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Stereoselective glycosylation of *endo*-glycals by microwave- and $AlCl_3$-assisted catalysis

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ABSTRACT

α-2-Deoxyglycosides were synthesized in good to excellent yields by microwave-assisted reaction of *endo*-glycals with various *O*-nucleophiles in the presence of catalytic amount of $AlCl_3$. These glycosyl additions occurred with high α-stereoselectivity and were complete in 5–35 min in 65–93% yield.

1. Introduction

Many biologically important natural products[1] contain one or more 2-deoxyglycosides in their scaffolds, such as anthracyclin antibiotics,[2] aureolic acids,[3] avermectins,[4] orthosomycins,[5] cardiac glycosides,[6] and angucycline.[7] Because the moiety of 2-deoxyglycosides was essential for their biological activities, many methods have been developed to synthesize 2-deoxyglycosides.[8–10] For instance, they can be prepared by formation of 2-iodo-2-deoxyglycoside, followed by dehalogenation.[8] Likewise, similar procedures also include the formation of 2-chloro-2-deoxyglycoside and subsequent radical dechlorination,[9] as well as the preparation of 2-deoxy-2-phenylthio-glycoside followed by the reduction of Raney Nickel.[10] Previous reports indicated that acid-catalyzed addition to glycals represents the most direct method that can be operated under various conditions, including hydrogen bromide,[11] triphenylphosphine hydrogenbromide,[12] Dowex-50 [H^+] in the presence of LiBr,[13] $CeCl_3{\cdot}7H_2O$/NaI,[14] $LaCl_3{\cdot}7H_2O$/NaI,[15] TMSOTf–NEt_3,[16] BCl_3 (or BBr_3),[17] ceric ammonium nitrate,[18] $GaCl_3$,[19] and Rhenium(V) [$ReOCl_3(SMe_2)(OPPh_3)$].[20] We recently applied microwave-assisted glycosylation of hex-1-en-3-uloses to synthesize α-2-deoxyulosides.[21] Herein we present the synthesis of α-*O*-2-deoxyglycoside by $AlCl_3$-catalyzed additions of *endo*-galactals. Several issues were addressed in depth, including the effects of Lewis acid, the substituent at C3-position and nucleophile substrates, plus the mechanistic study.

2. Result and discussion

3,4,6-Tri-*O*-benzyl-D-galactal (**1**), prepared from 3,4,6-tri-*O*-acetyl-D-galactal based on a reported procedure,[22] first reacted with cyclohexanol under a solvent-free condition. Several Lewis acids (0.2 equiv) were examined as the catalyst, including aluminum chloride ($AlCl_3$), samarium chloride ($SmCl_3$), iron chloride ($FeCl_3$), cerium chloride ($CeCl_3$), zinc chloride ($ZnCl_2$), tin chloride ($SnCl_2$), and europium trifluoromethanesulfonate ($Eu(OTf)_3$). The reactions were carried out at 50 °C in an open vessel with 100 W of microwave energy that was generated by the CEM 'Discover' Focused Microwave™ Synthesis System. Most of the reactions were complete within 10 min, as shown in Table 1. Among the reactions, the use of $AlCl_3$ was found to provide the desired product, cyclohexyl 2-deoxy-α-galactopyranoside (**5**), in the highest isolated yield (90%) with high stereoselectivity (ratio of α/β–anomers: 8/1). The same condition applied to other alcohol nucleophiles also led to similar yields and excellent stereoselectivity (see entries v–vii in Table 2). Interestingly, formation of the rearranged product (**6**) was also observed in the presence of several Lewis acids (see entries iv–vii in Table 1), indicating that the glycosylations likely occurs via two different reaction routes, such as protonation and allylic

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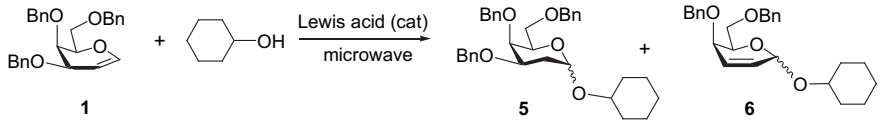
Table 1
Effect of Lewis acid on the glycosylations of *endo*-glycal **1** with cyclohexanol[a]

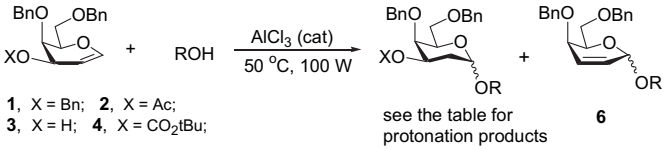


1 **5** **6**

Entry	Lewis acid (cat)	Time (min)	Protonation+rearrangement products (yield, α/β ratio)[b]
i	$AlCl_3$	5	**5** (90%, 8/1)+**6** (0%)
ii	$SmCl_3$	5	**5** (88%, 8/1)+**6** (0%)
iii	$CeCl_3$	10	**5** (88%, 7/1)+**6** (0%)
iv	$FeCl_3$	5	**5** (78%)[c]+**6** (11%)
v	$ZnCl_2$	10	**5** (52%)[c]+**6** (34%)
vi	$SnCl_2$	25	**5** (72%)[c]+**6** (18%)
vii	$Eu(OTf)_3$	20	**5** (81%)[c]+**6** (12%)
viii	$AlCl_3$	60	**5** (92%, 4/1)[d]+**6** (0%)
ix	—	20	**5** (0%)[b]+**6** (0%)

[a] The glycosyl additions were all under a solvent-free condition in the presence of cyclohexanol (>30 equiv).
[b] All the reactions were carried out at 50 °C with 100 W of microwave energy.
[c] The α-anomer is predominant with α/β ratio of 5/1 to 8/1 on the basis of ^{1}H NMR integration.
[d] The reaction was carried out without microwave heating in a CH_2Cl_2 solution containing $AlCl_3$ (1.0 equiv) and cyclohexanol at room temperature.

Table 2
Glycosylations of glycals **1**–**4** with various alcohols[a]



1, X = Bn; **2**, X = Ac;
3, X = H; **4**, X = CO_2tBu;

see the table for protonation products

6

Entry	Donor	Acceptor (ROH)	Time (min)	Protonation+rearrangement products (yield, α/β)
i	**1**	Cyclohexanol	5	**5** (90%, 8/1), —(0%)
ii	**2**	Cyclohexanol	5	**7** (85%, 9/1), —(0%)
iii	**3**	Cyclohexanol	10	**8** (81%, 8/1), —(0%)
iv	**4**	Cyclohexanol	5	**9** (69%)[b]+**6** (10%)[b]
v	**1**	*n*-Octanol	5	**10** (94%, 6/1), —(0%)
vi	**1**	Benzyl alcohol	5	**11** (95%, 7/1), —(0%)
vii	**1**	Isopropanol	5	**12** (92%, 10/1), —(0%)

[a] The glycosyl additions were all under a solvent-free condition in the presence of $AlCl_3$ (0.2 equiv) and excessive alcohol nucleophile (>30 equiv).
[b] The α-anomer is predominant with α/β ratio of 5/1 to 8/1 on the basis of ^{1}H NMR integration.

rearrangement.[25] Apparently the presence of $AlCl_3$ allows the former pathway only.

Although both $AlCl_3$ and the microwave energy were used for these reactions, each one was found to play a different role. Without the microwave heating, the reaction of compound **1** with cyclohexanol took much longer time for completion (see entry viii in Table 1). The resulting stereoselectivity was lower than that observed in the aforementioned examples, indicating that microwave energy is necessary for accelerating the reaction and enhancing the selectivity. In contrast, there was no reaction in the absence of $AlCl_3$ (entry ix in Table 1), indicating that the glycosylation reactions require Lewis acid to take place.

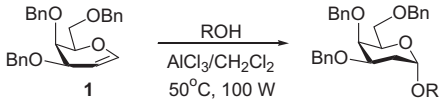
Furthermore, we examined how C3-substituents of *endo*-galactal affect the glycosylation reaction, including benzyl (compounds **1**), acetate (**2**), hydroxyl (**3**) and *tert*-butyl carbonate groups (**4**). The exclusive formation of 2-deoxy-D-galactosides (**5**, **7**, and **8**, see entries i–iii) was still observed with high stereoselectivity (ratio of α/β-anomers: 8/1 to 9/1), except for the reaction of compound **4** that generated both the desired product **9** (69%) and the minor rearranged product (10%). It seemed that the change on C3-substituent did not make significant difference.

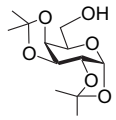
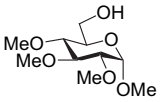
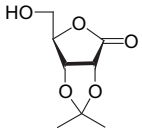
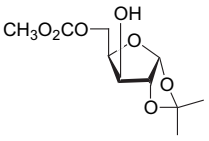
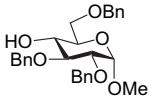
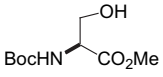
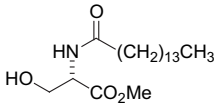
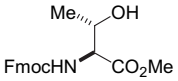
The aforementioned reactions were carried out under solvent-free conditions. When the acceptor substrate no longer exists as liquid or oil, usage of solvent is required to promote the reactivity. For instance, when the glycosyl donor **1** reacted with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (**13**), there was no reaction in the absence of solvent. But the addition of CH_2Cl_2 led to formation of the desired product **21** in 82% yield (see entry i in Table 3). The same glycosyl donor (**1**) further reacted with several *O*-nucleophiles in 0.5 mL CH_2Cl_2, including sugars **14**–**17** (entries ii–v in Table 3), and amino acid derivatives **18**–**20** (entries vi–viii in Table 3), to give 2-deoxy-D-galactoside products **22**–**28** in moderate to good yields, as shown in Table 3. As a result, we demonstrated that this $AlCl_3$- and microwave-assisted glycosylation is useful for formation of various glycosides, glycopeptides and glycolipids.

We previously investigated trifluoroacetic acid (TFA)-catalyzed glycosylations of *endo*- and *exo*-glycals where these reactions were also found to proceed via two pathways, such as Ferrier rearrangement and protonation.[24] The results indicated that protecting group and allylic substituent (equivalent to C3-substituent in this study) are critical to determine the favored reaction route. Interestingly we discovered that the usage of $AlCl_3$ not only becomes an additional factor, but also leads to exclusive formation of 2-deoxygalactosides via the protonation pathway.

The reactions all displayed high α-stereoselectivity, i.e., the nucleophiles attacked from the bottom face of the sugar ring. This result is not only consistent with the anomeric effect, but also favorable by the less steric hindrance (i.e., the axial hydroxyl group at C4-position prefers α-stereoselectivity). In contrast, the reactions of tri-*O*-benzyl-D-glucal with alcohol substrates (analogues to those of

Table 3
Glycosylations of glycals **1** with various alcohols

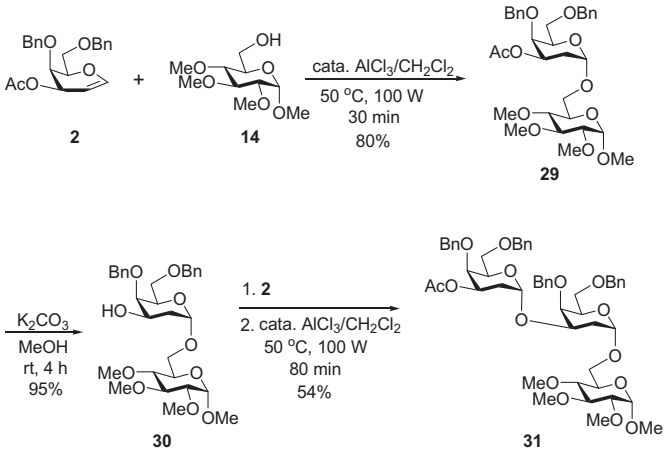


Entry	Acceptor (ROH)[a]		Time (min)	Products (yield, α/β)[b]
i		**13**	15	**21** (82%, 94/6)
ii		**14**	15	**22** (76%, 92/8)
iii		**15**	20	**23** (71%, 95/5)
iv		**16**	15	**24** (72%, 93/7)
v		**17**	35	**25** (65%, 94/6)
vi		**18**	15	**26** (83%, 94/6)
viii		**19**	15	**27** (78%, 93/7)
vii		**20**	20	**28** (74%, 92/8)

[a] The glycosyl additions were all catalyzed by $AlCl_3$ (0.2 equiv) with 2 equiv of the acceptor was dissolved in 0.5 mL CH_2Cl_2.
[b] The α-anomer is predominant with α/β ratio of 92/8 to 95/5 on basis of ^1H NMR integration.

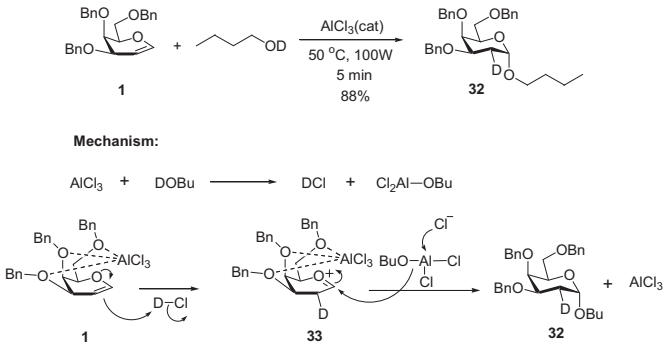
compound **1**) offered similar reactivity and yield, but with lower stereoselectivity (ratio of α/β-anomers: 1.5/1 to 3/1). Furthermore, the product structure and stereochemistry were rigorously determined by using DEPT and COSY, in agreement with previous reports.[20,23] For example, the ^1H NMR spectrum of compound **21** showed the characteristic signals, such as the resonance of the new anomeric proton at δ 5.03, H2a at δ 2.22 (ddd) and H2b at δ 2.02 (dd). In the corresponding ^{13}C NMR spectrum, δ 96.3 and 31.3 were assigned for C1 and C2 of 2-deoxy-D-galactoside, respectively.

Our developed method was further applied for the rapid assembly of trisaccharide **31**. As previously described (see entry ii of Table 3), the addition of alcohol **14** to the CH_2Cl_2 solution of 3-*O*-acetyl-4,6-di-*O*-benzyl-D-galactal **2** afforded the disaccharide **29** in 80% yield, as shown in Scheme 1. After deprotection under basic condition, the product was subjected to another glycosylation with the glycosyl donor **2** to give the trisaccharide **31** in 54% yield as a mixture of α/β anomers (ratio of 96/4). Both glycosylation additions were carried out with 0.2 equiv of $AlCl_3$ at 50 °C with 100 W of microwave energy.



Scheme 1.

In order for examining the mechanistic detail, 3,4,6-tri-*O*-benzyl-D-galactal **1** was treated with deuterium butanoxide. Intriguingly the resulting product (**32**, in 88% yield) contained the deuterium exclusively at the C2-equatorial position. Since it was a solvent-free operation, deuterium chloride was rationalized to result from the reaction of deuterium butanoxide with $AlCl_3$ (Scheme 2). Therefore, the benzyl group at C4 appeared to prevent the protonation from the top face of the sugar ring, but we cannot rule out the possibility that the steric hindrance is owing to the coordination of Lewis acid with the benzyl groups and the ring oxygen. Following the protonation with deuterium chloride, the oxocarbonium ion (**33**) then formed as the intermediate to react with the activated butanoxide (the nucleophile, see Scheme 2). Under such circumstances, anomeric effect or/and the aforementioned hindrance plays a role in favoring the α-glycosyl addition to generate the desired 2-deoxyglycoside **32**.



Scheme 2.

In conclusion, α-2-deoxygalactosides were successfully synthesized by glycosyl addition of *endo*-galactals with several nucleophiles, including simple alcohols, sugars, and amino acid derivatives. The synthesis was operated in the presence of $AlCl_3$ to occur via tandem protonation and glycosylation under microwave-assisted condition. This developed method was also applied for preparing the trisaccharide **31** with high stereoselectivity in a high overall yield.

3. Experimental section

3.1. General procedure

All purchased chemicals were of reagent grade. All reactions were carried out under a nitrogen atmosphere and monitored by TLC analysis (layer thickness: 250 μm). Column chromatography was carried out with silica gel 60 (70–230 mesh for gravity column, or 230–400 mesh for flash column). Commercially available reagents were directly used without further purification unless otherwise noted. Dichloromethane, ethyl acetate, hexanes, and methanol were purchased from Mallinckrodt Chemical Co. The following compounds were purchased from Acros Chemical Co, including benzyl alcohol, *n*-octanol, cyclohexanol, isopropanol, iodomethane, tri-*O*-acetyl-D-galactal, benzyl chloride, potassium carbonate, sodium hydride, $AlCl_3$, $SmCl_3$, $FeCl_3$, $CeCl_3$, $ZnCl_2$, $SnCl_2$, $Eu(OTf)_3$, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, *N*-*tert*-butoxycarbonyl-L-serine methyl ester, *N*-(9-fluorenylmethoxycarbonyl)-L-threonine methyl ester. Proton NMR spectra were recorded at a Bruker spectrometer (200 or 400 MHz) with $CDCl_3$ (δ_H 7.24) and DMSO-d_6 (δ_H 2.50) as the internal standard; Carbon-13 NMR spectra were recorded at 50 or 100 MHz with $CDCl_3$ [δ_C 77.0 (central line of a triplet)]. Splitting patterns are shown by the abbreviations, such as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Microwave irradiation experiments were performed using a single-mode Discover System from 'Discover' Focused MicrowaveTM Synthesis System.

3.2. Typical procedure of solvent-free glycosylation for preparing 2-deoxygalacoside derivatives 5, 7–12

endo-Galactal (e.g., **1**–**4**, 1.0 equiv) was mixed with alcohol substrate (30 equiv) and $AlCl_3$ (0.2 equiv), and then treated with 100 W of microwave energy at 50 °C for 5–10 min. The reaction mixture was concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography with EtOAc/hexanes (1:5) to give the desired product (e.g., **5**, **7**–**12**) in 70–90% yield.

*3.2.1. Cyclohexyl-2-deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranoside (**5**).* Pale yellow oil; $[\alpha]_D^{25}$ +21.5 (*c* 0.037, $CHCl_3$); IR ($CHCl_3$) 2931, 1650, 1254, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34–7.23 (15H, m, ArH), 5.13 (1H, d, $J_{1,2a}$=3.6 Hz, H1), 4.93 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.62 (1H, d, *J*=9.6 Hz, *PhCH*$_2$), 4.60 (2H, br s, CH_2Ph), 4.51 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.43 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 3.98 (1H, dd, $J_{3,4}$=6.4 Hz, $J_{3,2a}$=12.8 Hz, H3), 3.95(2H, br, H4, H5), 3.61 (1H, dd, $J_{6a,5}$=7.2 Hz, $J_{6a,6b}$=9.6 Hz, H6a), 3.57 (1H, dd, $J_{6b,5}$=6.0 Hz, $J_{6b,6a}$=9.6 Hz, H6b), 3.54–3.51 (1H, m, H1′), 2.22 (1H, ddd, $J_{2a,1}$=3.6 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 1.94 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.4 Hz, H2b), 1.84 (2H, br s, H2′), 1.70 (2H, br s, H6′), 1.52 (1H, br s, H3a′), 1.23 (5H, m, Cyclohexyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.99, 138.65, 138.22, 128.36, 128.35, 128.34, 128.19, 128.18, 128.17, 128.16, 128.15, 127.65, 127.64, 127.60, 127.59, 127.45, 127.44, 127.31, 95.57, 75.05, 74.45, 74.26, 73.39, 73.22, 70.45, 69.84, 69.66, 33.48, 31.73, 31.62, 25.71, 24.33, 24.07; HRMS (ESI) for $C_{33}H_{40}O_5Na^+$ [M+Na^+] calcd 539.2773, found: 539.2770. Anal. Calcd for $C_{33}H_{40}O_5$; C: 76.71; H: 7.80. Found: C: 76.75; H: 7.83.

*3.2.2. Cyclohexyl-2-deoxy-3-O-acetyl-4,6-di-O-benzyl-α-D-lyxo-hexopyranoside (**7**).* Pale yellow oil; $[\alpha]_D^{25}$ +43.6 (*c* 0.024, $CHCl_3$); IR ($CHCl_3$) 2929, 1741, 1644, 1238, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34–7.25 (10H, m, ArH), 5.24 (1H, ddd, $J_{3,4}$=2.8 Hz, $J_{3,2b}$=4.8 Hz, $J_{3,2a}$=12.4 Hz, H3), 5.12 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.67 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.54 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.53 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.44 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.11 (1H, dd, $J_{5,6a}$=6.4 Hz, $J_{5,6b}$=6.8 Hz, H5), 3.93 (1H, br, H4), 3.61–3.51 (3H, m, H6, H1′), 2.25 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.4 Hz, H2a), 1.97 (3H, s, CH_3), 1.82–1.70 (3H, m, H2b, H2′), 1.69–19 (8H, m, cyclohexyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.34, 138.48, 138.09, 128.32, 128.31, 128.27, 128.26, 128.06, 128.05, 127.60, 127.59, 127.58, 127.57, 95.24, 74.75, 74.64, 73.80, 73.29, 69.82, 69.16, 69.11, 33.38, 31.50, 31.08, 25.65, 24.22, 23.97, 21.12; HRMS (ESI) for $C_{28}H_{36}O_6Na^+$ [M+Na^+] calcd 491.2410, found: 491.2407. Anal. Calcd for $C_{28}H_{36}O_6$; C: 71.77; H: 7.74. Found: C: 72.01; H: 7.76.

*3.2.3. Cyclohexyl-2-deoxy-4,6-di-O-benzyl-α-D-lyxo-hexopyranoside (**8**).* Pale yellow oil; $[\alpha]_D^{25}$ +23.5 (*c* 0.022, $CHCl_3$); IR ($CHCl_3$) 3400–3200, 2960, 1633, 1240, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.25 (10H, m, ArH), 5.07 (1H, d, $J_{1,2a}$=2.8 Hz, H1), 4.73 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.62 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.57 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.50 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.06 (2H, m, H3, H5), 3.80 (1H, d, $J_{4,3}$=2.4 Hz, H4), 3.68 (1H, dd, $J_{6a,5}$=8.0 Hz, $J_{6a,6b}$=10.2 Hz, H6a), 3.60 (1H, dd, $J_{6b,5}$=6.4 Hz, $J_{6b,6a}$=10.2 Hz, H6b), 3.54–3.50 (1H, m, H1′), 1.90 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 1.87–1.81 (2H, m, H2a′,H2b), 1.73–1.19 (9H, m, cyclohexyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.49, 137.98, 128.56, 128.55, 128.38, 128.37, 127.99, 127.98, 127.90, 127.89, 127.69, 127.68, 95.41, 76.68, 75.13, 74.59, 73.40, 69.24, 69.14, 65.80, 35.08, 33.41, 31.54, 25.68, 24.25, 23.99; HRMS (ESI) for $C_{26}H_{34}O_5Na^+$ [M+Na^+] calcd 449.2304, found: 449.2310. Anal. Calcd for $C_{26}H_{34}O_5$; C: 73.21; H: 8.03. Found: C: 73.23; H: 8.05.

*3.2.4. Cyclohexyl-2-deoxy-3-O-tert-butoxycarbonyl-4,6-di-O-benzyl-α-D-lyxo-hexopyranoside (**9**).* Pale yellow oil; $[\alpha]_D^{25}$ +23.6 (*c* 0.018, $CHCl_3$); IR ($CHCl_3$) 2991, 1750, 1648, 1230, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33–7.24 (10H, m, ArH), 5.13 (1H, d, $J_{1,2a}$=2.8 Hz, H1), 5.07 (1H, ddd, $J_{3,4}$=3.2 Hz, $J_{3,2b}$=4.4 Hz, $J_{3,2a}$=12.8 Hz, H3), 4.76 (1H, d, *J*=11.5 Hz, *PhCH*$_2$), 4.50 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.48 (1H, d, *J*=10.0 Hz, *PhCH*$_2$), 4.41 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.07 (1H, dd, $J_{5,6a}$=6.0 Hz, $J_{5,6b}$=6.4 Hz, H5), 3.99 (1H, br s, H4), 3.55–3.49 (3H, m, H6, H1′), 2.29 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 1.89–184 (3H, m, H2b, H2′), 1.70 (2H, br s, H6′), 1.49 (9H, s, 3× CH_3), 1.48–1.23 (6H, m, cyclohexyl); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 152.93, 138.37, 138.19, 128.43, 128.42, 128.29, 128.26, 128.23, 128.15, 127.83, 127.63, 127.55, 127.52, 95.21, 82.19, 74.69, 74.55, 73.36, 73.26, 72.74, 69.42, 69.30, 33.39, 31.51, 31.09, 27.81, 27.80, 27.79, 25.67, 24.24, 23.98; HRMS (ESI) for $C_{32}H_{44}O_{11}Na^+$ [M+Na^+] calcd 549.2828, found: 549.2819. Anal. Calcd for $C_{32}H_{44}O_{11}$; C: 70.70; H: 7.74. Found: C: 70.74; H: 7.77.

*3.2.5. Octyl-2-deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranoside (**10**).* Pale yellow oil; $[\alpha]_D^{25}$ +29.4 (*c* 0.009, $CHCl_3$); IR ($CHCl_3$) 2935, 1631, 1250, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27–7.16 (15H, m, ArH), 4.88 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.85 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.53 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.52 (2H, br s, *CH*$_2$*Ph*), 4.43 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 4.34 (1H, d, *J*=12.0 Hz, *PhCH*$_2$), 3.87–3.81 (3H, m, H3, H4, H5), 3.55–3.46 (3H, m, H6, H1a′), 3.30–3.25 (1H, m, H1b′), 2.17–2.10 (1H, m, H2a), 1.92–1.89 (1H, m, H2b), 1.48–1.43 (2H, m, H2′), 1.24–1.19 (10H, m, H3′–H7′), 0.80 (3H, t, *J*=6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.92, 138.57, 138.14, 128.32, 128.31, 128.30, 128.17, 128.16, 128.15, 128.14, 128.13, 128.12, 127.70, 127.69, 127.68, 127.58, 127.42, 127.41, 127.28, 127.27, 127.26, 97.68, 74.91, 74.23, 73.41, 73.07, 70.41, 69.76, 69.60, 67.47, 31.80, 31.27, 29.51, 29.37, 29.22, 26.20, 22.62, 14.06; HRMS (ESI) for $C_{35}H_{46}O_5Na^+$ [M+Na^+] calcd 569.3243, found: 569.3247. Anal. Calcd for $C_{35}H_{46}O_5$; C: 76.89; H: 8.48. Found: C: 76.93; H: 8.51.

*3.2.6. Benzyl-2-deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranoside (**11**).* Pale yellow oil; $[\alpha]_D^{25}$ +30.1 (*c* 0.013, $CHCl_3$); IR ($CHCl_3$) 2955, 1650, 1235, 1022 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27–7.12 (20H, m, ArH), 4.98 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.84 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.56 (2H, br s, *PhCH*$_2$), 4.50 (2H, br s, CH_2Ph), 4.41 (1H, d, *J*=11.6 Hz, *PhCH*$_2$), 4.37 (1H, d, *J*=12.4 Hz, *PhCH*$_2$), 4.33 (1H, d,

J=12.4 Hz, *PhCH*$_2$), 3.89–3.84 (3H, m, H3, H4, H5), 3.52–3.45 (2H, m, H6), 2.21–2.12 (1H, m, H2a), 1.95 (1H, dd, $J_{2b,3}$=3.6 Hz, $J_{2b,2a}$=12.4 Hz, H2b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.90, 138.53, 138.13, 137.87, 128.52, 128.40, 128.39, 128.38, 128.37, 128.36, 128.35, 128.22, 128.21, 128.20, 128.19, 127.94, 127.93, 127.76, 127.75, 127.62, 127.49, 127.33, 127.32, 126.94, 97.11, 74.85, 74.28, 73.46, 73.05, 70.47, 70.11, 69.59, 68.90, 31.13; HRMS (ESI) for $C_{34}H_{36}O_5Na^+$ [M+Na$^+$] calcd 547.2460, found: 547.2462. Anal. Calcd for $C_{34}H_{36}O_5$; C: 77.84; H: 6.92. Found: C: 77.87; H: 6.97.

*3.2.7. Isopropyl-2-deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranoside (**12**).* Pale yellow oil; $[\alpha]_D^{25}$ +130.3 (*c* 0.014, $CHCl_3$); IR ($CHCl_3$) 2934, 1641, 1242, 1034 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41–7.28 (15H, m, ArH), 5.15 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.99 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.68 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.67 (2H, br s, *CH*$_2$*Ph*), 4.57 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.49 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.05–4.00 (3H, m, H3, H4, H5), 3.97–3.91 (1H, m, H1a′), 3.69 (1H, dd, $J_{6a,5}$=7.2 Hz, $J_{6a,6b}$=9.6 Hz, H6a), 3.62 (1H, dd, $J_{6b,5}$=6.0 Hz, $J_{6b,6a}$=9.6 Hz, H6b), 2.34–2.27 (1H, m, H2a), 2.03–1.98 (1H, m, H2b), 1.24 (3H, d, J=6.4 Hz, CH_3), 1.18 (3H, d, J=6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.97, 138.64, 138.17, 128.35, 128.34, 128.33, 128.32, 128.17, 128.16, 128.15, 128.14, 127.69, 127.68, 127.59, 127.41, 127.27, 127.26, 127.25, 95.56, 75.04, 74.25, 73.42, 73.14, 70.44, 69.75, 69.55, 68.03, 31.65, 23.32, 21.35; HRMS (ESI) for $C_{30}H_{36}O_5Na^+$ [M+Na$^+$] calcd 499.2460, found: 499.2465. Anal. Calcd for $C_{30}H_{36}O_5$; C: 75.60; H: 7.61. Found: C: 75.63; H: 7.63.

3.3. Typical procedure of glycosylation for preparing 2-deoxyglycoside derivatives (21–28)

To a stirred solution of *endo*-galactal (e.g., **1**, 1.0 equiv) in CH_2Cl_2 (2.0 mL) were added alcohol substrate (3 equiv) and $AlCl_3$ (0.2 equiv). The reaction mixture was subjected to microwave radiation of 100 W at 50 °C for 15–35 min. Upon reaction completion, the mixture was concentrated under reduced pressure and then purified by silica gel chromatography with EtOAc/hexanes (1:5) to give the desired glycoside product (e.g., **21**–**28**) in 65–80% yield.

*3.3.1. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→6)-1,2:3,4-di-O-isopropylidene-D-galactopyranose **21**.* Pale yellow oil; $[\alpha]_D^{25}$ +2.4 (*c* 0.037, $CHCl_3$); IR ($CHCl_3$) 2923, 1649, 1230, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.21 (15H, m, ArH), 5.51 (1H, d, $J_{1',2'}$=5.2 Hz, H1′), 5.03 (1H, d, $J_{1,2a}$=2.8 Hz, H1), 4.92 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.62 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.62–4.57 (3H, m, H3′, *CH*$_2$*Ph*), 4.49 (1H, d, J=12.0 Hz, *PhCH*$_2$), 4.42 (1H, d, J=12.0 Hz, *PhCH*$_2$), 4.30 (1H, dd, $J_{2'1'}$=2.4 Hz, $J_{2'3'}$=5.2 Hz, H2′), 4.21 (1H, dd, $J_{4'3'}$=1.6 Hz, $J_{4'5'}$=8.0 Hz, H4′), 3.95–3.94 (4H, m, H3, H4, H5, H5′), 3.74 (1H, dd, $J_{6a,5}$=6.8 Hz, $J_{6a,6b}$=10.4 Hz, H6a), 3.66 (1H, dd, $J_{6b,5}$=6.4 Hz, $J_{6b,6a}$=10.4 Hz, H6b), 3.62 (1H, dd, $J_{6a',5'}$=7.6 Hz, $J_{6a',6b'}$=9.2 Hz, H6a′), 3.54 (1H, dd, $J_{6b',5'}$=5.6 Hz, $J_{6b',6a'}$=9.2 Hz, H6b′), 2.22 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,3}$=12.0 Hz, $J_{2a,2b}$=12.4 Hz, H2a), 2.02 (1H, dd, $J_{2b,3}$=4.0 Hz, $J_{2b,2a}$=12.4 Hz, H2b), 1.51 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.33 (6H, s, 2× CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.95, 138.61, 138.14, 128.37,128.36, 128.35, 128.34, 128.21, 128.20, 128.18, 128.17, 127.81, 127.80, 127.61, 127.45, 127.44, 127.30, 127.29, 109.30, 108.51, 97.53, 96.35, 74.70, 74.30, 73.37, 72.91, 71.09, 70.68, 70.63, 70.41, 69.83, 69.20, 65.85, 65.54, 31.11, 26.11, 25.96, 24.93, 24.54; HRMS (ESI) for $C_{39}H_{48}O_{10}Na^+$ [M+Na$^+$] calcd 699.3125, found: 699.3125. Anal. Calcd for $C_{39}H_{48}O_{10}$; C: 69.21; H: 7.15. Found: C: 69.26; H: 7.19.

*3.3.2. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→6)-1,2,3,4-tetra-O-methyl-α-D-glucopyranose (**22**).* Pale yellow oil; $[\alpha]_D^{25}$ +23.9 (*c* 0.038, $CHCl_3$); IR ($CHCl_3$) 2932, 1632, 1240, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34–7.22 (15H, m, ArH), 5.04 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.93 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.74 (1H, d, $J_{1',2'}$=3.6 Hz, H1′), 4.62 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.59 (2H, br s, *PhCH*$_2$), 4.50 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.43 (1H, d, J=11.6 Hz, *PhCH*$_2$), 3.95–3.88 (3H, m, H3, H4, H5), 3.79 (1H, dd, $J_{6a',5'}$=5.2 Hz, $J_{6a',6b'}$=11.6 Hz, H6a′), 3.62 (3H, s, OCH_3), 3.59–3.54 (4H, m, H6a, H6b, H5′, H6b′), 3.51–3.42 (7H, m, H3′, OCH_3), 3.33 (3H, s, OCH_3), 3.17 (1H, dd, $J_{2',1'}$=3.6 Hz, $J_{2',3'}$=9.6 Hz, H2′), 3.09 (1H, dd, $J_{4',3'}$=9.2 Hz, $J_{4',5'}$=9.2 Hz, H4′), 2.23 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 2.04 (1H, dd, $J_{2b,3}$=3.6 Hz, $J_{2b,2a}$=12.4 Hz, H2b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.86, 138.39, 138.13, 128.38, 128.37, 128.34, 128.33, 128.20, 128.19, 128.18, 128.17, 127.70, 127.62, 127.54, 127.53, 127.47, 127.37, 127.36, 98.05, 97.23, 83.61, 81.85, 79.51, 74.36, 74.25, 73.34, 72.94, 70.27, 69.98, 69.63, 69.44, 65.82, 60.81, 60.29, 58.92, 54.96, 31.01; HRMS (ESI) for $C_{37}H_{48}O_{10}Na^+$ [M+Na$^+$] calcd 675.3145, found: 675.3146. Anal. Calcd for $C_{37}H_{48}O_{10}$; C: 68.08; H: 7.41. Found: C: 68.12; H: 7.42.

*3.3.3. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→5)-2,3-O-isopropylidene-D-lyxono-1,4-lactone (**23**).* Pale yellow oil; $[\alpha]_D^{25}$ +0.1 (*c* 0.023, $CHCl_3$); IR ($CHCl_3$) 2936, 1742, 1649, 1236, 1062 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40–7.25 (15H, m, ArH), 4.94 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.89 (1H, d, $J_{1,2a}$=2.8 Hz, H1), 4.69–4.58 (4H, m, H3, *PhCH*$_2$), 4.50 (1H, dd, $J_{3',4'}$=3.6 Hz, $J_{3',2'}$=6.4 Hz, H3′), 4.48 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.41 (1H, d, J=12 Hz, *PhCH*$_2$), 4.31 (1H, d, $J_{2',3'}$=6.4 Hz, H2′), 3.85 (1H, br s, H4), 3.77 (1H, dd, $J_{5a',4'}$=1.2 Hz, $J_{5a',5b'}$=11.2 Hz, H5a′), 3.69–3.63 (2H, m, H4′, H6a), 3.59–3.53 (3H, m, H5b′, H6b, H5), 2.18 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,3}$=12.4 Hz, $J_{2a,2b}$=12.8 Hz, H2a), 1.88 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.8 Hz, H2b), 1.46 (3H, s, CH_3), 1.34 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.94, 138.57, 137.81, 137.80, 128.59, 128.58, 128.44, 128.43, 128.27, 128.26, 128.25, 128.24, 127.93, 127.87, 127.86, 127.82, 127.63, 127.54, 127.53, 113.22, 99.01, 80.68, 78.00, 75.37, 74.26, 73.66, 72.95, 72.49, 70.92, 69.89, 69.57, 67.04, 30.38, 26.76, 25.56; HRMS (ESI) for $C_{35}H_{40}O_9Na^+$ [M+Na$^+$] calcd 627.2570, found: 627.2560. Anal. Calcd for $C_{35}H_{40}O_9$; C: 69.52; H: 6.67. Found: C: 69.55; H: 6.71.

*3.3.4. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→3)-5-O-carbomethoxy-1,2-O-isopropylidene-D-xylofuranose (**24**).* Pale yellow oil; $[\alpha]_D^{25}$ +5.0 (*c* 0.043, $CHCl_3$); IR ($CHCl_3$) 2928, 1726, 1644, 1244, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31 (15H, m, ArH), 5.85 (1H, d, $J_{1',2'}$=3.6 Hz, H1′), 5.08 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.92 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.83 (1H, d, $J_{2',1'}$=3.6 Hz, H2′), 4.59 (2H, br s, *PhCH*$_2$), 4.58 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.50 (1H, d, J=12.0 Hz, *PhCH*$_2$), 4.42 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.41 (1H, dd, $J_{4',3'}$=3.6 Hz, $J_{4',5a'}$=6.8 Hz, H4′), 4.32–4.30 (2H, m, H5a′, H5b′), 4.14 (1H, d, $J_{3',4'}$=2.8 Hz, H3′), 3.88 (1H, dd, $J_{5,6b}$=4.8 Hz, $J_{5,6a}$=7.2 Hz, H5), 3.85–3.82 (2H, m, H3, H4), 3.79 (3H, s, OCH_3), 3.60 (1H, dd, $J_{6a,5}$=7.2 Hz, $J_{6a,6b}$=10.0 Hz, H6a), 3.46 (1H, dd, $J_{6b,5}$=4.8 Hz, $J_{6b,6a}$=10.0 Hz, H6b), 2.21 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,3}$=12.4 Hz, $J_{2a,2b}$=12.8 Hz, H2a), 1.96 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.8 Hz, H2b), 1.45 (3H, s, CH_3), 1.14 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.51, 138.61, 138.23, 137.95, 128.45, 128.44, 128.39, 128.38, 128.24, 128.23, 128.22, 128.21, 127.75, 127.74, 127.68, 127.64, 127.60, 127.39, 127.38, 111.78, 105.07, 100.14, 82.89, 82.17, 77.49, 74.24, 74.18, 73.60, 73.09, 71.19, 70.52, 70.35, 65.01, 54.94, 31.15, 26.72, 25.99; HRMS (ESI) for $C_{37}H_{44}O_{11}Na^+$ [M+Na$^+$] calcd 687.2781, found: 687.2785. Anal. Calcd for $C_{37}H_{44}O_{11}$; C: 66.85; H: 6.67. Found: C: 66.87; H: 6.69.

*3.3.5. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→4)-2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose (**25**).* Pale yellow oil; $[\alpha]_D^{25}$ +23.9 (*c* 0.038, $CHCl_3$); IR ($CHCl_3$) 2929, 1641, 1235, 1052 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.20 (30H, m, ArH), 5.47 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.99 (1H, d, J=10.8 Hz, *PhCH*$_2$), 4.88 (1H, d, J=11.6 Hz, *PhCH*$_2$), 4.73 (1H, d, J=12.0 Hz, *PhCH*$_2$), 4.65 (1H, d, J=11.2 Hz, *PhCH*$_2$), 4.61 (1H, d, J=10.4 Hz, *PhCH*$_2$), 4.59 (1H, d,

$J_{1',2'}$=3.6 Hz, H1′), 4.58 (1H, d, J=11.2 Hz, $PhCH_2$), 4.54 (1H, d, J=12.0 Hz, $PhCH_2$), 4.52 (1H, d, J=11.6 Hz, $PhCH_2$), 4.49 (1H, d, J=11.6 Hz, $PhCH_2$), 4.38 (1H, d, J=12.0 Hz, $PhCH_2$), 4.37 (1H, d, J=12.0 Hz, $PhCH_2$), 4.31 (1H, d, J=11.6 Hz, $PhCH_2$), 3.89–3.76 (4H, m, H3, H3′, H6a, H6b), 3.73–3.59 (4H, m, H4′, H5′, H6a′, H6b′), 3.51–3.43 (3H, m, H2′, H4, H5), 3.39 (3H, s, OCH_3), 2.12 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 1.87 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.4 Hz, H2b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.78, 138.77, 138.45, 138.44, 138.04, 138.03, 128.45, 128.44, 128.43, 128.42, 128.41, 128.40, 128.39, 128.38, 128.33, 128.32, 128.31, 128.30, 128.29, 128.19, 128.13, 128.12, 127.92, 127.91, 127.90, 127.82, 127.81, 127.80, 127.63, 127.62, 127.61, 127.51, 127.50, 127.49, 127.30, 127.29, 99.68, 97.78, 82.05, 80.04, 75.91, 75.51, 74.48, 74.24, 73.46, 73.45, 73.26, 73.05, 72.78, 70.71, 70.39, 69.90, 69.55, 55.19, 31.60; HRMS (ESI) for $C_{55}H_{60}O_{10}Na^+$ [M+Na^+] calcd 903.4084, found: 903.34088. Anal. Calcd for $C_{55}H_{60}O_{10}$; C: 74.98; H: 6.86. Found: C: 75.02; H: 6.88.

*3.3.6. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→O)-N-tert-butoxycarbonyl-L-serine methyl ester (**26**).* Pale yellow oil; $[\alpha]_D^{25}$ +16.9 (*c* 0.052, $CHCl_3$); IR ($CHCl_3$) 2950, 1726, 1647, 1240, 1065 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37–7.23 (15H, m, ArH), 5.45 (1 H, d, $J_{NH,2'}$=8.4 Hz, NH), 4.92 (1H, br s, H1), 4.90 (1H, d, J=11.6 Hz, $PhCH_2$), 4.61–4.52 (3H, m, $PhCH_2$), 4.52 (1H, d, J=11.6 Hz, $PhCH_2$), 4.45–4.41 (2H, m, H2′, $PhCH_2$), 3.91–3.80 (5H, m, H1a′ H1b′, H3, H6a, H6b), 3.71 (3H, s, OCH_3), 3.58–3.56 (2H, m, H4, H5), 2.20 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,2b}$=12.4 Hz, $J_{2a,3}$=12.8 Hz, H2a), 1.93 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.4 Hz, H2b), 1.44 (9H, s, CH_3×3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.06, 155.45, 138.74, 138.32, 137.98, 128.37, 128.36, 128.35, 128.34, 128.18, 128.17, 128.16, 128.15, 127.76, 127.75, 127.63, 127.53, 127.48, 127.36, 127.35, 98.83, 79.98, 74.27, 73.42, 72.69, 70.38, 70.21, 69.17, 68.51, 53.96, 53.37, 52.35, 30.95, 28.28, 28.27, 28.26; HRMS (ESI) for $C_{36}H_{45}NO_9Na^+$ [M+Na^+] calcd 658.2992, found: 658.3001. Anal. Calcd for $C_{36}H_{45}NO_9$; C: 68.01; H: 7.13. Found: C: 68.06; H: 7.17.

*3.3.7. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→O)-N-(1-oxopentadecyl)-L-serine methyl ester (**27**).* Pale yellow oil; $[\alpha]_D^{25}$ +42.5 (*c* 0.016, $CHCl_3$); IR ($CHCl_3$) 2950, 1750, 1645, 1244, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37–7.24 (15H, m, ArH), 6.51 (1H, d, $J_{NH,2'}$=8.4 Hz, NH), 4.92–4.89 (2H, m, H1, $PhCH_2$), 4.78–4.75 (1H, m, H2′), 4.59 (1H, d, J=11.2 Hz, $PhCH_2$), 4.58 (2H, s, $PhCH_2$), 4.51 (1H, d, J=11.6 Hz, $PhCH_2$), 4.43 (1H, d, J=12.0 Hz, $PhCH_2$), 3.99 (1H, dd, $J_{1a',2'}$=3.6 Hz, $J_{1a',1b'}$=10.8 Hz, H1a′), 3.88–3.77 (4H, m, H1b′, H3, H4, H5), 3.72 (3H, s, OCH_3), 3.56 (1H, dd, $J_{6a,5}$=8.4 Hz, $J_{6a,6b}$=9.6 Hz, H6a), 3.53 (1H, dd, $J_{6b,5}$=8.8 Hz, $J_{6b,6a}$=9.6 Hz, H6b), 2.21 (1H, ddd, $J_{2a,1}$=2.8 Hz, $J_{2a,3}$=12.4 Hz, $J_{2a,2b}$=12.8 Hz, H2a), 2.14–2.12 (2H, m, H3′), 1.95 (1H, dd, $J_{2b,3}$=4.4 Hz, $J_{2b,2a}$=12.8 Hz, H2b), 1.62–1.55 (2H, m, H4′), 1.28 (22H, m, H5′–H15′), 0.88 (3H, d, $J_{16',15'}$=7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.05, 170.78, 138.64, 138.30, 137.83, 128.40, 128.39, 128.38, 128.37, 128.23, 128.22, 128.21, 127.76, 127.75, 127.74, 127.57, 127.56, 127.34, 127.33, 127.32, 99.23, 74.25, 74.24, 73.49, 72.74, 70.49, 70.34, 69.62, 69.10, 52.52, 52.41, 36.30, 31.89, 31.07, 29.64, 29.63, 29.62, 29.50, 29.49, 29.43, 29.42, 29.33, 29.24, 25.45, 22.65, 14.08; HRMS (ESI) for $C_{46}H_{65}NO_8Na^+$ [M+Na^+] calcd 782.4608, found: 782.4603. Anal. Calcd for $C_{46}H_{65}NO_8$; C: 72.70; H: 8.62. Found: C: 72.74; H: 8.64.

*3.3.8. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→O)-N-(9-fluorenylmethoxycarbonyl)-L-threonine methyl ester (**28**).* Pale yellow oil; $[\alpha]_D^{25}$ +11.3 (*c* 0.047, $CHCl_3$); IR ($CHCl_3$) 2936, 1745, 1645, 1248, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (2H, d, J=7.6 Hz, ArH), 7.63 (2H, m, ArH), 7.41–7.24 (19H, m, ArH), 5.41 (1H, d, $J_{NH,2'}$=9.6 Hz, NH), 4.93–4.90 (2H, m, H1, $PhCH_2$), 4.61 (2H, br s, $PhCH_2$), 4.60 (1H, d, J=11.6 Hz, $PhCH_2$), 4.51–4.40 (4H, m, H2′, H4′, $PhCH_2$), 4.36–425 (3H, m, H1′, H3a′, H3b′), 3.93 (2H, br s, H4, H5), 3.86 (1H, ddd, $J_{3,4}$=1.6 Hz, $J_{3,2b}$=3.6 Hz, $J_{3,2a}$=12.4 Hz, H3), 3.73 (3H, s, OCH_3), 3.58–3.52 (2H, m, H6a, H6b), 2.17 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,3}$=12.4 Hz, $J_{2a,2b}$=12.8 Hz, H2a), 1.85 (1H, dd, $J_{2b,3}$=4.0 Hz, $J_{2b,2a}$=12.8 Hz, H2b), 1.24 (3H, d, $J_{1',5'}$=6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.18, 156.59, 143.89, 143.71, 141.31, 141.30, 138.76, 138.31, 138.02, 128.40, 128.39, 128.36, 128.35, 128.19, 128.18, 128.14, 128.13, 127.72, 127.71, 127.70, 127.66, 127.65, 127.51, 127.50, 127.40, 127.39, 127.07, 127.06, 125.05, 119.98, 119.97, 119.96, 99.35, 75.10, 74.26, 74.25, 73.49, 72.89, 70.45, 70.38, 69.46, 67.14, 58.73, 52.38, 47.20, 31.26, 18.50; HRMS (ESI) for $C_{47}H_{49}NO_9Na^+$ [M+Na^+] calcd 794.3305, found: 794.3309. Anal. Calcd for $C_{47}H_{49}NO_9$; C: 73.13; H: 6.40. Found: C: 73.17; H: 6.43.

*3.3.9. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→6)-3-acetyl-1,2,4-tri-O-methyl-α-D-glucopyranose (**29**).* Pale yellow oil; $[\alpha]_D^{25}$ +61.0 (*c* 0.027, $CHCl_3$); IR ($CHCl_3$) 2960, 1741, 1642, 1248, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.25 (10H, m, ArH), 5.26 (1H, ddd, $J_{3,4}$=3.2 Hz, $J_{3,2b}$=4.8 Hz, $J_{3,2a}$=12.4 Hz, H3), 5.04 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.78 (1H, d, $J_{1',2'}$=3.6 Hz, H1′), 4.67 (1H, d, J=11.6 Hz, $PhCH_2$), 4.53 (1H, d, J=11.6 Hz, $PhCH_2$), 4.52 (1H, d, J=11.6 Hz, $PhCH_2$), 4.44 (1H, d, J=12.0 Hz, $PhCH_2$), 4.08 (1H, dd, $J_{5,6a}$=6.8 Hz, $J_{5,6b}$=6.4 Hz, H5), 3.94 (1H, br s, H4), 3.82 (1H, dd, $J_{6a',5'}$=8.0 Hz, $J_{6a',6b'}$=10.2 Hz, H6a′), 3.61–3.54 (7H, m, OCH_3, H6a, H6b, H6b′, H5′), 3.53–3.47 (7H, m, 2× OCH_3, H3′), 3.39 (3H, s, OCH_3), 3.18 (1H, dd, $J_{2',1'}$=3.6 Hz, $J_{2',3'}$=9.6 Hz, H2′), 3.12 (1H, dd, $J_{4',3'}$=9.2 Hz, $J_{4',5'}$=9.6 Hz, H4′), 2.26 (1H, ddd, $J_{2a,1}$=3.2 Hz, $J_{2a,3}$=12.4 Hz, $J_{2a,2b}$=12.8 Hz, H2a), 1.98 (3H, s, CH_3), 1.92 (1H, dd, $J_{2b,3}$=3.6 Hz, $J_{2b,2a}$=12.8 Hz, H2b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.22, 138.38, 138.01, 128.34, 138.33, 128.28, 128.27, 128.08, 128.07, 128.06, 128.05, 127.65, 127.64, 97.73, 97.27, 83.65, 81.80, 79.52, 74.74, 73.54, 73.27, 69.72, 69.51, 69.34, 68.93, 65.94, 60.76, 60.42, 58.94, 55.04, 30.44, 21.08; HRMS (ESI) for $C_{32}H_{44}O_{11}Na^+$ [M+Na^+] calcd 627.2781, found: 627.2780. Anal. Calcd for $C_{32}H_{44}O_{11}$; C: 63.56; H: 7.33. Found: C: 63.59; H: 7.35.

*3.3.10. 2-Deoxy-3,4,6-tri-O-benzyl-α-D-lyxo-hexopyranosyl-(1→6)-3-hyroxy-1,2,4-tri-O-methyl-α-D-glucopyranose (**30**).* Pale yellow oil; $[\alpha]_D^{25}$ +45.4 (*c* 0.058, $CHCl_3$); IR ($CHCl_3$) 3400–3200, 1642, 1250, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.26 (10H, m, ArH), 4.99 (1H, d, $J_{1,2a}$=2.0 Hz, H1), 4.78 (1H, d, $J_{1',2'}$=3.6 Hz, H1′), 4.73 (1H, d, J=11.6 Hz, $PhCH_2$), 4.63 (1H, d, J=11.2 Hz, $PhCH_2$), 4.57 (1 H, d, J=11.6 Hz, $PhCH_2$), 4.50 (1H, d, J=12.0 Hz, $PhCH_2$), 4.05–4.00 (2H, m, H3, H5), 3.82–3.78 (2H, m, H4, H5′), 3.69–3.57 (7H, m, H6a, H6b, H6a′, H6b′, OCH_3), 3.52–3.48 (7H, m, H3, OCH_3), 3.37 (3H, s, OCH_3), 3.17 (1H, dd, $J_{2',1'}$=3.6 Hz, $J_{2',3'}$=9.6 Hz, H2′), 3.11 (1H, dd, $J_{4',3'}$=8.8 Hz, $J_{4',5'}$=9.2 Hz, H4′), 1.93–1.80 (2H, m, H2a, OH), 1.79 (1H, d, $J_{2b,2a}$=10.0 Hz, H2b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.35, 137.86, 128.53, 128.52, 128.36, 128.35, 127.95, 127.94, 127.90, 127.89, 127.69, 127.68, 97.85, 97.23, 83.56, 81.81, 79.45, 76.24, 75.10, 73.32, 69.64, 69.29, 68.91, 65.91, 65.69, 60.74, 60.28, 58.89, 54.97, 34.32; HRMS (ESI) for $C_{30}H_{42}O_{10}Na^+$ [M+Na^+] calcd 585.2676, found: 585.2673. Anal. Calcd for $C_{30}H_{42}O_{10}$; C: 64.04; H: 7.52. Found: C: 64.08; H: 7.55.

*3.3.11. Trisaccharide (**31**).* Pale yellow oil; $[\alpha]_D^{25}$ +16.3 (*c* 0.036, $CHCl_3$); IR ($CHCl_3$) 2930, 1743, 1647, 1232, 1049 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.23 (20H, m, ArH), 5.23 (1H, ddd, $J_{3,4}$=2.8 Hz, $J_{3,2b}$=4.4 Hz, $J_{3,2a}$=9.6 Hz, H3), 5.10 (1H, d, $J_{1,2a}$=3.2 Hz, H1), 4.98 (1H, d, $J_{1',2a'}$=3.2 Hz, H1′), 4.83 (1H, d, J=11.6 Hz, $PhCH_2$), 4.72 (1H, d, $J_{1'',2''}$=3.6 Hz, H1″), 4.67 (1H, d, J=11.6 Hz, $PhCH_2$), 4.58 (1H, d, J=11.6 Hz, $PhCH_2$), 4.54 (1H, d, J=12.0 Hz, $PhCH_2$), 4.53 (1H, d, J=11.2 Hz, $PhCH_2$), 4.52 (1H, d, J=12.0 Hz, $PhCH_2$), 4.44 (1H, d, J=11.6 Hz, $PhCH_2$), 4.42 (1H, d, J=12.0 Hz, $PhCH_2$), 4.15–4.05 (2H, m, H3′, H5), 3.97 (1H, dd, $J_{5',6a'}$=6.0 Hz, $J_{5',6b'}$=6.4 Hz, H5′), 3.94 (1H, br s, H4), 3.83 (1H, br s, H4′), 3.76 (1H, dd, $J_{6a'',5''}$=4.8 Hz,

$J_{6a'',6b''}$=10.8 Hz, H6a″), 3.63–3.56 (8H, m, H6a, H6b, H6a′, H6b″, H5″, OCH_3), 3.50–3.45 (8H, m, H6b′, H3″, OCH_3), 3.34 (3H, s, OCH_3), 3.13 (1H, dd, $J_{2'',1''}$=4.0 Hz, $J_{2'',3''}$=9.6 Hz, H2″), 3.07 (1H, dd, $J_{4'',3''}$=8.4 Hz, $J_{4'',5''}$=9.2 Hz, H4″), 2.28–2.19 (2H, m, H2a, H2a′), 2.16–1.97 (4H, m, H2b, CH_3), 1.80 (1H, dd, $J_{2b',3'}$=4.8 Hz, $J_{2b',2a'}$=12.4 Hz, H2b′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.21, 138.68, 138.40, 138.08, 137.80, 128.58, 128.44, 128.35, 128.25, 128.03, 128.02, 127.93, 127.80, 127.69, 127.56, 97.95, 97.20, 96.73, 83.65, 81.87, 79.69, 76.16, 76.15, 74.49, 73.48, 73.33, 73.01, 72.89, 69.74, 69.70, 69.38, 69.23, 68.61, 65.94, 65.53, 60.78, 60.41, 58.89, 54.96, 34.83, 32.06, 29.68; HRMS (ESI) for $C_{52}H_{66}O_{15}Na^+$ [M+Na^+] calcd 953.4299, found: 953.4293. Anal. Calcd for $C_{52}H_{66}O_{15}$; C: 67.08; H: 7.14. Found: C: 67.10; H: 7.18.

*3.3.12. Butyl-3,4,6-tri-O-benzyl-2-deoxy-2R-deuterium-α-D-lyxo-hexopyranoside (**32**).* Pale yellow oil; $[\alpha]_D^{25}$ +16.8 (*c* 0.064, $CHCl_3$); IR ($CHCl_3$) 2924, 1646, 1248, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34–7.21 (15H, m, ArH), 4.96 (1H, d, $J_{1,2}$=3.6 Hz, H1), 4.93 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.62 (1H, d, *J*=11.6 Hz, $PhCH_2$), 4.59 (2H, s, $PhCH_2$), 4.51 (1H, d, *J*=12.0 Hz, $PhCH_2$), 4.42 (1H, d, *J*=11.6 Hz, $PhCH_2$), 3.94–3.89 (3H, m, H3, H4, H5), 3.64–3.54 (3H, m, H6a, H6b, H1a′), 3.38–3.33 (1H, m, H1b′), 2.21 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=12.4 Hz, H2), 1.55–1.49 (2H, m, H2′), 1.37–1.25 (2H, m, H3′), 0.90 (3H, t, $J_{4',3'}$=7.6 Hz, H4′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.88, 138.54, 138.11, 128.32, 128.31, 128.30, 128.17, 128.16, 128.14, 128.13, 127.69, 127.68, 127.59, 127.58, 127.43, 127.42, 127.27, 127.26, 97.63, 74.83, 74.21, 73.39, 72.99, 70.38, 69.74, 69.56, 67.11, 31.59, 19.39, 19.38, 13.86; HRMS (ESI) for $C_{31}H_{37}DO_5Na^+$ [M+Na^+] calcd 514.2680, found: 514.2688. Anal. Calcd for $C_{31}H_{37}DO_5$; C: 75.73; H: 8.00. Found: C: 75.76; H: 7.01.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.05.124.

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