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

Aoife Smith

Technological University Dublin, Aoife.Smith@tudublin.ie

Patricia Nobmann

Technological University Dublin, Patricia.Nobmann@tudublin.ie

Gary Henehan

Technological University Dublin, gary.henehan@tudublin.ie

See next page for additional authors

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Authors

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

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

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

4 School of Food Science & Environmental Health, Dublin Institute of Technology.

5 Cathal Brugha Street, Dublin 1, Ireland.

6

7 **Abstract**

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

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19 **Keywords**

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

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1. Introduction

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

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

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

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

1 The most common carbohydrate fatty acid ester utilised to date is sucrose ester. They
2 are commercially available and used for a variety of food applications. Kato and
3 Shibasaki (1975) showed that the sucrose ester of lauric acid had potent antimicrobial
4 activity against certain Gram-positive bacteria and fungi. They further showed that,
5 in contrast to findings with glycerides, the diester of sucrose was more active, than the
6 monoester. Of the diesters tested, sucrose dicaprylate showed the highest activity.¹³
7 Other oligosaccharide fatty acid esters, including maltose and maltotriose, have been
8 synthesised. These sugar esters were shown to inhibit the growth of *Streptococcus*
9 *sobrinus*, and are therefore potentially of significant value in the development of oral-
10 hygiene products.¹⁴ One study investigating the effect of carbohydrate monoesters
11 reported that among those synthesised, galactose laurate, fructose laurate and the
12 reducing 6-*O*-lauroylmannose showed the highest inhibitory effect against
13 *Streptococcus mutans*, while other analogs of hexose laurates showed no activity.¹⁵
14 This finding strongly suggests that the carbohydrate moiety can markedly affect the
15 antimicrobial activity of the fatty acid and therefore further investigation is merited.
16 Recent work in the area of carbohydrate fatty acid esters has focused on establishing
17 an effective regioselective, enzyme catalysed, synthesis of sugar derivatives for use as
18 surfactants for industrial applications,^{16,17,18,19,20} however relatively few studies have
19 examined role of the carbohydrate in antimicrobial activity.^{14,21,22}
20 This study is concerned with the synthesis of carbohydrate and polyhydroxylated non-
21 carbohydrate fatty acid derivatives for evaluation as antibacterial agents, with a view
22 to examining the effect of variation of the hydrophilic moiety on antimicrobial
23 activity. Therefore, we designed chemical syntheses to investigate the effects of
24 carbohydrate versus non-carbohydrate hydrophilic cores, the number of fatty acids
25 attached to the hydrophilic core, the monosaccharide core itself (and the anomeric

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

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

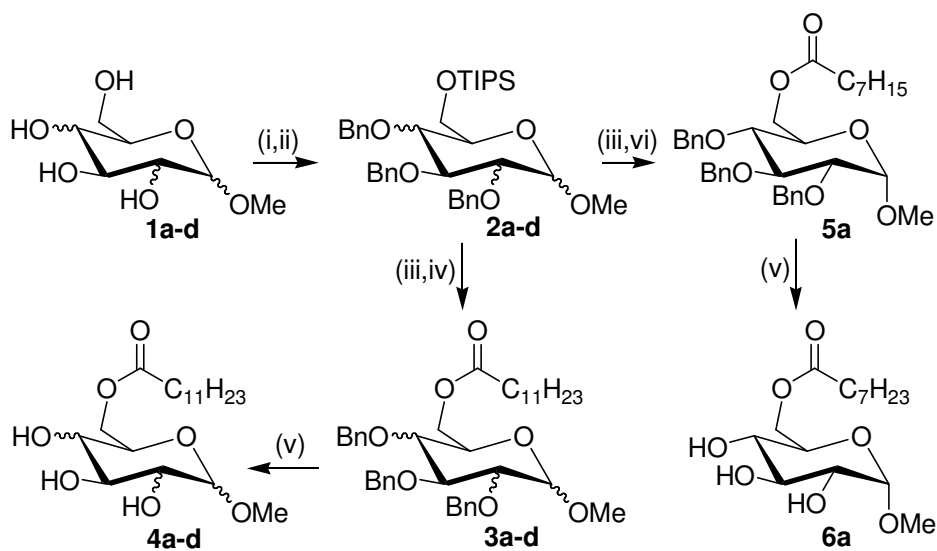
6 Enzymatic synthesis of novel sugar fatty acid esters has been widely employed and
7 can be highly regioselective, although for some carbohydrates minor regiomer
8 isomers may be obtained. For this study, we have developed a chemical route to allow
9 us synthesise a number of pure, regio-defined, monosaccharide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

17 **2. Results and Discussion**

18 **2.1 Synthesis**

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

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



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6 **Scheme 1** Reagents and Conditions: (i) DMF anhydr., TIPSCl, imidazole, rt. (ii) DMF anhydr., NaH,
7 BnBr, rt. (iii) THF anhydr., 0 °C, TBAF, rt. (iv) Pyr anhydr., DMAP, Lauroyl Cl, rt. (v) EtOH, Pd-C,
8 H₂. (vi) Pyr anhydr., DMAP, Octanoyl Cl, rt.

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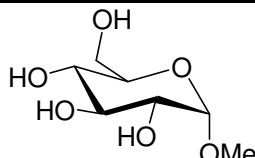
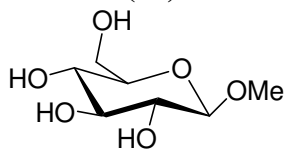
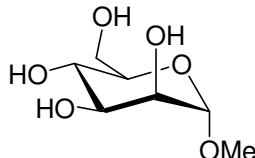
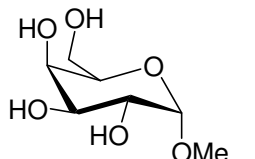
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Table 1 Percentage yields of compounds **2a-d**, **3a-d**, **4a-d**, **5a** and **6a**.

<i>Carbohydrate</i> (1)	<i>2,3,4-tri-O-Bn-6-O-TIPS</i> (2)	<i>2,3,4-tri-O-Bn-6-O-lauroyl</i> (3)	<i>6-O-lauroyl</i> (4)	<i>2,3,4-tri-O-Bn-6-O-octanoyl</i> (5)	<i>6-O-octanoyl</i> (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%		

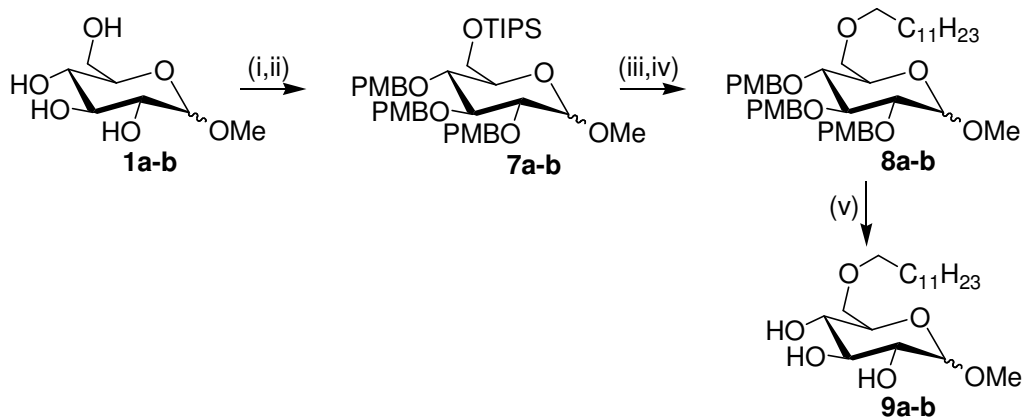
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7 Synthesis of the ether derivatives also commenced with the protection of the primary
8 hydroxyl with a triisopropylsilyl group (**Scheme 2**). The sugars were then fully
9 protected using paramethoxybenzyl chloride (PMB), to yield **7a-b**. Removal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

1 oxidative cleavage of the PMB groups with CAN gave the mono-dodecanyl sugars

2 **9a-b**.

3



5

6 **Scheme 2** Reagents and Conditions: (i) DMF anhydr., TIPSCl, imidazole, rt. (ii) DMF anhydr., THF

7 anhydr., 0 °C, NaH, PMBCl, TBAI, rt. (iii) THF anhydr., 0 °C, TBAF, rt. (iv) DMF anhydr., dodecanyl

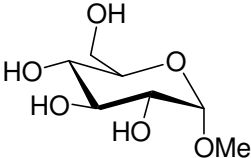
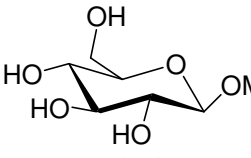
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chloride, 0 °C, NaH, rt. (v) MeCN:H₂O 3:1, CAN, rt.

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

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

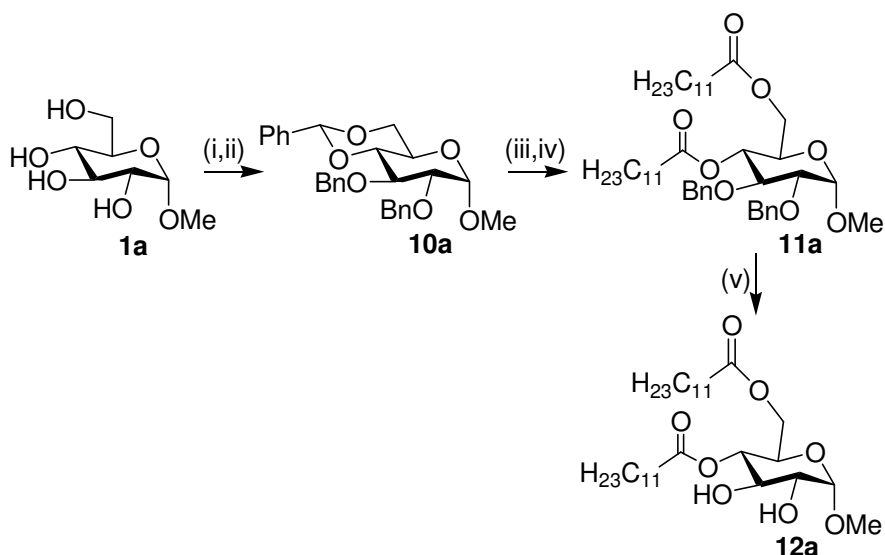
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12 The method used to synthesise di-lauroyl derivative **12a** is shown in **Scheme 3**. The 4

13 and 6-OH positions of methyl α -D-glucopyranoside **1a** were protected with a

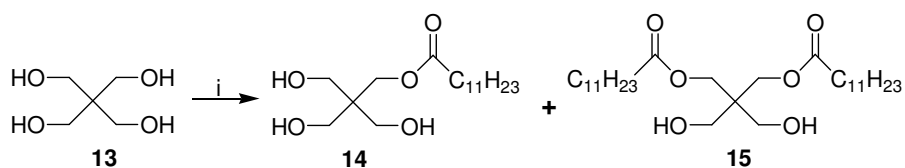
benzylidene group using benzaldehyde dimethylacetal. The remaining free OH's

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



5
 6 **Scheme 3.** Reagents and Conditions: (i) pTSA, PhCH(OMe)₂, MeCN anhydr., rt. (ii) DMF anhydr.,
 7 NaH, BnBr, rt. (95% yield over 2 steps) (iii) MeOH, TsOH. (iv) Pyr anhydr., DMAP, Lauroyl Cl, rt.
 8 (38% yield over 2 steps) (v) EtOH, Pd/, H₂. (75% yield)

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



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

15 2.2 Antimicrobial activity of fatty acid derivatives

16 Two non-carbohydrate polyhydroxylated fatty acid ester derivatives, six carbohydrate
 17 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

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

* Not determined due to insolubility

12

1 The data in **Table 3** show that the monoglycerides monolaurin and monocaprylin, had
2 greater activity compared to the free fatty acids lauric acid and caprylic acid against *S.*
3 *aureus*. Of the monoglycerides and free fatty acids tested, monolaurin had the lowest
4 MIC values for *S. aureus*, with a value of 0.04 mM compared to a value of 0.63 mM
5 for lauric acid. Furthermore, monocaprylin showed MIC values of 2.5 mM against *S.*
6 *aureus* compared to the value of 5.0 mM for caprylic acid. With respect to *E. coli*,
7 monolaurin showed less inhibitory effect than lauric acid with values of 20 mM and
8 10 mM respectively. In contrast, monocaprylin showed activity against *E. coli* at
9 concentrations of 6.25 mM compared with caprylic acid value of 12.5 mM.

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

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

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

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

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6 **2.3 Discussion**

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

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

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

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

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

6 With regard to the influence of different sugar cores, the results showed that the lauric
7 ester derivative of methyl α -D-mannopyranoside **4c** and methyl β -D-glucopyranoside
8 **4b**, showed higher activity than any other ester derivatives against *S. aureus*,
9 supporting the observation that the nature of the carbohydrate is involved in the
10 antimicrobial efficacy of the derivatives. This conclusion is consistent with results of
11 an earlier study by Watanabe *et al.*¹⁵

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

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

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

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

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

13 **3. Experimental**

14 **3.1 Synthesis**

15 **3.1.1 General methods**

16 All air and moisture-sensitive reactions were performed under an inert nitrogen
17 atmosphere. All reactions performed under a hydrogen atmosphere were performed
18 in a Parr Hydrogenator Apparatus. Anhydrous DMF, THF, Pyridine and MeCN were
19 purchased from Sigma Aldrich. TLC was performed on aluminium sheets precoated
20 with Silica Gel 60 (HF₂₅₄, Fluka) and spots visualised by UV and charring with
21 H₂SO₄-EtOH (1:20). Flash Column Chromatography was carried out with Silica Gel
22 60 (0.040-0.630 mm, E. Merck) and using stepwise solvent polarity gradient
23 correlated with TLC mobility. Chromatography solvents used were EtOAc (Riedel-
24 deHaen), MeOH (Riedel-deHaen) and petroleum ether (b.p. 40-60 °C, Fluka). Optical
25 rotations were determined with an AA-% Series Optical Activity Ltd Polarimeter.

1 NMR spectra were recorded with Varian Inova 300 and Varian NMRAS 400
2 spectrometers. Chemical shifts are reported relative to internal Me₄Si in CDCl₃ (δ
3 0.0) for ¹H and CDCl₃ (δ 77.0) for ¹³C. Coupling constants are reported in hertz.
4 FTIR spectra were recorded with a Nicolet FT-IR 5DXB infrared spectrometer,
5 samples were prepared in a KBr matrix. Low resolution mass spectra were measured
6 on a Quatromicro tandem quadrupole mass spectrometer. Methyl- α -D-
7 glucopyranoside, methyl- β -D-glucopyranoside, methyl- α -D-mannopyranoside,
8 methyl- α -D-galactopyranoside, pentaerythritol, 1-chlorododecane, lauroyl chloride
9 and octanoyl chloride were purchased from Sigma Aldrich.

10 **3.1.2 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl- α -D-glucopyranoside (2a)**

11 A solution of **1a** (5 g, 25 mmol) in DMF anhydrous (120 mL) was treated with
12 triisopropylsilyl chloride (15 mL, 75 mmol) and imidazole (5 g, 75 mmol) and
13 allowed to stir at room temperature for 24 h. The crude TIPS protected intermediate
14 was then concentrated *in vacuo* and dissolved in EtOAc. It was washed with 10%
15 HCl, water, followed by sat. aq. NaHCO₃, and finally sat. aq. NaCl. It was then dried
16 over anhydrous MgSO₄, and concentrated under reduced pressure.²³ The crude
17 product was dissolved in DMF anhydrous (50 mL) and cooled to 0 °C. NaH (5 g, 125
18 mmol) was added portion wise, BnBr (9 mL, 75 mmol) was added and the mixture
19 was allowed to warm to room temperature and stir for 24 h. MeOH (50 mL) was
20 added to quench the mixture which was stirred for 1 h. The fully protected sugar was
21 then concentrated *in vacuo* and dissolved in EtOAc. The solution was washed with
22 water, dried over anhydrous MgSO₄, and concentrated under diminished pressure.²⁴
23 The resulting residue was purified by chromatography (petroleum ether-EtOAc) to
24 give **2a** (13.2 g, 85%); [α]_D 10.7° (*c* 0.07, CHCl₃); FTIR (KBr): 2923, 1733, 1498,
25 1455, 909, 884, 791, 695 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.27 (ms, 15H,

1 aromatic H), 4.91, (AB d, 2H, J 11.0, OCH_2Ph), 4.78, (AB d, 2H, J 11.0, OCH_2Ph),
2 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,
3 $J_{3,4}$ 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
4 (overlapping signals, 2H, H-2,4), 3.37 (s, 3H, OCH_3), 1.10-1.02 (ms, 18H, each TIPS
5 CH_3), 0.88 (m, 3H, each TIPS CH); ^{13}C NMR (CDCl_3): δ 139.1, 138.7, 138.5 (each s,
6 each aromatic C), 128.65, 128.63, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8 (each d,
7 each aromatic CH), 98.0 (d, C-1), 82.5, 80.5, 78.1, 76.1 (each d), 76.1, 75.3, 73.6
8 (each t, each CH_2Ph), 62.9 (t, C-6), 55.0 (q, OCH_3), 18.3, 18.2 (each q, each TIPS
9 CH_3), 12.2 (each d, each TIPS CH); LRMS: Found, 643.3; required, 643.9; $[\text{M} +$
10 $\text{Na}]^+$.

11 **3.1.3 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl- β -D-glucopyranoside (2b)**

12 Treatment of **1b** (4.5 g, 23.17 mmol) as described for **1a** gave **2b** (8.7 g, 80%); $[\alpha]_{\text{D}}$
13 23° (c 0.01, CHCl_3); FTIR (KBr): 2863, 1730, 1497, 1454, 1399, 1277, 882, 802, 751,
14 697. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.37-7.28 (ms, 15H, aromatic H), 4.90,
15 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
16 (overlapping signals, 3H, H-5,6), 3.66 (m, 1H, H-3), 3.53 (s, 3H, OCH_3), 3.41 (m, 1H,
17 H-2), 3.34 (m, 1H, H-4), 1.26-1.05 (ms, 21H, TIPS); ^{13}C NMR (CDCl_3): δ 138.98,
18 138.92, 138.7 (each s, each aromatic C), 128.69, 128.65, 128.62, 128.5, 128.3, 128.2,
19 128.0, 127.9, 127.8 (each d, each aromatic CH), 104.7 (d, C-1), 84.9, 82.9, 77.8, 76.2
20 (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,
21 18.2 (each q, each TIPS CH_3), 12.3 (d, TIPS CH); LRMS: Found, 643.3 required,
22 643.9 $[\text{M} + \text{Na}]^+$.

23 **3.1.4 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl- α -D-mannopyranoside (2c)**

24 Treatment of **1c** (4 g, 20 mmol) as described for **1a** gave **2c** (6.5 g, 51%); $[\alpha]_{\text{D}}$ 25.5° (c
25 0.05, CHCl_3); FTIR (KBr): 3056, 2864, 1496, 1363, 1324, 970, 882, 790, 734, 696

1 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.38-7.24 (multiple signals, 15H, each aromatic
2 H), 4.79 (AB d, 2H, *J* 11.0, OCH₂Ph), 4.72 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.71-4.64
3 (overlapping signals, 3H, OCH₂Ph, H-1), 3.95 (dd, 1H, *J*_{2,3} 2.0, *J*_{3,4} 11.0, H-3), 3.93-
4 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 5.5, *J* 7.0, H-5), 3.31 (s, 3H, OMe), 1.12-1.04 (multiple signals, 21H, TIPS); ¹³C
6 NMR (CDCl₃): δ 138.68, 138.61, 138.4 (each s, each aromatic C), 128.3, 128.2,
7 127.9, 127.67, 128.63, 127.5, 127.4 (each d, each aromatic CH), 98.5 (d, C-1), 80.3,
8 76.7, 74.9, 73.3 (each d), 75.1, 72.5, 72.1 (each t, each CH₂Ph), 63.2 (t, C-6), 54.4 (q,
9 OMe), 18.0, 17.9 (each q, each TIPS CH₃), 12.3 (each d, each TIPS CH₂); LRMS:
10 Found, 638.5 required, 638.9; [M + H₂O]⁺.

11 **3.1.5 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl- α -D-galactopyranoside**

12 **(2d)**

13 Treatment of **1d** (4.0 g, 20.0 mmol) as described for **1a** gave **2d** (6.4 g, 50%); [α]_D
14 20.6° (*c* 0.07, CHCl₃); FTIR (KBr): 3030, 2865, 1496, 1454, 1350, 1194, 1054, 882,
15 793, 734, 696 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ; 7.41-7.22 (multiple signals, 15H,
16 each aromatic H), 4.82 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.71 (AB d, 2H, *J* 11.5,
17 OCH₂Ph), 4.77 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.68 (d, 1H, *J*_{1,2} 3.5, H-1), 4.04 (dd, 1H,
18 *J*_{2,3} 10.0, H-2), 3.95-3.92 (overlapping signals, 2H, H-3,5), 3.74-3.64 (overlapping
19 signals, 3H, H-4,6), 3.36 (s, 3H, OMe), 1.12-0.86 (multiple signals, 21H, TIPS); ¹³C
20 NMR (CDCl₃): δ 137.9, 137.7, 137.5 (each s, each aromatic C), 127.33, 127.28,
21 127.22, 127.15, 127.06, 126.62, 126.48, 126.45 (each d, each aromatic CH), 97.6 (d,
22 C-1), 78.1, 75.4, 74.0, 70.1 (each d), 73.7, 72.5, 72.2 (each t, each CH₂Ph), 61.4 (t, C-
23 6), 54.1 (q, OMe), 16.94, 16.93 (each q, each TIPS CH₃), 10.8 (each d, each TIPS
24 CH₂); LRMS: Found, 638.5 required, 638.9; [M + H₂O]⁺.

25 **3.1.6 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl- α -D-glucopyranoside (3a)**

1 Compound **2a** (3.0 g, 4.8 mmol) was dissolved in THF anhydrous (80 mL) and was
2 cooled to 0 °C. Tetrabutylammonium fluoride (1 g, 4 mmol) was added and the
3 solution was allowed to warm to room temperature and stir for 1 h.²⁵ It was then
4 concentrated *in vacuo* and approximately 1 mmol of the resulting 6-OH residue was
5 dissolved in pyridine anhydrous (25 mL). 4-Dimethylaminopyridine and lauroyl
6 chloride (0.29 mL, 1.22 mmol) were added and the solution was allowed to stir at
7 room temperature for 24 h.²⁶ It was then concentrated under reduced pressure and the
8 resulting benzylated ester derivative was purified by chromatography (petroleum
9 ether-EtOAc) to give **3a** (0.47 g, 72%); $[\alpha]_D$ 7.5° (*c* 0.02, CHCl₃); FTIR (KBr): 2924,
10 2853, 1738, 1603, 1502, 1454, 1249, 1072 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.35-
11 7.26 (ms, 15H, aromatic H), 4.92, (AB d, 2H, *J* 10.5, OCH₂Ph), 4.72, (AB d, 2H, *J*
12 10.5, OCH₂Ph), 4.64 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.59 (d, 1H, *J*_{1,2} 3.5, H-1), 4.27
13 (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}
14 10.0, H-5), 3.53 (dd, 1H, H-2), 3.48 (apt t, 1H, H-4) 3.37 (s, 3H, OCH₃), 2.35 (m, 2H,
15 aliphatic OCOCH₂C₁₀H₂₁), 1.61 (m, 2H, aliphatic OCOCH₂CH₂C₉H₁₉), 1.28-1.24
16 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.87 (m, 3H, aliphatic OCOC₁₀H₂₀CH₃);
17 ¹³C NMR (CDCl₃): δ 171.1 (s, C=O), 138.6, 138.1, 137.9 (each s, each aromatic C),
18 128.5, 128.48, 128.46, 128.1, 128.03, 127.98, 127.90, 127.7 (each d, each aromatic
19 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
20 CH₂Ph), 60.4 (t, C-6), 55.2 (q, OCH₃), 34.2, 31.9, 29.8, 29.6, 29.5, 29.3, 29.2, 24.9,
21 22.7, 21.1 (each t, each aliphatic CH₂), 14.2 (q, aliphatic CH₃); LRMS: Found,
22 669.39; required, 669.85; [M + Na]⁺; Anal. Calcd. for C₄₀H₅₄O₇: C, 74.27; H, 8.41.
23 Found: C, 73.98; H, 8.30.

24 3.1.7 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl-β-D-glucopyranoside (**3b**)

1 Treatment of **2b** (3.0 g, 4.8 mmol) as described for **2a** gave **3b** (2.2 g, 70%); $[\alpha]_D$ 8.3°
2 (*c* 0.03, CHCl₃); FTIR (KBr): 2924, 2853, 1739, 1497, 1454, 1356, 1151, 1070, 735
3 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.24 (ms, 15H, aromatic H), 4.87, 4.84,
4 4.72 (each AB d, 6H, *J* 10.5, OCH₂Ph), 4.37 (d, 2H, *J*_{5,6} 11.5, H-6a,6b), 4.31 (d, 1H,
5 *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,
6 OCH₃), 3.54 (m, 1H, H-4), 3.43 (dd, 1H, H-2), 2.32 (m, 2H, aliphatic
7 OCOCH₂C₁₀H₂₁), 1.62 (m, 2H, aliphatic OCOCH₂CH₂C₉H₁₉), 1.26-1.24 (ms, 16H,
8 each aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 3H, *J* 6.0, *J* 7.0, aliphatic
9 OCOC₁₁H₂₃CH₃); ¹³C NMR (CDCl₃): δ 173.6 (s, C=O), 138.43, 138.42, 137.8 (each
10 s, each aromatic C), 128.8, 128.5, 128.4, 128.38, 128.34, 128.26, 128.11, 128.07,
11 127.97, 127.92, 127.8, 127.7, 127.69, 127.64, 127.5 (each d, each aromatic CH),
12 104.7 (d, C-1), 84.6, 82.3, 77.6, 72.9 (each d), 75.7, 75.1, 74.8 (each t, each OCH₂Ph),
13 62.9 (t, C-6), 57.1 (q, OCH₃), 34.2, 31.9, 29.6, 29.5, 29.3, 29.2, 29.1, 24.9, 24.7, 22.6
14 (each t, each aliphatic CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 669.2 required,
15 669.9 [M + Na]⁺; Anal. Calcd. for C₄₀H₅₄O₇: C, 74.27; H, 8.41. Found: C, 73.91; H,
16 8.79.

17 **3.1.8 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl- α -D-mannopyranoside (**3c**)**

18 Treatment of **2c** (6.2 g, 10.0 mmol) as described for **2a** gave **3c** (4.1 g, 64%); $[\alpha]_D$
19 23.3° (*c* 0.04, CHCl₃); FTIR (KBr): 3031, 2924, 2853, 1737, 1496, 1454, 1362, 1066,
20 1027, 970, 909, 735, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.38-7.25 (multiple
21 signals, 15H, each aromatic H), 4.77 (AB d, 2H, *J* 10.5, OCH₂Ph), 4.74 (d, 1H, *J*_{1,2}
22 2.0, H-1), 4.72 (AB d, 2H, *J* 12.5, OCH₂Ph), 4.61 (s, 2H, OCH₂Ph), 4.38 (dd, 1H, *J*_{5,6a}
23 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,
24 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,
25 2H, *J* 7.5, *J* 7.5, aliphatic OCOCH₂C₁₀H₂₁), 1.61 (m, 2H, aliphatic

1 OCOCH₂CH₂C₉H₁₉), 1.31-1.54 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.91-0.86
2 (m, 3H, aliphatic OCOC₁₀H₂₀CH₃); ¹³C NMR (CDCl₃): δ 173.7, (s, C=O), 138.32,
3 138.21, 138.17 (each s, each aromatic C), 128.4., 128.38, 128.33, 128.05. 127.90,
4 127.76, 127.63, 127.23 (each d, each aromatic CH), 98.9 (d, C-1), 75.2, 74.6, 74.4,
5 69.9 (each d), 80.1, 72.6, 72.1 (each t, each CH₂Ph), 63.3 (t, C-6), 54.8 (q, OCH₃),
6 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,
7 22.7, 21.1 (each t, each aliphatic CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 664.6
8 required, 664.9; [M + H₂O]⁺; Anal. Calcd. for C₄₀H₅₄O₇: C, 74.27; H, 8.41. Found: C,
9 74.35; H, 8.25.

10 **3.1.9 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-lauroyl- α -D-galactopyranoside (3d)**

11 Treatment of **2d** (5.7 g, 9.2 mmol) as described for **2a** gave **3d** (3.6 g, 60%); [α]_D
12 27.8° (c 0.09, CHCl₃); FTIR (KBr): 3030, 2924, 2853, 1738, 1496, 1454, 1350, 1099,
13 1049, 735, 696 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.41-7.23 (multiple signals, 15H,
14 each aromatic H), 4.83 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.81 (AB d, 2H, *J* 11.5,
15 OCH₂Ph), 4.77 (AB d, 2H, *J* 12.0, OCH₂Ph), 4.68 (d, 1H, *J*_{1,2} 3.5, H-1), 4.16 (dd, 1H,
16 *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*
17 10.0 H-6a), 3.86-3.84 (overlapping signals, 2H, H-3,6b), 3.35 (s, 3H, OMe), 2.23 (m,
18 2H, aliphatic OCOCH₂C₁₀H₂₁), 1.57 (m, 2H, aliphatic OCOCH₂CH₂C₉H₁₉), 1.31-1.18
19 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic
20 OCOC₁₀H₂₀CH₃); ¹³C NMR (CDCl₃): δ 173.4 (s, C=O), 138.7, 138.4, 138.2 (each s,
21 each aromatic C), 128.42, 128.36, 128.32, 128.11, 127.90, 127.75, 127.59, 127.51,
22 127.21 (each d, each aromatic CH), 98.7 (d, C-1), 78.9, 76.3, 74.9, 68.4 (each d), 74.6,
23 73.63, 73.54 (each t, each CH₂Ph), 63.3 (t, C-6), 55.3 (q, OCH₃), 34.1, 33.8, 31.9,
24 29.359, 29.45, 29.32, 29.26, 29.12, 24.9, 24.8, 22.7 (each t, each aliphatic CH₂), 14.1

1 (q, aliphatic CH₃); LRMS: Found, 664.6 required, 664.9; [M + H₂O]⁺; Anal. Calcd.
2 for C₄₀H₅₄O₇: C, 74.27; H, 8.41. Found: C, 74.67; H, 8.68.

3 **3.1.10 Methyl 6-*O*-lauroyl- α -D-glucopyranoside (4a)**

4 Compound **3a** (0.34 g, 0.2 mmol) was dissolved in EtOH (1 mL) and Pd-C (0.1 g)
5 was added. The mixture was allowed to shake under hydrogen atmosphere of 2 psi
6 until all protecting groups had been removed, as shown by TLC, to yield **4a**. The
7 suspension was filtered and concentrated *in vacuo*.²⁷ (0.17 g, 86%); [α]_D 19° (*c* 0.02,
8 CHCl₃); FTIR (KBr): 3734, 3445, 2955, 2924, 2850, 2359, 2341, 1728. cm⁻¹; ¹H
9 NMR (400 MHz, CDCl₃): δ 4.75 (d, 1H, *J*_{1,2} 3.5, H-1), 4.33 (m, 2H, H-6), 3.75-3.73
10 (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,
11 *J*_{2,3} 9.5, H-2), 3.41 (s, 3H, OMe), 2.35 (t, 2H, *J* 7.5, aliphatic OCOCH₂C₁₀H₂₁), 1.63
12 (m, 2H, aliphatic OCOCH₂CH₂C₉H₁₉), 1.38-1.23 (ms, 16H, aliphatic
13 OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 3H, *J* 7.0, aliphatic OCOC₁₀H₂₀CH₃); ¹³C NMR
14 (CDCl₃): 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),
15 55.2 (q, OCH₃), 34.2, 31.9, 29.66, 29.64, 29.5, 29.4, 29.3, 29.2, 24.9, 22.7 (each t,
16 each aliphatic CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 399.3 required, 399.5; [M
17 + Na]⁺; Anal. Calcd. for C₁₉H₃₆O₇: C, 60.61; H, 9.64. Found: C, 60.69; H, 9.83.

18 **3.1.11 Methyl 6-*O*-lauroyl- β -D-glucopyranoside (4b)**

19 Treatment of **3b** (2.0 g, 3.0 mmol) as described for **3a** gave **4b** (0.86 g, 75%); [α]_D -
20 25.5° (*c* 0.05, CHCl₃); FTIR (KBr): 3421, 2921, 1744, 1703, 1016 cm⁻¹; ¹H NMR (400
21 MHz, CDCl₃): 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,
22 *J*_{5,6} 7.5, H-6), 3.54 (s, 3H, OCH₃), 3.49 (m, 1H, H-3), 3.39-3.31 (overlapping signals,
23 2H, H-4,5), 2.34 (m, 2H, aliphatic OCOCH₂C₁₀H₂₁), 2.02 (s, 3H, OH), 1.62 (m, 2H,
24 aliphatic OCOCH₂CH₂C₉H₁₉), 1.28-1.26 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃),
25 0.88 (t, 3H, *J* 6.5, aliphatic OCOC₁₀H₂₀CH₃); ¹³C NMR (CDCl₃): δ 174.2 (s, C=O),

1 103.6 (d, C-1), 76.5, 73.9, 73.4, 70.3 (each d), 63.6 (t, C-6), 57.0 (q, OCH₃), 34.2,
2 31.9, 29.61, 29.60, 29.5, 29.3, 29.2, 29.1, 24.9, 22.7 (each t, each aliphatic CH₂), 14.1
3 (q, aliphatic CH₃); LRMS: Found, 399.1 required, 399.5 [M + Na]⁺; Anal. Calcd. for
4 C₁₉H₃₆O₇: C, 60.61; H, 9.64. Found: C, 60.25; H, 9.91.

5 **3.1.12 Methyl 6-O-lauroyl- α -D-mannopyranoside (4c)**

6 Treatment of **3c** (3.3 g, 5.0 mmol) as described for **3a** gave **4c** (1.4 g, 75%); [α]_D
7 33.3° (c 0.01, CHCl₃); FTIR (KBr): 3421, 2923, 1736, 1466, 1197, 1057 cm⁻¹; ¹H
8 NMR (400 MHz, CDCl₃): δ 4.70 (s, 1H, H-1), 4.45 (br s, 1H, OH), 4.36 (d, 2H, *J* 4.0,
9 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-
10 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*
11 7.5, *J* 7.5, aliphatic OCOCH₂C₁₀H₂₁), 1.61 (m, 2H, aliphatic OCOCH₂CH₂C₉H₁₉),
12 1.29-1.25 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic
13 OCOC₁₀H₂₀CH₃); ¹³C NMR (CDCl₃): δ 174.7 (s, C=O), 100.9 (d, C-1), 71.5, 70.5,
14 70.4, 67.7 (each d), 63.9 (t, C-6), 54.9 (q, OCH₃), 34.2, 31.9, 29.7, 29.6, 29.5, 29.4,
15 29.36, 29.34, 29.19, 24.9, 22.7 (each t, each aliphatic CH₂), 14.1 (q, aliphatic CH₃);
16 LRMS: Found, 377.3 required, 377.5; [M + H]⁺; Anal. Calcd. for C₁₉H₃₆O₇: C, 60.61;
17 H, 9.64. Found: C, 60.71; H, 9.53.

18 **3.1.13 Methyl 6-O-lauroyl- α -D-galactopyranoside (4d)**

19 Treatment of **3d** (2.8 g, 4.4 mmol) as described for **3a** gave **4d** (1.43 g, 86%); [α]_D
20 56.25° (c 0.01, CHCl₃); FTIR (KBr): 3250, 2918, 1741, 1467, 1194, 1025cm⁻¹; ¹H
21 NMR (400 MHz, CDCl₃): δ 4.63 (apt t, 1H, *J* 6.5, *J* 5.0, OH-3), 4.57 (d, 1H, *J* 6.5,
22 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,
23 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
24 (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,
25 2H, *J* 7.5, aliphatic OCOCH₂C₁₀H₂₁), 1.63 (t, 2H, *J* 7.0, aliphatic

1 OCOCH₂CH₂C₉H₁₉), 1.28-1.23 (ms, 16H, aliphatic OCOC₂H₄C₈H₁₆CH₃), 0.85 (t, 3H,
2 *J* 7.0, aliphatic OCOC₁₀H₂₀CH₃); ¹³C NMR (CDCl₃): δ 178.2 (s, C=O), 104.8 (d, C-
3 1), 74.9, 74.1, 73.7, 73.1 (each d), 68.8 (t, C-6), 59.8 (q, OCH₃), 38.9, 36.5, 34.24,
4 34.10, 33.97, 33.93, 33.75, 29.5, 27.3, (each t, each aliphatic CH₂), 18.9 (q, aliphatic
5 CH₃); LRMS: Found, 399.3 required, 399.5; [M + Na]⁺; Anal. Calcd. for C₁₉H₃₆O₇: C,
6 60.61; H, 9.64. Found: C, 60.60; H, 9.88.

7 **3.1.14 Methyl 2,3,4-tri-*O*-benzyl-6-*O*-octanoyl- α -D-glucopyranoside (5a)**

8 Compound **2a** (5.0 g, 8.5 mmol) was dissolved in THF anhydrous (150 mL) and was
9 cooled to 0 °C. Tetrabutylammonium fluoride (2.2 g, 8.5 mmol) was added and the
10 solution was warmed to room temperature and stirred for 1 h.²⁵ The mixture was then
11 concentrated *in vacuo* and the resulting 6-OH residue was dissolved in pyridine
12 anhydrous (100 mL). 4-Dimethylaminopyridine and octanoyl chloride (2.9 mL, 17
13 mmol) was added and the mixture was stirred at room temperature for 24 h.²⁶ The
14 solution was then concentrated under reduced pressure and purified by
15 chromatography (petroleum ether-EtOAc) to give **5a** (3.9 g, 63%); [α]_D 20.8° (*c* 0.07,
16 CHCl₃); FTIR (KBr): 2927, 1738, 1497, 1454, 1360, 1163, 1093, 738, 697 cm⁻¹; ¹H
17 NMR (400 MHz, CDCl₃): δ 7.37-7.26 (ms, 15H, aromatic H), 4.93, (AB d, 2H, *J*
18 10.5, OCH₂Ph), 4.74, (AB d, 2H, *J* 12.0, OCH₂Ph), 4.73 (AB d, 2H, *J* 10.5, OCH₂Ph),
19 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,
20 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,
21 OCH₃), 2.31 (m, 2H, aliphatic OCOCH₂C₆H₁₃), 1.62 (m, 2H, aliphatic
22 OCH₂CH₂C₅H₁₁), 1.30-1.05 (ms, 8H, aliphatic OC₂H₄C₄H₈CH₃), 0.87 (m, 3H,
23 aliphatic OC₆H₁₂CH₃); ¹³C NMR (CDCl₃): δ 173.8 (s, C=O), 138.8, 138.3, 138.1
24 (each s, each aromatic C), 128.7, 128.6, 128.3, 128.29, 128.27, 128.3, 128.25, 128.20,
25 128.1 127.9 (each d, each aromatic CH), 98.3 (d, C-1), 82.2, 80.2, 77.8, 68.9 (each d),

1 76.1, 75.3, 73.6 (each t, each OCH₂Ph), 63.1 (t, C-6), 55.4 (q, OCH₃), 34.4, 31.9,
2 29.2, 25.0, 22.8, 17.9 (each t, each aliphatic CH₂), 14.3 (q, aliphatic CH₃); LRMS:
3 Found, 613.4 required, 613.7; [M + Na]⁺; Anal. Calcd. for C₃₆H₄₆O₇: C, 73.19; H,
4 7.85. Found: C, 73.25; H, 7.61

5 **3.1.15 Methyl 6-O-octanoyl- α -D-glucopyranoside (6a)**

6 Treatment of **5a** (3.6 g, 6.2 mmol) as described for **3a** gave **6a** (1.44 g, 73%); [α]_D
7 27.9° (c 0.4, CHCl₃); FTIR (KBr): 3388, 2922, 1712, 1465, 1193, 1106, 724 cm⁻¹; ¹H
8 NMR (400 MHz, CDCl₃): δ 5.82 (s, 3H, each OH), 4.76 (d, 1H, *J*_{1,2} 3.5, H-1), 4.35 (d,
9 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,
10 H-2), 3.41 (s, 3H, OCH₃), 3.36 (dd, 1H, *J*_{3,4} 9.5, *J*_{4,5} 10.0, H-4), 2.35 (m, 2H, aliphatic
11 COCH₂C₆H₁₃) 1.64 (t, 2H, *J* 7.0, aliphatic COCH₂CH₂C₅H₁₁), 1.31-1.05 (ms, 8H,
12 aliphatic COC₂H₄C₄H₈CH₃), 0.88 (t, 3H, *J* 5.5, *J* 7.0, aliphatic COC₆H₁₂CH₃); ¹³C
13 NMR (CDCl₃): δ 179.5 (s, C=O), 99.4 (d, C-1), 74.1, 72.0, 69.7, 70.3 (each d), 63.4
14 (t, C-6), 55.3 (q, OCH₃), 34.1, 31.7, 31.6, 29.9, 28.9, 24.8 (each t, each aliphatic
15 CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 343.1 required, 343.4; [M + Na]⁺; Anal.
16 Calcd. for C₁₅H₂₈O₇: C, 56.23; H, 8.81. Found: C, 56.47; H, 8.73.

17 **3.1.16 Methyl 2,3,4-tri-O-paramethoxybenzyl-6-O-triisopropylsilyl- α -D-** 18 **glucopyranoside (7a)**

19 A solution of **1a** (5.0 g, 25.0 mmol) in DMF anhydrous (120 mL) was treated with
20 triisopropylsilyl chloride (15 mL, 75 mmol) and imidazole (5 g, 75 mmol) and
21 allowed to stir at room temperature for 24 h. The crude TIPS protected intermediate
22 was then concentrated *in vacuo* and the resulting residue dissolved in EtOAc. It was
23 then washed with 10% HCl, water, followed by sat. aq. NaHCO₃, and finally sat. aq.
24 NaCl, before being dried over anhydrous MgSO₄, and concentrated under reduced
25 pressure.²³ The TIPS protected crude residue was then split in two and half was

1 dissolved in DMF anhydrous (30 mL) and THF anhydrous (20 mL). This solution
2 was then added dropwise at 0 °C to a suspension of NaH (2.5 g, 62.5 mmol) in DMF
3 anhydrous (10 mL) and THF anhydrous (7 mL), paramethoxybenzyl chloride (17 mL,
4 125 mmol) and tetrabutylammonium iodide (18.5 g, 50 mmol). This was stirred at
5 approximately 10 °C for 30 min and then allowed to warm to room temperature and
6 stir for 24 h. MeOH (50 mL) was added to quench the mixture which was stirred for
7 1 h. The solution was then concentrated under diminished pressure and dissolved in
8 EtOAc. It was washed with water, dried over anhydrous MgSO₄, and concentrated *in*
9 *vacuo*.²⁸ The resulting residue was purified by chromatography (petroleum ether-
10 EtOAc) to give **7a**. (5.15 g, 59%); [α]_D 11.6° (*c* 0.05, CHCl₃); FTIR (KBr): 3479,
11 2936, 2864, 1464, 1421, 1360, 1302, 883, 820. cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ
12 7.34-6.73 (ms, 12H, aromatic H), 4.88 (AB d, 2H, *J* 10.5 OCH₂Ph), 4.78 (d, 1H, *J*_{1,2}
13 5.0, H-1), 4.75, 4.71 (each AB d, 2H, *J* 12.0 OCH₂Ph), 4.63 (m, 1H, H-2), 3.99 (apt t,
14 1H, *J*_{3,4} 9.0, *J*_{4,5} 9.0, H-4), 3.89 (m, 2H, H6), 3.77 (m, 9H, each PhOCH₃), 3.57-3.49
15 (overlapping signals, 2H, H-3,5), 3.39 (s, 3H, OCH₃), 1.28 (m, 3H, each TIPS CH),
16 1.16-1.06 (ms, 18H, each TIPS CH₃); ¹³C NMR (CDCl₃): δ 159.6, 159.5, 159.4,
17 131.6, 131.4, 131.0 (each s, each aromatic C), 129.99, 129.93, 129.8, 114.13, 114.08,
18 113.6 (each d, each aromatic CH), 98.1 (d, C-1), 82.2, 80.2, 77.8, 72.1 (each d), 75.8,
19 74.9, 73.2 (each t, each OCH₂Ph), 63.1 (t, C-6), 55.47, 55.40, 55.36 (each q, each
20 PhOCH₃), 55.0 (q, OCH₃), 18.27, 18.25 (each q, each TIPS CH₃), 12.3 (d, each TIPS
21 CH); LRMS: Found, 733.3 required, 733.9 [M + Na]⁺.

22 **3.1.17 Methyl 2,3,4-tri-*O*-paramethoxybenzyl-6-*O*-triisopropylsilyl-β-D-**
23 **glucopyranoside (7b)**

24 Treatment of **1b** (4.5 g, 23.17 mmol) as described for **1a** gave **7b** (10.1 g, 61%); [α]_D
25 4.8° (*c* 0.05, CHCl₃); FTIR (KBr): 2939, 1586, 1464, 883, 821, 760, 683. cm⁻¹; ¹H

1 NMR (400 MHz, CDCl₃): δ 7.30-6.84 (ms, 12H, aromatic H), 4.85, 4.80, 4.73 (each
2 AB d, 2H, *J* 10.5, OCH₂Ph), 4.27 (d, 1H, *J*_{1,2} 7.5, H-1), 3.95 (m, 1H, H-6a), 3.87 (dd,
3 1H, *J*_{4,5} 11.0, *J*_{5,6} 4.5, H-5), 3.78 (m, 9H, PhOCH₃), 3.59 (m, 1H, H-3), 3.53 (s, 3H,
4 OCH₃) 3.36 (apt t, 1H, *J*_{2,3} 9.0, H-2), 3.29-3.24 (overlapping signals, 2H, H-4,6b),
5 1.10-1.04 (ms, 21H, TIPS); ¹³C NMR (CDCl₃): δ 159.5, 159.4, 131.2, 131.1, 130.9,
6 (each s, each aromatic C), 129.9, 129.8, 128.7, 114.1, 114.04, 114.01 (each d, each
7 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,
8 each OCH₂PH), 62.7 (t, C-6), 56.8 (q, OCH₃), 55.5 (each q, each PhOCH₃), 18.3, 18.2
9 (each q, each TIPS CH₃), 12.2 (d, each TIPS CH); LRMS: Found, 733.3; required,
10 733.9 [M + Na]⁺.

11 **3.1.18 Methyl 2,3,4-tri-*O*-paramethoxybenzyl-6-*O*-dodecanyl- α -D-**
12 **glucopyranoside (8a)**

13 Compound **7a** (4.0 g, 5.5 mmol) was dissolved in THF anhydrous (100 mL) and was
14 cooled to 0 °C. Tetrabutylammonium fluoride (1.4 g, 5.5 mmol) was added and the
15 solution was allowed to warm to room temperature and stir for 1 h.²⁵ The mixture
16 was then concentrated *in vacuo*, and the resulting 6-OH residue was dissolved in
17 DMF anhydrous (100 mL). 1-chlorododecane (1.8 mL, 11 mmol) was added and the
18 solution was cooled to 0 °C before NaH (0.11 g, 2.75 mmol) was added portion wise.
19 The mixture was then allowed to warm to room temperature and was stirred for 24 h.
20 MeOH (50 mL) was added to quench the solution which was stirred for 1 h.²⁹ The
21 crude PMB protected ether was then concentrated under diminished pressure and
22 purified by chromatography (petroleum ether-EtOAc) to give **8a** (1.89 g, 50%); [α]_D –
23 8.6° (*c* 0.06, CHCl₃); FTIR (KBr): 2924, 2854, 1613, 1586, 1464, 1359, 1301, 1248,
24 1172, 1037, 820 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 6.85-7.30 (ms, 12H, aromatic
25 H), 4.92 (d, 1H, *J*_{1,2} 10.5, H-1), 4.85 (AB d, 2H, *J* 10.5, OCH₂PhOCH₃), 4.74 (dd, 1H,

1 $J_{2,3}$ 9.5, H-2), 4.69, (AB d, 2H, J 10.5, $\text{OCH}_2\text{PhOCH}_3$), 4.60 (AB d, 2H, J 11.5
2 $\text{OCH}_2\text{PhOCH}_3$), 4.55 (apt t, 1H, $J_{3,4}$ 9.5, H-3), 3.95 (m, 1H, H-5), 3.80 (s, 9H, each
3 PhOCH_3), 3.53-3.37 (overlapping signals, 3H, H-4,6a,6b), 3.36 (s, 3H, OCH_3), 1.60
4 (m, 2H, aliphatic $\text{CH}_2\text{C}_{11}\text{H}_{23}$), 1.30-1.25 (ms, 20H, aliphatic $\text{CH}_2\text{C}_{10}\text{H}_{20}\text{CH}_3$), 0.89 (t,
5 3H, J 7.0, aliphatic $\text{C}_{11}\text{H}_{20}\text{CH}_3$); ^{13}C NMR (CDCl_3): δ 159.6, 159.5, 159.4, 131.3,
6 131.0, 130.6 (each s, each aromatic C), 130.0, 129.8, 129.6, 114.07, 114.05, 114.03
7 (each d, each aromatic CH), 98.5 (d, C-1), 82.1, 79.8, 77.7, 70.2 (each d), 75.7, 74.9,
8 73.3 (each t, each OCH_2Ph), 72.0 (t, aliphatic $\text{OCH}_2\text{C}_{11}\text{H}_{23}$), 69.5 (t, C-6), 55.5 (q,
9 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
10 (each t, each aliphatic CH_2), 14.4 (q, aliphatic CH_3); LRMS: Found, 745.5; required,
11 745.9; $[\text{M} + \text{Na}]^+$; Anal. Calcd. for $\text{C}_{43}\text{H}_{62}\text{O}_9$: C, 71.44; H, 8.64. Found: C, 71.09; H,
12 8.73.

13 **3.1.19 Methyl 2,3,4-tri-*O*-paramethoxybenzyl-6-*O*-dodecanyl- β -D-**
14 **glucopyranoside (8b)**

15 Treatment of **7b** (3.2 g, 4.5 mmol) as described for **7a** gave **8b** (0.55 g, 85%); $[\alpha]_{\text{D}}^{20}$
16 (c 0.01, CHCl_3); FTIR (KBr): 2923, 2851, 1614, 1464.40, 1421, 1359, 1302, 1254,
17 1173, 1072, 813 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.29-6.84 (ms, 12H, aromatic
18 H), 4.79, 4.75, 4.67 (each AB d, 2H, J 10.5, OCH_2Ph), 4.26 (d, 1H, $J_{1,2}$ 7.5, H-1),
19 3.79-3.58 (overlapping signals, 2H, H-3,5), 3.79 (m, 9H, PhOCH_3), 3.68 (m, 2H, H-
20 6a,6b), 3.56 (s, 3H, OCH_3), 3.43-3.39 (overlapping signals, 2H, H-2,4), 1.63 (m, 2H,
21 aliphatic $\text{OCH}_2\text{C}_{11}\text{H}_{23}$), 1.29-1.24 (ms, 20H, aliphatic $\text{OCH}_2\text{C}_{10}\text{H}_{20}\text{CH}_3$), 0.88 (t, 3H,
22 J 7.0, aliphatic $\text{OC}_{11}\text{H}_{22}\text{CH}_3$); ^{13}C NMR (CDCl_3): δ 159.3, 159.2, 159.1, 130.9, 130.8,
23 130.5 (each s, each aromatic C), 129.8, 129.6, 129.5, 113.8, 113.7 (each d, each
24 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,
25 each OCH_2Ph), 71.9 (t, aliphatic CH_2), 69.7 (t, C-6), 57.1 (q, OCH_3), 55.3, 55.2 (each

1 q, each PhOCH₃), 31.9, 29.7, 29.68, 29.65, 29.63, 29.5, 29.4, 26.2, 22.7 (each t, each
2 aliphatic CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 745.3; required, 745.9; [M +
3 Na]⁺; Anal. Calcd. for C₄₃H₆₂O₉: C, 71.44; H, 8.64. Found: C, 71.19; H, 8.70.

4 **3.1.20 Methyl 6-O-dodecanyl- α -D-glucopyranoside (9a)**

5 Compound **8a** (1.45 g, 2.0 mmol) was dissolved in a mixture of MeCN:H₂O (3:1) (21
6 mL) and ceric ammonium nitrate (8.85 g, 16.16 mmol) was added. The solution was
7 allowed to stir at room temperature for 24 h.³⁰ It was then concentrated *in vacuo* and
8 purified by chromatography (petroleum ether-EtOAc) to give **9a** (0.53 g, 73%); [α]_D
9 78.8° (*c* 0.04, CHCl₃); FTIR (KBr): 3416, 2919, 2851, 1467, 1372, 1128, 1043, 1019
10 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 4.98 (br s, 1H, OH), 4.75 (d, 1H, *J*_{1,2} 3.5, H-1),
11 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
12 (m, 2H, H-6), 3.54-3.44 (overlapping signals, 3H, H-2,4,5), 3.37 (s, 3H, OCH₃), 1.58
13 (m, 2H, aliphatic CH₂C₁₁H₂₃), 1.28-1.25 (ms, 20H, each aliphatic CH₂C₁₀H₂₀CH₃),
14 0.88 (t, 3H, *J* 6.5, *J* 7.0, aliphatic C₁₁H₂₀CH₃); ¹³C NMR (CDCl₃): δ 99.7 (d, C-1),
15 74.5, 72.3, 72.2, 71.2 (each d) 70.6 (t, aliphatic CH₂), 69.5 (t, C-6), 55.4 (q, OCH₃),
16 32.1, 29.9, 29.88, 29.86, 29.83, 29.7, 29.6, 26.3, 22.9 (each t, each aliphatic CH₂),
17 14.3 (q, aliphatic CH₃); LRMS: Found, 385.2; required, 385.5; [M + Na]⁺; Anal.
18 Calcd. for C₁₉H₃₈O₆: C, 62.95; H, 10.57. Found: C, 62.60; H, 10.67.

19 **3.1.21 Methyl 6-O-dodecanyl- β -D-glucopyranoside (9b)**

20 Treatment of **8b** (0.44 g, 0.6 mmol) as described for **8a** gave **9b** (0.17 g, 76%); [α]_D –
21 1° (*c* 0.03, CHCl₃); FTIR (KBr): 3405, 2922, 2850, 1470, 1391, 1128, 1109, 1048 cm⁻¹;
22 ¹H NMR (400 MHz, CDCl₃): δ 4.20 (d, 1H, *J*_{1,2} 7.5, H-1), 3.89 (s, 1H, OH), 3.74
23 (m, 2H, H-6a,6b), 3.66 (m, 1H, H-5), 3.54 (s, 3H, OCH₃), 3.52-3.44 (overlapping
24 signals, 2H, H-3,4), 3.35 (apt t, 1H, *J*_{2,3} 8.0, H-2), 1.58 (m, 2H, aliphatic
25 OCH₂C₁₁H₂₃), 1.28-1.11 (ms, 20H, aliphatic OCH₂C₁₀H₂₀CH₃), 0.88 (t, 3H, *J* 6.5, *J*

1 7.0, aliphatic $\text{OC}_{11}\text{H}_{22}\text{CH}_3$); ^{13}C NMR (CDCl_3): δ 103.5 (d, C-1), 76.5, 74.4, 73.4,
2 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,
3 29.65, 29.58, 29.53, 29.4, 26.0, 22.7 (each t, each aliphatic CH_2), 14.1 (q, aliphatic
4 CH_3); LRMS: Found, 385.2; required, 385.5; $[\text{M} + \text{Na}]^+$; Anal. Calcd. for $\text{C}_{19}\text{H}_{38}\text{O}_6$:
5 C, 62.95; H, 10.57. Found: C, 62.83; H, 10.36.

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

7 A solution of **1a** (1.0 g, 5.2 mmol), *p*-toluenesulfonic acid (10 mg) and benzaldehyde
8 dimethylacetal (1.5 mL, 10.3 mmol) in acetonitrile anhydrous (25 mL) was stirred for
9 24 h at room temperature. Trimethylamine (0.5 mL) was added to neutralise the
10 solution which was then stirred for 1 h. The product was filtered off as a white solid,
11 washed with petroleum ether and dried. The benzylidene protected intermediate was
12 then dissolved in DMF anhydrous (15 mL) and the solution was cooled to 0 °C. NaH
13 (0.74 g, 18.4 mmol) was added slowly, followed by benzyl bromide (2.5 mL, 20
14 mmol). The mixture was then warmed to room temperature and stirred over night.
15 MeOH (10 mL) was added to quench the solution which was stirred for a further 1
16 hr.²⁴ The mixture was then concentrated under diminished pressure and purified by
17 chromatography (petroleum ether-EtOAc) to give **10a**. (2.0 g, 95%); $[\alpha]_{\text{D}} 0.7^\circ$ (*c* 0.05,
18 CHCl_3); FTIR (KBr): 3063, 3031, 1109, 1088, 735, 692 cm^{-1} ; ^1H NMR (400 MHz,
19 CDCl_3): δ 7.50-7.22 (ms, 15H, each aromatic H), 5.54 (s, 1H, *CHPh*), 4.85 (AB d, 2H,
20 *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
21 (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,
22 1H, H-5), 3.70 (apt t, 1H, *J*_{5,6b} 10.5, H-6b), 3.62-3.54 (overlapping signals, 2H, H-
23 2,4), 3.39 (s, 3H, OCH_3); ^{13}C NMR (CDCl_3): δ 138.7, 138.1, 137.4 (each s, each
24 aromatic C), 128.89, 128.43, 128.29, 128.20, 128.10, 128.01, 127.90, 127.57, 126.0
25 (each d, each aromatic CH), 101.2 (d, C-1), 99.2 (d, *CHPh*), 82.1, 79.2, 78.6, 62.3

1 (each d), 75.3, 73.8 (each t), 69.1 (t, C-6), 55.3 (q, OCH₃); LRMS: Found, 463.3
2 required, 463.5; [M + H]⁺; Anal. Calcd. for C₂₈H₃₀O₆: C, 72.71; H, 6.54. Found: C,
3 72.31; H, 6.56.

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

5 **3.1.23.1 Methyl 2,3-di-*O*-benzyl-4,6-di-*O*-lauroyl- α -D-glucopyranoside (11a)**

6 Compound **10a** (1.7 g, 3.6 mmol) was dissolved in MeOH (50 mL) and a catalytic
7 amount of TsOH was added. The solution was stirred at room temperature overnight,
8 after which Et₃N (2 mL) was added to quench the reaction.³¹ The mixture was
9 concentrated under diminished pressure and the crude diol residue was dissolved in
10 pyridine anhydrous (70 mL). 4-Dimethylaminopyridine and lauroyl chloride (3.3 mL,
11 14.4 mmol) was added and the reaction was stirred at room temperature for 3 h.²⁶ The
12 solution was then concentrated under diminished pressure and purified by
13 chromatography (petroleum ether-EtOAc) to give **11a**. (1.0 g, 38%); FTIR (KBr):
14 2925, 2853, 1743, 1455, 1360, 1167, 1105, 1045, 734 cm⁻¹; ¹H NMR (400 MHz,
15 CDCl₃): δ 7.34-7.26 (multiple signal, 10H, each aromatic H), 5.01 (dd, 1H, $J_{3,4}$ 9.5,
16 $J_{4,5}$ 10.0, H-4), 4.78 (AB d, 2H, J 11.5, OCH₂Ph), 4.73 (AB d, 2H, J 12.0,
17 OCH₂Ph), 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
18 (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
19 (dd, 1H, H-2), 2.36-2.27 (m, 4H, each aliphatic OCOCH₂C₁₀H₂₁), 1.67-1.56 (m, 4H,
20 each aliphatic OCOCH₂CH₂C₉H₁₉), 1.26-1.16 (ms, 32H, each aliphatic
21 OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 6H, J 6.5, J 7.0, each aliphatic OCOC₁₀H₂₀CH₃); ¹³C
22 NMR (CDCl₃): δ 173.6, 172.4 (each s, each C=O), 138.4, 137.9 (each s, each
23 aromatic C), 128.51, 128.32, 128.18, 128.05, 127.69, 127.57 (each d, each aromatic
24 CH), 98.2 (d, C-1), 79.51, 79.18, 69.5, 67.7 (each d), 75.4, 73.6 (each t, each CH₂Ph),
25 62.2 (t, C-6), 55.4 (q, OCH₃), 34.15, 34.03, 33.99, 31.9, 29.62, 29.60, 29.49, 29.44,

1 29.35, 29.34, 29.28, 29.26, 29.15, 29.13, 29.07, 24.76, 24.70, 22.69 (each t, each
2 aliphatic CH₂), 14.1 (q, aliphatic CH₃).

3 **3.1.23.2 Methyl 4,6-di-*O*-lauroyl- α -D-glucopyranoside (12a)**

4 Compound **11a** (0.84 g, 1.14 mmol) was dissolved in EtOH (2.5 mL) and Pd/C (0.3 g)
5 was added. The mixture was allowed to shake under hydrogen atmosphere of 2 psi
6 until all protecting groups had been removed as shown by TLC to yield **12a**. The
7 suspension was filtered and concentrated *in vacuo*.²⁷ (0.47 g, 75%); [α]_D 4.33° (c
8 0.03, CHCl₃); FTIR (KBr): 3456, 2918, 2849, 1737, 1701, 1468, 1301, 1240, 1187,
9 1046 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 4.87 (dd, 1H, $J_{3,4}$ 9.5, $J_{4,5}$ 10, H-4), 4.82 (d,
10 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-
11 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,
12 OMe), 2.37-2.32 (m, 4H, each aliphatic OCOCH₂C₁₀H₂₁), 1.68-1.55 (m, 4H, each
13 aliphatic OCOCH₂CH₂C₉H₁₉), 1.30-1.26 (multiple signals, 32 H, each aliphatic
14 OCOC₂H₄C₈H₁₆CH₃), 0.88 (t, 6H, J 6.5, J 7.0, each aliphatic OCOC₁₀H₂₀CH₃); ¹³C
15 NMR (CDCl₃): δ 173.63, 173.58 (each s, each C=O), 99.0 (d, C-1), 72.9, 72.7, 70.3,
16 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,
17 29.47, 29.45, 29.36, 29.30, 29.27, 29.14, 29.08, 24.84, 24.82, 24.70, 22.70 (each t,
18 each aliphatic CH₂), 14.1 (q, aliphatic CH₃); LRMS: Found, 559.5 required, 559.8; [M
19 + H]⁺; Anal. Calcd. for C₃₁H₅₈O₈: C, 66.63; H, 10.46. Found: C, 66.66; H, 10.79.

20

21 **3.1.24 General procedure for the preparation of pentaerythritol esters**

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

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

3 **3.1.25 Mono lauroyl pentaerythritol (14)**

4 (0.33 g, 14%); FTIR (KBr): 3462, 2914, 2848, 1737, 1712, 1476, 1187, 1038, 1005
5 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 4.10 (s, 2H, $\text{CH}_2\text{OC}=\text{O}$), 3.80-3.61 (overlapping
6 signals, 9H, 3 x CH_2OH , 3 x OH), 2.34 (t, 2H, J 6.0, J 7.0, aliphatic
7 $\text{OCOCH}_2\text{C}_{10}\text{H}_{21}$), 1.61 (m, 2H, aliphatic $\text{OCOCH}_2\text{CH}_2\text{C}_9\text{H}_{19}$), 1.26 (ms, 16H,
8 aliphatic $\text{OCOC}_2\text{H}_4\text{C}_8\text{H}_{16}\text{CH}_3$), 0.88 (m, 3H, aliphatic $\text{OCOC}_{10}\text{H}_{20}\text{CH}_3$); ^{13}C NMR
9 (CDCl_3): δ 175.0 (s, $\text{C}=\text{O}$), 62.7, 62.4 (each t, each CH_2O), 45.3 (s, $\text{C}(\text{CH}_2)_4$), 34.2,
10 31.9, 29.59, 29.57, 29.44, 29.30, 29.23, 29.15, 24.9, 22.6 (each t, each aliphatic CH_2),
11 14.1 (q, aliphatic CH_3); LRMS: Found 341.2, required 341.45 $[\text{M}+\text{Na}]^+$; Anal. Calcd.
12 for $\text{C}_{17}\text{H}_{34}\text{O}_5$: C, 64.12; H, 10.76. Found: C, 64.08; H, 10.79.

13 **3.1.26 Di lauroyl pentaerythritol (15)**

14 (1.074 g, 29%); FTIR (KBr): 3351, 2915, 2850, 1739, 1701, 1471, 1163, 978, 719 cm^{-1}
15 ^1H NMR (400 MHz, CDCl_3): δ 4.12 (s, 4H, each $\text{CH}_2\text{OC}=\text{O}$), 3.58 (s, 4H, each
16 CH_2OH), 3.22 (br s, 2H, each OH) 2.34 (t, 4H, J 7.5, J 7.5, each aliphatic
17 $\text{OCOCH}_2\text{C}_{10}\text{H}_{21}$), 1.62 (t, 4H, J 6.5, J 6.5, each aliphatic $\text{OCOCH}_2\text{CH}_2\text{C}_9\text{H}_{19}$), 1.29-
18 1.26 (ms, 32H, each aliphatic $\text{OCOC}_2\text{H}_4\text{C}_8\text{H}_{16}\text{CH}_3$), 0.88 (t, 6H, J 6.5, J 6.5, each
19 aliphatic $\text{OCOC}_{10}\text{H}_{20}\text{CH}_3$); ^{13}C NMR (CDCl_3): δ 174.4 (s, each $\text{C}=\text{O}$), 62.4 (t, each
20 CH_2O), 44.7 (s, $\text{C}(\text{CH}_2)_4$), 34.2, 31.9, 29.56, 29.29, 29.21, 29.11, 24.9, 22.6 (each t,
21 each aliphatic CH_2), 14.1 (q, each aliphatic CH_3); LRMS: Found 501.5, required
22 501.75 $[\text{M}+\text{H}]^+$; Anal. Calcd. for $\text{C}_{29}\text{H}_{56}\text{O}_6$: C, 69.56; H, 11.27. Found: C, 69.64; H,
23 11.31.

24 **3.1.27 Tetra lauroyl pentaerythritol**

1 (0.39 g, 6%); FTIR (KBr): 2917, 2849, 1735, 1336, 1299, 1250, 1154, 1111, 1002 cm^{-1} ;
2 ^1H NMR (400 MHz, CDCl_3): δ 4.11 (s, 8H, each $\text{CH}_2\text{OC}=\text{O}$), 2.30 (t, 8H, J 7.5, J
3 8.0, each aliphatic $\text{OCOCH}_2\text{C}_{10}\text{H}_{21}$), 1.60 (t, 8H, J 6.5, J 7.0, each aliphatic
4 $\text{OCOCH}_2\text{CH}_2\text{C}_9\text{H}_{19}$), 1.41-1.26 (ms, 64H, each aliphatic $\text{OCOC}_2\text{H}_4\text{C}_8\text{H}_{16}\text{CH}_3$), 0.88
5 (t, 12H, J 6.5, J 7.0, each aliphatic $\text{OCOC}_{10}\text{H}_{20}\text{CH}_3$); ^{13}C NMR (CDCl_3): δ 173.2 (s,
6 each $\text{C}=\text{O}$), 62.1 (t, each CH_2O), 41.8 (s, $\text{C}(\text{CH}_2)_4$), 34.1, 31.9, 29.59, 29.45, 29.31,
7 29.23, 29.11, 24.8, 22.7 (each t, each aliphatic CH_2), 14.1 (each q, each aliphatic
8 CH_3); LRMS: Found 888.7, required 888.36 $[\text{M}+\text{Na}]^+$; Anal. Calcd. for $\text{C}_{53}\text{H}_{100}\text{O}_8$: C,
9 73.56; H, 11.65. Found: C, 73.60; H, 11.58.

10 **3.2 Evaluation of anti-microbial activity**

11 **3.2.1 Preparation of bacterial cultures**

12 Bacteria used in this study were *Staphylococcus aureus* ATCC 25923 and *Escherichia*
13 *coli* ATCC 25922. Stock cultures were maintained in tryptic soy broth (TSB, Sharlau
14 Chemie, Spain) supplemented with 20% glycerol at -70 $^\circ\text{C}$. Cultures were routinely
15 grown by subculturing 100 μL of stock culture into 9 mL TSB and incubating at 35
16 $^\circ\text{C}$ for 18 h. Cultures were then maintained on tryptic soy agar (TSA, Sharlau
17 Chemie, Spain) plates at 4 $^\circ\text{C}$. Working cultures were prepared by inoculating a loop
18 of pure culture into TSB and incubating at 35 $^\circ\text{C}$ for 18 h. A bacterial suspension was
19 prepared in saline solution (NaCl 0.85%, BioMérieux, France) equivalent to a
20 McFarland standard of 0.5, using the Densimat photometer (BioMérieux, SA, France),
21 to obtain a concentration of 1×10^8 cfu/mL. This suspension was then serially diluted
22 in TSB to obtain a working concentration of 1×10^6 cfu/mL.

23 **3.2.2 Anti-microbial activity assay**

24 Stock solutions (100 mmol) of test compounds and standards were prepared in sterile
25 hydroalcoholic diluent (ethanol-distilled water, 1:1) and stored at -20 $^\circ\text{C}$. Stock

1 solutions were diluted in TSB to obtain initial working concentrations (10 or 20
2 mmol). Working test compounds and standards were serially diluted in sterile TSB to
3 a final volume of 100 μ L within the 96-well plate. 100 μ L of freshly prepared
4 inoculum of the organism under study was added to each appropriate well. The final
5 concentration of each microorganism in each well was approximately 5×10^5 cfu/mL
6 and the concentration range of chemical compounds was from 1:2 to 1:256. Each
7 concentration was assayed in duplicate. The following controls were used in the
8 microplate assay for each organism and test compound; blank: uninoculated media
9 without test compound to account for changes in the media during the experiment;
10 negative control: uninoculated media containing only the test compound; positive
11 control 1: inoculated media without compound; positive control 2: inoculated media
12 without compound but including the corresponding sugar to evaluate any effect of the
13 sugar alone; and positive control 3: inoculated media without compound but with the
14 equivalent concentration of ethanol used to dissolve the test compound, thereby
15 assessing any activity of the alcohol. The 96-well plates were incubated at 35 °C for
16 18 hours in a microtiterplate reader (PowerWave microplate Spectrophotometer,
17 BioTek) and effects were monitored by measuring the optical density (OD) at 600 nm
18 for each well every 20 minutes with 20 seconds agitation before each OD
19 measurement. Each experiment was replicated three times. The MIC was defined as
20 the lowest concentration of compound that showed no increase in OD values for all
21 the replicates compared to the negative control after 18 hours. Subtraction of the
22 absorbance of the negative control eliminated interferences due to variation in the
23 media.

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