c* 0.6, $CHCl_3$); IR (neat): 2927, 2866, 1727, 1589, 1494, 1446, 1356 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.17-7.36 (m, Ar-H, 15H), 4.93 (d, benzyl-CH, 1H, J = 11.2 Hz), 4.83 (d, benzyl-CH, 1H, J = 10.4 Hz), 4.80 (d, C8a-H, 1H, J = 3.6 Hz), 4.66 (d, benzyl-CH_2, 2H, J = 11.6 Hz), 4.58 (d, benzyl-CH, 1H, J = 11.2 Hz), 4.52 (d, benzyl-CH, 1H, J = 12.0 Hz), 3.97-4.04 (m, C2-H, C7-H_a, 2H), 3.91 (dd, C4-H, 1H, J = 8.8 Hz, J = 10.4 Hz), 3.78 (dd, C2-methylene H_a, 1H, J = 3.2 Hz, J = 10.8 Hz), 3.72 (t, C3-H, 1H, J = 9.6 Hz), 3.67 (dd, C2-methylene H_b, 1H, J = 2.0 Hz, J = 10.4 Hz), 3.53 (td, C7-H_b, 1H, J = 2.0 Hz, J = 12.4 Hz), 2.08 (d, C5-H_a, 1H, J = 12.8 Hz), 1.92 (dd, C4a-H, 1H, J = 2.0 Hz, J = 10.8 Hz), 1.51-1.55 (m, C5-H_b, 1H), 1.41-1.48 (m, C6-H_a, 1H), 1.18 (d, C6-H_b,1H, J = 13.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.4, 138.3, 138.0, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.6, 127.5, 98.5, 79.5, 77.1, 75.0, 74.6, 73.5, 73.1, 68.5, 67.6, 40.9, 22.7, 20.2. HRMS (ESI): calcd for $C_{30}H_{34}O_5$ +Na 497.2304 found 497.2309.

*4.25. (2S,4R,5S,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(((R)-1-phenylallyl)oxy)-3-methylenetetrahydro-2H-pyran (**40**)*

Compound **40** (major isomer) was synthesized from glycal **38** by following the general experimental procedure A. Yield 25% as a colourless gum. R_f = 0. 6 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +63.2 (*c* 1.0, $CHCl_3$); IR (neat): 3090, 2915, 2858, 1603, 1489, 1453, 1360, 1303 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.18-7.43 (m, Ar-H, 20H), 5.96-6.04 (m, C2'-H, 1H), 5.21-5.27 (m, C3-methylene CH_a, C3'-H_a, 2H), 5.19 (d, C2'-H, 1H, J = 6.0 Hz), 5.14 (dt, C3'-H_b, 1H, J = 1.2 Hz, J = 10.4 Hz), 5.11 (s, C3-methylene CH_b, 1H), 4.98 (s, C2-H (anomeric), 1H), 4.90 (d, benzyl-CH, 1H, J = 10.8 Hz), 4.81 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.76 (d, benzyl-CH, 1H, J = 11.2 Hz), 4.68 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.51-4.56 (m, benzyl-CH_2, C4-H, 3H), 4.10-4.14 (m, C6-H, 1H), 3.82 (dd, C6-methylene H_b, 1H, J = 4.0 Hz, J = 11.6 Hz), 3.74 (dd, C6-methylene H_a, 1H, J = 2.0 Hz, J = 10.8 Hz), 3.65 (t, C5-H, 1H, J = 9.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.3, 139.8, 138.6, 138.3, 138.3, 138.2, 128.5, 128.4, 128.3, 128.3, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.3, 115.5, 110.3, 98.5, 81.3, 80.1, 77.9, 75.0, 73.5, 73.4, 71.9, 68.8. HRMS (ESI): calcd for $C_{37}H_{38}O_5+NH_4^+$ 580.3063 found 580.3066.

*4.26. (2R,4R,5S,6R,7aS)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-phenyl-4,5,6,7a-tetrahydro-2H-furo[2,3-b]pyran (**41**)*

Compound **41** was synthesized from **40** by following the general experimental procedure B. Yield 50%, as a colourless gum. R_f = 0. 42 (10% EtOAc/hexanes). $[\alpha]_D^{25}$ +3.0 (*c* 0.6, $CHCl_3$); IR (neat): 3023, 2920, 2858, 1722, 1593, 1448, 1360, 1288 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.16-7.39 (m, Ar-H, 20H), 6.31 (t, C7a-H, 1H, J = 1.6 Hz), 6.18 (t, C3-H, 1H, J = 1.6 Hz), 5.89 (s, C2-H, 1H), 4.68 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.67 (d, benzyl-CH, 1H, J = 12.4 Hz), 4.57 (d, benzyl-CH, 1H, J = 12.0 Hz), 4.53 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.45 (d, benzyl-CH, 1H, J = 11.2 Hz), 4.44 (d, benzyl-CH, 1H, J = 11.6 Hz), 4.38 (d, C4-H, 1H, J = 2.0 Hz), 3.92 (dd, C5-H, 1H, J = 1.6 Hz, J = 7.6 Hz), 3.73-3.82 (m, C6-H, C8-$H_{a,b}$, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.1, 138.4, 137.5, 137.5, 134.6, 134.2, 128.6, 128.5, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7, 127.4, 125.9, 104.3, 86.7, 79.7, 76.0, 73.3, 72.4, 71.7, 70.5, 68.8. HRMS (ESI): calcd for $C_{35}H_{34}O_5$+Na 557.2304 found 557.2300.

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(a) Supplementary Material

^{1}H and ^{13}C NMR spectra of all new compounds and the 2D NMR of **8**, **12**, **13**, **17**, **30**, **36**, **37** and **41** are provided.