Tetrahedron 64 (2008) 5124–5131

Contents lists available at ScienceDirect

Tetrahedron

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

Oxidatively induced glycosylation starting from hydroquinone glycosides

Hans Günter Thomas [a], Jean-Luc Mieusset [b,*]

[a] Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule Aachen, Professor-Pirlet-Straße 1, 52074 Aachen, Germany
[b] Institut für Organische Chemie, Universität Wien, Währinger Straße 38, A-1090 Wien, Austria

ARTICLE INFO

Article history:
Received 13 February 2008
Received in revised form 12 March 2008
Accepted 17 March 2008
Available online 21 March 2008

Keywords:
Glycosylation
Oxidation
Electrochemistry
Carbohydrates
Hydroquinones

ABSTRACT

As a new class of glycosyl donors, hydroquinone glycosides can be used for glycosylation reactions. Their activation can be performed either electrochemically or under homogeneous chemical conditions. Conventionally, several glucosides were produced with yields greater than 77% using DDQ in CH_2Cl_2 as oxidizing agent. For electrolyses, glycosides of trimethylhydroquinone are preferably used because their low oxidation potentials allow the utilization of an undivided cell. The synthesis of the glycosyl donors was achieved with high efficiency by direct coupling of the phenols with peracetylated monosaccharides employing boron trifluoride etherate as the catalyst. The oxidation of hydroquinone derivatives can also be applied to the generation of other stabilized cations.

1. Introduction

Carbohydrate derivatives play a central role in biological systems, especially in the modification of proteins and in molecular recognition processes. Therefore, a wide range of methodologies have been developed to perform glycosylations.[1] The most commonly used glycosyl donors are glycosyl halides, thioglycosides, and trichloroacetimidates. For this purpose, electrochemistry offers some advantages; it enables the activation of stable glycosides, which are resistant to a wide range of reaction conditions. The first reported use was the oxidation of aryl glycosides by Noyori.[2] During the following years, this method was applied to glycosylations that start from thio-,[3–5] seleno-[5,6] or telluroglycosides.[6] The disadvantage of this reaction path is that radical species are produced during the reaction and therefore the prepared glycosides contain many side products. The leaving group also is a cause of side reactions. For phenyl compounds, a mixture of aryl ethers[2] is formed. By the use of thioglycosides, the thio radical dimerizes first to a disulfide, which is further oxidized during the course of the electrolysis.[3] In the absence of a good nucleophile, the initially produced glycosyl cations tend to react with the supporting electrolyte, generating more or less stable glycosyl halides, perchlorates or triflates.[7] Therefore, the choice of the conducting salt is of crucial importance in order to minimize the amount of side products and to control the stereoselectivity of the reaction. Alternatively, glycosylation was also achieved by electrochemical reduction of glycosyl halides[8] and electrooxidative N-glycosylations leading to the formation of nucleosides that have already been reported.[9]

Johnson[10] showed that the oxidation of hydroquinone esters permits to realize a transacylation. With this method, the only byproduct is benzoquinone. Assuming that the glycosyl cation could be formed as easily as an acyl cation, we will show in this paper that hydroquinone glycosides can be used for glycosylations (Scheme 1) and that the sole side product is the corresponding quinone, a compound that can be removed very easily. Interestingly, hydroquinone bis-glucosides are found in traditional medicinal plants.[11] They are also used for the modification of the properties of conducting polymers in order to enhance their solubility or improve their binding properties.[12] Moreover, 4-hydroxyphenyl-β-D-glucopyranoside, a compound commonly called arbutin, is a readily available and cheap natural product especially found in bearberries. Since it has already been shown that unprotected sugars can serve as glycosyl donors, this methodology may be promising for glycosylation reactions in water.[13]

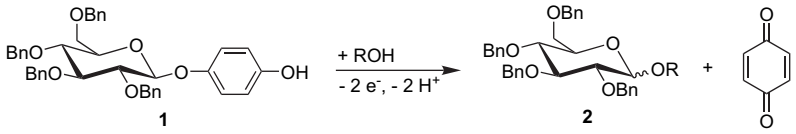
2. Results and discussion

2.1. Synthesis of the starting material

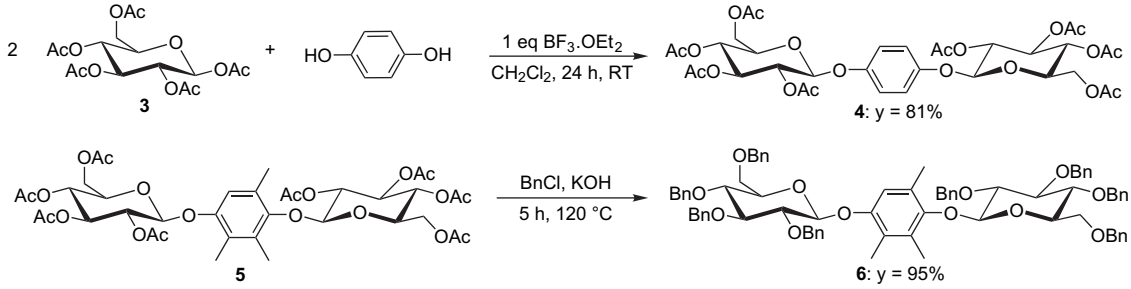
Aryl glycosides like **4**, **5**, and **25** can be easily prepared from pentaacetyl-β-D-glucose with $BF_3 \cdot OMe_2$ as activator (Scheme 2).[14] The corresponding benzylated compounds **6** and **9** were prepared by substitution of the protecting groups with benzyl chloride and KOH.[15]

* Corresponding author. Tel.: +43 1 4277 52112; fax: +43 1 4277 52140.
E-mail address: jeanluc.mieusset@univie.ac.at (J.-L. Mieusset).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.03.056



Scheme 1.



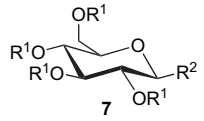
Scheme 2. Representative synthesis of the glycosyl donors.

4-Hydroxyphenyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (**1**) was prepared by the imidate method.[16]

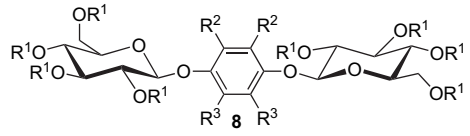
The glycosyl donors were investigated by cyclic voltammetry and their oxidation potentials are listed in Table 1. All oxidations are irreversible, a sign that the generated radical cation decomposes rapidly. In all cases, benzylated donors (armed sugars) have a lower oxidation potential than their acetylated counterparts (disarmed sugars). Hence, a quinone, which may activate a benzylated donor may not be suitable for a glycoside bearing acetyl protecting groups. Oxidation of the benzylic protecting groups occurs only with potentials higher than 2 V.

Initially, compound **1** (E_{ox}=1.3 V) was oxidized in an undivided cell. The produced glucosyl cation reacted with cyclohexanol to produce the corresponding glucoside[17] **11**. To obtain the best yield of 85%, 1 equiv $BF_3{\cdot}OMe_2$ was used as an electrolyte in MeCN/THF 95:5. Acetonitrile was necessary to make the reaction mixture conductive, but we needed tetrahydrofuran as an additional solvent, because the donor **1** cannot be dissolved in pure acetonitrile. This method favors the β-anomer with an anomeric ratio of 1:3, but it is not stereospecific. Utilization of tetrabutylammonium tetrafluoroborate as conducting salt improves the stereoselectivity (α/β=1:9), but the crude product contains 30% of α-tetrabenzyl glucosyl fluoride. Similarly, the use of tin tetrachloride leads to contamination by the glucosyl chloride and utilization of lithium perchlorate favors the formation of tetrabenzyl glucose. When higher alcohols were used, there was a competitive reaction with the free hydroxy group of **1** and bisglucosyloxybenzene **9** (E_{ox}=1.6 V) became the most important product, because it could not be oxidized under these conditions.

Table 1
Oxidation potentials of the glycosyl donors



7a: R^1=Ac; R^2=SPh
7b: R^1=Ac; R^2=*p*-MeOPhO
7c: R^1=Bn; R^2=*p*-MeOPhO
7d: R^1=Ac; R^2=*p*-HOPhO
7e: R^1=Bn; R^2=*p*-HOPhO
7f: R^1=Bn; R^2=*p*-CF_3CO_2PhO
7g: R^1=Bn; R^2=*p*-Me_3SiOPhO
7h: R^1=Bn; R^2=*p*-$HOMe_3$PhO



8b: R^1=Ac; R^2=Cl; R^3=Cl
8c: R^1=Ac; R^2=CN; R^3=H

Hydroquinone glycoside	$E_{ox1/2}$[a] (V)
7a	1.80
16	1.75
9	1.60
5	1.60
7b	1.55
6	1.50
7c	1.45
25	1.40
7d	1.35
7e	1.30
7f	1.20
7g	1.20
29	1.10
7h	1.05
8a	>2.0
8b	>2.0

[a] Against Ag, AgCl/3 M KCl in acetonitrile.

2.2. Indirect electroglycosylation

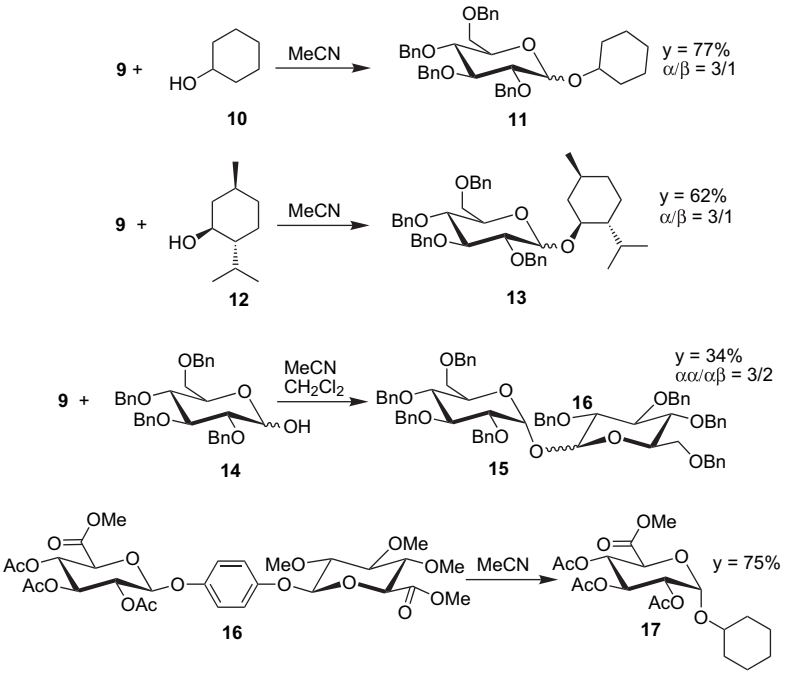
When the glycosyl donor **9** was oxidized in an undivided cell in the presence of cyclohexanol, only traces of products could be detected through TLC. The conversion was so low that no compounds could be isolated. Probably, with this procedure, the reaction begins and generates a small quantity of glucoside and benzoquinone. The latter compound is directly reduced at the cathode to hydroquinone. This compound prevents a further oxidation of the reactant **9** and the reaction stops. Therefore, **9** must be oxidized in a divided cell. In this device, the conductivity of the solution is limited and a mediator has to be used in order to obtain a better selectivity during the oxidation. $CoCl_2$ and tris(2,4-dibromophenyl)amine[18] could be employed for this purpose. Indeed, under these conditions, cyclohexyl glucoside **11** is produced in a yield of 77% (Table 2, Scheme 3), the favored anomer being the α-anomer. As a side product, 7–15% of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose[19] **20** is formed. These observations let us assume that the reaction proceeds through the trialkyloxonium ion **19** as an intermediate (Scheme 4). A further reason for the predominance of the α-anomer is that the anodic compartment is significantly more acidic than in the other experiments conducted in this work and that isomerization to the more stable α-glycoside takes place. In contrast, during the electrolyses in an undivided cell

Table 2
Glycosylation of some alcohols by means of an indirect electrolysis of 1,4-bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)benzene (**9**) or 1,4-bis(methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyloxyuronate)benzene (**16**)

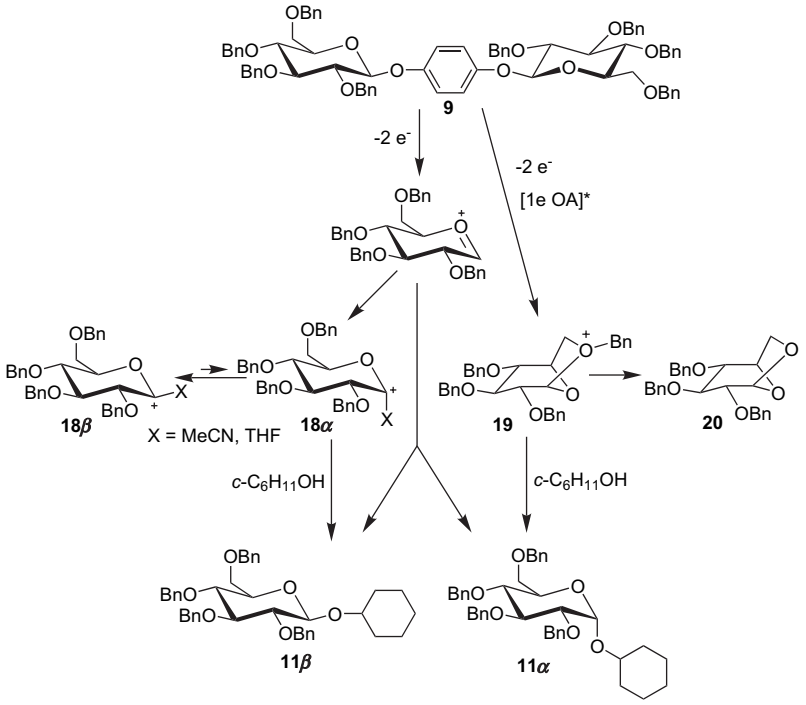
Donor	Acceptor	Product	Solvent	Yield (%)	α/β
9	**10**	**11**	MeCN	77	3:1
9	**12**	**13**	MeCN	62	3:1
9	**14** (α/β 3:1)	**15**	$MeCN/CH_2Cl_2$	34	3:2 (αα/αβ)
16	**10**	**17**	MeCN	75	α

in tetrahydrofuran and in acetonitrile, the β-anomer predominates; a possible explanation is that the glucosyl cation is stabilized by the solvent. As a consequence of the reverse anomeric effect,[20] the α-anomer **18α** is less stable and therefore more reactive than the corresponding β-anomer. Overall, it leads to formation of a β-glucoside.[21]

Hydroquinone bis-glucoside **9** reacts cleanly in a divided cell with (−)-menthol **12** and tetrabenzyl glucose[15] **14** (α/β=3:1). The glucosides **13** and **15** were obtained in 62 and 34% yield,



Scheme 3. Glycosylation in a divided cell in presence of $CoCl_2$.



Scheme 4. Proposed mechanism for the oxidative transglycosidation of hydroquinone glycosides.

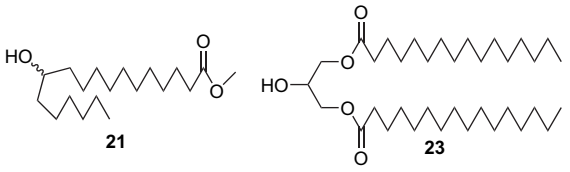
Table 3
Glucoside formation by direct electrolysis of 1,4-bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**) and its peracetylated analog **5** in the presence of alcohols

Donor	Acceptor	Product	Solvent	Yield (%)	α/β
6	**10**	**11**	$MeCN/CH_2Cl_2$	88	3:2
6	**12**	**13**	CH_2Cl_2	82	1:1
5	**12**	**27**	MeCN	61	β
5	**21**	**28**	MeCN	43	β

Table 4
Reaction between 1,4-bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**) and alcohols in the presence of DDQ

Acceptor	Product	Catalyst quantity	Reaction time (h)	Yield (%)	α/β
10	**11**	0.3 equiv TfOH	2.5	98	2:1
12	**13**	0.3 equiv TfOH	2.5	93	2:1
14	**15**	0.3 equiv TfOH	1.5	89	1:1[a]
21	**22**	0.45 equiv TfOH	2	87	2:1
23	**24**	1 equiv $SnCl_4$	1	77	2:1

[a] αα/αβ.



respectively (Table 2). Also with these alcohols, merely α-anomer was produced with the anomeric ratios α/β=3:1 and αα/αβ=3:2, respectively.

The behavior of 1,4-bis(methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyloxyuronate)benzene (**16**) (E_{ox}=1.75 V) is not exactly the same. This compound can be oxidized in a divided cell and it yields specifically the α-glucuronoside **17** of cyclohexanol (yield=75%). The reason for this α-glycosylation is probably that the carbonyl group at C(6) stabilizes the intermediate in a way that the alcohol can attack the glycosyl cation only in the α-position.[22]

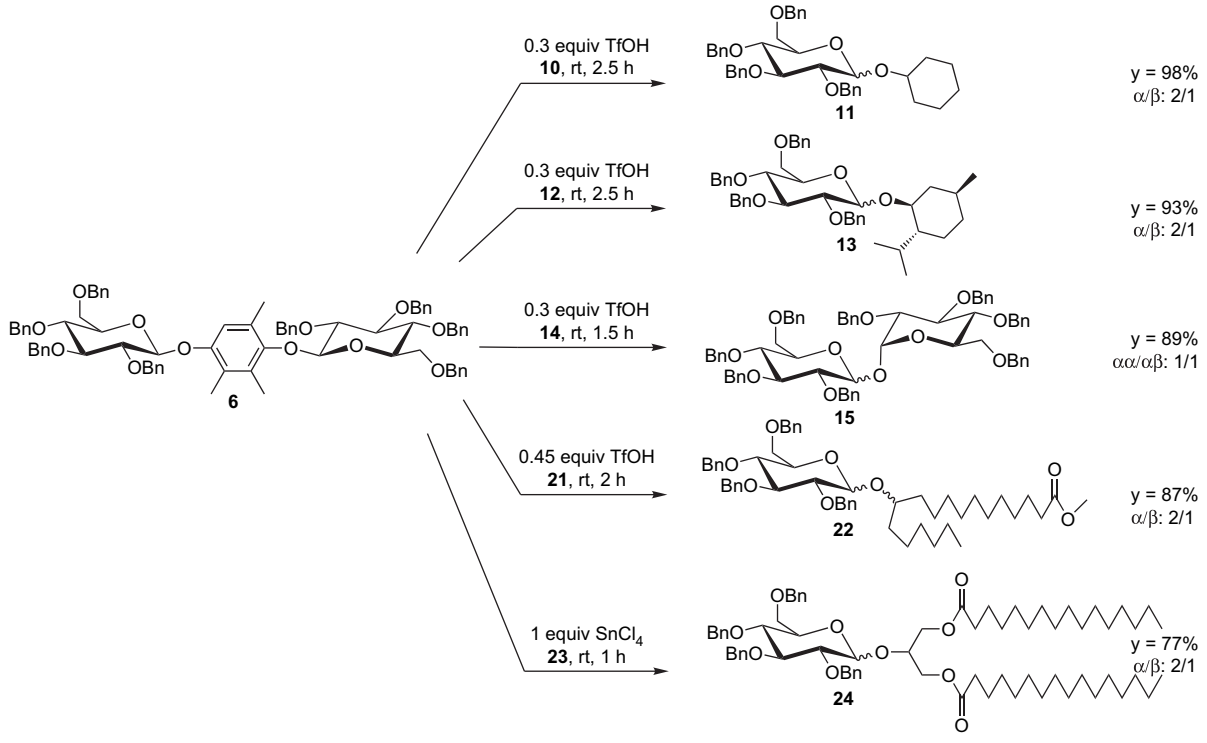
2.3. Direct electroglycosylation

Tris(4-bromophenyl)amine or $LiCl{\cdot}MnCl_2$ can be used as mediator for donors with a low oxidation potential like 1,4-bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**) (E_{ox}=1.5 V). However, because of the low oxidation potential of **6**, this compound can also be directly oxidized in an undivided cell. Due to this fact, solvents with low polarity like CH_2Cl_2 could be used. In this way, the glycosylation system becomes more efficient and the yields improve (Table 3). The disadvantage of this method is, however, that the anomeric selectivity is very low. For example, with (−)-menthol **12** as acceptor, the corresponding glucoside **13** is obtained in a yield of 82% with an anomeric ratio of 1:1.

With acetylated donors, glucoside formation occurs only in the presence of an acid. In the case of suitable reaction conditions, the *trans*-glucoside will be exclusively formed due to the stabilization of the intermediate compound through the ester group at C(2). We compared the results obtained with the Lewis acids $BF_3{\cdot}OMe_2$, $FeCl_3$, $ZnCl_2$, $SnCl_4$, and trimethylsilyl trifluoromethanesulfonate (TMSOTf), which were already used in glycosylation reactions, especially for the activation of 1-*O*-acyl sugars.[1b] The best results were obtained when tin(IV) chloride was used as the activator in acetonitrile. In this solvent, $SnCl_4$ dissociates and no other electrolyte is necessary. Under these conditions, 1,4-bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**5**) produces only the β-glucosides **27**[23] and **28** during the glycosylation of (−)-menthol **12** and methyl 12-hydroxyoctadecanoate (**21**). The yields are 61 and 43%, respectively.

2.4. Oxidation under homogeneous chemical conditions

Alternatively the oxidation could be performed with oxidizing agents instead of an anode. In our case, one-electron oxidizing agents like cobalt(III) acetylacetonate and tris(2,4-dibromophenyl)-ammoniumyl hexachloroantimonate[18] could not be used, because they provide tribenzyl anhydroglucose **20** as main product. In contrast, when 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)

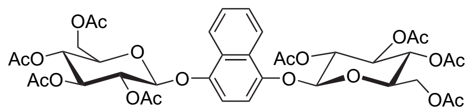


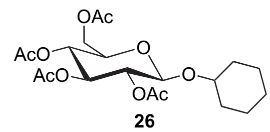
Scheme 5. Glycosylations with DDQ under homogeneous conditions.

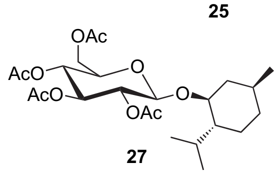
Table 5
Glucosylation of some alcohols by oxidation of the diglucosylated naphthohydroquinone **25** with DDQ

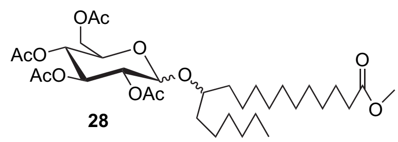
Acceptor	Product	Reaction conditions	Turnover (%)	Yield[a] (%)	α/β
10	**26**	0.1 equiv $BF_3 \cdot OMe_2$, CH_2Cl_2	100	64	1:2
10	**26**	2 h, MeCN/$SnCl_4$	37	63	1:9
12	**27**	2 days, MeCN/$SnCl_4$	52	81	β
21	**28**	2 days, MeCN/$SnCl_4$	52	78	β

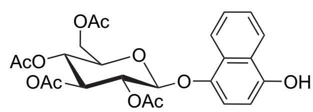
[a] Based on the turnover.


25


26


27


28


29

is used, **20** is not observed. The difference between these two methods is that the electron transfer occurs through a CT-complex when DDQ is used and that two electrons are rapidly transferred. Similarly, this oxidizing agent was already applied for glycosylations starting from methoxybenzyl-2-deoxyglucosides.[24]

With bisglucosyloxytrimethylbenzene **6**, glucoside formation succeeds only under specific conditions. Dichloromethane is the solvent of choice because the reaction proceeds faster than in THF or toluene. Of course, dry conditions are required but the usage of molecular sieves is prohibited because it inhibits the reaction. With benzylated compounds the reaction should last no longer than a few hours, because benzaldehyde is very slowly produced through cleavage of the protecting groups.[25] Therefore, a catalytic quantity of trifluoromethane sulfonic acid (TfOH), $BF_3 \cdot OMe_2$ or $SnCl_4$ is needed. In this way, the glucoside **11** of cyclohexanol was formed quantitatively in less than 3 h in the presence of TfOH (Table 4, Scheme 5). With the higher alcohols **12**, **14**, and **21**, we obtained the glucosides **13**, **15**, and **22** in yields greater than 87%. Only dipalmitine[26] **23** did not react in the presence of TfOH or $BF_3 \cdot OMe_2$ as catalyst and needs $SnCl_4$ to give glucoside **24**.

This methodology is especially convenient because $DDQH_2$ is insoluble in CH_2Cl_2 and can easily be removed by filtration. The facile recovery of the side products and the inexpensive regeneration of the reagents, for example, electrochemically,[27] make this procedure particularly attractive and sustainable. The acetylated glucoside **5** of trimethylhydroquinone could not be used in combination with DDQ because its oxidation potential (E_{ox}=1.6 V) is too high. Instead, we employed 1,4-bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)naphthalene (**25**) (E_{ox}=1.4 V). With $BF_3 \cdot OMe_2$ in CH_2Cl_2 in the presence of cyclohexanol, compound **25** reacts faster quantitatively and the purification procedure is simple. Unfortunately, a 1:2 mixture of α- and β-anomers of cyclohexyl glucoside **26** is formed. Therefore, the use of the combination $SnCl_4$/MeCN is recommended because it provides *trans*-glucosides like **27** and **28** in good yields (Table 5).

3. Conclusion

We have developed an efficient glycosylation method starting from a readily available glycoside donor that is stable under a wide range of reaction conditions allowing a further transformation of the carbohydrate in presence of the prospective leaving group. Nevertheless, these hydroquinone glycosides can be activated under mild conditions at room temperature by oxidation with DDQ and can even glycosylate poorly accessible hydroxy groups with good yields.

4. Experimental section

4.1. General methods and material

Melting points were determined on a Tottoli apparatus, Büchi 510 and are uncorrected. IR spectra were recorded with a Perkin–Elmer FTIR 1750 spectrophotometer. The locations of the absorption peaks are given in cm^{-1}. NMR spectra were recorded on a Varian VXR 300. Tetramethylsilane (TMS) was used as an internal standard. ^1H spectra were recorded at 300 MHz and ^{13}C spectra at 75 MHz in $CDCl_3$. The chemical shifts (δ) are listed in parts per million against TMS. The coupling constants (J) are given in hertz and the following abbreviations are used for the description of the patterns: s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, m=multiplet. Mass spectra were obtained with a Varian MAT 212 spectrometer. The masses of the ions are characterized through their *m*/*z* value. The peak intensity is expressed as a percentage of the basis peak. Elemental analyses were performed with a Heraeus CHN-O-Rapid analyzer. Reactions were monitored by TLC on precoated Silica Gel 60 F_{254} plates (E. Merck). The spots were made visible with phosphomolybdic acid (3% in EtOH). Cyclic voltammetry was performed in 30 ml of acetonitrile with 0.1 M tetrabutylammonium tetrafluoroborate as electrolyte and a platinum electrode as working electrode against Ag/AgCl/3 M KCl. Compounds, which are insoluble in pure MeCN were first dissolved in 1 ml of CH_2Cl_2.

4.1.1. *4-Hydroxyphenyl 2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**1**)*

Hydroquinone (32.5 g, 296 mmol, 4 mol equiv) was dissolved with tetrabenzylglucosyl trichloracetimidate (50.7 g, 74 mmol) in 600 ml of ether/dichloromethane 1:1 and cooled to −30 °C in the presence of molecular sieves. Then, $BF_3 \cdot OMe_2$ (0.2 mol equiv) was added and the solution was stirred for 2 h, while the temperature was slowly raised up to 20 °C. During the reaction, the product

precipitated. Before the crude reaction mixture could be washed with a potassium carbonate solution and water, the aryl glucoside should be dissolved by addition of dichloromethane. Then, the organic phase was dried over magnesium sulfate, filtered, and the solvent was removed by distillation. The obtained solid was recrystallized from ethyl acetate and ethanol. Yield 32.5 g (51 mmol, 69%); mp 156 °C (EtOH); IR (KBr) 3305 (OH), 3088, 3064, 3027 (=C–H), 2939, 2905, 2878 (–C–H), 1602, 1512 (Ph), 1453 (CH_2), 1086, 1066, 1048 (C–O–C), 736, 698 (Ph, monosubstitution) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.55–3.80 (m, 5H, H-2, H-3, H-4, H-5, H-6), 3.78 (dd, J=10.7, 1.7 Hz, 1H, H-6), 4.87 (d, J=7.4 Hz, 1H, H-1), 4.50–5.07 (8d, 8H, 4PhCH_2), 6.65, 6.93 (2d, J=8.73 Hz, 4H, O–Ph–O), 7.15–7.35 (m, 20H, 4Ph); ^{13}C NMR ($CDCl_3$) δ 68.85 (C-6), 74.93 (C-5), 73.48, 75.05, 75.05, 75.76 (PhCH_2), 77.70 (C-4), 82.05 (C-2), 84.61 (C-3), 102.75 (C-1), 115.99, 118.52 (O–Ph–O), 127.66–128.41 (arom CH, *Ph*CH_2), 137.94, 137.94, 138.18, 138.45 (arom C, *Ph*CH_2), 151.29, 151.35 (arom C–O); MS 522 (0.53) M^+−aglycon, 415 (0.50) 522−BnO, 307 (0.27) 522−2BnO−H, 181 (19.13), 179 (2.41), 110 (1.19) $HOPhOH^+$, 91 (100) Bn^+, 65 (2.20) $C_5H_5^+$. Anal. Calcd for $C_{40}H_{40}O_7$ (632.75): C, 75.93; H, 6.37. Found: C, 76.15; H, 6.60.

4.2. Method A

Hydroquinone was dissolved in ether and 2 g of pulverized molecular sieves as well as the peracetylated sugar dissolved in dichloromethane were added. After 30 min, 5 mol equiv of boron trifluoride etherate was added and the reaction mixture was stirred for 3 days. Then, this solution was extracted with water and with a $NaHCO_3$ solution, and dried over $MgSO_4$. The crude product was recrystallized from ethanol.

*4.2.1. 1,4-Bis(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**5**)*

Glucose-β-pentaacetate (**3**) (50 g, 129 mmol) dissolved in 500 ml of dichloromethane, 59 ml (641 mmol, 5 mol equiv) of boron trifluoride etherate, and 7.85 g (51.6 mmol, 0.4 mol equiv) of trimethylhydroquinone dissolved in 200 ml of ether were combined using method A. Yield 26.4 g (32.5 mmol, 50%); mp 213 °C (EtOH); IR (KBr) 2965, 2876 (–C–H), 1747 (C=O), 1226, 1041 (C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01–2.24 (11s, 33H, 11Me), 3.54 (ddd, J=9.4, 4.5, 3.0 Hz, 1H, H-5′), 3.87 (ddd, J=10.0, 5.5, 2.7 Hz, 1H, H-5), 4.07 (dd, J=12.0, 2.7 Hz, 1H, H-6), 4.16–4.30 (m, 3H, H-6, H-6′), 4.74 (d, J=7.7 Hz, 1H, H-1′), 4.98 (d, J=7.7 Hz, 1H, H-1), 5.10–5.40 (m, 6H, H-2, H-3, H-2′, H-3′, H-4′), 6.69 (s, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 12.06, 13.63, 17.23 (3Me), 20.62 (8MeCO), 61.62, 62.17 (C-6, C-6′), 68.45, 68.50, 71.16, 71.60, 71.80, 71.96, 72.72, 72.98 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.78, 101.79 (C-1, C-1′), 115.31 (arom CH), 125.47, 129.22, 131.73 (arom C), 148.30, 151.78 (arom C–O), 169.25–170.50 (8C=O); MS 812 (0.05) M^+, 482 (0.24) M^+−333+H, 331 (18) M^+−aglycon, 289 (0.11) 331−H_2C=C=O, 271 (7.9) 331−AcOH, 229 (1.5) 331−AcOH−H_2C=C=O, 211 (5.4) 331−2AcOH, 169 (100) 331−2AcOH−H_2C=C=O, 127 (17) 331−2AcOH−$2H_2C$=C=O, 109 (61) 331−3AcOH−H_2C=C=O. Anal. Calcd for $C_{37}H_{48}O_{20}$ (812.78): C, 54.68; H, 5.95. Found: C, 54.64; H, 6.02.

*4.2.2. 1,4-Bis(methyl 2,3,4-tri-O-acetyl-β-D-glucopyranosyloxy-uronate)benzene (**16**)*

Methyl tetraacetyl-β-glucuronate (19.7 g, 52.2 mmol), hydroquinone (2.3 g, 20.9 mmol, 0.4 mol equiv), and $BF_3{\cdot}OMe_2$ (24 ml, 261 mmol, 5 mol equiv) were dissolved in 500 ml of dichloromethane/diethyl ether 2:1 using method A. Yield 8.1 g (10.9 mmol, 42%); mp 206 °C (Et_2O); IR (KBr) 2959 (–C–H), 1757 (C=O), 1219, 1043 (C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.04, 2.04, 2.06 (2s, 18H, 6MeCO), 3.74 (s, 6H, 2OMe), 4.16 (d, J=9.40 Hz, 2H, H-5), 5.05 (d, J=7.39 Hz, 2H, H-1), 5.21–5.36 (m, 6H, H-2, H-3, H-4), 6.94 (s, 4H, Ph); ^{13}C NMR ($CDCl_3$) δ 20.49, 20.60, 20.60 (6MeCO), 52.98 (2OMe), 69.13, 71.08, 71.87, 72.59 (C-2, C-3, C-4, C-5), 99.80 (C-1), 118.54 (arom CH), 152.79 (arom C–O), 166.90 (C-6), 169.22, 169.36, 170.08 (3MeCO); MS 742 (0.02) M^+, 683 (0.01) M^+−AcO, 623 (0.005) M^+−2AcOH+H, 317 (22) M^+−aglycon, 275 (0.20) 317−H_2C=C=O, 257 (41) 317−AcOH, 215 (18) 317−AcOH−H_2C=C=O, 197 (29) 317−2AcOH, 155 (100) 317−2AcOH−H_2C=C=O, 127 (60). Anal. Calcd for $C_{52}H_{58}O_{20}$ (742.65): C, 51.75; H, 5.16. Found: C, 51.46; H, 5.48.

*4.2.3. 1,4-Bis(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-naphthalene (**25**)*

According to method A, naphthohydroquinone (5.0 g, 31.2 mmol, 0.4 mol equiv) was combined with pentaacetyl-β-D-glucose (30.4 g, 78 mmol) and $BF_3{\cdot}OMe_2$ (36 ml, 390 mmol, 5 mol equiv) in CH_2Cl_2/Et_2O 200:100 ml. The crude reaction mixture was filtered before it was extracted. Yield 9.8 g (11.94 mmol, 31%); mp 179 °C (EtOH); IR (KBr) 3077 (=C–H), 2961, 2889 (–C–H), 1756 (C=O), 1229, 1038 (C–O–C), 769, 758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05, 2.06, 2.07, 2.08 (4s, 24H, 8MeCO), 3.95 (ddd, J=9.4, 4.7, 2.3 Hz, 2H, H-5), 4.22 (dd, J=2.3, 12.1 Hz, 2H, H-6), 4.35 (dd, J=12.1, 4.7 Hz, 2H, H-6), 5.18 (d, J=7.7 Hz, 2H, H-1), 5.24, 5.37 (2t, J=9.4 Hz, 4H, H-3, H-4), 5.47 (dd, J=9.4, 7.7 Hz, 2H, H-2), 7.01 (s, 2H, O–Ph–O), 7.54, 8.03 (2dd, J=6.4, 3.0 Hz, Ph); ^{13}C NMR ($CDCl_3$) δ 20.54, 20.58, 20.64, 20.64 (8MeCO), 61.88 (C-6), 68.39, 71.14, 71.99, 72.59 (C-2, C-3, C-4, C-5), 100.02 (C-1), 109.50 (O–Ph–O), 121.53, 126.76 (arom CH), 126.58 (arom C), 148.68 (arom C–O), 169.44, 169.47, 170.11, 170.48 (4CO); MS 490 (0.01) M^+−331+H, 331 (6.3) M^+−aglycon, 271 (2.8) 331−AcOH, 229 (1.4) 331−AcOH−H_2C=C=O, 211 (2.5) 331−2AcOH, 187 (1.3) 331−AcOH−$2H_2C$=C=O, 169 (100) 331−2AcOH−H_2C=C=O, 160 (5.0) $aglycon^+$, 127 (20) 331−2AcOH−$2H_2C$=C=O, 109 (68) 331−3AcOH−H_2C=C=O. Anal. Calcd for $C_{38}H_{44}O_{20}$ (820.76): C, 55.61; H, 5.40. Found: C, 55.21; H, 5.42.

4.3. Method B

The acetylated aryl glucoside was heated with 20 mol equiv KOH, 15 mol equiv of benzyl chloride, and 0.1 mol equiv of water for 5 h at 100 °C. After the mixture had cooled down, it was extracted with dichloromethane and water, and dried over potassium carbonate. The volatile compounds were removed under reduced pressure until 160 °C was reached. The residue was recrystallized from ethanol.

*4.3.1. 1,4-Bis(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**)*

1,4-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**5**) (15 g, 18.46 mmol) was treated according to method B. Yield 21.1 g (17.6 mmol, 95%); mp 184 °C (EtOH); IR (KBr) 3088, 3063, 3030 (=C–H), 2902, 2867 (–C–H), 1497 (Ph), 1453 (CH_2), 1072 (C–O–C), 734, 696 (Ph, monosubstitution) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20, 2.27, 2.28 (3s, 9H, 3Me), 3.28 (ddd, 1H, J=9.7, 5.5, 2.7 Hz, H-5′), 3.50–3.80 (m, 11H, H-2, H-3, H-4, H-5, H-6, H-2′, H-3′, H-4′, H-6′), 4.50–5.07 (9d, 18H, 8PhCH_2, H-1, H-1′), 6.81 (s, 1H, O–Ph–O), 7.15–7.35 (m, 40H, 8Ph); ^{13}C NMR ($CDCl_3$) δ 12.76, 14.09, 13.35 (3Me), 68.90 (C-6, C-6′), 73.49, 73.54, 74.99, 74.99, 75.17, 75.38, 75.75, 75.75 (8PhCH_2), 74.93, 75.06, 77.78, 77.83, 82.30, 82.94, 84.82, 84.87 (C-2, C-2′, C-3, C-3′, C-4, C-4′, C-5, C-5′), 102.41, 104.58 (C-1, C-1′), 116.19 (arom CH, O–Ph–O), 125.43, 129.43, 131.80 (arom C, O–Ph–O), 127.54–128.38 (arom CH, *Ph*CH_2), 138.10–138.74 (arom C, *Ph*CH_2), 148.52, 151.91 (arom C–O). Anal. Calcd for $C_{77}H_{80}O_{12}$ (1197.48): C, 77.23; H, 6.73. Found: C, 77.03; H, 6.73.

*4.3.2. 1,4-Bis(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyloxy)-benzene (**9**)*

1,4-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)benzene[14] (**4**) (1 g, 1.3 mmol) was treated according to method B. Yield 710 mg (0.615 mmol, 47%); mp 123 °C (EtOH); IR (KBr) 3062, 3030 (=C–H),

2912, 2860 (–C–H), 1505 (Ph), 1454 (CH_2), 1070 (C–O–C), 735, 697 (Ph, monosubstitution) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.55–3.80 (m, 12H, H-2, H-3, H-4, H-5, H-6), 4.93 (d, J=7.72 Hz, 2H, H-1), 4.50–5.07 (8d, 16H, 8PhCH_2), 7.02 (s, 4H, O–Ph–O), 7.15–7.35 (m, 40H, 8*Ph*CH_2); ^{13}C NMR ($CDCl_3$) δ 68.72 (C-6), 75.01 (C-5), 73.41, 75.01, 75.01, 75.71 (4PhCH_2), 77.60 (C-4), 81.96 (C-2), 84.59 (C-3), 102.37 (C-1), 118.45 (O–Ph–O), 127.68–128.37 (arom CH, *Ph*CH_2), 137.96, 138.04, 138.17, 138.45 (arom C, *Ph*CH_2), 152.93 (arom C–O). Anal. Calcd for $C_{74}H_{74}O_{12}$ (1155.40): C, 76.93; H, 6.45. Found: C, 76.91; H, 6.45.

4.4. Electrolysis in an undivided cell

*4.4.1. (−)-Menthyl 2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**13**)*

This electrolysis was performed in an undivided 100 ml cell. The cell was fitted with a ground glass lid and was provided with openings for a thermometer and a gas inlet. The electrodes were two cylindrical platinum gauzes with a surface of 25 cm^2 and a space of 2 mm between them. 1,4-Bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**) (1 g, 0.834 mmol) was mixed together with 261 mg (1.67 mmol) (−)-menthol in CH_2Cl_2 and NEt_4ClO_4. The electrolyses were carried out at room temperature at a constant current intensity of 50 mA and under stirring. The oxidation was monitored by TLC until complete disappearance of the glycosyl donor. The complete reaction requires between 2 and 3 F/mol. Then, the solution was washed with water, dried over magnesium sulfate, filtered, and evaporated. The product was isolated as an anomer mixture by column chromatography with hexane/CH_2Cl_2 1:9 as the eluent. The β-anomer could be separated by repeated chromatographies. Yield 930 mg (1.37 mmol, 82%) (−)-menthyl 2,3,4,6-tetrabenzylglucopyranoside (α/β 1:1); mp 84 °C (EtOH); IR (KBr) 3063, 3033 (=C–H), 2953, 2927, 2867 (C–H), 1454 (CH_2), 1073 (C–O–C), 746, 698 (Ph, monosubstitution) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83, 0.90, 0.92 (3d, J=6.9 Hz, 9H, 3Me), 1.00, 1.27, 1.34, 1.64, 2.12 (5m, 8H, CH), 2.36 (hd, J=6.9, 2.5 Hz, 1H, C*H*Me_2), 3.41 (dd, J=8.5, 2.7 Hz, 1H, H-6), 3.43 (dd, J=8.5, 4.7 Hz, 1H, H-6), 3.50 (td, J=10.4, 4.1 Hz, 1H, HC–$O_{aglycon}$), 3.55–3.72 (m, 4H, H-2, H-3, H-4, H-5), 4.47 (d, J=7.9 Hz, 1H, H-1), 4.50–5.00 (8d, J=10.0–12.4 Hz, 8H, 4CH_2Ph), 7.15–7.40 (m, 20H, 4Ph); ^{13}C NMR ($CDCl_3$) δ 15.98, 21.09, 22.25 (3Me), 23.22, 34.47, 40.98 (CH_2), 25.29, 31.47, 48.14 (CH), 69.34 (C-6), 74.83 (C-5), 73.68, 74.83, 75.00, 75.59 (CH_2Ph), 77.76, 77.97 (C-4, HC–$O_{aglycon}$), 82.24, 84.99 (C-2, C-3), 100.80 (C-1), 127.49–128.40 (arom CH, *Ph*CH_2), 138.27, 138.42, 138.60, 138.87 (arom C, *Ph*CH_2); MS 678 (0.01) M^+, 587 (0.25) M^+−Bn, 522 (0.08) M^+−aglycon−H, 495 (0.01) M^+−2Bn−H, 481 (0.10) M^+−Bn−BnO+H, 431 (2.0) 522−Bn, 325 (1.9) 522−Bn−BnO+H, 301 (2.0), 275 (6.8), 253 (21) $(BnOCH)_2CH^+$, 240 (8.6) $(BnOCH)_2^+$, 181 (14) Bn_2^+−H, 139 (13) aglycon$^+$−OH, 91 (100) Bn^+. Anal. Calcd for $C_{44}H_{54}O_6$ (678.91): C, 77.84; H, 8.02. Found: C, 77.72; H, 7.98.

4.5. Electrolysis in a divided cell

*4.5.1. Methyl (cyclohexyl 2,3,4-tri-O-acetyl-α-D-glucopyranosid)-uronate (**17**)*

This electrolysis was performed in a divided cell. A 'H'-cell was employed. Each of the two electrode compartments held approximately 100 ml of electrolyte. They were connected by a 4 cm diameter glass frit (No. 4). The cell was hermetically closed and the lids had an inlet and outlet for the passage of nitrogen gas. The electrodes were suspended from the lids. The anode was a platinum gauze and the cathode a carbon cylinder. Lithium perchlorate (3 g) was placed into each compartment and dissolved in 90 ml acetonitrile. 1,4-Bis(methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyloxyuronate)benzene (**16**) (1 g, 1.34 mmol) and 269 mg (2.68 mmol) of cyclohexanol were added together with 50 mg of cobalt (II) chloride as mediator. The electrolysis was performed at room temperature at a constant current intensity of 20 mA, until the reaction was complete. Then, the reaction mixture was first concentrated and taken in ether, washed with water, dried over magnesium sulfate, filtered, and evaporated. The product was isolated by column chromatography with hexane/ethyl acetate 1:1 as the eluent. Yield 840 mg (2.01 mmol, 75%); mp 114 °C (EtOH); IR (KBr) 2940, 2860 (C–H), 1749 (C=O) 1220, 1044 (C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2–1.9 (m, 10H, CH_2), 2.03, 2.03, 2.05 (2s, 9H, 3*Me*CO), 3.59 (tt, J=8.3, 4.1 Hz, 1H, HC–$O_{aglycon}$), 3.75 (s, 3H, OMe), 4.44 (d, J=10.2 Hz, 1H, H-5), 4.84 (dd, J=10.2, 3.8 Hz, 1H, H-2), 5.15 (dd, J=10.2, 9.4 Hz, 1H, H-3 or H-4), 5.31 (d, J=3.8 Hz, 1H, H-1), 5.54 (dd, J=10.2, 9.4 Hz, 1H, H-3 or H-4); ^{13}C NMR ($CDCl_3$) δ 20.54, 20.63, 20.73 (3*Me*CO), 23.55, 23.88 (*C*H_2CH_2CH–O), 25.45 (*C*$H_2CH_2CH_2CH$–O), 31.28, 33.18 (*C*H_2CH–O), 52.84 (OMe), 68.28, 69.43, 69.90, 70.82 (C-2, C-3, C-4, C-5), 94.15 (C-1), 168.42 (C-6), 169.64, 170.01, 170.15 (3C=O); MS 417 (0.09) M^++H, 405 (0.24), 357 (3.9) M^+−AcO, 317 (4.6) M^+−aglycon, 296 (4.5) M^+−2AcOH, 274 (17) 317−Ac, 228 (70) 317−AcOH−(C-1)−OH, $AcO_3C_4H_4^+$, 186 (65) 228−H_2C=C=O, 157 (100) $(AcOCH)_2CH^+$. Anal. Calcd for $C_{19}H_8O_{10}$ (416.42): C, 54.80; H, 6.78. Found: C, 54.79; H, 6.69.

4.6. Method C

1,4-Bis(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyloxy)-2,3,5-trimethylbenzene (**6**) (500 mg, 0.418 mmol), DDQ (95 mg, 0.42 mmol), and 0.84 mmol of alcohol were dissolved in 20 ml of dry dichloromethane. TfOH (10 mg) was added and the solution was stirred for 10 min. If no turbidity appeared, 10 mg of TfOH was added again. The progress of the reaction was monitored by TLC. The reaction mixture was filtered, washed with $NaHCO_3$ and water, dried over magnesium sulfate, and evaporated. The product was isolated by column chromatography.

*4.6.1. Methyl 12-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyloxy)-octadecanoate (**22**)*

Methyl 12-hydroxyoctadecanoate (**21**) (264 mg, 0.84 mmol) was treated according to method C with 30 mg of TfOH. The reaction lasted 2 h and the product was isolated by column chromatography with hexane/ethyl acetate 3:1 as eluent. Yield 610 mg (0.73 mmol, 87%) α/β 2:1; IR (capillar) 3088, 3063, 3030 (=C–H), 2927, 2855 (C–H), 1739 (C=O), 1454 (CH_2), 1072 (C–O–C), 736, 698 (Ph, monosubstitution) cm^{-1}; ^1H NMR ($CDCl_3$) α-anomer: δ 0.87 (t, J=6.0 Hz, 3H, Me), 1.26 ('s', 24H, CH_2), 1.53, 1.59 (2 m, 4H, CH_2CH–O), 2.26 (t, J=7.4 Hz, 2H, CH_2C=O), 3.44 (br t, J=7.7 Hz, 1H, HC–$O_{aglycon}$), 3.61 (s, 3H, OMe), 3.52–3.73 (m, 3H, HC–O), 3.74 (dd, J=10.4, 3.4 Hz, 1H, H-6), 3.90 (br d, J=9.4 Hz, 1H, H-5), 4.00 (t, J=9.4 Hz, 1H, H-3 or H-4), 4.4–5.0 (9d, 9H, H-1, 4PhCH_2), 7.10–7.40 (m, 20H, Ph); ^{13}C NMR ($CDCl_3$) α-anomer: δ 14.12 (Me), 22.65 (MeCH_2), 24.89 (CH_2CH_2C=O), 24.89, 25.67 (*C*H_2CH_2CH–O), 29.10, 29.23, 29.39, 29.56, 29.66, 29.81, 29.94 (CH_2), 31.77 (MeCH_2CH_2), 33.17, 34.47 (CH_2CH–O), 51.29 (OMe), 68.50 (C-6), 73.18, 73.41, 74.98, 75.51 (*Ph*CH_2), 70.41, 73.18, 77.94, 80.09, 82.09 (HC–O), 95.66 (C-1), 127.44–128.28 (arom CH, *Ph*CH_2), 137.97, 138.29, 138.33, 138.93 (arom C, *Ph*CH_2), 174.08 (C=O); characteristic peaks of the β-anomer: δ 25.13, 25.29 (*C*H_2CH_2CH–O), 31.75 (MeCH_2CH_2), 34.21, 34.90 (*C*H_2CH–O), 69.17 (C-6), 73.52, 74.88, 74.98, 75.57 (*Ph*CH_2), 74.88, 78.02, 79.84, 82.40, 84.91 (HC–O), 102.63 (C-1), 138.22, 138.39, 138.59, 138.73 (arom C, *Ph*CH_2); MS 745 (0.0006) M^+−Bn, 698 (0.0008), 639 (0.0001) M^+−BnO−Bn+H, 607 (0.004), 539 (0.04) 522+OH, 522 (0.03) M^+−aglycon−H, 431 (0.64) 522−Bn, 355 (1.1), 325 (1.1) 522−Bn−BnO+H, 297 (11) aglycon$^+$−OH, 253 (10) $(BnOCH)_2CH^+$, 240 (6.6) $C_{17}H_{36}^+$, 181 (13) Bn_2^+−H, 91 (100) Bn^+. Anal. Calcd for $C_{53}H_{72}O_8$ (837.15): C, 76.04; H, 8.67. Found: C, 76.27; H, 8.54.

4.6.2. 1,3-Bis(hexadecanoyloxy)prop-2-yl 2,3,4,6-tetra-O-benzyl-D-glucopyranoside (**24**)

Dipalmitine **23** (477 mg, 0.84 mmol) was treated according to method C with $SnCl_4$ (218 mg, 0.84 mmol). The reaction lasted 1 h and the product was isolated by column chromatography with hexane/ethyl acetate 6:1 as eluent. Yield 700 mg (0.64 mmol, 77%); α/β 2:1; IR (KBr) 3087, 3063, 3030 (=C–H), 2918, 2852 (C–H), 1739 (C=O), 1457 (CH_2), 1072 (C–O–C), 738, 699 (Ph, mono-substitution) cm^{-1}; ^1H NMR ($CDCl_3$) α-anomer: δ 0.88 (t, *J*=6.5 Hz, 6H, Me), 1.26, 1.76 (2m, 48H and 4H, CH_2), 2.26 (m, 4H, CH_2C=O), 3.4–4.4 (m, 11H, HC–O), 4.4–5.0 (8d, 8H, 4PhCH_2), 5.05 (d, *J*=3.4 Hz, 1H, H-1), 7.10–7.40 (m, 20H, Ph); ^{13}C NMR ($CDCl_3$) α-anomer: δ 14.13 (Me), 22.70 ($MeCH_2$), 24.85 (CH_2CH_2C=O), 29.38–29.71 (CH_2), 31.94 ($MeCH_2CH_2$), 34.09, 34.13 (CH_2C=O), 62.77, 63.67 (CH_2O), 68.35 (C-6), 73.07, 73.53, 75.01, 75.68 (*Ph*CH_2), 70.71, 72.92, 77.53, 79.75, 81.80 (HC–O), 96.40 (C-1), 127.55–128.47 (arom CH, *Ph*CH_2), 138.12, 138.12, 138.31, 138.82 (arom C, *Ph*CH_2), 173.32 (C=O); characteristic peaks of the β-anomer: δ 24.81 (CH_2CH_2C=O), 34.01, 34.28 (CH_2C=O), 63.32, 63.50 (CH_2O), 68.86 (C-6), 73.52, 74.69, 75.02, 75.68 (*Ph*CH_2), 75.01, 81.99, 84.63 (HC–O), 103.47 (C-1), 137.86, 137.86, 138.47, 138.59 (arom C, *Ph*CH_2), 173.47 (C=O); MS 1123 (<0.1) M^++CO_2−H, 595 (1.7) aglycon$^+$+CO_2−OH, 551 (30) aglycon$^+$−OH, 522 (<1) M^+−aglycon−H, 431 (4.0) 522−Bn, 341 (7.0) 522−2Bn+H, 325 (3.9) 522−Bn−BnO+H, 313 (21), 299 (8.9), 253 (12) $(BnOCH)_2CH^+$, 239 (14) $C_{15}H_{31}CO^+$, 181 (8.7) Bn_2^+−H, 106 (92) BnO^+−H, 91 (100) Bn^+. Anal. Calcd for $C_{69}H_{102}O_{10}$ (1091.56): C, 75.92; H, 9.42. Found: C, 75.80; H, 9.24.

4.6.3. Methyl 12-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-octadecanoate (**28**)

1,4-Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)naphthalene (**25**) (500 mg, 0.61 mmol), DDQ (138 mg, 0.61 mmol), methyl 12-hydroxyoctadecanoate (337 mg, 1.22 mmol, 1 mol equiv) dissolved in 2 ml of dry dichloromethane and $SnCl_4$ (318 mg, 1.22 mmol) were stirred together in 20 ml of MeCN. After 2 days, the reaction mixture was concentrated and the residue was dissolved in CH_2Cl_2, washed with $NaHCO_3$ and water, and dried over magnesium sulfate. The product was isolated by column chromatography with hexane/ethyl acetate 3:1 as eluent. Yield 320 mg (0.5 mmol, 41%); IR (KBr) 2929, 2856 (C–H), 1757 (C=O) 1225, 1040 (C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J*=6.8 Hz, 3H, Me), 1.2–1.65 (m, 28H, CH_2), 2.00, 2.02, 2.02, 2.07 (3s, 12H, 4*Me*CO), 2.30 (t, *J*=7.5 Hz, 2H, CH_2C=O), 3.55 (p, *J*=5.5 Hz, 1H, HC–$O_{aglycon}$), 3.66 (s, 3H, OMe), 3.68 (ddd, *J*=9.5, 5.4, 2.3 Hz, 1H, H-5), 4.12 (dd, *J*=12.1, 2.3 Hz, 1H, H-6), 4.23 (dd, *J*=12.1, 5.4 Hz, 1H, H-6), 4.56 (d, *J*=8.0 Hz, 1H, H-1), 4.96 (dd, *J*=9.4, 8.0 Hz, 1H, H-2), 5.06, 5.20 (2t, *J*=9.4 Hz, 2H, H-3, H-4); ^{13}C NMR ($CDCl_3$) δ 14.08 (Me), 20.60, 20.60, 20.64, 20.68 (4*Me*CO), 22.65 ($MeCH_2$), 24.96 (CH_2CH_2C=O), 25.02, 25.10 (CH_2CH_2CH-O), 29.15, 29.26, 29.46, 29.55, 29.59, 29.67 (CH_2), 31.89 ($MeCH_2CH_2$), 34.08 (CH_2C=O), 34.17, 34.81 (CH_2CH–O), 51.38 (OMe), 62.30 (C-6), 68.74, 71.55, 71.73, 73.08 (C-2, C-3, C-4, C-5), 81.35 (HC–$O_{aglycon}$), 100.48 (C-1), 169.18, 169.43, 170.32, 170.55 (4MeCO); MS 645 (0.06) M^++H, 613 (0.16) M^+−MeO, 585 (0.09) M^+−$C_2H_3O_2$, 553 (0.66) M^+−AcOH−MeO, 524 (0.05) M^+−2AcOH, 493 (0.13) M^+−2AcOH−MeO, 464 (0.55) M^+−3AcOH, 422 (0.50) M^+−3AcOH−H_2C=C=O, 331 (56) M^+−aglycon, 297 (59) aglycon$^+$−OH, 289 (20) 331−H_2C=C=O, 271 (16) 331−AcOH, 242 (82) 331−AcOH−(C-1)−OH, 229 (23) 331−AcO−Ac, 200 (46) 242−H_2C=C=O, 169 (100) 331−2AcOH−HC=C=O. Anal. Calcd for $C_{33}H_{56}O_{12}$ (644.80): C, 61.47; H, 8.75. Found: C, 61.17; H, 8.81.

References and notes

1. (a) Fügedi, P. *Organic Chemistry of Sugars*; Levy, D. E., Fügedi, P., Eds.; CRC: Boca Raton, FL, 2006; pp 89–179; (b) Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503–1531; (c) Boons, G. J. *Tetrahedron* **1996**, *52*, 1095–1121; (d) Davis, B. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2137–2160; (e) Toshima, K. *Carbohydr. Res.* **2006**, *341*, 1282–1297.
2. Noyori, R.; Kurimoto, I. *J. Org. Chem.* **1986**, *51*, 4320–4322.
3. (a) Amatore, C.; Jutand, A.; Mallet, J.-M.; Meyer, G.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1990**, 718–719; (b) Mallet, J.-M.; Meyer, G.; Yvelin, F.; Jutand, A.; Amatore, C.; Sinaÿ, P. *Carbohydr. Res.* **1993**, *244*, 237–246; (c) Amatore, C.; Jutand, A.; Meyer, G.; Bourhis, P.; Machetto, F.; Mallet, J.-M.; Sinaÿ, P.; Tabeur, C.; Zhang, Y.-M. *J. Appl. Electrochem.* **1994**, *24*, 725–729.
4. (a) Balavoine, G.; Gref, A.; Fischer, J. C.; Lubineau, A. *Tetrahedron Lett.* **1990**, *31*, 5761–5764; (b) Vijayakumar, S.; Nagarajan, P.; Sulochana, N. *Indian J. Chem., Sect. B* **1993**, *32*, 599–600; (c) Hamann, C. H.; Polligkeit, H.; Wolf, P.; Smiatacz, Z. *Carbohydr. Res.* **1994**, *265*, 1–7; (d) Patricia, J. F. R.; Jasintha, T.; Nagarajan, P.; Subramanian, N. S.; Sulochana, N. *Bull. Electrochem.* **1995**, *11*, 324–325; (e) Balavoine, G.; Berteina, S.; Gref, A.; Fischer, J. C.; Lubineau, A. J. *Carbohydr. Chem.* **1995**, *14*, 1217–1236; (f) Tanaka, N.; Ohnishi, F.; Uchihata, D.; Torii, S.; Nokami, J. *Tetrahedron Lett.* **2007**, *48*, 7383–7387.
5. (a) France, R. R.; Rees, N. V.; Wadhavan, J. D.; Fairbanks, A. J.; Compton, R. G. *Org. Biomol. Chem.* **2004**, *2*, 2188–2194; (b) France, R. R.; Compton, R. G.; Davis, B. G.; Fairbanks, A. J.; Rees, N. V.; Wadhavan, J. D. *Org. Biomol. Chem.* **2004**, *2*, 2195–2202; (c) Drouin, L.; Compton, R. G.; Fietkau, N.; Fairbanks, A. J. *Synlett* **2007**, 2711–2717.
6. (a) Yamago, S.; Kokubo, K.; Yoshida, J. *Chem. Lett.* **1997**, *26*, 111–112; (b) Yamago, S.; Kokubo, K.; Hara, O.; Masuda, S.; Yoshida, J. *J. Org. Chem.* **2002**, *67*, 8584–8592.
7. (a) Suzuki, S.; Matsumoto, K.; Kawamura, K.; Suga, S.; Yoshida, J. *Org. Lett.* **2004**, *6*, 3755; (b) Nokami, T.; Shibuya, A.; Tsuyama, H.; Suga, S.; Bowers, A. A.; Crich, D.; Yoshida, J. *J. Am. Chem. Soc.* **2007**, *129*, 10922–10928.
8. (a) Rondinini, S.; Mussini, P. R.; Sello, G.; Vismara, E. *J. Electrochem. Soc.* **1998**, *145*, 1108–1112; (b) Benedetto, M.; Miglierini, G.; Mussini, P. R.; Pelizzoni, F.; Rondinini, S.; Sello, G. *Carbohydr. Lett.* **1995**, *1*, 321–328; (c) Brevet, D.; Mugnier, Y.; Samreth, S.; Dellis, P. *Carbohydr. Res.* **2003**, *338*, 1543–1552.
9. (a) Nokami, J.; Osafune, M.; Ito, Y.; Miyake, F.; Sumida, S.-I.; Torii, S. *Chem. Lett.* **1999**, *28*, 1053–1054; (b) Mitsudo, K.; Kawaguchi, T.; Miyahara, S.; Matsuda, W.; Kuroboshi, M.; Tanaka, H. *Org. Lett.* **2005**, *7*, 4649–4652.
10. Johnson, R. W.; Bednarski, M. D.; O'Leary, B. F.; Grover, E. R. *Tetrahedron Lett.* **1981**, *22*, 3715–3718.
11. (a) Nguyen Van, T.; Claessens, S.; Habonimana, P.; Abbaspour Tehrani, K.; Van Puyvelde, L.; De Kimpe, N. *Synlett* **2006**, 2469–2471; (b) Güvenalp, Z.; Kazaz, C.; Kaya, Y.; Demirezer, L. Ö. *Biochem. Syst. Ecol.* **2006**, *34*, 894–896; (c) Han, L.; Li, W.; Narimatsu, S.; Liu, L.; Fu, H.; Okuda, H.; Koike, K. *J. Nat. Med.* **2007**, *61*, 184–186.
12. (a) Tanese, M. C.; Torsi, L.; Cioffi, N.; Zotti, L. A.; Colangiuli, D.; Farinola, G. M.; Babudri, F.; Naso, F.; Giangregorio, M. M.; Sabbatini, L.; Zambonin, P. G. *Sens. Actuators, B* **2004**, *100*, 17–21; (b) Kim, I.-B.; Erdogan, B.; Wilson, J. N.; Bunz, U. H. F. *Chem.—Eur. J.* **2004**, *10*, 6247–6254; (c) Takasu, A.; Iso, K.; Dohmae, T.; Hirabayashi, T. *Biomacromolecules* **2006**, *7*, 411–414; Yamashita, Y.; Kaneko, Y.; Kadokawa, J.-I. *Eur. Polym. J.* **2007**, *43*, 3795–3806.
13. (a) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095–3165; (b) Li, C.-J.; Chen, L. *Chem. Soc. Rev.* **2006**, *35*, 68–82; (c) Herrerias, C. I.; Yao, X.; Li, Z.; Li, C.-J. *Chem. Rev.* **2007**, *107*, 2546–2562.
14. Smits, E.; Engberts, J. B. F. N.; Kellog, R. M.; van Doren, H. A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2873–2878.
15. Schmidt, O. T.; Auer, T.; Schmadel, H. *Chem. Ber.* **1960**, *93*, 556–557.
16. Schmidt, R. R.; Stumpp, M. *Liebigs Ann. Chem.* **1983**, *7*, 1249–1256.
17. Shoda, S.; Mukayama, T. *Chem. Lett.* **1979**, 847–848.
18. (a) Schmidt, W.; Steckhan, E. *Chem. Ber.* **1980**, *113*, 577–585; (b) Mehta, S.; Pinto, B. M. *Carbohydr. Res.* **1998**, *310*, 43–51; (c) Wain, A. J.; Streeter, I.; Thompson, M.; Fietkau, N.; Drouin, L.; Fairbanks, A. J.; Compton, R. G. *J. Phys. Chem. B* **2006**, *110*, 2681–2691.
19. Zemplen, G.; Csuros, Z.; Angyal, S. *Chem. Ber.* **1937**, *70*, 1848–1856.
20. (a) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2205–2213; (b) Perrin, C. *Tetrahedron* **1995**, *51*, 11901–11935.
21. (a) Sinaÿ, P.; Pougny, J. *Tetrahedron Lett.* **1976**, *17*, 4073–4076; (b) Fraser-Reid, B.; Konradsson, P.; Ratcliffe, A. J. *J. Am. Chem. Soc.* **1990**, *112*, 5665–5667; (c) Hadd, M. J.; Gervay, J. *Carbohydr. Res.* **1999**, *320*, 61–69.
22. Dayal, B.; Salen, G.; Padia, J.; Shefer, S.; Tint, G. S.; Sasso, G.; Williams, T. H. *Carbohydr. Res.* **1993**, *240*, 133–142.
23. Treibs, W.; Franke, I. *Ann. Chem.* **1950**, *570*, 76–87.
24. Inanaga, J.; Yokoyama, Y.; Hanamoto, T. *Chem. Lett.* **1993**, 85–88.
25. Classon, B.; Samuelsson, B.; Garegg, P. J. *Acta Chem. Scand. B* **1984**, *38*, 419–422.
26. Hartman, L. *J. Chem. Soc.* **1957**, 3572–3575.
27. Brinker, U. H.; Tyner, M., III; Jones, W. M. *Synthesis* **1975**, 671.