Carbohydrate Research 343 (2008) 2557–2566

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

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

Aoife Smith, Patricia Nobmann, Gary Henehan, Paula Bourke, Julie Dunne *

School of Food Science and Environmental Health, Dublin Institute of Technology, Cathal Brugha Street, Dublin 1, Ireland

ARTICLE INFO

Article history:
Received 28 May 2008
Received in revised form 14 July 2008
Accepted 21 July 2008
Available online 26 July 2008

Keywords:
Fatty acid derivatives
Lauric acid
Monolaurin
Antimicrobial activity
Staphylococcus aureus
Escherichia coli

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.

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 (a 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 that has broad applications in the food industry is that of the 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 are non-toxic.[12]

The most common carbohydrate fatty acid esters utilised to date are sucrose esters. They are commercially available and used for a variety of food applications. Kato and Shibasaki 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 analogues 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.

* Corresponding author. Tel.: +353 14024400.
E-mail address: julie.dunne@dit.ie (J. Dunne).

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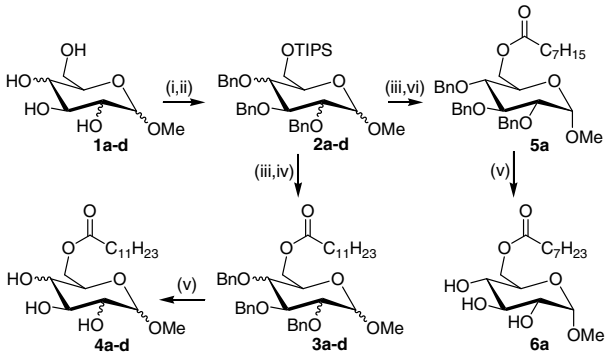
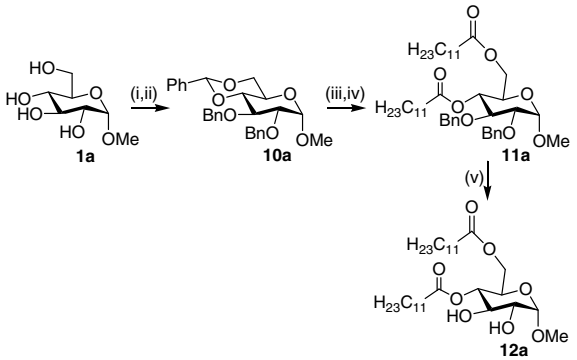
doi:10.1016/j.carres.2008.07.012



Scheme 1. Reagents and conditions: (i) DMF anhyd, TIPSCl, imidazole, rt; (ii) anhyd DMF, NaH, BnBr, rt; (iii) THF anhyd, 0 °C, TBAF, rt; (iv) anhyd Pyr, DMAP, Lauroyl Cl, rt; (v) EtOH, Pd/C, H_2; (vi) Pyr anhyd, DMAP, octanoyl Cl, rt.



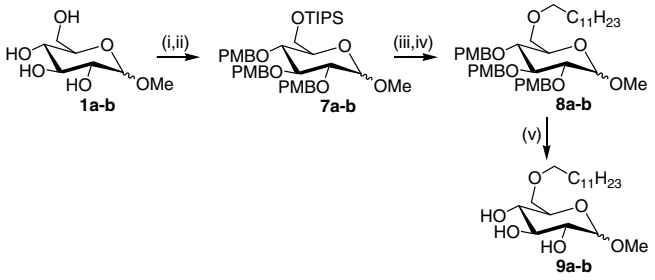
Scheme 3. Reagents and conditions: (i) pTSA, $PhCH(OMe)_2$, anhyd MeCN, rt; (ii) anhyd DMF, NaH, BnBr, rt (95% yield over 2 steps); (iii) MeOH, TsOH; (iv) anhyd Pyr, DMAP, lauroyl Cl, rt (38% yield over 2 steps); (v) EtOH, Pd/C, H_2 (75% yield).

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;[16–20] however, relatively few studies have examined role of the carbohydrate in antimicrobial activity.[14,21,22]

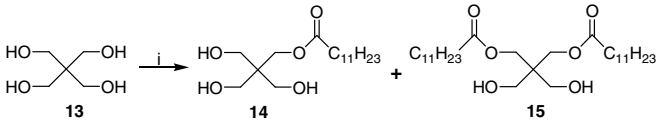
This study is concerned with the synthesis of carbohydrate and polyhydroxylated non-carbohydrate fatty acid derivatives for evaluation as antibacterial agents, with a view to examining the effect of variation of the hydrophilic moiety on antimicrobial activity. Therefore, we designed chemical syntheses 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 the synthesis of 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).



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



Scheme 4. Reagents and conditions: (i) Pyr anhyd, DMAP, lauroyl Cl, rt (**14**, 14%; **15**, 29%).

2. Results and discussion

2.1. Synthesis

A chemical route designed to obtain monoester sugars is shown in Scheme 1 and is based on the following carbohydrate starting materials: methyl α-D-glucopyranoside (**1a**), methyl β-D-glucopyranoside (**1b**), methyl α-D-mannopyranoside (**1c**) and methyl α-D-galactopyranoside (**1d**). The synthesis commenced with the selective protection of the primary hydroxyl group 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 (Table 1).

Synthesis of the ether derivatives also commenced with the protection of the primary hydroxyl group with a triisopropylsilyl group (Scheme 2). The sugars were then fully protected using *p*-methoxybenzyl chloride (PMB), to yield **7a**–**b**. Removal of the TIPS group gave the free primary hydroxyl. Next, the lauryl ether group was attached using dodecanyl chloride to give the fully protected ether derivatives **8a**–**b**. Finally, oxidative cleavage of the PMB groups with ceric ammonium nitrate (CAN) gave the monododecanyl sugars **9a**–**b** (Table 2).

The method used to synthesise di-*O*-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 OHs were then converted to benzyl ethers to give **10a**. Removal of the benzylidene acetal using a catalytic amount of 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**.

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

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

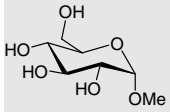
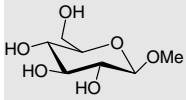
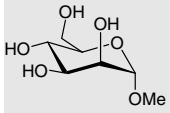
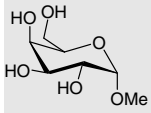
Carbohydrate (**1**)	2,3,4-Tri-*O*-Bn-6-*O*-TIPS (**2**)	2,3,4-Tri-*O*-Bn-6-*O*-lauroyl (**3**)	6-*O*-Lauroyl (**4**)	2,3,4-Tri-*O*-Bn-6-*O*-octanoyl (**5**)	6-*O*-Octanoyl (**6**)
 **(1a)**	**2a** 85%	**3a** 72%	**4a** 86%	**5a** 63%	**6a** 73%
 **(1b)**	**2b** 80%	**3b** 70%	**4b** 75%		
 **(1c)**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

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

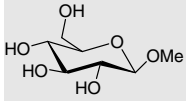
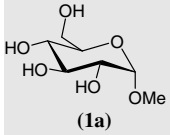
Carbohydrate (**1**)	2,3,4-Tri-*O*-PMB-6-*O*-TIPS (**7**)	2,3,4-Tri-*O*-PMB-6-*O*-dodecanyl (**8**)	6-*O*-Dodecanyl (**9**)
 **(1b)**	**7a** 59%	**8a** 50%	**9a** 73%
 **(1a)**	**7b** 61%	**8b** 85%	**9b** 76%

Table 3
MIC values of fatty acid derivatives and controls

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

[a] Not determined due to insolubility.

2.2. Antimicrobial activity of the 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, together with their corresponding polyhydric alcohols, fatty acids and monoglycerides as controls, were tested against a Gram-positive bacterium, *Staphylococcus aureus*, and a Gram-negative bacterium, *Escherichia coli*, to assess their antimicrobial activity. The efficacy of the derivatives and controls was compared using minimum inhibitory concentration values (MIC), which is defined as the lowest concentration of compound that shows no increase in cell growth for all the replicates compared to a negative control after 18 h.

The polyhydric alcohols (carbohydrates and pentaerythritol) showed no antimicrobial activity or growth-promoting effects for the microorganisms under the conditions used (results not shown).

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 as those for **6a** for *S. aureus* with values of 2.5 mM. The galactopyranoside ester derivative **4d** and the mono-*O*-lauroyl pentaerythritol **14** were the least active compounds tested, both with comparatively negligible MIC values of >10 mM for *S. aureus* and >20 mM 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 monosubstituted 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 efficacies 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 *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 glucopyranosides **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 glucopyranosides **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 such 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. 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 were visualised by UV and charring with 1:20 H_2SO_4–EtOH. Flash column chromatography was carried out with Silica Gel 60 (0.040–0.630 mm, E. Merck) using a stepwise solvent polarity gradient correlated with TLC mobility. Chromatography solvents used were EtOAc (Riedel-deHaen), MeOH (Riedel-deHaen) and petroleum ether (bp 40–60 °C, Fluka). Optical rotations were determined with an AA-% Series Optical Activity Ltd polarimeter. NMR spectra were recorded with Varian Inova 300 and Varian AS 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 (Hz). FTIR spectra were recorded with a Nicolet FT-IR 5DXB infrared spectrometer, samples were prepared in a KBr matrix. Low-resolution electrospray-ionisation mass spectra (LRESIMS) were measured in the positive-ion mode on a Micromass Quattro 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 anhyd DMF (120 mL) was treated with chlorotriisopropylsilane (TIPSCl, 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. The organic extract was washed with 10% HCl and water, followed by satd aq $NaHCO_3$ and finally satd aq NaCl. It was then dried over anhyd $MgSO_4$ and concentrated under reduced pressure.[23] The crude product was dissolved in anhyd DMF (50 mL) and cooled to 0 °C. NaH (5 g,

125 mmol) was added portionwise, BnBr (9 mL, 75 mmol) was added, and the mixture was allowed to warm to room temperature and stirred for 24 h. MeOH (50 mL) was added to quench the reaction, and the mixture was stirred for 1 h. The solution of the fully protected sugar was then concentrated in vacuo, and the residue was dissolved in EtOAc. The solution was washed with water, dried over anhyd $MgSO_4$ and concentrated under diminished pressure.[24] The resulting crude product was purified by chromatography (petroleum ether–EtOAc) to give **2a** (13.2 g, 85%); $[\alpha]_D$ 10.7 (*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, OCH_2Ph), 4.78, (AB d, 2H, *J* 11.0, OCH_2Ph), 4.74 (AB d, 2H, *J* 12.0, OCH_2Ph), 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, OCH_3), 1.10–1.02 (ms, 18H, each TIPS CH_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); LRESIMS: Found, *m/z* 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}; ^1H 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, OCH_2Ph), 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, OCH_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); LRESIMS: Found, *m/z* 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}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.24 (multiple signals, 15H, each aromatic H), 4.79 (AB d, 2H, *J* 11.0, OCH_2Ph), 4.72 (AB d, 2H, *J* 12.0, OCH_2Ph), 4.71–4.64 (overlapping signals, 3H, OCH_2Ph, 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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$ 20.6 (*c* 0.07, $CHCl_3$); FTIR (KBr): 3030, 2865, 1496, 1454, 1350, 1194, 1054, 882, 793, 734, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41–7.22 (multiple signals, 15H, each aromatic H), 4.82 (AB d, 2H, *J* 12.0, OCH_2Ph), 4.71 (AB d, 2H, *J* 11.5, OCH_2Ph), 4.77 (AB d, 2H, *J* 12.0, OCH_2Ph), 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); LRESIMS: Found, *m/z* 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 anhyd THF (80 mL), and the solution was cooled to 0 °C. Tetrabutylammonium fluoride (1 g, 4 mmol) was added, and the solution was allowed to warm to room temperature and stirred for 1 h.[25] It was then concentrated in vacuo, and approximately 1 mmol of the resulting 6-OH residue was dissolved in anhyd pyridine (25 mL). 4-Dimethylaminopyridine (DMAP, catalytic amt) 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%); $[\alpha]_D$ 7.5 (*c* 0.02, $CHCl_3$); FTIR (KBr): 2924, 2853, 1738, 1603, 1502, 1454, 1249, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ *7.35–7.26* (ms, 15H, aromatic H), 4.92, (AB d, 2H, *J* 10.5, OCH_2Ph), 4.72, (AB d, 2H, *J* 10.5, OCH_2Ph), 4.64 (AB d, 2H, *J* 12.0, OCH_2Ph), 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, OCH_3), 2.35 (m, 2H, aliphatic OCOC$H_2C_{10}H_{21}$), 1.61 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.28–1.24 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.87 (m, 3H, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$ 8.3 (*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, OCH_2Ph), 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, OCH_3), 3.54 (m, 1H, H-4), 3.43 (dd, 1H, H-2), 2.32 (m, 2H, aliphatic OCOC$H_2C_{10}H_{21}$), 1.62 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.26–1.24 (ms, 16H, each aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 3H, *J* 6.0, *J* 7.0, aliphatic $OCOC_{11}H_{23}CH_3$); ^{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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$ 23.3 (*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, OCH_2Ph), 4.74 (d, 1H, $J_{1,2}$ 2.0, H-1), 4.72 (AB d, 2H, *J* 12.5, OCH_2Ph), 4.61 (s, 2H, OCH_2Ph), 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 $OCOCH_2C_{10}H_{21}$), 1.61 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.31–1.54 (ms, 16H, aliphatic $OCOC_2H_4$-$C_8H_{16}CH_3$), 0.91–0.86 (m, 3H, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$ 27.8 (*c* 0.09, $CHCl_3$); FTIR (KBr): 3030, 2924, 2853, 1738, 1496, 1454, 1350, 1099, 1049, 735, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41–7.23 (multiple signals, 15H, each aromatic H), 4.83 (AB d, 2H, *J* 12.0, OCH_2Ph), 4.81 (AB d, 2H, *J* 11.5, OCH_2Ph), 4.77 (AB d, 2H, *J* 12.0, OCH_2Ph), 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 $OCOCH_2C_{10}H_{21}$), 1.57 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.31–1.18 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m/z* 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] to give **4a** (0.17 g, 86%); $[\alpha]_D$ 19 (*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 $OCOCH_2C_{10}H_{21}$), 1.63 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.38–1.23 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 3H, *J* 7.0, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m*/z 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%); $[\alpha]_D$ −25.5 (*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, OCH_3), 3.49 (m, 1H, H-3), 3.39–3.31 (overlapping signals, 2H, H-4,5), 2.34 (m, 2H, aliphatic $OCOCH_2C_{10}H_{21}$), 2.02 (s, 3H, OH), 1.62 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.28–1.26 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 3H, *J* 6.5, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$ 33.3 (*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 $OCOCH_2C_{10}H_{21}$), 1.61 (m, 2H, aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.29–1.25 (ms, 16H, aliphatic $OCOC_2H_4C_8H_{16}CH_3$), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic $OCOC_{10}H_{20}CH_3$); ^{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); LRESIMS: Found, *m*/z 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%); $[\alpha]_D$ 56.25 (*c* 0.01, $CHCl_3$); FTIR (KBr): 3250, 2918, 1741, 1467, 1194, 1025 cm^{-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 $OCOCH_2C_{10}H_{21}$), 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); LRESIMS: Found, *m/z* 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 anhyd THF (150 mL), and the solution 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 anhyd pyridine (100 mL). 4-Dimethylaminopyridine (DMAP, catalytic amt) and octanoyl chloride (2.9 mL, 17 mmol) were 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, OC*H*$_2$Ph), 4.74, (AB d, 2H, *J* 12.0, OC*H*$_2$Ph), 4.73 (AB d, 2H, *J* 10.5, OC*H*$_2$Ph), 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, OC*H*$_3$), 2.31 (m, 2H, aliphatic OCOC*H*$_2$C$_6$H$_{13}$), 1.62 (m, 2H, aliphatic OCH$_2$C*H*$_2$C$_5$H$_{11}$), 1.30–1.05 (ms, 8H, aliphatic OC$_2$H$_4$C$_4$*H*$_8$CH$_3$), 0.87 (m, 3H, aliphatic OC$_6$H$_{12}$C*H*$_3$); ^{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$_2$Ph), 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$_3$); LRESIMS: Found, *m*/z 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%); $[\alpha]_D$ 27.9 (*c* 0.4, $CHCl_3$); FTIR (KBr): 3388, 2922, 1712, 1465, 1193, 1106, 724 cm^{-1}; ^{1}H 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, OC*H*$_3$), 3.36 (dd, 1H, $J_{3,4}$ 9.5, $J_{4.5}$ 10.0, H-4), 2.35 (m, 2H, aliphatic COC*H*$_2$C$_6$H$_{13}$) 1.64 (t, 2H, *J* 7.0, aliphatic COCH$_2$C*H*$_2$C$_5$H$_{11}$), 1.31–1.05 (ms, 8H, aliphatic COC$_2$H$_4$C$_4$*H*$_8$CH$_3$), 0.88 (t, 3H, *J* 5.5, *J* 7.0, aliphatic COC$_6$H$_{12}$C*H*$_3$); ^{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$_3$); LRESIMS: Found, *m*/z 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*-*p*-methoxybenzyl-6-*O*-triisopropylsilyl-α-D-glucopyranoside (7a)

A solution of **1a** (5.0 g, 25.0 mmol) in anhyd DMF (120 mL) was treated with chlorotriisopropylsilane (TIPSCl, 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 was dissolved in EtOAc. The organic extract was then washed with 10% HCl and water, followed by satd aq $NaHCO_3$ and finally satd aq NaCl. It was then dried over anhyd $MgSO_4$ and concentrated under reduced pressure.[23] The TIPS-protected crude product was then split into two parts, and half was dissolved in a mixture of anhyd DMF (30 mL) and anhyd THF (20 mL). This solution was then added dropwise at 0 °C to a suspension of NaH (2.5 g, 62.5 mmol) in anhyd DMF (10 mL) and anhyd THF (7 mL), *p*-methoxybenzyl chloride (17 mL, 125 mmol) and tetrabutylammonium iodide (18.5 g, 50 mmol). The mixture was stirred at ~10 °C for 30 min and then allowed to warm to room temperature and stirred for 24 h. MeOH (50 mL) was added to quench the reaction, and the mixture was stirred for 1 h. The solution was then concentrated under diminished pressure and dissolved in EtOAc. The organic extract was washed with water, dried over anhyd $MgSO_4$ and concentrated in vacuo.[28] The resulting residue was purified by chromatography (petroleum ether–EtOAc) to give **7a** (5.15 g, 59%); $[\alpha]_D$ 11.6 (*c* 0.05, $CHCl_3$); FTIR (KBr): 3479, 2936, 2864, 1464, 1421, 1360, 1302, 883, 820 cm^{-1}; ^{1}H 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$_2$Ph), 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); LRESIMS: Found, *m*/z 733.3; required, 733.9 [M+Na]$^+$.

3.1.17. Methyl 2,3,4-tri-*O*-*p*-methoxybenzyl-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%); $[\alpha]_D$ 4.8 (*c* 0.05, $CHCl_3$); FTIR (KBr): 2939, 1586, 1464, 883, 821, 760, 683 cm^{-1}; ^{1}H 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$_2$PH), 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); LRESIMS: Found, *m*/z 733.3; required, 733.9 [M+Na]$^+$.

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

Compound **7a** (4.0 g, 5.5 mmol) was dissolved in anhyd THF (100 mL), and the solution was cooled to 0 °C. Tetrabutylammonium fluoride (1.4 g, 5.5 mmol) was added, and the solution was allowed to warm 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 anhyd DMF (100 mL). 1-Chlorododecane (1.8 mL, 11 mmol) was added, and the solution was cooled to 0 °C before NaH (0.11 g, 2.75 mmol) was added portionwise. The mixture was then allowed to warm to room temperature and was stirred for 24 h. MeOH (50 mL) was added to quench the reaction, and the mixture 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%); $[\alpha]_D$ −8.6 (*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$_3$); LRESIMS: Found, *m*/z 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*-parametoxybenzyl-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%); $[\alpha]_D$ 2 (*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 $OCH_2C_{11}H_{23}$), 1.29–1.24 (ms, 20H, aliphatic $OCH_2C_{10}H_{20}CH_3$), 0.88 (t, 3H, *J* 7.0, aliphatic $OC_{11}H_{22}CH_3$); ^{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_2Ph), 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); LRESIMS: Found, *m/z* 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 3:1 MeCN–H_2O (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 the residue was purified by chromatography (petroleum ether–EtOAc) to give **9a** (0.53 g, 73%); $[\alpha]_D$ 78.8 (*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); LRESIMS: Found, *m/z* 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%); $[\alpha]_D$–1 (*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); LRESIMS: Found, *m/z* 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 anhyd MeCN (25 mL) was stirred for 24 h at room temperature. Me_3N (0.5 mL) was added to neutralise the solution, and the mixture 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 anhyd DMF (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 overnight. MeOH (10 mL) was added to quench the reaction, and the mixture was stirred for a further 1 h.[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, *CH*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, *CH*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); LRESIMS: Found, *m/z* 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 anhyd pyridine (70 mL). 4-Dimethylaminopyridine (DMAP, catalytic amt) and lauroyl chloride (3.3 mL, 14.4 mmol) were added, and the reaction was stirred at room temperature for 3 h.[26] The solution was then concentrated under diminished pressure, and the crude product was 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, OCH_2Ph), 4.73 (AB d, 2H, *J* 12.0, OCH_2Ph), 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 $OCOCH_2C_{10}H_{21}$), 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 a hydrogen atmosphere of 2 psi until all protecting groups had been removed (TLC) to yield **12a**. The suspension was filtered and concentrated in vacuo[27] to give **12a** (0.47 g, 75%). $[\alpha]_D$ 4.33 (*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 $OCOCH_2C_{10}H_{21}$), 1.68–1.55 (m, 4H, each aliphatic $OCOCH_2CH_2C_9H_{19}$), 1.30–1.26 (multiple signals, 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 173.63, 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); LRESIMS: Found, *m/z* 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 (DMAP, catalytic amt) were dissolved in anhyd pyridine (50 mL) and stirred at 50 °C for 24 h.[26] The solution was then concentrated in vacuo, and the following mono-*O*-lauroyl **14** and di-*O*-lauroyl **15** products were isolated by chromatography (petroleum ether–EtOAc). A tetra-*O*-lauroyl derivative was also isolated (0.39 g, 6%):

3.1.25. Mono-*O*-lauroyl pentaerythritol (14)

Yield: 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 × CH_2OH, 3 × 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); LRESIMS: Found *m/z* 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-*O*-lauroyl pentaerythritol (15)

Yiled: 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); LRESIMS: Found *m/z* 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-*O*-lauroyl pentaerythritol

Yield: 0.39 g (6%); FTIR (KBr): 2917, 2849, 1735, 1336, 1299, 1250, 1154, 1111, 1002 cm^{-1}; ^1H 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); LRESIMS: Found *m/z* 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 antimicrobial activity

3.2.1. Preparation of bacterial cultures

Bacteria used in this study were *S. aureus* ATCC 25923 and *E. 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 °C 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 1×10^8 cfu/mL. This suspension was then serially diluted in TSB to obtain a working concentration of 1×10^6 cfu/mL.

3.2.2. Antimicrobial activity assay

Stock solutions (100 mmol) of test compounds and standards were prepared in sterile aqueous-alcoholic diluent (1:1 EtOH–distilled H_2O) 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. Freshly prepared inoculum (100 μL) of the organism under study was added to each appropriate well. The final concentration of each microorganism in each well was $\sim 5 \times 10^5$ 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 EtOH used to dissolve the test compound, thereby assessing any activity of the alcohol. The 96-well plates were incubated at 35 °C for 18 h 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 min with 20 s 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 h. Subtraction of the absorbance of the negative control eliminated interferences due to variation in the media.

Acknowledgements

We thank Geraldine Fitzpatrick, Dr. Ken Glass and Dr. Yannick Ortin, NMR Center UCD, and Dr. Dilip Rye, Mass Spectroscopy Centre UCD for spectra. Funding for this project was provided by TSR Strand I Grant.

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