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Synthesis and Antimicrobial Evaluation of Carbohydrate and Polyhydroxylated Non-carbohydrate Fatty Acid Ester and Ether Derivatives

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Synthesis and antimicrobial evaluation of carbohydrate and polyhydroxylated non-carbohydrate fatty acid ester and ether derivatives.

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Abstract

A series of fatty acid ester and ether derivatives have been chemically synthesised based on carbohydrate and non-carbohydrate polyhydroxylated scaffolds. The synthesised compounds, along with their corresponding fatty acid monoglyceride antimicrobials, were evaluated for antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*. Of the derivatives synthesised several of the carbohydrate based compounds have antimicrobial efficacy comparable with commercially available antimicrobials. The results suggest that the nature of the carbohydrate core plays a role in the efficacy of carbohydrate fatty acid derivatives as antimicrobials.

Keywords

Fatty acid derivatives, lauric acid, monolaurin, antimicrobial activity, *Staphylococcus aureus* and *Escherichia coli*.

1. Introduction

The antimicrobial effects of fatty acids have been well documented.[1] Generally, long chain fatty acids have activity against Gram-positive bacteria while short chain fatty acids are more active against Gram-negative bacteria. Lauric acid (medium chain fatty acid) is regarded as the most active, with reported activity against both Gram-positive and Gram-negative bacteria.[2] Lauric acid and gentamicin combined have been reported to show activity against MRSA.[3] Lauric acid is inexpensive and therefore may be very useful for infection control in hospitals.

Esterification of fatty acids with monohydric alcohols such as methanol or ethanol has been shown to reduce their antimicrobial activity.[4] In contrast, esterification of fatty acids to the polyhydric alcohol glycerol increased their effectiveness.[5] One of the most active of these antimicrobial derivatives is monolaurin (Lauricidin®), the glycerol monoester of lauric acid, which is used as a key ingredient of antimicrobial food additives to inhibit the growth of undesirable microorganisms.[6,7]

More recently, a study has shown that the corresponding ether of monolaurin, dodecylglycerol, had greater potency against *Streptococcus faecium* than monolaurin itself, albeit depending on the incubation conditions.[8] The greater potency of dodecylglycerol was ascribed to its greater retention by the cell, and its action on specific receptors or enzymes.

Another class of fatty acid derivatives which have broad applications in the food industry are carbohydrate fatty acid esters.[9,10] While they are most commonly employed as surfactants, their antimicrobial properties have been documented.[11] The use of carbohydrate esters is increasingly favoured since they are biodegradable, are not harmful to the environment and they are non-toxic.[12]

The most common carbohydrate fatty acid ester utilised to date is sucrose ester. They are commercially available and used for a variety of food applications. Kato and Shibasaki (1975) showed that the sucrose ester of lauric acid had potent antimicrobial activity against certain Gram-positive bacteria and fungi. They further showed that, in contrast to findings with glycerides, the diester of sucrose was more active, than the monoester. Of the diesters tested, sucrose dicaprylate showed the highest activity.[13] Other oligosaccharide fatty acid esters, including maltose and maltotriose, have been synthesised. These sugar esters were shown to inhibit the growth of *Streptococcus sobrinus*, and are therefore potentially of significant value in the development of oral-hygiene products.[14] One study investigating the effect of carbohydrate monoesters reported that among those synthesised, galactose laurate, fructose laurate and the reducing 6-*O*-lauroylmannose showed the highest inhibitory effect against *Streptococcus mutans*, while other analogs of hexose laurates showed no activity.[15] This finding strongly suggests that the carbohydrate moiety can markedly affect the antimicrobial activity of the fatty acid and therefore further investigation is merited.

Recent work in the area of carbohydrate fatty acid esters has focused on establishing an effective regioselective, enzyme catalysed, synthesis of sugar derivatives for use as surfactants for industrial applications,[16,17,18,19,20] however relatively few studies have examined role of the carbohydrate in antimicrobial activity. [14,21,22]

This study is concerned with the synthesis of carbohydrate and polyhydroxylated non-carbohydrate fatty acid derivatives for evaluation as antibacterial agents, with a view to examining the effect of variation of the hydrophilic moiety on antimicrobial activity. Therefore, we designed chemical syntheses to investigate the effects of carbohydrate versus non-carbohydrate hydrophilic cores, the number of fatty acids attached to the hydrophilic core, the monosaccharide core itself (and the anomeric

configuration with respect to glucopyranoside), the glycoconjugate linkage and the length of fatty acid chain on antimicrobial activity.

A quantitative assay for antimicrobial activity was used to allow comparisons between compounds and all were measured relative to the free fatty acids and monolaurin as reference compounds.

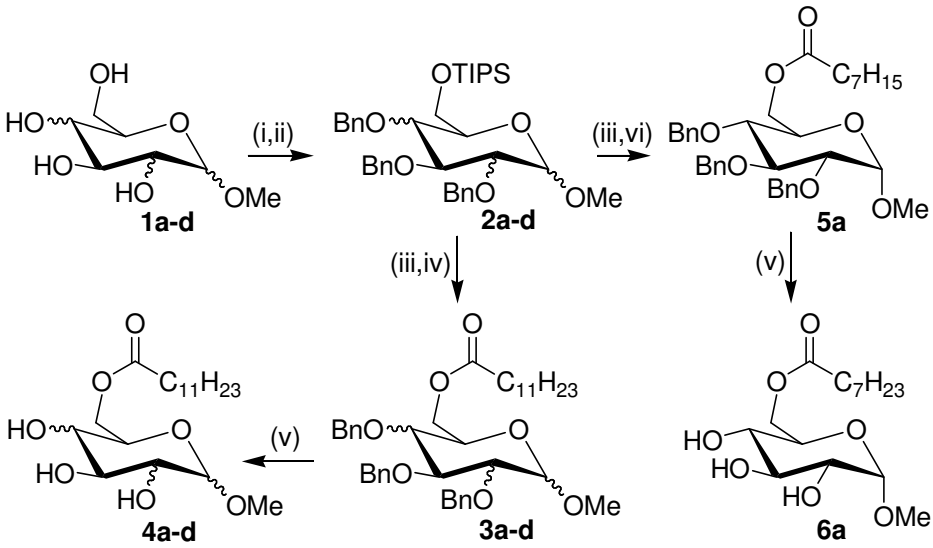
Enzymatic synthesis of novel sugar fatty acid esters has been widely employed and can be highly regioselective, although for some carbohydrates minor regiomeric isomers may be obtained. For this study, we have developed a chemical route to allow us synthesise a number of pure, regio-defined, monosaccharide mono fatty acid esters (**Scheme 1**). We have also developed a route to the corresponding ether derivatives (**Scheme 2**). In order to establish whether a second fatty acid conjugated to a monosaccharide would improve antimicrobial activity, a route was developed to synthesise a di-laurate derivative (**Scheme 3**). Furthermore, to investigate whether the structure and therefore the synthesis, could be simplified and retain activity, non-carbohydrate hydroxylated esters based on a pentaerythritol core were synthesised by a straightforward esterification (**Scheme 4**).

2. Results and Discussion

2.1 Synthesis

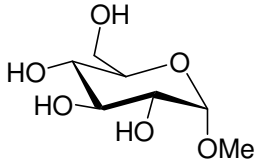
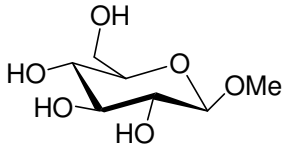
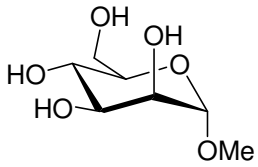
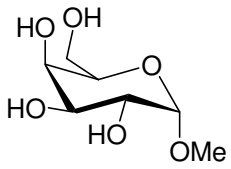
A designed chemical route to obtain mono-ester sugars is shown in **Scheme 1** and is based on the following carbohydrate starting materials: **1a** methyl α-D-glucopyranoside, **1b** methyl β-D-glucopyranoside, **1c** methyl α-D-mannopyranoside and **1d** methyl α-D-galactopyranoside. The synthesis commenced with the selective protection of the primary hydroxyl of sugars **1a-d** with a triisopropylsilyl (TIPS) group. The silyl derivatives were then fully protected with benzyl groups to give **2a-d**. The removal of the TIPS group by tetrabutylammonium

fluoride in THF allowed for the esterification of the free 6-OH position with either lauroyl chloride to yield **3a-d** or octanoyl chloride to yield **5a**. Removal of the benzyl groups by catalytic hydrogenation led to the unprotected carbohydrate esters **4a-d** and **6a** respectively.



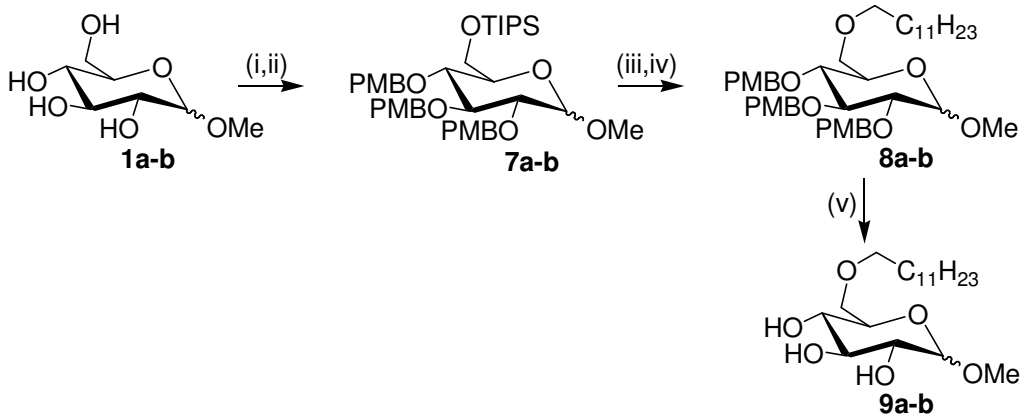
Scheme 1 Reagents and Conditions: (i) DMF anhydr., TIPSCl, imidazole, rt. (ii) DMF anhydr., NaH, BnBr, rt. (iii) THF anhydr., 0 ^{o}C, TBAF, rt. (iv) Pyr anhydr., DMAP, Lauroyl Cl, rt. (v) EtOH, Pd-C, H_2. (vi) Pyr anhydr., DMAP, Octanoyl Cl, rt.

Table 1 Percentage yields of compounds **2a-d**, **3a-d**, **4a-d**, **5a** and **6a**.

Carbohydrate ***(1)***	*2,3,4-tri-O-Bn-6-O-TIPS* ***(2)***	*2,3,4-tri-O-Bn-6-O-lauroyl* ***(3)***	*6-O-lauroyl* ***(4)***	*2,3,4-tri-O-Bn-6-O-octanoyl* ***(5)***	*6-O-octanoyl* ***(6)***
 **(1a)**	**2a**	**3a**	**4a**	**5a**	**6a**
	85%	72%	86%	63%	73%
 **(1b)**	**2b**	**3b**	**4b**		
	80%	70%	75%		
 **(1c)**	**2c**	**3c**	**4c**		
	51%	64%	75%		
 **(1d)**	**2d**	**3d**	**4d**		
	50%	60%	86%		

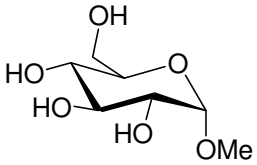
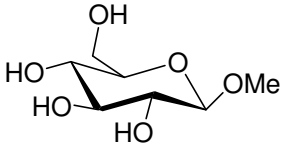
Synthesis of the ether derivatives also commenced with the protection of the primary hydroxyl with a triisopropylsilyl group (**Scheme 2**). The sugars were then fully protected using paramethoxybenzyl chloride (PMB), to yield **7a-b**. Removal of the TIPS group gave the free primary hydroxyl. Next, the lauric ether group was attached using dodecanyl chloride to give the fully protected ether derivatives **8a-b**. Finally

oxidative cleavage of the PMB groups with CAN gave the mono-dodecanyl sugars **9a-b**.



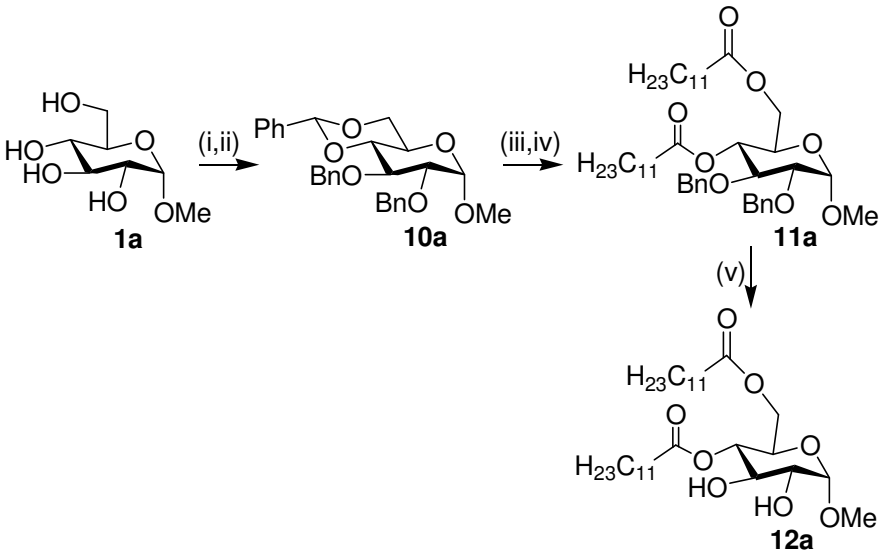
Scheme 2 Reagents and Conditions: (i) DMF anhydr., TIPSCl, imidazole, rt. (ii) DMF anhydr., THF anhydr., 0 °C, NaH, PMBCl, TBAI, rt. (iii) THF anhydr., 0 °C, TBAF, rt. (iv) DMF anhydr., dodecanyl chloride, 0 °C, NaH, rt. (v) MeCN:H_2O 3:1, CAN, rt.

Table 2 Percentage yields of compounds **7a-b**, **8a-b** and **9a-b**.

Carbohydrate ***(1)***	*2,3,4-tri-O-PMB-6-O-TIPS* ***(7)***	*2,3,4-tri-O-PMB-6-O-dodecanyl* ***(8)***	*6-O-dodecanyl* ***(9)***
 **(1a)**	**7a**	**8a**	**9a**
	59%	50%	73%
 **(1b)**	**7b**	**8b**	**9b**
	61%	85%	76%

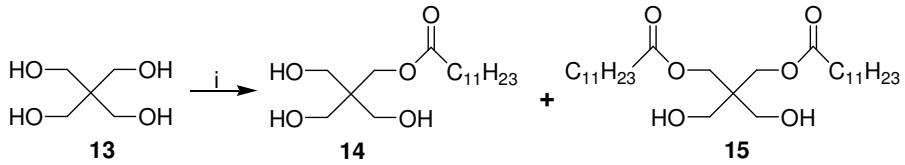
The method used to synthesise di-lauroyl derivative **12a** is shown in **Scheme 3**. The 4 and 6-OH positions of methyl α-D-glucopyranoside **1a** were protected with a benzylidene group using benzaldehyde dimethylacetal. The remaining free OH's

were then converted to benzyl ethers to give **10a**. Removal of the benzylidene acetal using catalytic TsOH in MeOH then enabled the esterification of the 4 and 6-OH to give **11a.** Finally, removal of the benzyl groups by catalytic hydrogenation gave the diester derivative **12a**.



Scheme 3. Reagents and Conditions: (i) pTSA, $PhCH(OMe)_2$, MeCN anhydr., rt. (ii) DMF anhydr., NaH, BnBr, rt. (95% yield over 2 steps) (iii) MeOH, TsOH. (iv) Pyr anhydr., DMAP, Lauroyl Cl, rt. (38% yield over 2 steps) (v) EtOH, Pd/, H_2. (75% yield)

Direct esterification of pentaerythritol **13** using lauroyl chloride and DMAP in pyridine, yielded the non-sugar derivatives **14** and **15**, shown in **Scheme 4**.



Scheme 4. Reagents and Conditions: (i) Pyr anhydr., DMAP, Lauroyl Cl, rt. (**14** 14%, **15** 29%)

2.2 Antimicrobial activity of fatty acid derivatives

Two non-carbohydrate polyhydroxylated fatty acid ester derivatives, six carbohydrate fatty acid ester derivatives and two carbohydrate long chain alkyl ether derivatives,

1 together with their corresponding polyhydric alcohols, fatty acids and monoglycerides
2 as controls, were tested against a Gram-positive bacteria, *Staphylococcus aureus*, and
3 a Gram-negative bacteria, *Escherichia coli*, to assess their antimicrobial activity. The
4 efficacy of the derivatives and controls were compared using Minimum Inhibitory
5 Concentration values (MIC), which was defined as the lowest concentration of
6 compound that showed no increase in cell growth for all the replicates compared to a
7 negative control after 18 hours.
8 The polyhydric alcohols (carbohydrates and pentaerythritol) showed no antimicrobial
9 activity or growth promoting effects for the microorganisms under the conditions used
10 (results not shown).

11 **Table 3** MIC values of Fatty Acid Derivatives and Controls

Compound	***S. aureus ATCC 25923***	***E. coli ATCC 25922***
Lauric acid	0.63 mM	10 mM
Monolaurin	0.04 mM	20 mM
Caprylic acid	5 mM	12.5 mM
Monocaprylin	2.5 mM	6.25 mM
Methyl 6-*O*-lauroyl-α-D-glucopyranoside (**4a**)	0.31 mM	20 mM
Methyl 6-*O*-lauroyl-β-D-glucopyranoside (**4b**)	0.04 mM	20 mM
Methyl 6-*O*-octanoyl-α-D-glucopyranoside (**6a**)	2.5 mM	12.5 mM
Methyl 6-*O*-dodecanyl-α-D-glucopyranoside (**9a**)	0.04 mM	20 mM
Methyl 6-*O*-dodecanyl-β-D-glucopyranoside (**9b**)	2.5 mM	20 mM
Methyl 4,6-di-*O*-lauroyl-α-D-glucopyranoside (**12a**)	ND*	ND
Methyl 6-*O*-lauroyl-α-D-mannopyranoside (**4c**)	0.04 mM	20 mM
Methyl 6-*O*-lauroyl-α-D-galactopyranoside (**4d**)	>10 mM	>20 mM
Mono lauroyl pentaerythritol (**14**)	>10 mM	>20 mM
Di lauroyl pentaerythritol (**15**)	ND	ND

12 * Not determined due to insolubility

The data in **Table 3** show that the monoglycerides monolaurin and monocaprylin, had greater activity compared to the free fatty acids lauric acid and caprylic acid against *S. aureus*. Of the monoglycerides and free fatty acids tested, monolaurin had the lowest MIC values for *S. aureus*, with a value of 0.04 mM compared to a value of 0.63 mM for lauric acid. Furthermore, monocaprylin showed MIC values of 2.5 mM against *S. aureus* compared to the value of 5.0 mM for caprylic acid. With respect to *E. coli*, monolaurin showed less inhibitory effect than lauric acid with values of 20 mM and 10 mM respectively. In contrast, monocaprylin showed activity against *E. coli* at concentrations of 6.25 mM compared with caprylic acid value of 12.5 mM.

All fatty acid derivatives showed greater antimicrobial activity against *S. aureus* than *E. coli*.

Among the sugar fatty acid esters and the sugar alkyl ethers prepared, methyl 6-*O*-dodecanyl-α-D-glucopyranoside **9a**, methyl 6-*O*-lauroyl-α-D-mannopyranoside **4c** and methyl 6-*O*-lauroyl-β-D-glucopyranoside **4b** showed the best inhibitory effects for *S. aureus*, with MIC values of 0.04 mM. The next derivative in order of efficacy was methyl 6-*O*-lauroyl-α-D-glucopyranoside **4a**, with a value of 0.31 mM. Methyl 6-*O*-octanoyl-α-D-glucopyranoside **6a** was comparable to monocaprylin against *S. aureus* with values of 2.5 mM. This compound was also more active than any of the lauric acid derivatives against *E. coli*. Methyl 6-*O*-dodecanyl-β-D-glucopyranoside **9b** gave similar results to **6a** for *S. aureus* with values of 2.5 mM. The galactopyranoside ester derivative **4d** and the mono-lauroyl pentaerythritol **14**, were the least active compounds tested, both with comparatively negligible MIC values of >10 mM for *S. aureus* and >20mM for *E. coli*.

The di-substituted methyl 4,6-di-*O*-lauroyl-α-D-glucopyranoside **12a** did not show any activity comparable with either the monoglycerides or indeed the mono-

substituted sugar derivatives. This was attributed to poor solubility in water, as was the case for the di-substituted non-sugar compound di-lauroyl pentaerythritol **15**.

2.3 Discussion

In this present study, we have evaluated the effect of polyhydroxylated fatty acid derivatives as inhibitors of a Gram-positive (*S. aureus*) and a Gram-negative (*E. coli)* microorganism of concern to the food and healthcare industries. Several of the synthesised compounds have antimicrobial efficacy comparable with commercially available antimicrobials against *S. aureus*.

We studied the effect of carbohydrate versus non-carbohydrate hydrophilic cores (carbohydrate and pentaerythritol laurates), the degree of substitution (monoester and diester), the monosaccharide core (glucopyranoside, mannopyranoside and galactopyranoside), the anomeric configuration (α and β glucopyranoside), the type of fatty acid carbohydrate linkage (ester and ether), and the length of fatty acid chain (lauric and caprylic) on antimicrobial activity.

As with the monoglycerides and free fatty acids, all of the fatty acid derivatives that were found to be active showed greater antimicrobial activity against the *S. aureus* than *E. coli*.

The non-carbohydrate pentaerythritol monoester **14**, which has the same number of free hydroxyl groups as the carbohydrate monoester derivatives, showed negligible activity against both microorganisms tested, indicating that the carbohydrate itself could play an important role in the antimicrobial activity of these compounds.

The degree of substitution of these derivatives was also shown to be crucial as both the non-sugar pentaerythritol diester **15** and the carbohydrate methyl α-D-glucopyranoside diester **12a** were much less soluble in water than the monoesters. As a consequence, no antimicrobial activity results for these compounds could be obtained.

With regard to the influence of different sugar cores, the results showed that the lauric ester derivative of methyl α-D-mannopyranoside **4c** and methyl β-D-glucopyranoside **4b**, showed higher activity than any other ester derivatives against *S. aureus,* supporting the observation that the nature of the carbohydrate is involved in the antimicrobial efficacy of the derivatives. This conclusion is consistent with results of an earlier study by Watanabe *et al*.[15]

Further evidence for this is noted in the results for the lauric ester anomers of methyl glucopyranoside **4a** and **4b**. A difference was noted when these compounds were tested against *S. aureus* with the beta configuration showing higher activity. The lauric ether anomers of methyl glucopyranoside **9a** and **9b** also showed a marked difference in activity when tested against *S. aureus*, with the alpha configuration showing a much higher activity.

In addition, the difference in activity between the ester and ether conjugates of the same carbohydrate showed that for the methyl α-D-glucopyranoside derivatives, the ether derivative **9a** was more active than the ester **4a**, however for methyl β-D-glucopyranoside, the ester **4b** was more active than the ether **9b**. These results indicate that, in combination with other factors, the nature of the bond conjugating the fatty acid to the carbohydrate could play some role in antimicrobial activity.

The importance of the chain length of the fatty acid ester was investigated using both lauric and caprylic derivatives. The lauric ester derivative **4a** showed much higher

activity against *S. aureus* compared to the corresponding caprylic ester derivative **6a**. Conversely, the caprylic ester derivative **6a** showed higher activity against *E. coli*, compared with the lauric derivative **4a**. This trend was also observed for the monoglyceride controls and is in accordance with general trends observed for medium and short chain fatty acids.[2]

In conclusion, these results suggest that the nature of the carbohydrate core plays a role in the efficacy of carbohydrate fatty acid derivatives as antimicrobials, and therefore further optimisation may be possible. However, to confirm the trends outlined with respect to the importance of the carbohydrate moiety and the role of the nature of the glycoconjugate bond, further studies are warranted using a wider range of Gram-positive and Gram-negative microorganisms, which would allow for evaluation of potential species and strain effects.

3. Experimental

3.1 Synthesis

3.1.1 General methods

All air and moisture-sensitive reactions were performed under an inert nitrogen atmosphere. All reactions performed under a hydrogen atmosphere were performed in a Parr Hydrogenator Apparatus. Anhydrous DMF, THF, Pyridine and MeCN were purchased from Sigma Aldrich. TLC was performed on aluminium sheets precoated with Silica Gel 60 (HF_{254}, Fluka) and spots visualised by UV and charring with H_2SO_4-EtOH (1:20). Flash Column Chromatography was carried out with Silica Gel 60 (0.040-0.630 mm, E. Merck) and using stepwise solvent polarity gradient correlated with TLC mobility. Chromatography solvents used were EtOAc (Riedel-deHaen), MeOH (Riedel-deHaen) and petroleum ether (b.p. 40-60 ^{o}C, Fluka). Optical rotations were determined with an AA-% Series Optical Activity Ltd Polarimeter.

NMR spectra were recorded with Varian Inova 300 and Varian NMRAS 400 spectrometers. Chemical shifts are reported relative to internal Me_4Si in $CDCl_3$ (δ 0.0) for ^1H and $CDCl_3$ (δ 77.0) for ^{13}C. Coupling constants are reported in hertz. FTIR spectra were recorded with a Nicolet FT-IR 5DXB infrared spectrometer, samples were prepared in a KBr matrix. Low resolution mass spectra were measured on a Quatromicro tandem quadropole mass spectrometer. Methyl-α-D-glucopyranoside, methyl-β-D-glucopyranoside, methyl-α-D-mannopyranoside, methyl-α-D-galactopyranoside, pentaerythritol, 1-chlorododecane, lauroyl chloride and octanoyl chloride were purchased from Sigma Aldrich.

3.1.2 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-glucopyranoside (2a)

A solution of **1a** (5 g, 25 mmol) in DMF anhydrous (120 mL) was treated with triisopropylsilyl chloride (15 mL, 75 mmol) and imidazole (5 g, 75 mmol) and allowed to stir at room temperature for 24 h. The crude TIPS protected intermediate was then concentrated *in vacuo* and dissolved in EtOAc. It was washed with 10% HCl, water, followed by sat. aq. $NaHCO_3$, and finally sat. aq. NaCl. It was then dried over anhydrous $MgSO_4$, and concentrated under reduced pressure.[23] The crude product was dissolved in DMF anhydrous (50 mL) and cooled to 0 ^oC. NaH (5 g, 125 mmol) was added portion wise, BnBr (9 mL, 75 mmol) was added and the mixture was allowed to warm to room temperature and stir for 24 h. MeOH (50 mL) was added to quench the mixture which was stirred for 1 h. The fully protected sugar was then concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with water, dried over anhydrous $MgSO_4$, and concentrated under diminished pressure.[24] The resulting residue was purified by chromatography (petroleum ether-EtOAc) to give **2a** (13.2 g, 85%); $[\alpha]_D$ 10.7º (*c* 0.07, $CHCl_3$); FTIR (KBr): 2923, 1733, 1498, 1455, 909, 884, 791, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.27 (ms, 15H,

aromatic H), 4.91, (AB d, 2H, *J* 11.0, OC*H*$_2$Ph), 4.78, (AB d, 2H, *J* 11.0, OC*H*$_2$Ph), 4.74 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.61 (d, 1H, $J_{1,2}$ 3.5, H-1), 3.99 (apt t, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, H-3), 3.84 (d, 2H, $J_{5,6}$ 4.5, H-6a,6b), 3.64 (m, 1H, H-5), 3.55-3.49 (overlapping signals, 2H, H-2,4), 3.37 (s, 3H, OC*H*$_3$), 1.10-1.02 (ms, 18H, each TIPS C*H*$_3$), 0.88 (m, 3H, each TIPS C*H*); ^{13}C NMR ($CDCl_3$): δ 139.1, 138.7, 138.5 (each s, each aromatic C), 128.65, 128.63, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8 (each d, each aromatic CH), 98.0 (d, C-1), 82.5, 80.5, 78.1, 76.1 (each d), 76.1, 75.3, 73.6 (each t, each CH_2Ph), 62.9 (t, C-6), 55.0 (q, OCH_3), 18.3, 18.2 (each q, each TIPS CH_3), 12.2 (each d, each TIPS CH); LRMS: Found, 643.3; required, 643.9; [M + Na]$^+$.

3.1.3 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl-β-D-glucopyranoside (2b)

Treatment of **1b** (4.5 g, 23.17 mmol) as described for **1a** gave **2b** (8.7 g, 80%); $[\alpha]_D$ 23° (*c* 0.01, $CHCl_3$); FTIR (KBr): 2863, 1730, 1497, 1454, 1399, 1277, 882, 802, 751, 697. cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.28 (ms, 15H, aromatic H), 4.90, 4.88, 4.83 (each AB d, 6H, *J* 11.0, OC*H*$_2$Ph), 4.30 (d, 1H, $J_{1,2}$ 7.5, H-1), 4.00-3.90 (overlapping signals, 3H, H-5,6), 3.66 (m, 1H, H-3), 3.53 (s, 3H, OC*H*$_3$), 3.41 (m, 1H, H-2), 3.34 (m, 1H, H-4), 1.26-1.05 (ms, 21H, TIPS); ^{13}C NMR ($CDCl_3$): δ 138.98, 138.92, 138.7 (each s, each aromatic C), 128.69, 128.65, 128.62, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8 (each d, each aromatic CH), 104.7 (d, C-1), 84.9, 82.9, 77.8, 76.2 (each d), 76.0, 75.3, 75.0 (each t, each CH_2Ph), 62.7 (t, C-6), 56.9 (q, OCH_3), 18.3, 18.2 (each q, each TIPS CH_3), 12.3 (d, TIPS CH); LRMS: Found, 643.3 required, 643.9 [M + Na]$^+$.

3.1.4 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranoside (2c)

Treatment of **1c** (4 g, 20 mmol) as described for **1a** gave **2c** (6.5 g, 51%); $[\alpha]_D$ 25.5° (*c* 0.05, $CHCl_3$); FTIR (KBr): 3056, 2864, 1496, 1363, 1324, 970, 882, 790, 734, 696

cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.24 (multiple signals, 15H, each aromatic H), 4.79 (AB d, 2H, *J* 11.0, OC*H*$_2$Ph), 4.72 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.71-4.64 (overlapping signals, 3H, OC*H*$_2$Ph, H-1), 3.95 (dd, 1H, $J_{2,3}$ 2.0, $J_{3,4}$ 11.0, H-3), 3.93-3.87 (overlapping signals, 3H, H-4,6a,6b), 3.76 (dd, 1H, $J_{1,2}$ 2.5, H-2), 3.59 (dd, 1H, *J* 5.5, *J* 7.0, H-5), 3.31 (s, 3H, OMe), 1.12-1.04 (multiple signals, 21H, TIPS); ^{13}C NMR ($CDCl_3$): δ 138.68, 138.61, 138.4 (each s, each aromatic C), 128.3, 128.2, 127.9, 127.67, 128.63, 127.5, 127.4 (each d, each aromatic CH), 98.5 (d, C-1), 80.3, 76.7, 74.9, 73.3 (each d), 75.1, 72.5, 72.1 (each t, each CH_2Ph), 63.2 (t, C-6), 54.4 (q, OMe), 18.0, 17.9 (each q, each TIPS CH_3), 12.3 (each d, each TIPS CH_2); LRMS: Found, 638.5 required, 638.9; $[M + H_2O]^+$.

3.1.5 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-galactopyranoside (2d)

Treatment of **1d** (4.0 g, 20.0 mmol) as described for **1a** gave **2d** (6.4 g, 50%); $[\alpha]_D$ 20.6º (*c* 0.07, $CHCl_3$); FTIR (KBr): 3030, 2865, 1496, 1454, 1350, 1194, 1054, 882, 793, 734, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ; 7.41-7.22 (multiple signals, 15H, each aromatic H), 4.82 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.71 (AB d, 2H, *J* 11.5, OC*H*$_2$Ph), 4.77 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.68 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.04 (dd, 1H, $J_{2,3}$ 10.0, H-2), 3.95-3.92 (overlapping signals, 2H, H-3,5), 3.74-3.64 (overlapping signals, 3H, H-4,6), 3.36 (s, 3H, OMe), 1.12-0.86 (multiple signals, 21H, TIPS); ^{13}C NMR ($CDCl_3$): δ 137.9, 137.7, 137.5 (each s, each aromatic C), 127.33, 127.28, 127.22, 127.15, 127.06, 126.62, 126.48, 126.45 (each d, each aromatic CH), 97.6 (d, C-1), 78.1, 75.4, 74.0, 70.1 (each d), 73.7, 72.5, 72.2 (each t, each CH_2Ph), 61.4 (t, C-6), 54.1 (q, OMe), 16.94, 16.93 (each q, each TIPS CH_3), 10.8 (each d, each TIPS CH_2); LRMS: Found, 638.5 required, 638.9; $[M + H_2O]^+$.

3.1.6 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl-α-D-glucopyranoside (3a)

Compound **2a** (3.0 g, 4.8 mmol) was dissolved in THF anhydrous (80 mL) and was cooled to 0 ^{o}C. Tetrabutylammonium fluoride (1 g, 4 mmol) was added and the solution was allowed to warm to room temperature and stir for 1 h.[25] It was then concentrated *in vacuo* and approximately 1 mmol of the resulting 6-OH residue was dissolved in pyridine anhydrous (25 mL). 4-Dimethylaminopyridine and lauroyl chloride (0.29 mL, 1.22 mmol) were added and the solution was allowed to stir at room temperature for 24 h.[26] It was then concentrated under reduced pressure and the resulting benzylated ester derivative was purified by chromatography (petroleum ether-EtOAc) to give **3a** (0.47 g, 72%); $[\alpha]_D$ 7.5º (*c* 0.02, $CHCl_3$); FTIR (KBr): 2924, 2853, 1738, 1603, 1502, 1454, 1249, 1072 cm^{1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.26 (ms, 15H, aromatic H), 4.92, (AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 4.72, (AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 4.64 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.59 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.27 (d, 2H, $J_{5,6}$ 3.5, H-6a,6b), 4.01 (apt t, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 9.0, H-3), 3.82 (d apt t, 1H, $J_{4,5}$ 10.0, H-5), 3.53 (dd, 1H, H-2), 3.48 (apt t, 1H, H-4) 3.37 (s, 3H, OC*H*$_3$), 2.35 (m, 2H, aliphatic OCOC*H*$_2$C$_{10}$H$_{21}$), 1.61 (m, 2H, aliphatic OCOCH$_2$C*H*$_2$C$_9$H$_{19}$), 1.28-1.24 (ms, 16H, aliphatic OCOC$_2$H$_4$C$_8$*H*$_{16}$CH$_3$), 0.87 (m, 3H, aliphatic OCOC$_{10}$H$_{20}$C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 171.1 (s, C=O), 138.6, 138.1, 137.9 (each s, each aromatic C), 128.5, 128.48, 128.46, 128.1, 128.03, 127.98, 127.90, 127.7 (each d, each aromatic CH), 98.0 (d, C-1), 88.0, 79.9, 77.6, 68.6 (each d), 75.8, 75.1, 73.4 (each t, each CH_2Ph), 60.4 (t, C-6), 55.2 (q, OCH_3), 34.2, 31.9, 29.8, 29.6, 29.5, 29.3, 29.2, 24.9, 22.7, 21.1 (each t, each aliphatic CH_2), 14.2 (q, aliphatic CH_3); LRMS: Found, 669.39; required, 669.85; $[M + Na]^+$; Anal. Calcd. for $C_{40}H_{54}O_7$: C, 74.27; H, 8.41. Found: C, 73.98; H, 8.30.

3.1.7 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl-β-D-glucopyranoside (3b)

Treatment of **2b** (3.0 g, 4.8 mmol) as described for **2a** gave **3b** (2.2 g, 70%); $[\alpha]_D$ 8.3º (*c* 0.03, $CHCl_3$); FTIR (KBr): 2924, 2853, 1739, 1497, 1454, 1356, 1151, 1070, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.24 (ms, 15H, aromatic H), 4.87, 4.84, 4.72 (each AB d, 6H, *J* 10.5, OC*H*$_2$Ph), 4.37 (d, 2H, $J_{5,6}$ 11.5, H-6a,6b), 4.31 (d, 1H, $J_{1,2}$ 8.0, H-1), 4.25 (m, 1H, H-5), 3.67 (apt t, 1H, $J_{2,3}$ 8.5, $J_{3,4}$ 8.5, H-3), 3.56 (s, 3H, OC*H*$_3$), 3.54 (m, 1H, H-4), 3.43 (dd, 1H, H-2), 2.32 (m, 2H, aliphatic OCOC*H*$_2$C$_{10}$H$_{21}$), 1.62 (m, 2H, aliphatic OCOCH$_2$C*H*$_2$C$_9$H$_{19}$), 1.26-1.24 (ms, 16H, each aliphatic OCOC$_2$H$_4$C$_8$*H*$_{16}$CH$_3$), 0.88 (t, 3H, *J* 6.0, *J* 7.0, aliphatic OCOC$_{11}$H$_{23}$C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 173.6 (s, C=O), 138.43, 138.42, 137.8 (each s, each aromatic C), 128.8, 128.5, 128.4, 128.38, 128.34, 128.26, 128.11, 128.07, 127.97, 127.92, 127.8, 127.7, 127.69, 127.64, 127.5 (each d, each aromatic CH), 104.7 (d, C-1), 84.6, 82.3, 77.6, 72.9 (each d), 75.7, 75.1, 74.8 (each t, each OCH_2Ph), 62.9 (t, C-6), 57.1 (q, OCH_3), 34.2, 31.9, 29.6, 29.5, 29.3, 29.2, 29.1, 24.9, 24.7, 22.6 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 669.2 required, 669.9 $[M + Na]^+$; Anal. Calcd. for $C_{40}H_{54}O_7$: C, 74.27; H, 8.41. Found: C, 73.91; H, 8.79.

3.1.8 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl-α-D-mannopyranoside (3c)

Treatment of **2c** (6.2 g, 10.0 mmol) as described for **2a** gave **3c** (4.1 g, 64%); $[\alpha]_D$ 23.3º (*c* 0.04, $CHCl_3$); FTIR (KBr): 3031, 2924, 2853, 1737, 1496, 1454, 1362, 1066, 1027, 970, 909, 735, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38-7.25 (multiple signals, 15H, each aromatic H), 4.77 (AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 4.74 (d, 1H, $J_{1,2}$ 2.0, H-1), 4.72 (AB d, 2H, *J* 12.5, OC*H*$_2$Ph), 4.61 (s, 2H, OC*H*$_2$Ph), 4.38 (dd, 1H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 12.0, H-6a), 4.33 (dd, 1H, $J_{5,6b}$ 5.0, H-6b), 3.94-3.88 (overlapping signals, 2H, H-3,4), 3.78 (dd, 1H, $J_{2,3}$ 2.5, H-2), 3.76 (m, 1H, H-5), 3.31 (s, 3H, OMe), 2.32 (t, 2H, *J* 7.5, *J* 7.5, aliphatic OCOC*H*$_2$C$_{10}$H$_{21}$), 1.61 (m, 2H, aliphatic

OCOCH$_2$C*H$_2$*C$_9$H$_{19}$), 1.31-1.54 (ms, 16H, aliphatic OCOC$_2$H$_4$C$_8$*H$_{16}$*CH$_3$), 0.91-0.86 (m, 3H, aliphatic OCOC$_{10}$H$_{20}$C*H$_3$*); ^{13}C NMR (CDCl$_3$): δ 173.7, (s, C=O), 138.32, 138.21, 138.17 (each s, each aromatic C), 128.4., 128.38, 128.33, 128.05. 127.90, 127.76, 127.63, 127.23 (each d, each aromatic CH), 98.9 (d, C-1), 75.2, 74.6, 74.4, 69.9 (each d), 80.1, 72.6, 72.1 (each t, each CH_2Ph), 63.3 (t, C-6), 54.8 (q, OCH_3), 34.2, 33.9, 31.9, 29.61, 29.48, 29.44, 29.33, 29.27, 29.17, 29.07, 24.9, 24.7, 23.8, 22.7, 21.1 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 664.6 required, 664.9; $[M + H_2O]^+$; Anal. Calcd. for $C_{40}H_{54}O_7$: C, 74.27; H, 8.41. Found: C, 74.35; H, 8.25.

3.1.9 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl-α-D-galactopyranoside (3d)

Treatment of **2d** (5.7 g, 9.2 mmol) as described for **2a** gave **3d** (3.6 g, 60%); $[\alpha]_D$ 27.8º (*c* 0.09, $CHCl_3$); FTIR (KBr): 3030, 2924, 2853, 1738, 1496, 1454, 1350, 1099, 1049, 735, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.23 (multiple signals, 15H, each aromatic H), 4.83 (AB d, 2H, *J* 12.0, OC*H$_2$*Ph), 4.81 (AB d, 2H, *J* 11.5, OC*H$_2$*Ph), 4.77 (AB d, 2H, *J* 12.0, OC*H$_2$*Ph), 4.68 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.16 (dd, 1H, *J* 7.5, *J* 11.5, H-4), 4.07-4.03 (overlapping signals, 2H, H-2,5), 3.94 (dd, 1H, *J* 3.0, *J* 10.0 H-6a), 3.86-3.84 (overlapping signals, 2H, H-3,6b), 3.35 (s, 3H, OMe), 2.23 (m, 2H, aliphatic OCOC*H$_2$*C$_{10}$H$_{21}$), 1.57 (m, 2H, aliphatic OCOCH$_2$C*H$_2$*C$_9$H$_{19}$), 1.31-1.18 (ms, 16H, aliphatic OCOC$_2$H$_4$C$_8$*H$_{16}$*CH$_3$), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic OCOC$_{10}$H$_{20}$C*H$_3$*); ^{13}C NMR (CDCl$_3$): δ 173.4 (s, C=O), 138.7, 138.4, 138.2 (each s, each aromatic C), 128.42, 128.36, 128.32, 128.11, 127.90, 127.75, 127.59, 127.51, 127.21 (each d, each aromatic CH), 98.7 (d, C-1), 78.9, 76.3, 74.9, 68.4 (each d), 74.6, 73.63, 73.54 (each t, each CH_2Ph), 63.3 (t, C-6), 55.3 (q, OCH_3), 34.1, 33.8, 31.9, 29.359, 29.45, 29.32, 29.26, 29.12, 24.9, 24.8, 22.7 (each t, each aliphatic CH_2), 14.1

(q, aliphatic CH_3); LRMS: Found, 664.6 required, 664.9; $[M + H_2O]^+$; Anal. Calcd. for $C_{40}H_{54}O_7$: C, 74.27; H, 8.41. Found: C, 74.67; H, 8.68.

3.1.10 Methyl 6-*O*-lauroyl-α-D-glucopyranoside (4a)

Compound **3a** (0.34 g, 0.2 mmol) was dissolved in EtOH (1 mL) and Pd-C (0.1 g) was added. The mixture was allowed to shake under hydrogen atmosphere of 2 psi until all protecting groups had been removed, as shown by TLC, to yield **4a**. The suspension was filtered and concentrated *in vacuo*.[27] (0.17 g, 86%); $[\alpha]_D$ 19º (*c* 0.02, $CHCl_3$); FTIR (KBr): 3734, 3445, 2955, 2924, 2850, 2359, 2341, 1728. cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.75 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.33 (m, 2H, H-6), 3.75-3.73 (overlapping signals, 2H, H-3,5), 3.35 (apt t, 1H, $J_{3,4}$ 9.5, $J_{4,5}$ 9.5, H-4), 3.54 (dd, 1H, $J_{2,3}$ 9.5, H-2), 3.41 (s, 3H, OMe), 2.35 (t, 2H, *J* 7.5, aliphatic $OCOC\mathit{H}_2C_{10}H_{21}$), 1.63 (m, 2H, aliphatic $OCOCH_2C\mathit{H}_2C_9H_{19}$), 1.38-1.23 (ms, 16H, aliphatic $OCOC_2H_4C_8\mathit{H}_{16}CH_3$), 0.88 (t, 3H, *J* 7.0, aliphatic $OCOC_{10}H_{20}C\mathit{H}_3$); ^{13}C NMR ($CDCl_3$): δ 174.2 (s, C=O), 99.4 (d, C-1), 74.1, 71.9, 70.4, 69.8 (each d), 63.5 (t, C-6), 55.2 (q, OCH_3), 34.2, 31.9, 29.66, 29.64, 29.5, 29.4, 29.3, 29.2, 24.9, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 399.3 required, 399.5; [M + Na]$^+$; Anal. Calcd. for $C_{19}H_{36}O_7$: C, 60.61; H, 9.64. Found: C, 60.69; H, 9.83.

3.1.11 Methyl 6-*O*-lauroyl-β-D-glucopyranoside (4b)

Treatment of **3b** (2.0 g, 3.0 mmol) as described for **3a** gave **4b** (0.86 g, 75%); $[\alpha]_D$ – 25.5º (*c* 0.05, $CHCl_3$); FTIR (KBr): 3421, 2921, 1744, 1703, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.40 (d, 1H, $J_{1,2}$ 11.5, H-1), 4.28 (dd, 1H, $J_{2,3}$ 6.0, H-2), 4.21 (d, 2H, $J_{5,6}$ 7.5, H-6), 3.54 (s, 3H, $OC\mathit{H}_3$), 3.49 (m, 1H, H-3), 3.39-3.31 (overlapping signals, 2H, H-4,5), 2.34 (m, 2H, aliphatic $OCOC\mathit{H}_2C_{10}H_{21}$), 2.02 (s, 3H, OH), 1.62 (m, 2H, aliphatic $OCOCH_2C\mathit{H}_2C_9H_{19}$), 1.28-1.26 (ms, 16H, aliphatic $OCOC_2H_4C_8\mathit{H}_{16}CH_3$), 0.88 (t, 3H, *J* 6.5, aliphatic $OCOC_{10}H_{20}C\mathit{H}_3$); ^{13}C NMR ($CDCl_3$): δ 174.2 (s, C=O),

103.6 (d, C-1), 76.5, 73.9, 73.4, 70.3 (each d), 63.6 (t, C-6), 57.0 (q, OCH_3), 34.2, 31.9, 29.61, 29.60, 29.5, 29.3, 29.2, 29.1, 24.9, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 399.1 required, 399.5 $[M + Na]^+$; Anal. Calcd. for $C_{19}H_{36}O_7$: C, 60.61; H, 9.64. Found: C, 60.25; H, 9.91.

3.1.12 Methyl 6-*O*-lauroyl-α-D-mannopyranoside (4c)

Treatment of **3c** (3.3 g, 5.0 mmol) as described for **3a** gave **4c** (1.4 g, 75%); $[\alpha]_D$ 33.3º (*c* 0.01, $CHCl_3$); FTIR (KBr): 3421, 2923, 1736, 1466, 1197, 1057 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 1H, H-1), 4.45 (br s, 1H, OH), 4.36 (d, 2H, *J* 4.0, H-6), 3.96-3.92 (overlapping signals, 2H, OH, H-2), 3.78 (dd, 1H, $J_{2,3}$ 2.5, $J_{3,4}$ 9.0, H-3), 3.71 (m, 1H, H-5), 3.62 (apt t, 1H, $J_{4,5}$ 9.5, H-4) 3.36 (s, 3H, OMe), 2.35 (t, 2H, *J* 7.5, *J* 7.5, aliphatic $OCOC\mathit{H}_2C_{10}H_{21}$), 1.61 (m, 2H, aliphatic $OCOCH_2C\mathit{H}_2C_9H_{19}$), 1.29-1.25 (ms, 16H, aliphatic $OCOC_2H_4C_8\mathit{H}_{16}CH_3$), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic $OCOC_{10}H_{20}C\mathit{H}_3$);); ^{13}C NMR ($CDCl_3$): δ 174.7 (s, C=O), 100.9 (d, C-1), 71.5, 70.5, 70.4, 67.7 (each d), 63.9 (t, C-6), 54.9 (q, OCH_3), 34.2, 31.9, 29.7, 29.6, 29.5, 29.4, 29.36, 29.34, 29.19, 24.9, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 377.3 required, 377.5; $[M + H]^+$; Anal. Calcd. for $C_{19}H_{36}O_7$: C, 60.61; H, 9.64. Found: C, 60.71; H, 9.53.

3.1.13 Methyl 6-*O*-lauroyl-α-D-galactopyranoside (4d)

Treatment of **3d** (2.8 g, 4.4 mmol) as described for **3a** gave **4d** (1.43 g, 86%); $[\alpha]_D$ 56.25º (*c* 0.01, $CHCl_3$); FTIR (KBr): 3250, 2918, 1741, 1467, 1194, 1025cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.63 (apt t, 1H, *J* 6.5, *J* 5.0, OH-3), 4.57 (d, 1H, *J* 6.5, OH-2), 4.55 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.13 (dd, 1H, $J_{5,6a}$ 8.0, $J_{6a,6b}$ 11.5, H-6a), 4.07 (dd, 1H, $J_{5,6b}$ 4.0, H-6b), 3.75 (dd, 1H, H-5), 3.68 (apt t, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ 3.0, H-4), 3.58 (ddd, 1H, $J_{2,3}$ 10.0, $J_{2,OH}$ 16.5, H-2), 3.52 (m, 1H, H-3), 3.24 (s, 3H, OMe), 2.28 (t, 2H, *J* 7.5, aliphatic $OCOC\mathit{H}_2C_{10}H_{21}$), 1.63 (t, 2H, *J* 7.0, aliphatic

$OCOCH_2CH_2C_9H_{19}$), 1.28-1.23 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.85 (t, 3H, *J* 7.0, aliphatic $OCOC_{10}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 178.2 (s, C=O), 104.8 (d, C-1), 74.9, 74.1, 73.7, 73.1 (each d), 68.8 (t, C-6), 59.8 (q, OCH_3), 38.9, 36.5, 34.24, 34.10, 33.97, 33.93, 33.75, 29.5, 27.3, (each t, each aliphatic CH_2), 18.9 (q, aliphatic CH_3); LRMS: Found, 399.3 required, 399.5; $[M + Na]^+$; Anal. Calcd. for $C_{19}H_{36}O_7$: C, 60.61; H, 9.64. Found: C, 60.60; H, 9.88.

3.1.14 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-octanoyl-α-D-glucopyranoside (5a)

Compound **2a** (5.0 g, 8.5 mmol) was dissolved in THF anhydrous (150 mL) and was cooled to 0 °C. Tetrabutylammonium fluoride (2.2 g, 8.5 mmol) was added and the solution was warmed to room temperature and stirred for 1 h.[25] The mixture was then concentrated *in vacuo* and the resulting 6-OH residue was dissolved in pyridine anhydrous (100 mL). 4-Dimethylaminopyridine and octanoyl chloride (2.9 mL, 17 mmol) was added and the mixture was stirred at room temperature for 24 h.[26] The solution was then concentrated under reduced pressure and purified by chromatography (petroleum ether-EtOAc) to give **5a** (3.9 g, 63%); $[\alpha]_D$ 20.8° (*c* 0.07, $CHCl_3$); FTIR (KBr): 2927, 1738, 1497, 1454, 1360, 1163, 1093, 738, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.26 (ms, 15H, aromatic H), 4.93, (AB d, 2H, *J* 10.5, OCH_2Ph), 4.74, (AB d, 2H, *J* 12.0, OCH_2Ph), 4.73 (AB d, 2H, *J* 10.5, OCH_2Ph), 4.60 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.28 (d, 2H, $J_{5,6}$ 3.0, H-6), 4.01 (apt t, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, H-3), 3.81 (m, 1H, H-5), 3.54 (dd, 1H, H-2), 3.48 (dd, 1H, $J_{4,5}$ 10.5, H-4), 3.37 (s, 3H, OCH_3), 2.31 (m, 2H, aliphatic $OCOCH_2C_6H_{13}$), 1.62 (m, 2H, aliphatic $OCH_2CH_2C_5H_{11}$), 1.30-1.05 (ms, 8H, aliphatic $OC_2H_4C_4H_8CH_3$), 0.87 (m, 3H, aliphatic $OC_6H_{12}CH_3$); ^{13}C NMR ($CDCl_3$): δ 173.8 (s, C=O), 138.8, 138.3, 138.1 (each s, each aromatic C), 128.7, 128.6, 128.3, 128.29, 128.27, 128.3, 128.25, 128.20, 128.1 127.9 (each d, each aromatic CH), 98.3 (d, C-1), 82.2, 80.2, 77.8, 68.9 (each d),

76.1, 75.3, 73.6 (each t, each OCH_2Ph), 63.1 (t, C-6), 55.4 (q, OCH_3), 34.4, 31.9, 29.2, 25.0, 22.8, 17.9 (each t, each aliphatic CH_2), 14.3 (q, aliphatic CH_3); LRMS: Found, 613.4 required, 613.7; $[M + Na]^+$; Anal. Calcd. for $C_{36}H_{46}O_7$: C, 73.19; H, 7.85. Found: C, 73.25; H, 7.61

3.1.15 Methyl 6-*O*-octanoyl-α-D-glucopyranoside (6a)

Treatment of **5a** (3.6 g, 6.2 mmol) as described for **3a** gave **6a** (1.44 g, 73%); $[\alpha]_D$ 27.9º (*c* 0.4, $CHCl_3$); FTIR (KBr): 3388, 2922, 1712, 1465, 1193, 1106, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (s, 3H, each O*H*), 4.76 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.35 (d, 2H, $J_{5,6}$ 4.0, H-6), 3.78-3.72 (overlapping signals, 2H, H-3,5), 3.54 (dd, 1H, $J_{2,3}$ 9.5, H-2), 3.41 (s, 3H, O*C*H_3), 3.36 (dd, 1H, $J_{3,4}$ 9.5, $J_{4.5}$ 10.0, H-4), 2.35 (m, 2H, aliphatic CO*C*$H_2C_6H_{13}$) 1.64 (t, 2H, *J* 7.0, aliphatic $COCH_2CH_2C_5H_{11}$), 1.31-1.05 (ms, 8H, aliphatic $COC_2H_4C_4H_8CH_3$), 0.88 (t, 3H, *J* 5.5, *J* 7.0, aliphatic $COC_6H_{12}CH_3$); ^{13}C NMR ($CDCl_3$): δ 179.5 (s, C=O), 99.4 (d, C-1), 74.1, 72.0, 69.7, 70.3 (each d), 63.4 (t, C-6), 55.3 (q, OCH_3), 34.1, 31.7, 31.6, 29.9, 28.9, 24.8 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 343.1 required, 343.4; $[M + Na]^+$; Anal. Calcd. for $C_{15}H_{28}O_7$: C, 56.23; H, 8.81. Found: C, 56.47; H, 8.73.

3.1.16 Methyl 2,3,4-tri-*O*-parmethoxybenzyl-6-*O*-triisopropylsilyl-α-D-glucopyranoside (7a)

A solution of **1a** (5.0 g, 25.0 mmol) in DMF anhydrous (120 mL) was treated with triisopropylsilyl chloride (15 mL, 75 mmol) and imidazole (5 g, 75 mmol) and allowed to stir at room temperature for 24 h. The crude TIPS protected intermediate was then concentrated *in vacuo* and the resulting residue dissolved in EtOAc. It was then washed with 10% HCl, water, followed by sat. aq. $NaHCO_3$, and finally sat. aq. NaCl, before being dried over anhydrous $MgSO_4$, and concentrated under reduced pressure.[23] The TIPS protected crude residue was then split in two and half was

dissolved in DMF anhydrous (30 mL) and THF anhydrous (20 mL). This solution was then added dropwise at 0 °C to a suspension of NaH (2.5 g, 62.5 mmol) in DMF anhydrous (10 mL) and THF anhydrous (7 mL), paramethoxybenzyl chloride (17 mL, 125 mmol) and tetrabutylammonium iodide (18.5 g, 50 mmol). This was stirred at approximately 10 °C for 30 min and then allowed to warm to room temperature and stir for 24 h. MeOH (50 mL) was added to quench the mixture which was stirred for 1 h. The solution was then concentrated under diminished pressure and dissolved in EtOAc. It was washed with water, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*.[28] The resulting residue was purified by chromatography (petroleum ether-EtOAc) to give **7a**. (5.15 g, 59%); $[\alpha]_D$ 11.6º (*c* 0.05, $CHCl_3$); FTIR (KBr): 3479, 2936, 2864, 1464, 1421, 1360, 1302, 883, 820. cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34-6.73 (ms, 12H, aromatic H), 4.88 (AB d, 2H, *J* 10.5 OC*H*$_2$Ph), 4.78 (d, 1H, $J_{1,2}$ 5.0, H-1), 4.75, 4.71 (each AB d, 2H, *J* 12.0 OC*H*$_2$Ph), 4.63 (m, 1H, H-2), 3.99 (apt t, 1H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.0, H-4), 3.89 (m, 2H, H6), 3.77 (m, 9H, each PhOC*H*$_3$), 3.57-3.49 (overlapping signals, 2H, H-3,5), 3.39 (s, 3H, OC*H*$_3$), 1.28 (m, 3H, each TIPS C*H*), 1.16-1.06 (ms, 18H, each TIPS C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 159.6, 159.5, 159.4, 131.6, 131.4, 131.0 (each s, each aromatic C), 129.99, 129.93, 129.8, 114.13, 114.08, 113.6 (each d, each aromatic CH), 98.1 (d, C-1), 82.2, 80.2, 77.8, 72.1 (each d), 75.8, 74.9, 73.2 (each t, each OCH_2Ph), 63.1 (t, C-6), 55.47, 55.40, 55.36 (each q, each $PhOCH_3$), 55.0 (q, OCH_3), 18.27, 18.25 (each q, each TIPS CH_3), 12.3 (d, each TIPS CH); LRMS: Found, 733.3 required, 733.9 $[M + Na]^+$.

3.1.17 Methyl 2,3,4-tri-*O*-paramethoxybenzyl-6-*O*-triisopropylsilyl-β-D-glucopyranoside (7b)

Treatment of **1b** (4.5 g, 23.17 mmol) as described for **1a** gave **7b** (10.1 g, 61%); $[\alpha]_D$ 4.8º (*c* 0.05, $CHCl_3$); FTIR (KBr): 2939, 1586, 1464, 883, 821, 760, 683. cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$): δ 7.30-6.84 (ms, 12H, aromatic H), 4,85, 4.80, 4.73 (each AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 4.27 (d, 1H, $J_{1,2}$ 7.5, H-1), 3.95 (m, 1H, H-6a), 3.87 (dd, 1H, $J_{4,5}$ 11.0, $J_{5,6}$ 4.5, H-5), 3.78 (m, 9H, PhOC*H*$_3$), 3.59 (m, 1H, H-3), 3.53 (s, 3H, OC*H*$_3$) 3.36 (apt t, 1H, $J_{2,3}$ 9.0, H-2), 3.29-3.24 (overlapping signals, 2H, H-4,6b), 1.10-1.04 (ms, 21H, TIPS); ^{13}C NMR ($CDCl_3$): δ 159.5, 159.4, 131.2, 131.1, 130.9, (each s, each aromatic C), 129.9, 129.8, 128.7, 114.1, 114.04, 114.01 (each d, each aromatic CH), 104.7 (d, C-1), 84.7, 82.6, 77.5, 76.2 (each d), 75.7, 74.9, 74.7 (each t, each OCH_2PH), 62.7 (t, C-6), 56.8 (q, OCH_3), 55.5 (each q, each $PhOCH_3$), 18.3, 18.2 (each q, each TIPS CH_3), 12.2 (d, each TIPS CH); LRMS: Found, 733.3; required, 733.9 $[M + Na]^+$.

3.1.18 Methyl 2,3,4-tri-*O*-parametoxybenzyl-6-*O*-dodecanyl-α-D-glucopyranoside (8a)

Compound **7a** (4.0 g, 5.5 mmol) was dissolved in THF anhydrous (100 mL) and was cooled to 0 ^{o}C. Tetrabutylammonium fluoride (1.4 g, 5.5 mmol) was added and the solution was allowed to warm to room temperature and stir for 1 h.[25] The mixture was then concentrated *in vacuo*, and the resulting 6-OH residue was dissolved in DMF anhydrous (100 mL). 1-chlorododecane (1.8 mL, 11 mmol) was added and the solution was cooled to 0 ^{o}C before NaH (0.11 g, 2.75 mmol) was added portion wise. The mixture was then allowed to warm to room temperature and was stirred for 24 h. MeOH (50 mL) was added to quench the solution which was stirred for 1 h.[29] The crude PMB protected ether was then concentrated under diminished pressure and purified by chromatography (petroleum ether-EtOAc) to give **8a** (1.89 g, 50%); $[\alpha]_D$ – 8.6º (*c* 0.06, $CHCl_3$); FTIR (KBr): 2924, 2854, 1613, 1586, 1464, 1359, 1301, 1248, 1172, 1037, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85-7.30 (ms, 12H, aromatic H), 4.92 (d, 1H, $J_{1,2}$ 10.5, H-1), 4.85 (AB d, 2H, *J* 10.5, OC*H*$_2$PhOCH$_3$), 4.74 (dd, 1H,

$J_{2,3}$ 9.5, H-2), 4.69, (AB d, 2H, *J* 10.5, OC*H*$_2$PhOCH$_3$), 4.60 (AB d, 2H, *J* 11.5 OC*H*$_2$PhOCH$_3$), 4.55 (apt t, 1H, $J_{3,4}$ 9.5, H-3), 3.95 (m, 1H, H-5), 3.80 (s, 9H, each PhOC*H*$_3$), 3.53-3.37 (overlapping signals, 3H, H-4,6a,6b), 3.36 (s, 3H, OC*H*$_3$), 1.60 (m, 2H, aliphatic C*H*$_2$C$_{11}$H$_{23}$), 1.30-1.25 (ms, 20H, aliphatic CH$_2$C$_{10}$*H*$_{20}$CH$_3$), 0.89 (t, 3H, *J* 7.0, aliphatic C$_{11}$H$_{20}$C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 159.6, 159.5, 159.4, 131.3, 131.0, 130.6 (each s, each aromatic C), 130.0, 129.8, 129.6, 114.07, 114.05, 114.03 (each d, each aromatic CH), 98.5 (d, C-1), 82.1, 79.8, 77.7, 70.2 (each d), 75.7, 74.9, 73.3 (each t, each OCH$_2$Ph), 72.0 (t, aliphatic OCH$_2$C$_{11}$H$_{23}$), 69.5 (t, C-6), 55.5 (q, PhOCH$_3$), 55.3 (s, OCH$_3$), 32.2, 29.94, 29.91, 29.89, 29.87, 29.84, 29.7, 29.5, 28.4 (each t, each aliphatic CH$_2$), 14.4 (q, aliphatic CH$_3$); LRMS: Found, 745.5; required, 745.9; $[M + Na]^+$; Anal. Calcd. for C$_{43}$H$_{62}$O$_9$: C, 71.44; H, 8.64. Found: C, 71.09; H, 8.73.

3.1.19 Methyl 2,3,4-tri-*O*-paramethoxybenzyl-6-*O*-dodecanyl-β-D-glucopyranoside (8b)

Treatment of **7b** (3.2 g, 4.5 mmol) as described for **7a** gave **8b** (0.55 g, 85%); $[\alpha]_D$ 2º (*c* 0.01, $CHCl_3$); FTIR (KBr): 2923, 2851, 1614, 1464.40, 1421, 1359, 1302, 1254, 1173, 1072, 813 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-6.84 (ms, 12H, aromatic H), 4.79, 4.75, 4.67 (each AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 4.26 (d, 1H, $J_{1,2}$ 7.5, H-1), 3.79-3.58 (overlapping signals, 2H, H-3,5), 3.79 (m, 9H, PhOC*H*$_3$), 3.68 (m, 2H, H-6a,6b), 3.56 (s, 3H, OC*H*$_3$), 3.43-3.39 (overlapping signals, 2H, H-2,4), 1.63 (m, 2H, aliphatic OC*H*$_2$C$_{11}$H$_{23}$), 1.29-1.24 (ms, 20H, aliphatic OCH$_2$C$_{10}$*H*$_{20}$CH$_3$), 0.88 (t, 3H, *J* 7.0, aliphatic OC$_{11}$H$_{22}$C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 159.3, 159.2, 159.1, 130.9, 130.8, 130.5 (each s, each aromatic C), 129.8, 129.6, 129.5, 113.8, 113.7 (each d, each aromatic CH), 104.8 (d, C-1), 84.4, 82.1, 77.7, 75.3 (each d), 74.9, 74.6, 74.4 (each t, each OCH$_2$Ph), 71.9 (t, aliphatic CH$_2$), 69.7 (t, C-6), 57.1 (q, OCH$_3$), 55.3, 55.2 (each

q, each $PhOCH_3$), 31.9, 29.7, 29.68, 29.65, 29.63, 29.5, 29.4, 26.2, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 745.3; required, 745.9; $[M + Na]^+$; Anal. Calcd. for $C_{43}H_{62}O_9$: C, 71.44; H, 8.64. Found: C, 71.19; H, 8.70.

3.1.20 Methyl 6-*O*-dodecanyl-α-D-glucopyranoside (9a)

Compound **8a** (1.45 g, 2.0 mmol) was dissolved in a mixture of MeCN:H_2O (3:1) (21 mL) and cerric ammonium nitrate (8.85 g, 16.16 mmol) was added. The solution was allowed to stir at room temperature for 24 h.[30] It was then concentrated *in vacuo* and purified by chromatography (petroleum ether-EtOAc) to give **9a** (0.53 g, 73%); $[\alpha]_D$ 78.8º (*c* 0.04, $CHCl_3$); FTIR (KBr): 3416, 2919, 2851, 1467, 1372, 1128, 1043, 1019 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.98 (br s, 1H, OH), 4.75 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.34 (br s, 1H, OH), 4.01 (br s, 1H, OH), 3.75 (apt t, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, H-3), 3.66 (m, 2H, H-6), 3.54-3.44 (overlapping signals, 3H, H-2,4,5), 3.37 (s, 3H, OCH_3), 1.58 (m, 2H, aliphatic $CH_2C_{11}H_{23}$), 1.28-1.25 (ms, 20H, each aliphatic $CH_2C_{10}H_{20}CH_3$), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic $C_{11}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 99.7 (d, C-1), 74.5, 72.3, 72.2, 71.2 (each d) 70.6 (t, aliphatic CH_2), 69.5 (t, C-6), 55.4 (q, OCH_3), 32.1, 29.9, 29.88, 29.86, 29.83, 29.7, 29.6, 26.3, 22.9 (each t, each aliphatic CH_2), 14.3 (q, aliphatic CH_3); LRMS: Found, 385.2; required, 385.5; $[M + Na]^+$; Anal. Calcd. for $C_{19}H_{38}O_6$: C, 62.95; H, 10.57. Found: C, 62.60; H, 10.67.

3.1.21 Methyl 6-*O*-dodecanyl-β-D-glucopyranoside (9b)

Treatment of **8b** (0.44 g, 0.6 mmol) as described for **8a** gave **9b** (0.17 g, 76%); $[\alpha]_D$ – 1º (*c* 0.03, $CHCl_3$); FTIR (KBr): 3405, 2922, 2850, 1470, 1391, 1128, 1109, 1048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.20 (d, 1H, $J_{1,2}$ 7.5, H-1), 3.89 (s, 1H, OH), 3.74 (m, 2H, H-6a,6b), 3.66 (m, 1H, H-5), 3.54 (s, 3H, OCH_3), 3.52-3.44 (overlapping signals, 2H, H-3,4), 3.35 (apt t, 1H, $J_{2,3}$ 8.0, H-2), 1.58 (m, 2H, aliphatic $OCH_2C_{11}H_{23}$), 1.28-1.11 (ms, 20H, aliphatic $OCH_2C_{10}H_{20}CH_3$), 0.88 (t, 3H, *J* 6.5, *J*

7.0, aliphatic $OC_{11}H_{22}CH_3$); ^{13}C NMR ($CDCl_3$): δ 103.5 (d, C-1), 76.5, 74.4, 73.4, 72.1, (each d), 71.6 (t, aliphatic CH_2), 70.9 (t, C-6), 57.1 (q, OCH_3), 31.9, 29.7, 29.66, 29.65, 29.58, 29.53, 29.4, 26.0, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 385.2; required, 385.5; $[M + Na]^+$; Anal. Calcd. for $C_{19}H_{38}O_6$: C, 62.95; H, 10.57. Found: C, 62.83; H, 10.36.

3.1.22 Methyl 2,3-di-*O*-benzyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside (10a)

A solution of **1a** (1.0 g, 5.2 mmol), p-toluenesulfonic acid (10 mg) and benzaldehyde dimethylacetal (1.5 mL, 10.3 mmol) in acetonitrile anhydrous (25 mL) was stirred for 24 h at room temperature. Trimethylamine (0.5 mL) was added to neutralise the solution which was then stirred for 1 h. The product was filtered off as a white solid, washed with petroleum ether and dried. The benzylidene protected intermediate was then dissolved in DMF anhydrous (15 mL) and the solution was cooled to 0 °C. NaH (0.74 g, 18.4 mmol) was added slowly, followed by benzyl bromide (2.5 mL, 20 mmol). The mixture was then warmed to room temperature and stirred over night. MeOH (10 mL) was added to quench the solution which was stirred for a further 1 hr.[24] The mixture was then concentrated under diminished pressure and purified by chromatography (petroleum ether-EtOAc) to give **10a**. (2.0 g, 95%); $[\alpha]_D$ 0.7° (*c* 0.05, $CHCl_3$); FTIR (KBr): 3063, 3031, 1109, 1088, 735, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50-7.22 (ms, 15H, each aromatic H), 5.54 (s, 1H, C*H*Ph), 4.85 (AB d, 2H, *J* 4.0, OCH_2Ph), 4.82 (AB d, 2H, *J* 12.0, OCH_2Ph), 4.59 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.26 (dd, 1H, $J_{5,6a}$ 10.0, $J_{6a,6b}$ 4.5, H-6a), 4.05 (apt t, 1H, $J_{2,3}$ 9.0, $J_{3,4}$ 9.0, H-3), 3.83 (m, 1H, H-5), 3.70 (apt t, 1H, $J_{5,6b}$ 10.5, H-6b), 3.62-3.54 (overlapping signals, 2H, H-2,4), 3.39 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 138.7, 138.1, 137.4 (each s, each aromatic C), 128.89, 128.43, 128.29, 128.20, 128.10, 128.01, 127.90, 127.57, 126.0 (each d, each aromatic CH), 101.2 (d, C-1), 99.2 (d, C*H*Ph), 82.1, 79.2, 78.6, 62.3

(each d), 75.3, 73.8 (each t), 69.1 (t, C-6), 55.3 (q, OCH_3); LRMS: Found, 463.3 required, 463.5; $[M + H]^+$; Anal. Calcd. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.31; H, 6.56.

3.1.23 Methyl 4,6-di-*O*-lauroyl-α-D-glucopyranoside (12a)

3.1.23.1 Methyl 2,3-di-*O*-benzyl-4,6-di-*O*-lauroyl-α-D-glucopyranoside (11a)

Compound **10a** (1.7 g, 3.6 mmol) was dissolved in MeOH (50 mL) and a catalytic amount of TsOH was added. The solution was stirred at room temperature overnight, after which Et_3N (2 mL) was added to quench the reaction.[31] The mixture was concentrated under diminished pressure and the crude diol residue was dissolved in pyridine anhydrous (70 mL). 4-Dimethylaminopyridine and lauroyl chloride (3.3 mL, 14.4 mmol) was added and the reaction was stirred at room temperature for 3 h.[26] The solution was then concentrated under diminished pressure and purified by chromatography (petroleum ether-EtOAc) to give **11a**. (1.0 g, 38%); FTIR (KBr): 2925, 2853, 1743, 1455, 1360, 1167, 1105, 1045, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34-7.26 (multiple signal, 10H, each aromatic H), 5.01 (dd, 1H, $J_{3,4}$ 9.5, $J_{4,5}$ 10.0, H-4), 4.78 (AB d, 2H, *J* 11.5, OC*H*$_2$Ph), 4.73 (AB d, 2H, *J* 12.0, OC*H*$_2$Ph),4.59 (d, 1H, $J_{1,2}$ 3.5, H-1), 4.15 (dd, 1H, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 12.5, H-6a), 4.04 (dd, 1H, $J_{5,6b}$ 2.0, H-6b), 3.92 (apt t, 1H, $J_{2,3}$ 9.5, H-3), 3.87-3.82 (m, 1H, H-5), 3.59 (dd, 1H, H-2), 2.36-2.27 (m, 4H, each aliphatic OCOC*H*$_2$$C_{10}H_{21}$), 1.67-1.56 (m, 4H, each aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.26-1.16 (ms, 32H, each aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 6H, *J* 6.5, *J* 7.0, each aliphatic $OCOC_{10}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 173.6, 172.4 (each s, each C=O), 138.4, 137.9 (each s, each aromatic C), 128.51, 128.32, 128.18, 128.05. 127.69, 127.57 (each d, each aromatic CH), 98.2 (d, C-1), 79.51, 79.18, 69.5, 67.7 (each d), 75.4, 73.6 (each t, each CH_2Ph), 62.2 (t, C-6), 55.4 (q, OCH_3), 34.15, 34.03, 33.99, 31.9, 29.62, 29.60, 29.49, 29.44,

29.35, 29.34, 29.28, 29.26, 29.15, 29.13, 29.07, 24.76, 24.70, 22.69 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3).

3.1.23.2 Methyl 4,6-di-*O*-lauroyl-α-D-glucopyranoside (12a)

Compound **11a** (0.84 g, 1.14 mmol) was dissolved in EtOH (2.5 mL) and Pd/C (0.3 g) was added. The mixture was allowed to shake under hydrogen atmosphere of 2 psi until all protecting groups had been removed as shown by TLC to yield **12a**. The suspension was filtered and concentrated *in vacuo*.[27] (0.47 g, 75%); $[\alpha]_D$ 4.33º (*c* 0.03, $CHCl_3$); FTIR (KBr): 3456, 2918, 2849, 1737, 1701, 1468, 1301, 1240, 1187, 1046 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.87 (dd, 1H, $J_{3,4}$ 9.5, $J_{4,5}$ 10, H-4), 4.82 (d, 1H, $J_{1,2}$ 4.0, H-1), 4.23 (dd, 1H, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 12.0, H-6b), 4.12 (dd, 1H, $J_{5,6a}$ 2.0, H-6a), 3.91 (ddd, 1H, H-5), 3.84 (apt t, 1H, $J_{2,3}$ 9.5, H-3), 3.64 (m, 1H, H-2), 3.44 (s, 3H, OMe), 2.37-2.32 (m, 4H, each aliphatic $OCOC\mathit{H}_2C_{10}H_{21}$), 1.68-1.55 (m, 4H, each aliphatic $OCOCH_2C\mathit{H}_2C_9H_{19}$), 1.30-1.26 (multiple signals, 32 H, each aliphatic $OCOC_2H_4C_8\mathit{H}_{16}CH_3$), 0.88 (t, 6H, *J* 6.5, *J* 7.0, each aliphatic $OCOC_{10}H_{20}C\mathit{H}_3$); ^{13}C NMR ($CDCl_3$): δ 173.63, 173.58 (each s, each C=O), 99.0 (d, C-1), 72.9, 72.7, 70.3, 67.7 (each d), 62.2 (t, C-6), 55.5 (q, OMe), 34.2, 34.1, 34.0, 31.9, 29.63, 29.61, 29.50, 29.47, 29.45, 29.36, 29.30, 29.27, 29.14, 29.08, 24.84, 24.82, 24.70, 22.70 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found, 559.5 required, 559.8; $[M + H]^+$; Anal. Calcd. for $C_{31}H_{58}O_8$: C, 66.63; H, 10.46. Found: C, 66.66; H, 10.79.

3.1.24 General procedure for the preparation of pentaerythritol esters

Pentaerythritol **13** (1.0 g, 7.3 mmol), lauroyl chloride (4.8 mL, 21 mmol) and 4-dimethylaminopyridine were dissolved in pyridine anhydrous (50 mL) and stirred at 50 ^oC for 24 h.[26] The solution was then concentrated *in vacuo*, and the following

mono-lauroyl **14** and di-lauroyl **15** products were isolated by chromatography (petroleum ether-EtOAc) a tetra-lauroyl derivative was also isolated (0.39 g, 6%):

3.1.25 Mono lauroyl pentaerythritol (14)

(0.33 g, 14%); FTIR (KBr): 3462, 2914, 2848, 1737, 1712, 1476, 1187, 1038, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.10 (s, 2H, $CH_2OC{=}O$), 3.80-3.61 (overlapping signals, 9H, 3 x CH_2OH, 3 x OH), 2.34 (t, 2H, *J* 6.0, *J* 7.0, aliphatic $OCOCH_2C_{10}H_{21}$), 1.61 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.26 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (m, 3H, aliphatic $OCOC_{10}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 175.0 (s, C=O), 62.7, 62.4 (each t, each CH_2O), 45.3 (s, $C(CH_2)_4$), 34.2, 31.9, 29.59, 29.57, 29.44, 29.30, 29.23, 29.15, 24.9, 22.6 (each t, each aliphatic CH_2), 14.1 (q, aliphatic CH_3); LRMS: Found 341.2, required 341.45 $[M+Na]^+$; Anal. Calcd. for $C_{17}H_{34}O_5$: C, 64.12; H, 10.76. Found: C, 64.08; H, 10.79.

3.1.26 Di lauroyl pentaerythritol (15)

(1.074 g, 29%); FTIR (KBr): 3351, 2915, 2850, 1739, 1701, 1471, 1163, 978, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.12 (s, 4H, each $CH_2OC{=}O$), 3.58 (s, 4H, each CH_2OH), 3.22 (br s, 2H, each OH) 2.34 (t, 4H, *J* 7.5, *J* 7.5, each aliphatic $OCOCH_2C_{10}H_{21}$), 1.62 (t, 4H, *J* 6.5, *J* 6.5, each aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.29-1.26 (ms, 32H, each aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 6H, *J* 6.5, *J* 6.5, each aliphatic $OCOC_{10}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 174.4 (s, each C=O), 62.4 (t, each CH_2O), 44.7 (s, $C(CH_2)_4$), 34.2, 31.9, 29.56, 29.29, 29.21, 29.11, 24.9, 22.6 (each t, each aliphatic CH_2), 14.1 (q, each aliphatic CH_3); LRMS: Found 501.5, required 501.75 $[M+H]^+$; Anal. Calcd. for $C_{29}H_{56}O_6$: C, 69.56; H, 11.27. Found: C, 69.64; H, 11.31.

3.1.27 Tetra lauroyl pentaerythritol

(0.39 g, 6%); FTIR (KBr): 2917, 2849, 1735, 1336, 1299, 1250, 1154, 1111, 1002 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.11 (s, 8H, each $CH_2OC{=}O$), 2.30 (t, 8H, *J* 7.5, *J* 8.0, each aliphatic $OCOCH_2C_{10}H_{21}$), 1.60 (t, 8H, *J* 6.5, *J* 7.0, each aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.41-1.26 (ms, 64H, each aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 12H, *J* 6.5, *J* 7.0, each aliphatic $OCOC_{10}H_{20}CH_3$); ^{13}C NMR ($CDCl_3$): δ 173.2 (s, each C=O), 62.1 (t, each CH_2O), 41.8 (s, $C(CH_2)_4$), 34.1, 31.9, 29.59, 29.45, 29.31, 29.23, 29.11, 24.8, 22.7 (each t, each aliphatic CH_2), 14.1 (each q, each aliphatic CH_3); LRMS: Found 888.7, required 888.36 $[M+Na]^+$; Anal. Calcd. for $C_{53}H_{100}O_8$: C, 73.56; H, 11.65. Found: C, 73.60; H, 11.58.

3.2 Evaluation of anti-microbial activity

3.2.1 Preparation of bacterial cultures

Bacteria used in this study were *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922. Stock cultures were maintained in tryptic soy broth (TSB, Sharlau Chemie, Spain) supplemented with 20% glycerol at -70 °C. Cultures were routinely grown by subculturing 100 µL of stock culture into 9 mL TSB and incubating at 35 °C for 18 h. Cultures were then maintained on tryptic soy agar (TSA, Sharlau Chemie, Spain) plates at 4 °C. Working cultures were prepared by inoculating a loop of pure culture into TSB and incubating at 35 ºC for 18 h. A bacterial suspension was prepared in saline solution (NaCl 0.85%, BioMérieux, France) equivalent to a McFarland standard of 0.5, using the Densimat photometer (BioMérieux, SA, France), to obtain a concentration of $1x10^8$ cfu/mL. This suspension was then serially diluted in TSB to obtain a working concentration of $1x10^6$ cfu/mL.

3.2.2 Anti-microbial activity assay

Stock solutions (100 mmol) of test compounds and standards were prepared in sterile hydroalcoholic diluent (ethanol-distilled water, 1:1) and stored at -20 °C. Stock

solutions were diluted in TSB to obtain initial working concentrations (10 or 20 mmol). Working test compounds and standards were serially diluted in sterile TSB to a final volume of 100 µL within the 96-well plate. 100 µL of freshly prepared inoculum of the organism under study was added to each appropriate well. The final concentration of each microorganism in each well was approximately $5x10^5$ cfu/mL and the concentration range of chemical compounds was from 1:2 to 1:256. Each concentration was assayed in duplicate. The following controls were used in the microplate assay for each organism and test compound; blank: uninoculated media without test compound to account for changes in the media during the experiment; negative control: uninoculated media containing only the test compound; positive control 1: inoculated media without compound; positive control 2: inoculated media without compound but including the corresponding sugar to evaluate any effect of the sugar alone; and positive control 3: inoculated media without compound but with the equivalent concentration of ethanol used to dissolve the test compound, thereby assessing any activity of the alcohol. The 96-well plates were incubated at 35 °C for 18 hours in a microtiterplate reader (PowerWave microplate Spectrophotometer, BioTek) and effects were monitored by measuring the optical density (OD) at 600 nm for each well every 20 minutes with 20 seconds agitation before each OD measurement. Each experiment was replicated three times. The MIC was defined as the lowest concentration of compound that showed no increase in OD values for all the replicates compared to the negative control after 18 hours. Subtraction of the absorbance of the negative control eliminated interferences due to variation in the media.

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