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Facile synthesis of tetrasaccharide fragments of bioactive Asterosaponins novaeguinosides I and II from starfish *Culcita novaeguineae*

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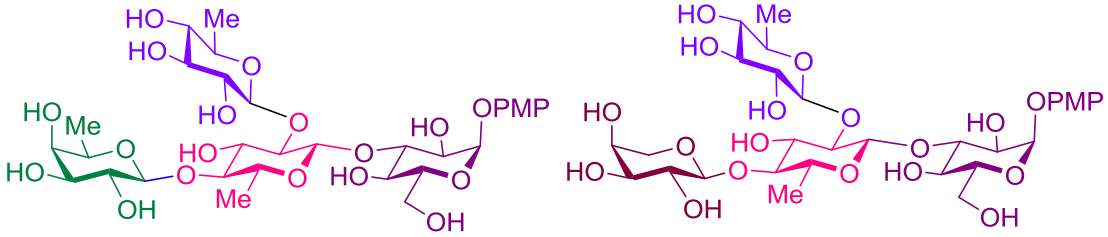
Abstract

Simple and straightforward synthesis of tetrasaccharide fragments of novaeguinosides I and II, isolated from the starfish *Culcita novaeguineae* that showed significant in *vitro* cytotoxicity activity against two human tumor cell lines (leukemia K-562 and hepatoma BEL-7402) is reported. The tetrasaccharide moieties have been synthesized as their *p*-methoxyphenyl (PMP) glycosides by sequential glycosylation strategy using suitably functionalized thioglycoside donors employing sulfuric acid immobilized on silica (H_2SO_4–silica) as a Brönsted acid catalyst to work as a promoter for all glycosylation reactions. All intermediate steps are high yielding and the glycosylation steps are stereoselective.



tetrasaccharide fragments of bioactive Asterosaponins novaeguinosides I and II

Keywords: Steroidal glycoside, natural products, glycosylation, tetrasaccharide, H_2SO_4–silica

Introduction

Steroidal glycosides are a structurally and biologically diverse class of molecules which occur widely and abundantly in terrestrial plants, are rarely found in the animal kingdom. The only exception so far is in species belonging to Asteroidea (starfish), in which steroidal oligoglycosides (asterosaponins) are the predominant and characteristic secondary metabolites that are present in and isolated from sea stars (starfish).[1-3]

The structures of steroidal glycosides seem to be quite peculiar in terms of both their carbohydrate and aglycon moieties. They have been subdivided into three main groups: asterosaponin (sulfated steroidal glycosides), steroidal cyclic glycosides, and polyhydroxysteroidal glycosides.[4] The common structures feature of all asterosaponins, occurring in almost all starfish species, contain $\Delta^{9(11)}$-3β,6α-dihydroxysteroidal nucleus bond with a sulfate residue at C-3 and an oligosaccharide residue attached at C-6 of the aglycon.[5] The glycans are mostly penta- or hexasaccharides with all 1,2-trans-pyranosidic linkages and a (1→2) branching point at the second sugar unit. An example in two new asterosaponins, novaeguinosides I and II (Figure 1) were isolated from the starfish *Culcita novaeguineae* Cushion stars (*Culcita novaeguineae* Muller et Troschel, order Valvatida, family Oreasteridae) distributed in the South China Sea.[6]

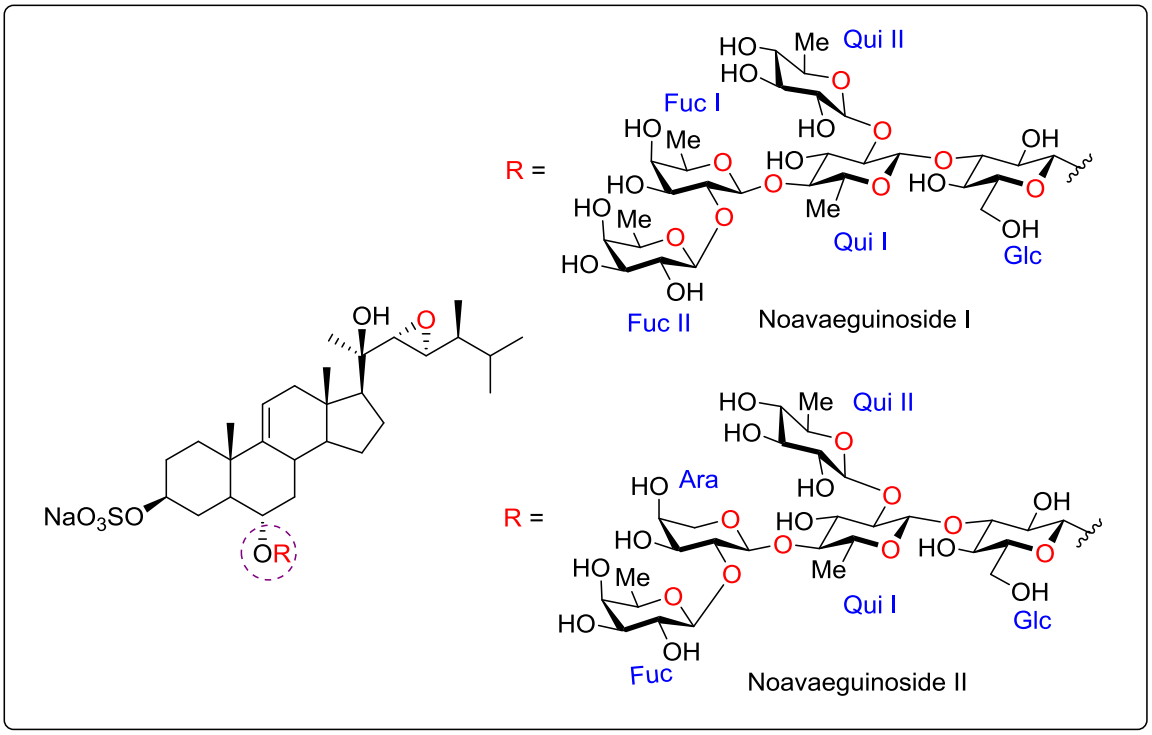


Figure 1. Starfish asterosaponin "novaeguinoside I and novaeguinoside II" from *Culcita novaeguineae.*

The species Asteroidea (starfish) persistently contains the steroidal glycosides. These are secondary metabolites produced in their regular growth and development program, also served as a source of medicines from long time ago. *Culcita novaeguineae* Muller et Troschel (Oreasteridae) is an abundant starfish distributed in the South China Sea and used as a folk medicine for the treatment of rheumatism and as a tonic in China.[7] Most traditional Chinese medicines contain saponins as major components and thus represent glycoconjugate templates in drug design and development.[8-10] The secondary metabolites of sulphated steroidal glycosides are therefore believed, and in many cases have been proven, to be defense chemicals against parasites and

predators.[1-3] These glycosides show excellent physiological and pharmacological activities, such as antiviral, antifungal, cytotoxic antitumor, antimicrobial, antifungal and hemolytic activities.[11-14] Attracted by the medicinal value of the steroidal glycosides Tang *et al.* have analyzed different extracts from the starfish *Culcita novaeguineae* (Figure 1) which showed significant in *vitro* cytotoxicity activity against two human tumor cell lines (leukemia K-562 and hepatoma BEL-7402).[6]

The oligosaccharides have a very important role in the bioactivity of asterosaponins. Profound studies on the activities of steroidal glycosides becomes less because the isolation of starfish saponin from natural resources in adequate quantity is extremely difficult, because they are scarce, often vulnerable towards acid and base and occur as complicated mixtures, whose separation into individual pure components is difficult.

Accordingly, due to the variety of pharmacological activities exhibited by these asterosaponins, it was decided to develop a synthetic route for tetrasaccharide fragments of bioactive Asterosaponins novaeguinosides I and II.

So, poor accessibility of these molecules has retarded in-depth studies on their biosynthetic pathway biological activities.[15,16] Also the structures of carbohydrate moieties in starfish asterosaponin are often very complex and so far there is only a few synthetic work reported on this field.[17-20] The efficient synthesis of the oligosaccharide chain is not a trivial task. In continuation to our constant effort towards synthesis of carbohydrate containing natural products,[21] here we report a simple and straightforward synthesis of a tetrasaccharide fragment (**1** & **2**) (Figure 2) of bioactive Asterosaponins novaeguinosides I and II as their 4-methoxyphenyl glycoside through a sequential glycosylation and stereocontrolled approach employing sulfuric acid immobilized on silica (H_2SO_4-silica) as an alternative user-friendly, solid acid catalyst to work as a promoter like TfOH[22] or TMSOTf.[23] The 4-methoxyphenyl group acts as a temporary protecting group of the anomeric position at the reducing end, that could easily be transformed into an *ortho*-alkynylbenzoate donor, which could be coupled with the aglycon under neutral conditions to form steroidal glycoside, catalysed by a gold(I) complex (e.g., $Ph_3PAuOTf$ or $Ph_3PAuNTf_2$).[24]

Results and Discussion

The tetrasaccharide fragments (**1** & **2**) of novaeguinoside I and novaeguinoside II respectively were synthesized in the form of their *p*-methoxyphenyl glycoside (PMP) using sequential glycosylation strategy using similar reaction conditions for stereoselective glycosylations and functional group manipulations. For the construction of the target molecules, suitably functionalized monosaccharide intermediates **3**, **4**,[25] **5**,[26] **6**[27] and **7** were prepared from commercially available reducing sugars using earlier reported reaction conditions (Figure 2).

Among these sugars the functionalized monosaccharide intermediates **4**, **5** and **6** were prepared from the commercially available monosaccharides using literature-reported reaction conditions, while the synthon **3** and **7** were synthesized as outlined in Scheme 1. A general iodonium ion promoted stereoselective glycosylation condition was used for the synthesis of tetrasaccharide derivatives (**19** & **20**) as well as its synthetic intermediates **14** and **16**.

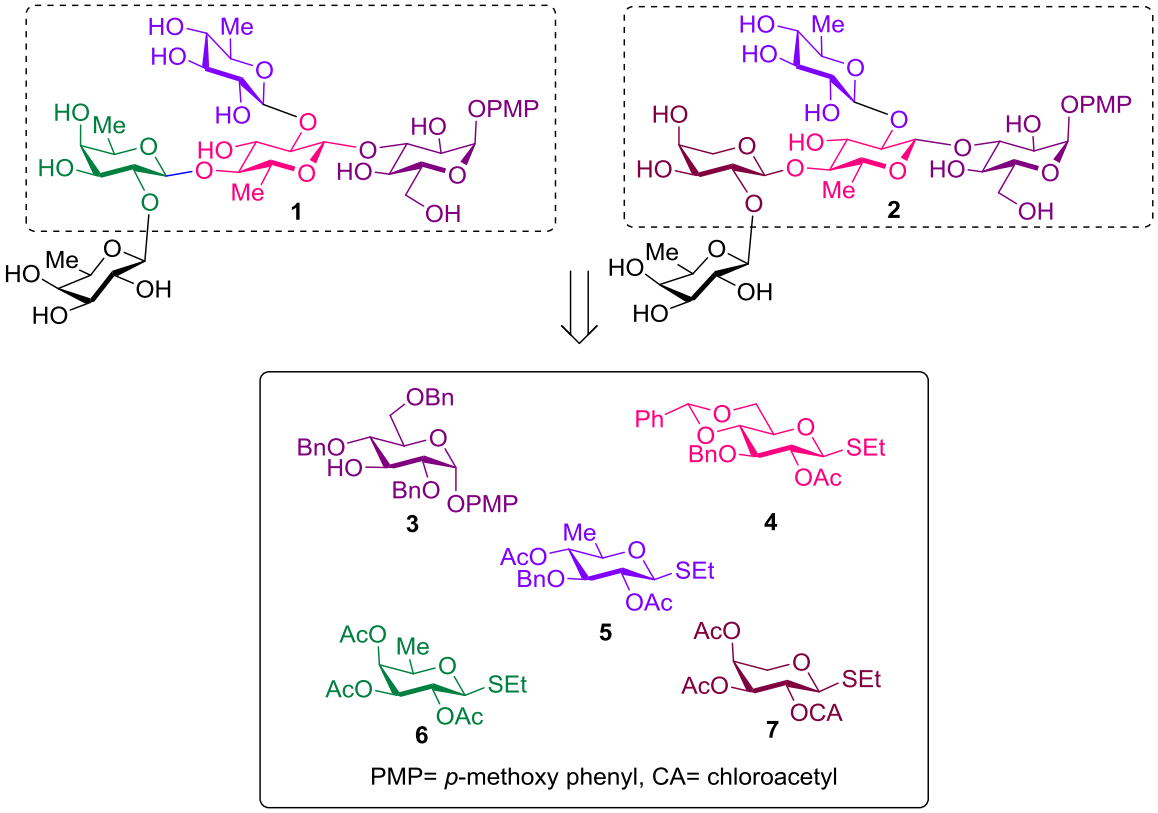
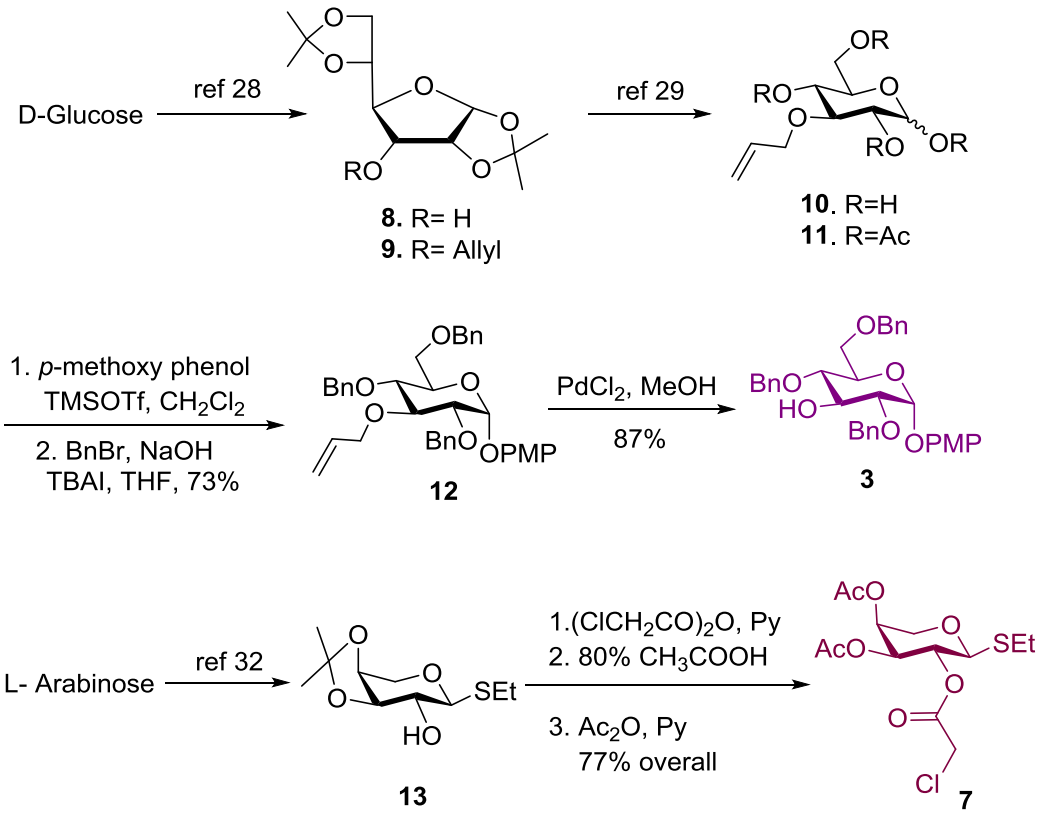


Figure 2. Structure of the synthesized tetrasaccharide **1** and **2** and it's precursors intermediates.

Synthesis of the building blocks 3 & 7. The route to glycosyl acceptor **3** began from the glucose di-isopropyl derivative **8,** which can be easily synthesized from commercial D-glucose (Scheme 1).[28] Transformation of 3-*O*-allyl-protected glucose derivative **11**[29] into *p*-methoxyphenyl 2,4,6-tri-*O*-benzyl-3-*O*-allyl-α-D-glucopyranoside (**12**) was carried out with *p* -methoxyphenol in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) followed by one-pot deacetylation-benzylation[30] to give compound **12** in a 73% overall yield in two steps. Deallylation of compound **12** using palladium chloride[31] afforded *p* -methoxyphenyl 2,4,6-tri-*O*-benzyl-α-D-glucopyranoside **3** in 87% yield.

Thioglycoside donor **7** was prepared by the treatment of compound **13**[32] with 1.5 equiv of chloroacetic anhydride [$(ClCH_2CO)_2O$] in pyridine followed by -removal of isopropylidene ketal using 80% aqueous acetic acid at 80 °C,[33] then acetylation with acetic anhydride in pyridine and purification by column chromatography afforded ethyl -3,4-di-*O*-acetyl-2- *O*-chloroacetyl-1-thio-β-L-arabinopyranoside (**7**) in 77% overall yield (Scheme 1).

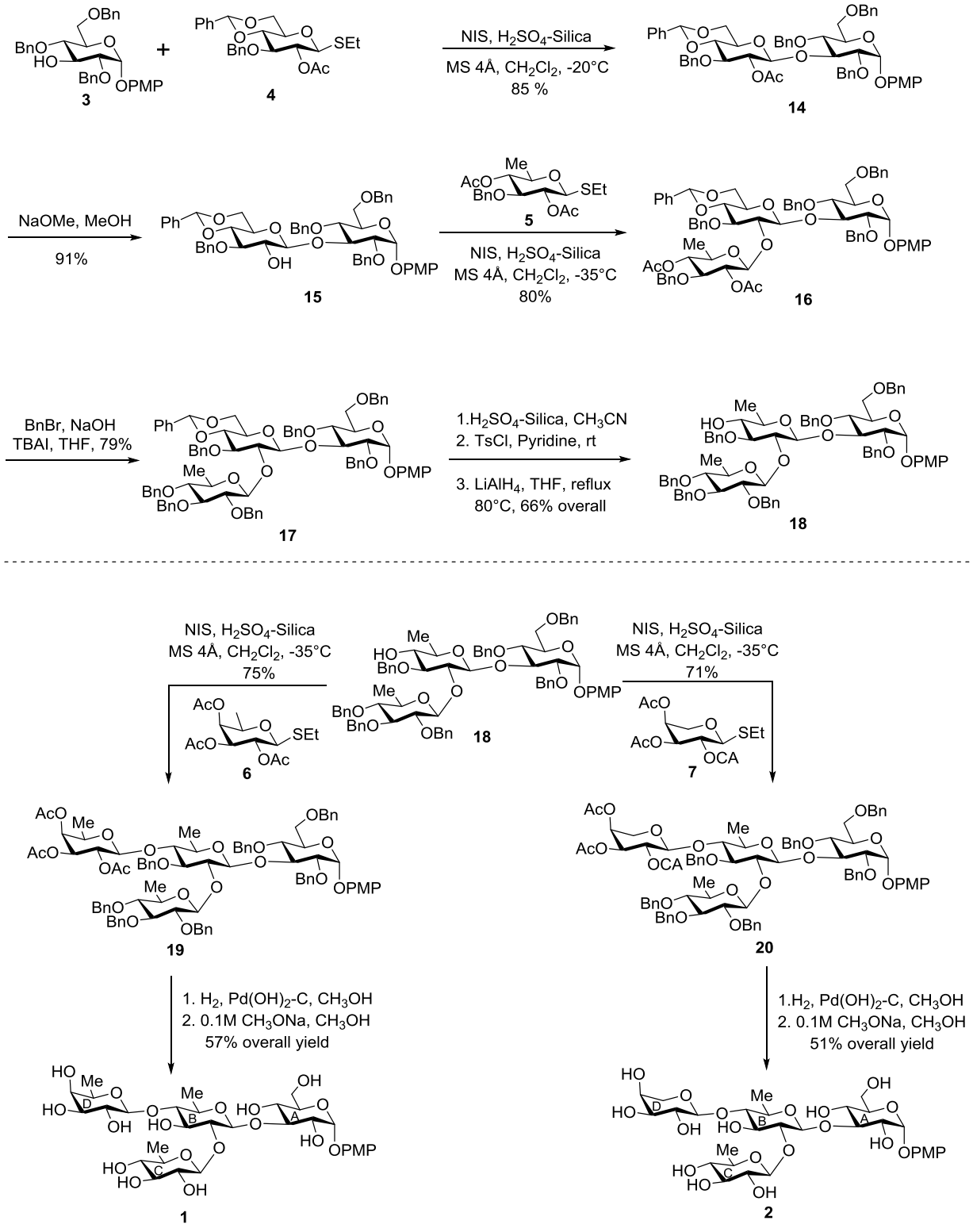


Scheme 1. Preparation of the building blocks **3** &**7**.

Synthesis of tetrasaccharide fragments 1 & 2. With all the required building blocks in hand, *p*-methoxyphenyl 2,4,6-tri-*O*-benzyl- α -D-glucopyranoside (**3**) was glycosylated with thioglycoside derivative **4** in the presence of *N*-iodosuccinimide (NIS) in conjunction with sulfuric acid immobilized on silica (H_2SO_4–silica)[34-39] to afford the disaccharide **14** in 85% yield. The use of H_2SO_4-silica instead of TfOH or TMSOTf as the acid source for the *N*-iodosuccinimide promoted activation of thioglycoside is particularly beneficial since it is a solid and can be weighed easily. Moreover, it is devoid of toxic fumes, highly stable at room temperature and also advantage to maintain the dry condition in a glycosylation reaction. The catalyst could be easily recovered from the reaction mixture and reusable.Once the disaccharide **14** is in hand, disaccharide **14** was then deacetylated under Zempl´en conditions[40] to furnish the disaccharide alcohol **15** in 91% yield (Scheme 2).

Iodonium ion promoted stereoselective glycosylation of compound **15** with thioglycoside donor **5** in the presence of *N*-iodosuccinimide (NIS) in conjunction with sulfuric acid immobilized on silica (H_2SO_4–silica)[34-39] to furnish β-(1→2)-linked trisaccharide **16** in 80% yield, which was transformed to trisaccharide derivative **17** under a one-pot deacetylation-benzylation[30] reaction condition in 79% yield. Then the benzylidene acetal was removed from compound **17** using silica supported sulfuric acid (H_2SO_4–SiO_2)[41] followed by selective tosylation of the primary hydroxyl group using tosyl chloride in the presence of DMAP in pyridine. The reaction mixture was then refluxed with $LiAlH_4$ in THF[42] to give the trisaccharide acceptor **18** in 66% overall yield (Scheme 2).

Stereoselective glycosylation of compound **18** with peracetyl-fucosyl thioglycoside donor **6** in the presence of a combination of *N*-iodosuccinimide (NIS) and H_2SO_4-silica afforded the β-(1→4)-coupled tetrasaccharide derivative **19** in 75% yield, which was confirmed from its spectral analysis [signals at δ(ppm) 5.20 (d, *J* 3.5 Hz, H-1_A), 5.11 (d, *J* 7.6 Hz, H-1_C), 4.91 (d, *J* 7.6 Hz, H-1_B), 4.68 (d, *J* 7.3 Hz, H-1_D) in the ^{1}H NMR and at δ (ppm) 102.7 (C-1_B), 101.1 (C-1_D), 100.3 (C-1_C), 96.5 (C-1_A) in the ^{13}C NMR spectra].



Scheme 2. Synthesis of the tetrasaccharide fragment (**1** & **2**) of novaeguinoside I and II as their *p*-methoxyphenyl glycoside (PMP).

Hydrogenolysis of tetrasaccharide derivative **19** over Pearlman's catalyst[31] followed by saponification using sodium methoxide furnished the tetrasaccharide (**1)** as its *p*-methoxyphenyl glycoside in 57% overall yield (Scheme 2). The structure of the tetrasaccharide (**1**) was elucidated by NMR techniques. The ^{1}H NMR spectrum

showed signals for four anomeric protons at δ (ppm) 5.57 (d, *J* 3.3 Hz, H-1_A), 4.72 (d, *J* 7.4 Hz, H-1_C), 4.71 (d, *J* 7.2 Hz, H-1_B), 4.45 (d, *J* 6.7 Hz, H-1_D), which were correlated in the HSQC experiment with the corresponding carbons at δ 103.8 (C-1_C), 103.2 (C-1_D), 102.1 (C-1_B), 97.5 (C-1_A).

In another experiment, the common trisaccharide intermediate **18** upon stereoselective glycosylation with thioglycoside arabinose donor **7** in the presence of a combination of *N*-iodosuccinimide (NIS) and H_2SO_4-silica afforded the β-(1→4)-coupled tetrasaccharide derivative **20** in 71% yield, which was confirmed from its spectral analysis [signals at δ(ppm) 5.10 (d, *J* 3.5 Hz, H-1_A), 5.02 (d, *J* 7.6 Hz, H-1_C), 4.86 (d, *J* 7.6 Hz, H-1_B), 4.56 (d, *J* 7.3 Hz, H-1_D) in the ^{1}H NMR and at δ(ppm) 102.6 (C-1_B), 101.1 (C-1_D), 100.2 (C-1_C), 96.6 (C-1_A) in the ^{13}C NMR spectra]. Hydrogenolysis of tetrasaccharide derivative **20** over Pearlman's catalyst[31] followed by saponification using sodium methoxide furnished targeted tetrasaccharide **2** as its *p*-methoxyphenyl glycoside in 51% overall yield (Scheme 2). The structure of the tetrasaccharide (**2**) was elucidated by NMR techniques. The presence of four anomeric protonsin the ^{1}H NMR δ 5.58 (d, *J* 3.3 Hz, 1H, H-1_A), 4.71 (d, *J* 7.4 Hz, 1H, H-1_C), 4.69 (d, *J* 7.2 Hz, 1H- H-1_B), 4.42 (d, *J* 6.7 Hz, 1H, H-1_D) and 103.3 (C- 1_C), 103.2 (C-1_D), 101.9 (C-1_B), 97.4 (C-1_A) in the ^{13}C NMR spectra confirmed the formation of compound **2**.

Conclusions

The synthesis of a tetrasaccharide fragments (**1** & **2**) as their *p*-methoxyphenyl glycoside corresponding to asterosaponin novaeguinoside I and novaeguinoside II originally isolated from the starfish *Culcita novaeguineae* has been successfully achieved in a straightforward manner. During the synthetic process, we have utilized H_2SO_4 immobilized on silica as an alternative promoter instead of TfOH or TMSOTf which are toxic, expensive and difficult to handle. All glycosylation steps gave good yields with excellent stereoselectivity. The *p*-methoxyphenyl group could act as a temporary protecting group of the anomeric position at the reducing end, which could be removed for coupling the tetrasaccharide with aglycon to form steroidal glycoside.

Experimental Section

General. All reactions were monitored by thin layer chromatography over silica gel-coated TLC plates. The spots on TLC were visualized by warming ceric sulfate [2% $Ce(SO_4)_2$ in 5% H_2SO_4 in EtOH sprayed plates on a hot plate. Silica gel 230–400 mesh was used for column chromatography. ^{1}H, ^{13}C NMR, DEPT 135, 2D COSY and HSQC, NMR spectra were recorded on Bruker DPX- 400 MHz spectrometer using $CDCl_3$ and D_2O as solvents and TMS as internal reference unless stated otherwise. Chemical shift values are expressed in δ ppm. Coupling constants are given in Hertz. HRMS was performed using 6520 QToF LC MS/MS mass spectrometer (Aligent technologies). IR spectra were recorded on Perkin Elmer Spectrum Two FT-IR Spectrometer. Optical rotations were determined on Autopol III polarimeter. Commercially available grades of organic solvents of adequate purity are used in all reactions.

***p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-allyl-α-D-glucopyranoside (12).** To solution of glucose derivative **11** (5 g, 12.88 mmol), *p*-methoxyphenol (1.9 g, 15.30 mmol) and MS 4Å (2 g) in anhydrous CH_2Cl_2 (80 mL) was cooled to 0 °C. To the cooled reaction was drop wise added TMSOTf (2.8 mL, 15.47 mmol) and the reaction mixture was allowed to stir at room temperature for 10 h. The reaction was quenched with Et_3N (4 mL),

filtered and evaporated to dryness. To a solution of crude product in THF (80 mL) were added powdered NaOH (1.03 g, 25.75 mmol), tetrabutylammonium iodide (TBAI) (95 mg, 0.26 mmol), and benzyl bromide (2.3 mL, 19.34 mmol) and the reaction mixture was allowed to stir briskly for 3 h at room temperature. After completion (as monitored by TLC), the reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and concentrated to dryness. The crude reaction product was purified over SiO_2 using hexane–EtOAc (8:1) as eluent to give pure compound **12** (5.6 g, 73%); Colorless liquid; $[\alpha]_D^{25}$ -33 (*c* 1.0, $CHCl_3$); IR (neat): 2935, 2849, 1535, 1375, 1120, 1018, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.25 (m, 13 H, Ar-H), 7.20-7.18 (m, 2 H, Ar-H), 6.99 (d, *J* 9.0 Hz, 2 H, Ar-H), 6.78 (d, *J* 9.0 Hz, 2 H, Ar-H), 6.08-5.98 (m, 1H, C*H*$_2$=CH), 5.34 (d, *J* 3.4 Hz, 1 H, H-1), 5.33 (d, *J* 17.2 Hz, 1 H, C*H*$_2$=CH), 5.19 (d, *J* 10.4 Hz, 1 H, C*H*$_2$=CH), 4.86 (d, *J* 12.0 Hz, 1 H, PhC*H*$_2$), 4.79 (d, *J* 12.0 Hz, 1H, PhC*H*$_2$), 4.67 (d, *J* 12.0 Hz, 1H, PhC*H*$_2$), 4.58 (d, *J* 12.0 Hz, 1 H, PhC*H*$_2$), 4.54–4.52 (m, 1 H, OC*H*$_2$), 4.49 (d, *J* 12.0 Hz, 1H, PhC*H*$_2$), 4.41 (d, *J* 12.0 Hz, 1H, PhC*H*$_2$), 4.37–4.34 (m, 1 H, OC*H*$_2$), 4.03 (t, *J* 9.2 Hz, 1 H, H-3), 3.90 – 3.88 (m, 1 H, H-5), 3.76 (s, 3 H, OC*H*$_3$), 3.75-3.68 (m, 2 H, H-6a, H-4), 3.63 (dd, *J* 9.6, 3.5 Hz, 1 H, H-2), 3.58-3.56 (m, 1 H, H-6_b); ^{13}C NMR (100 MHz,$CDCl_3$): δ 155.0-114.5 (Ar-C), 116.6 (CH_2=CH_2), 96.5 (C-1), 81.7 (C-3), 79.6 (C-2), 77.5 (C-4), 75.2 (Ph*C*H_2), 74.5 (Ph*C*H_2), 73.5 (Ph*C*H_2), 73.3 (O*C*H_2-CH=CH), 70.7 (C-5), 68.4 (C-6), 55.6 (O*C*H_3); HRMS (ESI-TOF) calcd for $C_{37}H_{40}NaO_7^+$ $[M + Na]^+$ 619.2666, found 619.2683.

***p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (3).** To a solution of compound **12** (4.0 g, 6.71 mmol) in CH_3OH (50 mL) was added $PdCl_2$ (1.3 g, 7.33 mmol) and the reaction mixture was allowed to stir at room temperature for 2 hours after which time TLC showed complete consumption of starting material. Then, the reaction mixture was filtered through a pad of Celite and the filtrate was removed under reduced pressure and the crude product was purified by flash chromatography using 4:1 n-hexane–EtOAc to afford pure compound **3** (3.2 g, 87%) as a colorless oil; $[\alpha]_D^{25}$–44 (*c* 1.0, $CHCl_3$); IR (neat): 3231, 2847, 1375, 1228, 1120, 1048, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.22 (m, 15 H, Ar-H), 6.98 (d, *J* 9.0 Hz, 2 H, Ar-H), 6.78 (d, *J* 9.0 Hz, 2 H, Ar-H), 5.38 (d, *J* 3.1 Hz, 1 H, H-1), 4.87 (d, *J* 11.2 Hz, 1 H, PhC*H*$_2$), 4.69 (brs, 2 H, PhC*H*$_2$), 4.57 (dd, *J* 11.1 Hz, 2 H, PhC*H*$_2$), 4.43 (d, *J* 11.4 Hz, 1 H, PhC*H*$_2$), 4.28 (t, *J* 9.3 Hz, 1 H, H-3), 3.91-3.89 (m, 1 H, H-5), 3.76 (s, 3 H, OC*H*$_3$), 3.72-3.60 (m, 3 H, H-6_{ab}, H-4), 3.56-3.54 (m, 1 H, H-2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1-114.6 (Ar-C), 95.8 (C-1), 79.3 (C-3), 77.3 (C-2), 74.7 (Ph*C*H_2), 73.5 (C-4), 73.4 (Ph*C*H_2), 72.9 (Ph*C*H_2), 70.4 (C-5), 68.4 (C-6), 55.7 (O*C*H_3); HRMS (ESI-TOF) calcd for $C_{34}H_{36}NaO_7^+$, $[M+Na]^+$ 579.2353, found 579.2373.

Ethyl-3,4-di-*O*-acetyl-2-*O*-chloroacetyl 1-thio-β-L-arabinopyranoside (7). To a solution of compound **13** (2.0 g, 8.54 mmol) in dry pyridine (40 mL) was added chloroacetic anhydride (2.19 g, 12.81 mmol) and the solution was stirred for 2 hours at room temperature. Solvents were evaporated *in vacuo* and the residual syrup was diluted with EtOAc (60 mL) and washed with 1 M HCl (10 mL), and brine (30 mL), dried over Na_2SO_4, and concentrated. The residue was purified by short silica gel column chromatography using hexane-EtOAc (5:1) as eluent, to give pure compound. To a solution of pure compound in 80% aq AcOH (50 mL) was stirred at 80 °C for 1 h. The solvent was then removed in vacuo. The residue was kept for next step. To a solution of crude product in pyridine (20 mL) and Ac_2O (1.9 mL, 20.10 mmol) was stirred at rt overnight. The solvent was removed in vacuo. The residue was purified by silica gel column chromatography (4:1 petroleum ether–EtOAc) to give **7** (2.3 g, 77% overall yield) as syrup; $[\alpha]_D^{25}$–22 (*c* 1.0, $CHCl_3$); IR (neat): 2978, 1448, 1220, 1053, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.69 (d, *J* 4.3 Hz, 1 H), 5.36 (dd, *J* 4.3, 8.3 Hz, 1 H), 5.33 (brs, 1 H), 5.25 (dd, *J* 2.7, 8.3 Hz, 1 H), 4.31 (d, *J* 10.4 Hz, 1 H, H-1), 4.08 (brs, 2 H, COC*H*$_2$Cl), 3.70 (dd, *J* 1.9, 10.4 Hz, 1 H), 2.60-2.53 (m, 2 H, SC*H*$_2$CH$_3$), 2.15 (s, 3 H, COC*H*$_3$), 2.02 (s, 3 H, COC*H*$_3$), 1.26 (t, *J* 6.9 Hz, 3 H, SCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz,$CDCl_3$): δ170.0 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 166.0 (*C*OCH$_2$Cl), 82.1 (C-1), 70.0 (C-2), 68.7 (C-4), 67.5 (C-3), 60.7 (C-5), 40.6 (CO*C*H$_2$Cl), 24.3 (S*C*H$_2$CH$_3$), 20.9 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 14.7 (SCH$_2$*C*H$_3$); HRMS (ESI-TOF) calcd for $C_{13}H_{19}ClNaO_7S^+$, $[M+Na]^+$ 377.0432, found 377.0451.

***p*-Methoxyphenyl (2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (14).** To a solution of compound **3** (3 g, 5.39 mmol) and compound **4** (2.8 g, 6.46 mmol) in anhydrous CH_2Cl_2 (60 mL) was added MS 4 Å (3 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon and cooled to -20 °C. To the cooled reaction mixture were added NIS (1.7 g, 7.56 mmol) and H_2SO_4–silica (50 mg) and it was stirred at the same temperature for 30 min, after which time TLC showed complete consumption of acceptor **3**. The mixture was filtered through a Celite® bed and then washed with CH_2Cl_2. The combined organic layer were successively washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, and water, dried (Na_2SO_4) and concentrated. The crude product was purified over SiO_2 using hexane-EtOAc (4:1) as eluent to give pure compound **14** (4.3 g, 85%); Yellow oil; $[\alpha]_D^{25}$ -43 (*c* 1.0, $CHCl_3$); IR (neat): 3351, 2924, 1777, 1507, 1250, 1202, 1048, 995, 796 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (m, 2 H, Ar-H), 7.31-7.29 (m, 2 H, Ar-H), 7.25-7.15 (m, 21 H, Ar-H), 6.86 (d, *J* 9.1 Hz, 2 H, Ar-H), 6.68 (d, *J* 9.1 Hz, 2 H, Ar-H), 5.46 (s, 1 H, PhC*H*), 5.20 (d, *J* 3.6 Hz, 1 H, H-1_A), 5.09 (d, *J* 8.0 Hz, 1 H, H-1_B), 5.04 (dd, *J* 8.9, 7.5 Hz, 1 H, H-2_B), 4.89 (d, *J* 11.4 Hz, 1 H, PhCH_2), 4.83 (d, *J* 12.0 Hz, 1 H, PhCH_2), 4.63 (dd, *J* 10.8 Hz, 2 H, PhCH_2), 4.46 (dd, *J* 11.8 Hz, 2 H, PhCH_2), 4.38 (t, *J* 9.1 Hz, 1 H, H-3_A), 4.37-4.31 (m, 2 H, PhCH_2), 4.22 (dd, *J* 10.6, 4.9 Hz, 1 H, H-6_{aB}), 3.82-3.79 (m, 1 H, H-5_A), 3.69-3.67 (m, 1 H, H-3_B), 3.66 (s, 3 H, OCH_3), 3.64-3.63 (m, 1 H, H-4_A), 3.62-3.55 (m, 2 H, H-6_{aA}, H-5_B), 3.56-3.52 (m, 2 H, H- H-6_{bB}, H-2_A), 3.37-3.34 (m, 1 H, H-4_B), 3.48 (dd, *J* 10.8, 1.2 Hz, 1 H, H-6_{bA}), 3.37-3.34 (m, 1 H, H-4_B), 1.97 (s, 3 H, COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4 (*C*OCH_3), 155.1-114.5 (Ar-C), 101.3 (Ph*C*H), 101.1 (C-1_B), 95.9 (C-1_A), 82.0 (C-3_B), 80.7 (C-2_A), 78.8 (C-4_A), 78.6 (C-3_A), 75.6 (C-5_B), 74.9 (Ph*C*H_2), 74.2 (Ph*C*H_2), 73.7 (C-2_B), 73.5 (2 C, Ph*C*H_2), 70.4 (C-5_A), 68.8 (C-6_B), 68.3 (C-6_A), 66.0 (C-4_B), 55.6 (O*C*H_3), 21.2 (CO*C*H_3); HRMS (ESI-TOF) calcd for $C_{56}H_{58}NaO_{13}^+$, $[M + Na]^+$ 961.3770, found 961.3786.

***p*-Methoxyphenyl (3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (15**). To a solution of compound **14** (3 g, 3.20 mmol) in MeOH (50 mL), few drops of 0.1M NaOMe were added and the reaction was stirred at room temperature for 3 h. The reaction was then neutralized with Dowex 50W-X8 (H^+) resin, filtered and evaporated to give the crude product, which was purified by column chromatography using hexane–EtOAc (2 : 1) as eluent, to give **15** (2.6 g, 91%); $[\alpha]_D^{25}$–31 (*c* 1.0, $CHCl_3$); IR (neat): 3348, 2887, 1273, 1140, 1107, 1048, 750, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.38 (m, 2 H, Ar-H), 7.32-7.24 (m, 7 H, Ar-H), 7.23-7.15 (m, 14 H, Ar-H), 7.12-7.09 (m, 2 H, Ar-H), 6.89 (d, *J* 9.1 Hz, 2 H, Ar-H), 6.72 (d, *J* 9.1 Hz, 2 H, Ar-H), 5.43 (s, 1 H, PhC*H*), 5.28 (d, *J* 3.6 Hz, 1 H, H-1_A), 4.90 (d, *J* 10.8 Hz, 1 H, PhCH_2), 4.84 (d, *J* 10.8 Hz, 1 H, PhCH_2), 4.78 (brs, 1 H, PhCH_2), 4.77 (d, *J* 7.6 Hz, 1 H, H-1_B), 4.67 (d, *J* 11.3 Hz, 1 H, PhCH_2), 4.58 (d, *J* 10.8 Hz, 1 H, PhCH_2), 4.51 (d, *J* 10.8 Hz, 1 H, PhCH_2), 4.38-4.33 (m, 3 H, H-3_A, PhCH_2), 3.88 (dd, *J* 10.6, 4.9 Hz, 1 H, H-6_{aB}), 3.83-3.81(m, 1 H, H-5_A), 3.69 (s, 3 H, OCH_3), 3.68-3.62 (m, 3 H, H-4_A, H-6_{aA}, H-5_B), 3.60-3.54 (m, 3 H, H-2_A, H-2_B, H-3_B), 3.52-3.49 (m, 2 H, H-6_{bA}, H-6_{bB}) 3.30-3.25 (m, 1 H, H-4_B); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2-114.6 (Ar-C), 105.6 (C-1_B), 101.3 (Ph*C*H), 95.6 (C-1_A), 81.6 (C-3_A), 81.2 (C-3_B), 80.2 (C-2_A), 78.9 (C-4_A), 77.3 (C-5_B), 76.3 (C-2_B), 74.6 (Ph*C*H_2), 74.5 (Ph*C*H_2), 73.5 (Ph*C*H_2), 73.1 (Ph*C*H_2), 70.7 (C-5_A), 68.7 (C-6_B), 68.2 (C-6_A), 66.7 (C-4_B), 55.7 (O*C*H_3); HRMS (ESI-TOF) calcd for $C_{54}H_{56}NaO_{12}^+$, $[M+Na]^+$ 919.3664, found 919.3683.

***p*-Methoxyphenyl (2,4-di-*O*-acetyl-3-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→2)-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (16):** To a solution of compound **15** (2.5 g, 2.78 mmol) and compound **5** (1.5 g, 3.48 mmol) in anhydrous CH_2Cl_2 (50mL) was added MS 4 Å (2 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon and cooled to -35 °C. To the cooled reaction mixture were added NIS (0.941 g, 4.18 mmol) and H_2SO_4–silica (30 mg) and it was stirred at the same temperature for 30 min, after which time TLC showed complete consumption of acceptor **15**. Then, the combined organic layer were successively washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, and water, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (petroleum

ether/EtOAc, 4:1) to give pure compound **16** (2.7 g, 80%); white foam.$[\alpha]_D^{25}$ +21 (*c* 1.0, $CHCl_3$); IR (neat): 3329, 2837, 1218, 1170, 1048, 976, 760, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.22 (m, 13 H, Ar-H), 7.21-7.14 (m, 15 H, Ar-H), 6.85 (d, *J* 9.1 Hz, 2 H, Ar-H), 6.68 (d, *J* 9.1 Hz, 2 H, Ar-H), 5.45 (s, 1 H, PhC*H*), 5.15 (d, *J* 7.7 Hz, 1 H, H-1_C), 5.09 (d, *J* 3.7 Hz, 1 H, H-1_A), 5.08-5.05 (m, 1 H, H-4_C), 4.94 (d, *J* 7.6 Hz, 1 H, H-1_B), 4.93-4.88 (m, 3 H, PhCH_2), 4.87-4.84 (m, 1 H, H-2_C), 4.65 (d, *J* 12.0 Hz, 1 H, PhCH_2), 4.58 (d, *J* 12.0 Hz, 1 H, PhCH_2), 4.49 (brs, 2 H, PhCH_2), 4.48 (d, *J* 12.0 Hz, 1 H, PhCH_2), 4.44 (t, *J* 9.2 Hz, 1 H, H-3_A), 4.34 (dd, *J* 11.0 Hz, 2 H, PhCH_2), 4.27 (dd, *J* 10.6, 4.9 Hz, 1 H, H-6_{aB}), 3.85-3.81 (m, 1 H, H-5_A), 3.71-3.68 (m, 3 H, H-2_B, H-3_B,H-3_C), 3.67 (s, 3 H, OCH_3), 3.63-3.59 (m, 2 H, H-2_A, H-6_{aA}), 3.58-3.47 (m, 4 H, H-4_A, H-5_B, H-6_{bA}, H-6_{bB}), 3.38-3.33 (m, 2 H, H-4_B, H-5_C), 1.94 (s, 3 H, COCH_3), 1.84 (s, 3 H, COCH_3), 1.18 (d, *J* 6.2 Hz, 3 H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6 (*C*OCH_3), 168.9 (*C*OCH_3), 155.1-114.5 (Ar-C), 101.2 (Ph*C*H), 100.8 (2 C, C-1_B, C-1_C), 96.4 (C-1_A), 82.4 (C-3_B), 82.3 (C-2_A), 80.7 (C-3_C), 80.4 (C-4_A), 79.4 (C-2_B), 77.8 (C-3_A), 75.9 (C-5_B),75.1 (Ph*C*H_2), 74.8 (Ph*C*H_2), 74.7 (C-2_C), 74.2 (Ph*C*H_2), 73.3 (2 C, Ph*C*H_2), 73.1 (C-4_C), 70.2 (C-5_A), 70.1 (C-5_C), 69.0 (C-6_B), 68.6 (C-6_A), 65.4 (C-4_B), 55.6 (O*C*H_3), 20.9 (2 C, CO*C*H_3), 17.7 (C*C*H_3); HRMS (ESI-TOF) calcd for $C_{71}H_{76}NaO_{18}^+$, $[M+Na]^+$ 1239.4924, found 1239.4944.

***p*-Methoxyphenyl (2,3,4-tri-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→2)-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (17):** To a solution of compound **16** (2.5 g, 2.05 mmol) in THF (10 mL) were added powdered NaOH (1.03 g, 25.7 mmol), tetrabutylammonium iodide (TBAI) (95 mg, 0.26 mmol), and benzyl bromide (2.3 mL, 19.34 mmol) and the reaction mixture was allowed to stir briskly for 3 h at room temperature. After completion (as monitored by TLC), the reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and concentrated to dryness. The crude reaction product was purified over SiO_2 using hexane-EtOAc (5:1) as eluent to give pure compound **17** (2.1 g, 79%); Colourless syrup.$[\alpha]_D^{25}$ +18 (*c* 1.0, $CHCl_3$); IR (neat): 3321, 2987, 1228, 1127, 1048, 760, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (m, 2 H, Ar-H), 7.46-7.22 (m, 38 H, Ar-H), 6.99 (d, *J* 9.1 Hz, 2 H, Ar-H), 6.80 (d, *J* 9.1 Hz, 2 H, Ar-H), 5.55 (s, 1 H, PhC*H*), 5.30 (d, *J* 7.6 Hz, 1 H, H-1_C), 5.22 (d, *J* 3.6 Hz, 1 H, H-1_A), 5.04-4.96 (m, 4 H, PhCH_2) 4.95 (d, *J* 7.7 Hz, 1 H, H-1_B), 4.87 (d, *J* 11.4 Hz, 1 H, PhCH_2), 4.80 (dd, *J* 11.6 Hz, 2 H, PhCH_2), 4.71 (d, *J* 11.0 Hz, 2 H, PhCH_2), 4.64 (dd, *J* 11.6 Hz, 3 H, PhCH_2),), 4.55 (t, *J* 9.2 Hz, 1 H, H-3_A), 4.47 (dd, *J* 11.6 Hz, 2 H, PhCH_2), 4.39 (dd, *J* 10.6, 4.9 Hz, 1 H, H-6_{aB}), 3.97-3.94 (m, 1 H, H-5_A), 3.93-3.85 (m, 2 H, H-3_B, H-3_C), 3.79 (s, 3 H, OCH_3), 3.77-3.71(m, 3 H, H-2_A, H-2_B, H-6_{aA}), 3.70-3.61 (m, 4 H, H-5_B, H-2_C, H-6_{bA}, H-6_{bB}), 3.57-3.52 (m, 1 H, H-4_B), 3.46 (t, *J* 9.2 Hz, 1 H, H-4_A), 3.42-3.38 (m, 1H, H-5_C), 3.31-3.24(m, 1 H, H-4_C),1.38 (d, *J* 6.2 Hz, 3 H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0-114.5 (Ar-C), 103.2 (C-1_B), 101.3 (C-1_C), 101.0 (Ph*C*H), 96.2 (C-1_A), 84.9 (C-2_C), 83.9 (C-4_C), 83.5 (C-4_A), 82.7 (C-3_C), 82.2 (C-2_A), 80.4 (C-2_B), 79.7 (C-3_B), 78.1 (C-3_A), 75.8 (2 C, C-5_B, Ph*C*H_2), 75.4 (Ph*C*H_2), 75.0 (2 C, Ph*C*H_2), 73.9 (Ph*C*H_2), 73.4 (2 C, Ph*C*H_2), 70.9 (C-5_C), 70.4 (C-5_A), 69.0 (C-6_B), 68.5 (C-6_A), 65.3 (C-4_B), 55.6 (O*C*H_3), 18.2 (C*C*H_3); HRMS (ESI-TOF) calcd for $C_{81}H_{84}NaO_{16}^+$, $[M+Na]^+$ 1335.5652, found 1335.5667.

***p*-Methoxyphenyl (2,3,4-tri-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→2)-(3-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (18).** To a solution of compound **17** (2.1 g, 1.59 mmol) in CH_3CN (42 mL) was added H_2SO_4–silica (0.25 g) and the reaction mixture was allowed to stir at room temperature for 20 min. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. To a cooled solution of crude product in pyridine (17 mL) was added *p*-toluenesulfonyl chloride (325 mg, 1.70 mmol) at 0 °C. The reaction mixture was gradually brought to rt and stirred for 6 h. After consumption of starting material, solvents were evaporated under reduced pressure and the crude product was purified by short column chromatography. A solution of tosylated compound in THF (30 mL) was added gradually LAH (173 mg, 4.55mmol) at 0 °C and the solution was refluxed for 2 h. After complete consumption of starting material the reaction mixture was brought to 0 °C and LAH was quenched with a drop wise addition of EtOAc followed by water, the so formed precipitate was dissolved in 2N H_2SO_4 (25 mL) and extracted with

EtOAc (50ml x 2). Separated organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography using hexan- EtOAc (2:1) to obtain pure compound **18** (1.2 g, 66% overall yield); white foam; $[\alpha]_D^{25}$ +12 (*c* 1.0, $CHCl_3$); IR (neat): 2927,2833, 1238, 1120, 1038, 976, 696, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.36-7.34 (m, 2 H, Ar-H), 7.28-7.18 (m, 26 H, Ar-H), 7.16-7.10 (m, 7 H, Ar-H), 6.87 (d, *J* 9.1 Hz, 2H, Ar –H), 6.68 (d, *J* 9.1 Hz, 2H, Ar-H), 5.14 (d, *J* 3.5 Hz, 1H, H-1_A), 5.05 (d, *J* 7.6 Hz, 1H, H-1_C), 4.99 (d, *J* 10.8 Hz, 1H, PhCH_2), 4.90 (d, *J* 11.2 Hz, 1H, PhCH_2), 4.87 (brs, 1H, PhCH_2), 4.84-4.81 (m, 3H, PhCH_2), 4.80 (d, *J* 7.6 Hz, 1H, H-1_B), 4.74 (d, *J* 11.3 Hz, 1H, PhCH_2), 4.66 – 4.59 (m, 3H, PhCH_2), 4.49-4.43 (m, 3H, PhCH_2, H-3_A), 4.35-4.30 (m, 2H, PhCH_2, H-5_A), 3.88-3.84 (m, 1H, H-5_C), 3.72-3.67 (m, 2H, H-2_B, H-2_A), 3.66 (s, 3H, OCH_3), 3.65-3.58 (m, 2H, H-6_{Aa}, H-5_B), 3.57-3.50 (m, 2H, H-6_{Ab}, H-4_A), 3.39-3.35 (m, 2H, H-3_C, H-2_C), 3.31-3.27 (m, 2H, H-4_B, H-5_A), 3.21-3.18 (m, 2H, H-4_C, H-3_B), 1.26 (d, *J* 6.3 Hz, 3H, CCH_3), 1.20 (d, *J* 6.3 Hz, 3H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ138.5-114.5 (Ar-C), 102.6 (C-1_B), 100.4 (C-1_C), 96.3 (C-1_A), 86.4 (C-2_C), 85.0 (C-4_A), 83.9 (C-4_C), 83.6 (C-3_C), 80.7 (C-2_A), 79.7 (C-2_B), 77.5 (C-3_A), 77.3 (C-5_B), 76.2 (C-3_B), 75.9 (Ph*C*H_2), 75.8 (Ph*C*H_2), 75.3 (Ph*C*H_2), 75.2 (C-5_A), 75.0 (Ph*C*H_2), 74.9 (Ph*C*H_2), 73.9 (Ph*C*H_2), 73.4 (Ph*C*H_2), 71.1 (C-4_B), 70.9 (C-5_C), 70.3 (C-6_A), 55.6 (O*C*H_3), 18.2 (C*C*H_3), 17.7 (C*C*H_3); HRMS (ESI-TOF) calcd for $C_{74}H_{81}O_{15}^+$, $[M+H]^+$ 1209.5570, found 1209.5591.

***p*-Methoxyphenyl (2,3,4-tri-*O*-acetyl-6-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,4-tri-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→2)-(3-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-gluco-pyranoside (19).** To a solution of compound **18** (600 mg, 0.49 mmol) and compound **6** (205 mg, 0.59 mmol) in anhydrous CH_2Cl_2 (50 mL) was added MS 4 Å (2 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon and cooled to -35 °C. To the cooled reaction mixture were added NIS (160 mg, 0.71 mmol) and H_2SO_4–silica (30 mg) and it was stirred at the same temperature for 30 min, after which time TLC showed complete consumption of acceptor **16**. Then, the combined organic layer were successively washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, and water, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (petroleum ether-EtOAc 5:1) to give pure compound **19** (551 mg, 75%) as colourless syrup; $[\alpha]_D^{25}$ +22 (*c* 1.0, $CHCl_3$); IR (neat): 2973, 2837, 1173, 1170, 1048, 976, 696, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.36-7.32 (m, 2H, Ar-H), 7.29-7.27 (m, 3H, Ar-H), 7.26-7.24 (m, 10H, Ar-H), 7.22-7.17 (m, 16H, Ar-H), 7.16-7.15 (m, 4H, Ar-H), 6.87 (d, *J* 9.1Hz, 2H, Ar-H), 6.69 (d, *J* 9.1 Hz, 2H, Ar-H), 5.20 (d, *J* 3.5 Hz, 1H, H-1_A), 5.19-5.17 (m, 1H, H-3_D), 5.11 (d, *J* 7.6 Hz, 1H, H-1_C), 5.09-5.07 (m, 1H, PhCH_2), 5.03-5.01 (m, 1H, H-4_D), 4.99-4.96 (m, 2H, PhCH_2),4.91(d, *J* 7.6 Hz, 1H, H-1_B), 4.90-4.89 (m, 1H, PhCH_2,), 4.88-4.85 (m, 1H, PhCH_2), 4.83-4.79 (m, 2H, PhCH_2), 4.72-4.69 (m, 1H, PhCH_2), 4.68 (d, *J* 7.3 Hz, 1H, H-1_D), 4.66-4.56 (m, 4H, PhCH_2), 4.47-4.40 (m, 2H, PhCH_2, H-3_A), 4.37-4.30 (m, 2H, PhCH_2, H-2_D), 3.85-3.82 (m, 1H, H-4_B), 3.80-3.78 (m, 1H, H-2_B), 3.77-3.72 (m, , 1H-H-2_A), 3.67 (s, 3H, OCH_3), 3.63-3.55 (m, 3H, H-6_{Aa}, H-4_A, H-5_A), 3.52-3.46 (m, 2H, H-5_D, H-6_{Ab}), 3.45-3.30 (m, 4H, H-2_C, H-3_C, H-3_B, H-5_B), 3.25-3.21 (m, 1H, H-5_C), 3.17-3.13 (m, 1H, H-4_C), 2.05 (s, 3H, COCH_3), 1.99 (s, 3H, COCH_3), 1.90 (s, 3H, COCH_3), 1.24 (d, *J* 6.3 Hz, 6H, CCH_3), 0.93 (d, *J* 6.4 Hz, 3H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ170.3 (*C*OCH_3), 170.2 (*C*OCH_3), 169.8 (*C*OCH_3), 155.0-114.5 (Ar-C), 102.7 (C-1_B), 101.1 (C-1_D), 100.3 (C-1_C), 96.5 (C-1_A), 84.8 (C-2_C), 84.1 (C-4_A), 83.9 (C-4_C), 83.6 (C-3_C), 83.4 (C-5_B), 80.5 (C-2_A) , 79.4 (C-2_B), 77.6 (C-3_A), 77.3 (C-5_A), 75.8 (Ph*C*H_2), 75.3 (Ph*C*H_2), 75.1 (C-2_D), 74.8 (Ph*C*H_2), 74.7 (Ph*C*H_2), 74.0 (Ph*C*H_2), 73.4 (Ph*C*H_2), 71.5 (Ph*C*H_2), 70.8 (C-5_C), 70.4 (C-3_B), 70.3 (C-4_C), 70.2 (C-4_B), 70.0 (C-3_D), 96.4 (C-5_D), 68.5 (C-6_A), 55.6 (O*C*H_3), 20.9 (CO*C*H_3), 20.7 (CO*C*H_3), 20.6 (CO*C*H_3), 18.1 (C*C*H_3), 17.9 (C*C*H_3), 15.9 (C*C*H_3); HRMS (ESI-TOF) calcd for $C_{86}H_{96}NaO_{22}^+$, $[M+Na]^+$ 1503.6285, found 1503.6294.

***p*-Methoxyphenyl (2-*O*-chloroacetyl-3,4-di-*O*-acetyl-β-L-arabinopyranosyl)-(1→4)-(2,3,4-tri-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→2)-(3-*O*-benzyl-6-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (20).** To a solution of compound **18 (**600 mg, 0.49 mmol) and compound **7** (210 mg, 0.59 mmol) in anhydrous CH_2Cl_2 (50mL) was added MS 4 Å (2 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon and cooled to −35 °C. To the cooled reaction mixture were added

NIS (0.160 g, 0.711 mmol) and H_2SO_4–silica (30 mg) and it was stirred at the same temperature for 30 min, after which time TLC showed complete consumption of acceptor **18**. Then, the combined organic layer were successively washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, and water, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (petroleum ether-EtOAc 5:1) to give pure compound **20** (523 mg, 71%) as colourless syrup; $[\alpha]_D^{25}$ +28 (*c* 1.0, $CHCl_3$); IR (neat): 3019, 2710, 2219, 1528, 1425, 1302, 1042, 988, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.38-7.32 (m, 4H, Ar-H), 7.28-7.23 (m, 7H- Ar-H), 7.21-7.18 (m, 11H, Ar-H), 7.17-7.14 (m, 13H, Ar-H), 6.86 (d, 2H, *J* 9.1 Hz, Ar-H), 6.68 (d, *J* 9.1 Hz, 2H, Ar-H), 5.22 (dd, *J* 6.8, 7.3 Hz, 1H, H-3_D), 5.18-5.17 (m, 1H, H-4_D), 5.10 (d, *J* 3.5 Hz, 1H, H-1A), 5.02 (d, *J* 7.6 Hz, H-1_C), 5.01-4.99 (m, 1H, H-2_B), 4.98-4.96 (m, 1H, PhCH_2), 4.94 (brs, 1H, PhCH_2), 4.88-4.87 (d, *J* 11.0 Hz, 1H, PhCH_2), 4.86 (d, *J* 7.6 Hz, 1H, H-1_B), 4.84 (d, *J* 11.2 Hz, 1H, PhCH_2), 4.80-4.74 (m, 3H, PhCH_2), 4.65-4.60 (m, 4H, PhCH_2), 4.56 (d, *J* 7.3 Hz, 1H, H-1_D), 4.48-4.40 (m, 2H, PhCH_2, H-3_A), 4.34-4.30 (m, 2H, PhCH_2), 3.96 (brs, 2H, COCH_2Cl), 3.92 (dd, *J* 1.2, 13.2 Hz, 1H, H-5_{Da}), 3.85-3.83 (m, 1H, H-4_B), 3.77-3.75 (m, 1H, H-2A), 3.67 (s, 3H, OCH_3), 3.66-3.62 (m, 1H, H-4_A), 3.60-3.59 (m, 1H, H-6_{Aa}), 3.57-3.54 (m, 3H, H-2_B, H-2_C, H-3_B), 3.51-3.49 (m, 1H, H-6_{Ab}), 3.47-3.44 (m, 1H, H-5_{Db}), 3.41 (brs, 1H, H-5C), 3.38-3.33 (m, 3H, H-2_B, H-3_C, H-5_A), 3.20-3.17 (m, 2H, H-5_B, H-4_C), 2.03 (s, 3H, COCH_3), 1.94 (s, 3H, COCH_3), 1.22 (d, *J* 6.3 Hz, 3H, CCH_3), 1.19 (d, *J* 6.3 Hz, 3H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ170.3 (*C*OCH_3), 170.1 (*C*OCH_3), 166.1 (*C*OCH_2Cl), 155.0-114.5 (C-Ar), 102.6 (C- 1_B), 101.1 (C-1_D), 100.2 (C-1_C), 96.6 (C-1_A), 84.9 (C- 2_C), 83.9 (C-4_C), 83.7 (C-3_C), 83.5 (C-2_B), 80.6 (C-3_B), 78.8 (C-4_A), 77.5 (C-2_A), 75.8 (C-3_A), 77.3 (Ph*C*H_2), 75.7 (Ph*C*H_2), 75.4 (Ph*C*H_2), 75.2 (Ph*C*H_2), 74.8 (Ph*C*H_2), 74.0 (Ph*C*H_2), 73.4 (Ph*C*H_2), 71.8 (C-3_D), 70.9 (C-5_B), 70.5 (C-2_D), 70.3 (C-5_C), 70.2 (C-4_B), 68.5 (C-4_D), 68.2 (C-6_A), 64.2 (C-5_D), 55.6 (O*C*H_3), 40.4 (CO*C*H_2Cl), 20.9 (CO*C*H_3), 20.6 (CO*C*H_3), 18.0 (C*C*H_3), 17.9 (C*C*H_3); HRMS (ESI-TOF) calcd for $C_{85}H_{93}ClNaO_{22}^+$, $[M+Na]^+$ 1523.5739, found 1523.5835.

***p*-Methoxyphenyl (6-deoxy-β-D-galactopyranosyl)-(1→4)-(6-deoxy-β-D glucopyranosyl)-(1→2)-(6-deoxy-β-D-glucopyranosyl)-(1→3)- α-D-glucopyranoside (1).** To a soln. of compound **19** (250 mg, 0.17 mmol) in CH_3OH (10 mL) was added 20% $Pd(OH)_2$–C (80 mg) and the mixture was stirred at room temperature for 24 h under a positive pressure of H_2. The mixture was filtered through a Celite bed and concentrated to dryness. A solution of the hydrogenated product in 0.1 M CH_3ONa in CH_3OH (15 mL) was allowed to stir at room temperature for 4 h. The reaction mixture was neutralized with Dowex 50W-X8 (H+) resin, filtered and evaporated to dryness. The crude product was passed through a Sephadex® LH-20 column using CH_3OH–H_2O (8:1 *v/v*) as eluant to give pure compound **1** (69 mg, 57%); Powder; $[\alpha]_D^{25}$ −12 (*c* 1.0, H_2O);IR (KBr): 3430, 2906, 2472, 1629, 1357, 1010, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.16 (d, *J* 7.7 Hz, 2H, Ar-H), 6.98 (d, *J* 7.7 Hz, 2H, Ar-H), 5.57 (d, *J* 3.3 Hz, 1H, H-1_A), 4.72 (d, *J* 7.4 Hz, 1H, H-1_C), 4.71 (d, *J* 7.2 Hz, 1H- H-1_B), 4.45 (d, *J* 6.7 Hz, 1H, H-1_D), 3.98-3.96 (m, 1H, H-3_A), 3.93-3.91 (m, 1H, H-2_D), 3.88-3.80 (m, 6H, H-4_D, H-3_C, H-5_B, H-5_D, H-6_{Aab}), 3.77 (s, 3H, OCH_3), 3.67-3.61 (m, 4H, H-2_A, H-2_D, H-4_A, H-4_C), 3.54-3.48 (m, 3H, H-5_A, H-3_B, H-2_B), 3.42-3.36 (m , 2H, H-2_C, H-4_B), 3.19-3.18 (m, 1H, H-5_C), 1.36 (d, *J* 6.3 Hz, 6H, CCH_3), 1.28 (d, *J* 6.3 Hz, 3H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ154.7-115.1 (Ar-C), 103.8 (C- 1_C), 103.2 (C-1_D), 102.1 (C-1_B), 97.5 (C-1_A), 85.1 (C-3_A), 83.8 (C-4_B), 82.3 (C-2_D), 75.1 (C-2_B), 74.8 (C- 3_C), 74.3 (C-5_A), 74.2 (C-2_C), 72.8 (C-4_C), 72.5 (C-3_D), 72.4 (C-3_B), 71.3 (C-5_C), 70.9 (C-2_A), 70.8 (2C, C-5_D, C-5_B), 70.2 (C-4_D), 67.9 (C-4_A), 60.2 (C-6_A), 55.9 (O*C*H_3), 16.7 (2C,C*C*H_3), 15.4 (C*C*H_3);); HRMS (ESI-TOF) calcd for $C_{31}H_{48}NaO_{19}^+$, $[M+Na]^+$ 747.2682, found 747.2686.

***p*-Methoxyphenyl (β-L-arabinopyranosyl)-(1→4)-(6-deoxy-β-D-glucopyranosyl)-(1→2)-(6-deoxy-β-D-glucopyranosyl)-(1→3)- α-D-glucopyranoside (2).** To a soln. of compound **20** (300 mg, 0.20 mmol) in CH_3OH (10 mL) was added 20% $Pd(OH)_2$–C (70 mg) and the mixture was stirred at room temperature for 24 h under a positive pressure of H_2. The mixture was filtered through a Celite bed and concentrated to dryness. A solution of the hydrogenated product in 0.1M CH_3ONa in CH_3OH (20 mL) was allowed to stir at room temperature for 4 h. The reaction mixture was neutralized with Dowex 50W-X8 (H^+) resin, filtered and evaporated to dryness.

The crude product was passed through a Sephadex® LH-20 column using $CH_3OH–H_2O$ (9:1 *v/v*) as eluant to give pure compound **2** (72 mg, 51%); Powder; $[\alpha]_D^{25}$ −18 (*c* 1.0, H_2O);IR (KBr): 3420, 2922, 2272,1511,1456, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, *J* 7.7 Hz, 2H, Ar-H), 6.98 (d, *J* 7.7 Hz, 2H, Ar-H), 5.58 (d, *J* 3.3 Hz, 1H, H-1_A), 4.71 (d, *J* 7.4 Hz, 1H, H-1_C), 4.69 (d, *J* 7.2 Hz, 1H- H-1_B), 4.42 (d, *J* 6.7 Hz, 1H, H-1_D), 3.94-3.90 (m, 3H, H-2_D, H-4_D, H-3_D), 3.81-3.76 (m, 4H, H-2_B, H-3_B, H-6_{Aab}), 3.76 (s, 3H, OCH_3), 3.68-3.66 (m, 2H, H-3_C, H-4_C), 3.58-3.49 (m, 3H, H-2_C, H-4_A, H-2_A), 3.41-3.36 (m, 2H, H-5_B, H-5_A), 3.35 (brs, 2H, H-3_A, H-4_B), 3.23-3.15 (m, 2H, H-5_C, H-5_D), 1.31 (d, *J* 6.3 Hz, 6H, CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ152.7-115.1 (Ar-C), 103.3 (C- 1_C), 103.2 (C-1_D), 101.9 (C-1_B), 97.4 (C-1_A), 84.2 (C-3_A), 83.5 (C-4_B), 82.1 (C-2_D), 75.3 (C-2_B), 75.1 (C- 3_C), 74.9 (C-2_C), 74.7 (C-4_C), 74.4 (C-5_A), 74.1 (C-3_D), 72.5 (C-3_B), 72.3 (C-5_C), 71.9 (C-5_B), 70.6 (C-2_A), 68.5 (C-4_D), 67.9 (C-4_A), 61.3 (C-6_A), 55.8 (OCH_3), 48.9 (C-5_D), 16.2 (2C, CCH_3); HRMS (ESI-TOF) calcd for $C_{30}H_{46}NaO_{19}^+$, $[M+Na]^+$ 733.2526, found 733.2593.

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Supplementary Material

Copies of ^1H and ^{13}C NMR and 2D NMR spectra of compound **1, 2, 3, 7, 12, 14-20**.

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