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Synthesis and characterization of phenolic antioxidants with surfactant properties: glucosyl- and glucuronosyl alkyl gallates

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ABSTRACT

In the search of better antioxidants for different applications, we have designed and synthesized two series of antioxidants that possess surfactant properties: glucosyl- and glucuronosyl alkyl gallates. They display better surface-active efficiency that alkyl gallates and some show critical micelle concentration (CMC) and surfactant effectiveness (γ_{cmc}) in the same range of worldwide known surfactants, such as Brij-30 or Tween-20. Moreover, they exhibit a high antioxidant activity due to the di-*ortho* phenolic moiety present in their structure. Nevertheless, glucosyl- and glucuronosyl alkyl gallates are worse antioxidants than the corresponding alkyl gallates.

1. Introduction

Oxidation in living cells causes the formation of reactive oxygen species that are counterbalanced by biological repairing systems. The oxidative stress produced when this equilibrium is unbalanced has been related with ageing[1] and diseases, such as atherosclerosis, stroke, rheumatoid arthritis and neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases.[2–5] Antioxidants have been proposed as potential preventive and therapeutic tools to counteract the oxidation damage and therefore control disease.[6–9] At the same time, antioxidants have been traditionally used as food additives to help guard against food deterioration and as stabilizers in fuels and lubricants to prevent oxidation.

Polyphenols are one of the main groups of antioxidants found in Nature. They have shown interesting biological properties, such as green tea catechins with anticancer[10] and brain-protective activities,[11] berries anthocyanins enhancing memory[12,13] or olive oil phenols, such as hydroxytyrosol capable of reducing the size of atherosclerotic lesions in rabbits.[14] At the same time, the potency of natural phenols, such as rosmarinic acid or hydroxytyrosol as food antioxidants has proven to be even better than α-tocopherol, BHT or ascorbyl palmitate commonly used food antioxidants.[15–18]

Different chemical modifications of natural phenols have been explored to improve their antioxidant potency and biological activity. Inspired by hydroxytyrosol **1** (Fig. 1), our group and others have recently prepared new phenolic derivatives varying the number of phenolic hydroxyl groups, length of the alkyl chain[19] or attaching lipophilic moieties to the central core.[20–24] This last group of new phenolic compounds containing a phenolic scaffold

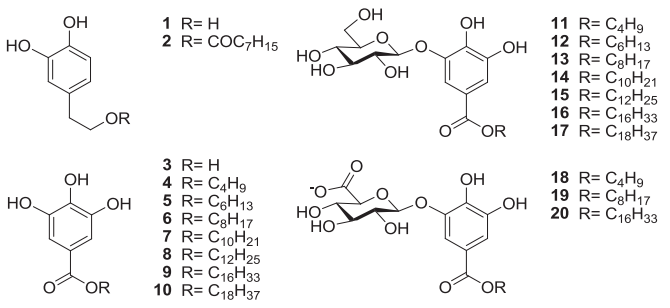

Fig. 1. Hydroxytyrosol (**1**), hydroxytyrosol octanoate (**2**), gallic acid (**3**), alkyl gallates (**4**–**10**) and glucosyl alkyl gallates (**11**–**17**) and glucuronosyl alkyl gallates (**18**–**20**) prepared in this work.

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with an attached alkyl chain has recently being named as phenolipids.[25] In oil-in-water emulsified systems we observed that acylation of hydroxytyrosol with medium-size alkyl chains (for example, hydroxytyrosol octanoate **2**) presented higher antioxidant activity than hydroxytyrosol or hydroxytyrosol fatty acid esters with longer alkyl chains.[26]

A similar behaviour has been described for other phenolipids, such as chlorogenate esters and rosmarinate esters modified with medium-size alkyl chains.[25,27–29] In fact, the best antioxidant in a series of hydroxytyrosol fatty acid esters was the most effective surfactant in aqueous media.[30] Since the phenolic unit, responsible for most of the antioxidant activity, is common to all these series of compounds, an effective surfactant would locate the antioxidant preferentially at the oil-water interface in the emulsions inhibiting lipid oxidation more efficiently (Fig. 2a). This reasoning can also be extended to the biological field where an antioxidant located at the cell membrane will be more efficient to protect the cell from reactive oxygen species in the exterior (Fig. 2b). Actually, tocopheryl derivatives as amphiphilic antioxidants have been prepared to be embedded within the membranes for a better protection of the cells.[31]

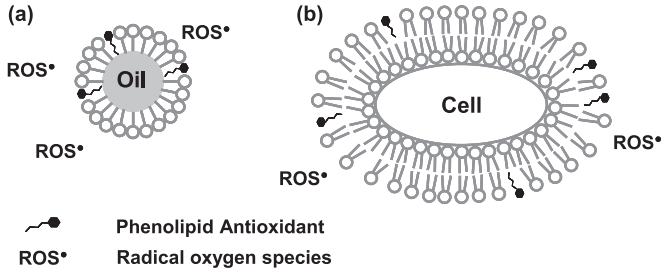


Fig. 2. (a) Oil-in-water emulsion containing antioxidants located at the interface; (b) Cell containing antioxidants placed within the membrane.

We have now focused in the potent and commonly used antioxidants gallic acid and alkyl gallates (**3**–**10**, Fig. 1) to design new antioxidant surfactants. Alkyl gallates, such as butyl gallate **4** or octyl gallate **6** are potent antioxidants used as additives in food, cosmetics and lubricants. Moreover, they have been reported to protect cells against oxidative damage induced by reactive oxygen species (ROS), as hydroxyl radicals or hydrogen peroxide, and reactive sulfur species (RSS).[32] Alkyl gallates are also known to cause apoptosis in several tumour cell lines and to inhibit lymphocyte proliferation.[33,34]

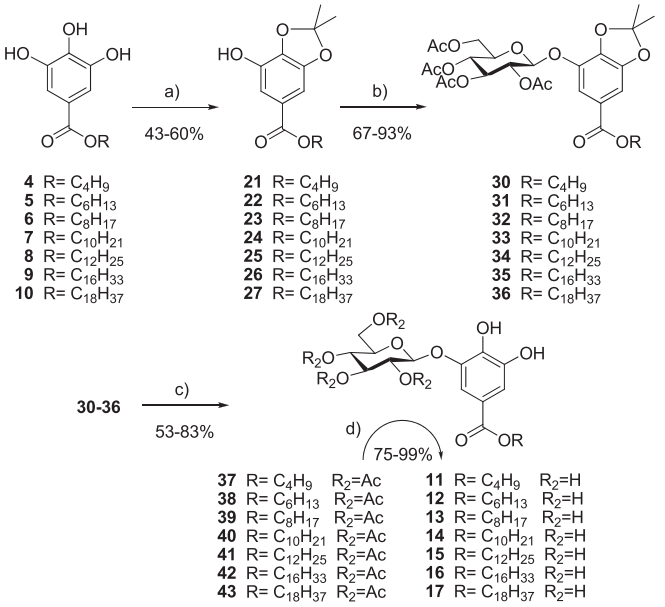
We tried to design antioxidants highly effective in emulsified systems and in cellular environments based in the structure of alkyl gallates. We found that the surface active properties of alkyl gallates could be improved (see below) and decided to attach a sugar moiety at the phenolic group at position 3 maintaining a di-*ortho* phenolic moiety in the overall structure. Previously, gallic esters of sucrose[35] and glucopyranosyl derivatives of tocopherols,[36] have been reported as radical scavengers and amphiphilic antioxidants, respectively. Also, acyl glyco-carotenoic acids have been isolated from a marine bacterium, Rubritalea squalenifaciens.[37,38] Here we report the synthesis of a series of glycosyl alkyl gallates (**11**–**20**) that contain glucose or glucuronic acid attached to the alkyl gallate scaffold (Fig. 2). Alkyl gallates (**4**–**10**) with different chain lengths from C4 to C18 have been used in the synthesis of the new derivatives in order to obtain an appropriate hydrophilic–lipophilic balance (HLB). Critical micelle concentration (CMC) and surface tension in aqueous media have been analyzed and discussed. Radical scavenging properties and reducing capacity have been measured for the new antioxidant surfactants using the DPPH and the FRAP test, respectively. The new antioxidants seem to display optimum properties to be used in emulsified systems and to protect cells from oxidation.

2. Results and discussion

2.1. Synthesis of glycosyl alkyl gallates (11–20)

We designed new compounds based on the potent antioxidants alkyl gallates that will carry a more polar head group within their amphiphilic structure that may improve their surface active properties. To do so, we decided to attach a glycosyl unit to the phenolic hydroxyl group at position 3 of alkyl gallates leaving a di-*ortho* phenolic moiety that should maintain most of their antioxidant activity.

*2.1.1. Synthesis of glucosyl alkyl gallates (**11**–**17**).* The synthesis started with the acetal protection of the corresponding alkyl gallates **4**–**10** (Scheme 1), all of them commercially available, except decyl gallate that was prepared by reaction of gallic acid and decanol in THF using DCC as catalyst.[39]



Scheme 1. Synthesis of glucosyl alkyl gallates (**11**–**17**). (a) 2,2-dimethoxypropane, acid, $CHCl_3$; (b) **28**, $BF_3{\cdot}OEt_2$, CH_2Cl_2; (c) TFA; (d) Na_2CO_3, MeOH.

The isopropyliden derivatives **21**–**27** were synthesized by standard reactions conditions with 2,2-dimethoxyisopropyliden acetal and camphor sulfonic acid with moderate yields (43–60%) (Scheme 1). Next, glycosylation reactions were carried out using classical Schmidt's glycosylation protocol[40–42] either with the glucosyl or the glucuronosyl trichloroacetimidates donors **28** and **29**, respectively (Fig. 3).

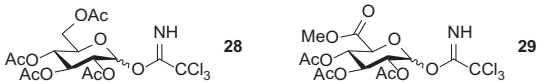


Fig. 3. Glucosyl and glucuronosyl tricholoacetimidate donors (**28**–**29**).

Fully protected glucosyl alkyl gallates **30**–**36** were obtained with good to excellent yields (67–93%, Table 1, entries 1–7) using $BF_3{\cdot}OEt_2$ as the promoter in CH_2Cl_2 at room temperature and short reaction times (30–60 min). These reaction conditions resulted in glycosylated products with β-stereoselectivity as expected. These compounds were then submitted to deprotection steps. First treatment with TFA to remove the isopropyliden group afforded compounds **37**–**43** (yields, 53–83%) followed by hydrolysis with

Table 1
Glycosylation reaction conditions and results obtained

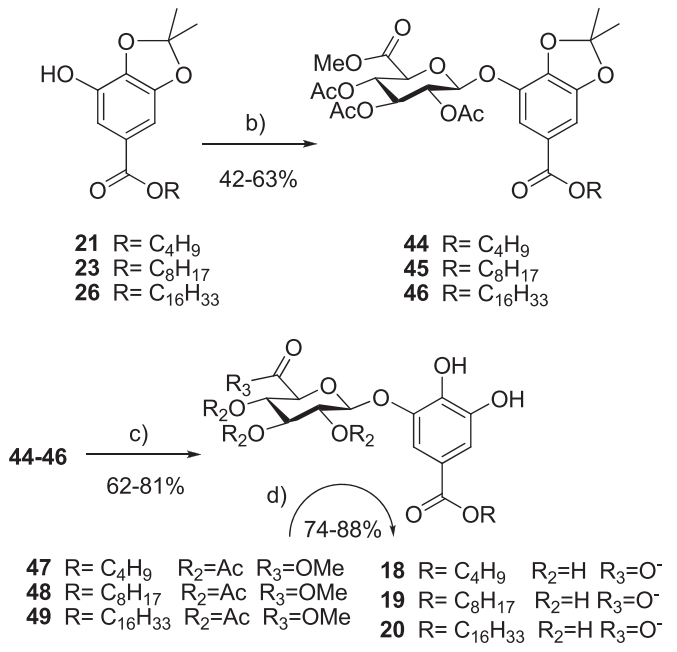
Entry	Acceptor	Donor	Product[a]	Yield[b] (%)
1	21	28	30	89
2	22	28	31	76
3	23	28	32	79
4	24	28	33	93
5	25	28	34	86
6	26	28	35	79
7	27	28	36	67
8	21	29	44	42
9	23	29	45	53
10	26	29	46	63

[a] All glycosylation reactions were performed in dichloromethane and $BF_3{\cdot}OEt_2$ was used like promoter.
[b] Isolated yield after chromatography.

Na_2CO_3 in MeOH to obtain the final products **11**–**17** (yields, 75–99%). Deprotection steps carried out in the reverse order yielded complex reaction mixtures.

*2.1.2. Synthesis of glucuronosyl alkyl gallates (**18**–**20**).* Next, we decided to include glucuronic acid, a charged glycosyl moiety, within the alkyl gallate scaffold to compare the surface active and antioxidant properties with the neutral polar heads of the glucosyl alkyl gallates **4**–**10**. The synthesis of glucuronic acid derivatives is not trivial since the corresponding glycosyl donors exhibit quite low reactivity with all kind of alcohols. This problem worsens when the alcohol acceptor is a phenol given that they tend to be less reactive than primary or secondary alcohols. Synthesis of glucuronosyl donor **29** (Fig. 2) is carried out in three steps from the commercially available D-glucurono-6,3-lactone in good yields via the 1-hydroxysugar.[43–46] Final conversion into the corresponding trichloroacetimidates donor is accomplished through activation of the hydroxyl group with DBU and reaction with trichloroacetonitrile in good yields.[47]

Butyl, octyl and hexadecyl gallates **4**, **6**, **9** were selected to be modified with the glucuronosyl moiety (Scheme 2). The same synthetic strategy was followed as in the case of the glucosyl derivatives. Glycosylation between acetal protected alkyl gallates **21**, **23** and **26** and glucuronosyl trichloroacetimidate **26** (Table 1, entries 8–10) was carried out using the same reaction conditions described for the glucosyl derivatives, to obtain glucuronosyl gallates **44**–**46** in moderate to good yields (42–63%). Deprotection with TFA yielded compounds **47**–**49** and final treatment with Na_2CO_3 in MeOH afforded the corresponding compounds **18**–**20**.



Scheme 2. Synthesis of glucuronosyl alkyl gallates (**18**–**20**). (b) **29**, $BF_3{\cdot}OEt_2$, CH_2Cl_2; (c) TFA; (d) Na_2CO_3, MeOH.

2.2. Physicochemical properties of alkyl gallates (4–10) and glycosyl alkyl gallates (11–20)

*2.2.1. Surface tension measurements for alkyl gallates (**4**–**10**).* The amphiphilic structure of alkyl gallates, especially those with long alkyl chains could indicate that they may behave as surfactants. To the best of our knowledge, there is no surface tension data reported for any alkyl gallate. Nevertheless, it has been described how their presence in small amounts (up to 0.2%) affects the properties of different micellar systems.[48] Therefore, we measured surface tension in aqueous media for alkyl gallates **4**–**10** that possess different length for the alkyl chain. The graphs of surface tension/log of the compound concentration are represented in Fig. 4. It can be observed that whereas for gallic acid (taken as a reference) no surface tension decrease is produced when the concentration increases up to its limit of solubility, the incorporation of alkyl groups with increasing hydrocarbon chain length in the alkyl gallates, promotes a drastic change in the profile of the graphs that attain in most of the cases the typical shape of a surfactant compound. When the alkyl chain length is increased, the hydrophilic-lipophilic balance (HLB) of the molecule diminishes gradually covering the appropriate range to display the best surfactant properties. This is the case for alkyl gallates **5**, **6** and **7** with hexyl, octyl and decyl chains, respectively. For longer alkyl chains the surfactant performance decreases until not behaving as surfactants because of an excess of hydrophobicity.

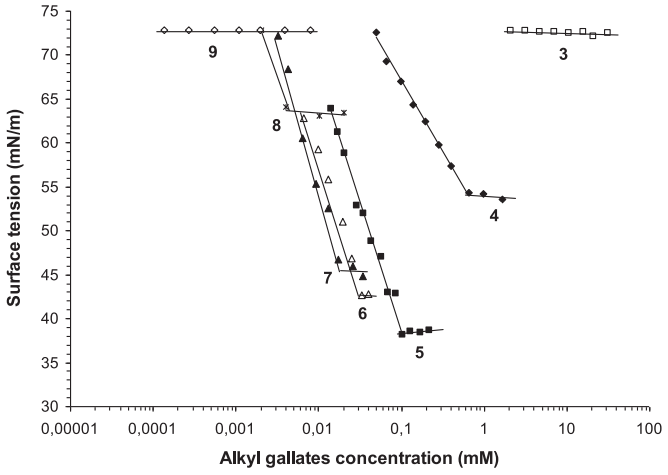


Fig. 4. Surface tension versus log of the concentration plots for the series of alkyl gallates **4**–**10** (gallic acid **3** is included as reference).

*2.2.2. Surface tension measurements for glucosyl alkyl gallates (**11**–**17**).* Next, we measured surface tension for the series of 1-*O*-β-glucosyl alkyl gallates (**11**–**17**) at different concentrations (Fig. 5). Similar considerations can be made for this series when going from a very hydrophilic molecule (gallic acid) to a very lipophilic one (glucosyl hexadecyl gallate). In this case, the appropriate range of compounds displaying surfactant properties is extended to derivatives with alkyl chains from butyl (**11**) to dodecyl (**15**). This behaviour must be due to the incorporation of a glucosyl group that makes more hydrophilic the polar head of these molecules and

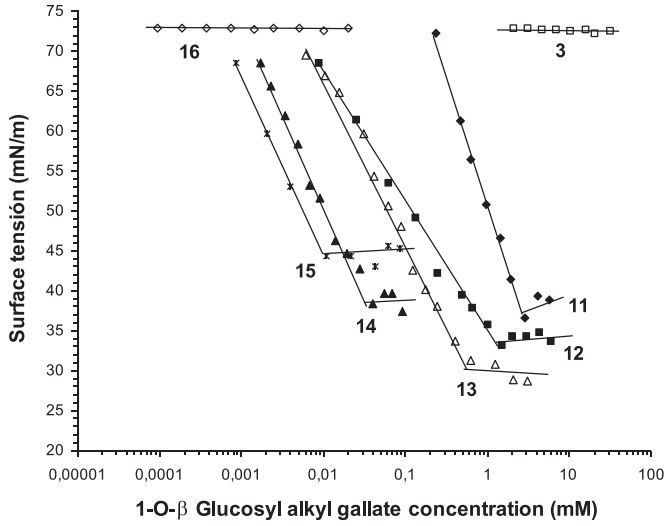


Fig. 5. Surface tension versus log of the concentration plots for the series of Glucosyl alkyl gallates **11**–**17** (gallic acid **3** is included as a reference).

consequently larger alkyl chains are useful to fit the proper range of HLB.

*2.2.3. Surface tension measurements for glucuronosyl alkyl gallates (**18**–**20**).* The plots of surface tension/log of compound concentration for the series of 1-*O*-β-glucuronosyl alkyl gallates (**18**–**20**) are reported in Fig. 6. The presence of a carboxylic group in the glucosyl ring makes these molecules more hydrophilic than those of the former series. The range of alkyl chain lengths able to compensate the strong hydrophilicity of these charged carbohydrates can be now notably longer than in the previous series. For example, glucuronosyl hexadecyl gallate **20** displays good surfactant behaviour, whereas its glucosyl homologue **16** and hexadecyl gallate **9** are not capable of changing the surface tension in the aqueous solution at all.

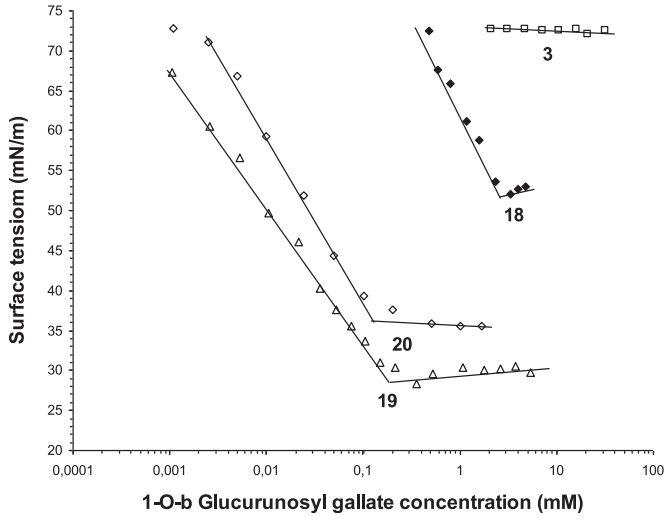


Fig. 6. Surface tension versus log of the concentration plots for the series of Glucuronosyl alkyl gallates **18**–**20** (gallic acid **3** is included as a reference).

*2.2.4. Physicochemical parameters for alkyl gallates (**4**–**10**) and glycosyl alkyl gallates (**11**–**20**).* The physicochemical parameters obtained for the alkyl gallates (**4**–**10**), glucosyl alkyl gallates (**11**–**17**) and glucuronosyl alkyl gallates (**18**–**20**) are summarized in Table 2. Besides the HLB values, the following physicochemical parameters were obtained from the graphs of surface tension/log of compound concentration: (1) CMC: critical micelle concentration, (2) γ_{cmc}: surface tension at the CMC related to the surfactant effectiveness, (3) C_{20}: necessary concentration to decrease in 20 units the surface tension of pure water, i.e., concentration to reach 52 mN/m, (4) pC_{20}: given by $-\log C_{20}$ related to the surfactant efficiency, (5) Γ_{max}: maximum surfactant adsorption and (6) A: area occupied per molecule in the saturated interface.

It can be observed for each of the series that an increase in the length of the ester alkyl chain leads to a decrease of the CMC as occurs for conventional surfactants. This observation is quite logical because the larger the hydrophobic alkyl chain, the faster will be the process of auto-aggregation into micelles avoiding the long alkyl chains their contact with the water molecules. The relationship between log of CMC and the alkyl chain length are represented in Fig. 7. Whereas for alkyl gallates and glucosyl alkyl gallates the CMC diminishes almost linearly, for glucuronosyl alkyl gallates the value corresponding to the hexadecyl alkyl (**20**) chain do not follow this tendency. This same evidence has been observed in some cases for large alkyl chains.[49,51] A possible explanation has been reported based on the eventual coiling of these long chains in water resulting in a smaller effective length.

It can be observed that for a given alkyl chain, the CMC values of glucosyl alkyl gallates and glucuronosyl alkyl gallates are higher than those of the alkyl gallates. A logical reasoning is that being the polar head of the formers more hydrophilic because the glucosyl or glucuronosyl groups, the micelle formation can be delayed to higher concentrations. It can also be noticed that these differences diminishes with the increase of the alkyl chain length. Again, this behaviour is logical because for moderate alkyl chain length the influence of the polar group is critical, but for molecules with large alkyl chains and consequently with predominant lipophilic character, the polar group looses gradually its capacity to discriminate between different polar heads. An extreme example is the case of the hexadecyl gallate and glucosyl hexadecyl gallate that show the same behaviour on surface tension in Figs. 4 and 5, in spite of their different polar head.

Concerning the surfactant effectiveness (γ_{cmc}), the compounds containing the sugar moiety at the polar head, the glucosyl and glucuronosyl alkyl gallate series (**11**–**20**) show better values than the corresponding alkyl gallates (**4**–**10**). In fact, the γ_{cmc} values for glucosyl hexyl gallate **11**, glucosyl octyl gallate **13** and glucuronosyl octyl gallate **19** (30–33.5 mN/m) are in the same range of relevant surfactants, such as Brij-30 or Tween-20.[50,49] γ_{cmc} values for the best alkyl gallate surfactants, such as hexyl, octyl and decyl gallates **5**–**7** are in the range of 40–46 mN/m. These values illustrate alkyl gallates **5**–**7** are optimum surfactants but worse than the new glycosyl alkyl gallate or other commonly used surfactants.

In comparison to other phenolic surfactants, such as tyrosol or hydroxytyrosol fatty acid esters, the values observed for alkyl gallates **5**–**7** are similar to those obtained for tyrosol octanoate or hydroxytyrosol hexanoate, whereas some glycosyl alkyl gallates (**12**–**13**) are close to those observed for hydroxytyrosol octanoate **2** or hydroxytyrosol decanoate (28–30 mN/m).

When the surfactant effectiveness is plotted against the number of carbons of the ester alkyl chain (Fig. 8) a minimum value associated to the compound structure appears. For the series of alkyl gallates the optimum effectiveness is produced for the hexyl derivative (**5**), whereas for glucosyl alkyl gallate series with a more hydrophilic polar group, the best alkyl chain moves up to the octyl group (**13**). Although only three compounds of the glucuronosyl alkyl gallate series were prepared, taking into account the values on the graph and considering the possibility of a similar graph shape, it could be deduced that the minimum could appear at an alkyl chain in the range of decyl or dodecyl and probably with a lower value than for the other series. It seems that alkyl gallates can behave as

Table 2
CMC, surface tension, area per molecule, C20, pC_{20} and Γ parameters of alkyl gallates (**4**–**8**), glycosyl alkyl gallates (**11**–**20**) and two common non-ionic surfactants

Compound	MW	HLB	CMC (mM)	γ_{cmc} (mN/m)	C_{20} (mM)	pC_{20}	Γ (mol/cm^2)	A (Å^2)
Butyl gallate (**4**)	226.2	11.1	0.60	54.0	—	—	3.103×10^{-10}	53.5
Hexyl gallate (**5**)	254.3	9.8	0.10	38.5	0.035	4.45	4.738×10^{-10}	35.0
Octyl gallate (**6**)	282.3	8.9	0.05	42.2	0.016	4.80	6.589×10^{-10}	25.2
Decyl gallate (**7**)	310.4	8.1	0.017	46.7	0.012	4.92	6.143×10^{-10}	27.0
Dodecyl gallate (**8**)	338.4	7.4	0.0041	64.1	—	—	5.172×10^{-10}	32.1
Glc-butyl gallate (**11**)	388.4	14.7	2.40	37.5	0.90	3.04	6.066×10^{-10}	27.4
Glc-hexyl gallate (**12**)	416.4	13.8	1.30	33.5	0.09	4.05	3.024×10^{-10}	54.9
Glc-octyl gallate (**13**)	444.5	12.9	0.50	31.0	0.055	4.26	3.926×10^{-10}	42.3
Glc-decyl gallate (**14**)	472.5	12.1	0.032	39.5	0.009	5.04	3.994×10^{-10}	41.6
Glc-dodecyl gallate (**15**)	500.6	11.5	0.010	44.3	0.0048	5.32	3.871×10^{-10}	42.9
GlcA-butyl gallate (**18**)	401.3	15.0	2.70	52.0	0.0027	2.57	4.554×10^{-10}	36.4
GlcA-octyl gallate (**19**)	457.4	13.1	0.18	30.0	0.0085	5.07	2.966×10^{-10}	56.0
GlcA-hexadecyl gallate (**20**)	569.7	10.5	0.10	37.0	0.022	4.66	3.674×10^{-10}	45.2
Brij 30® (Polyoxyethylene (4) lauryl ether)[a]	362.5	9.4	0.0035	30.0	0.0024	5.62	3.80×10^{-10}	44.0
Tween 20® (polyoxyethylene sorbitan monolaurate)[b,c]	1227.5	16.6	0.0169	35.0	0.0025	5.61	3.560×10^{-10}	46.6

[a] Data from Ref. 49.
[b] Data from Ref. 50.
[c] C_{20} and pC_{20} were calculated as noted in the experimental section.

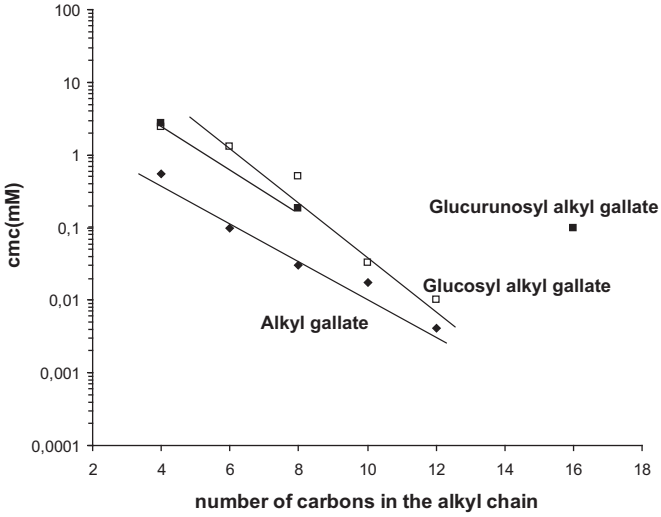


Fig. 7. Relationship between log of CMC and the length of the acyl alkyl chain in the gallate derivative series, for compounds displaying surfactant properties.

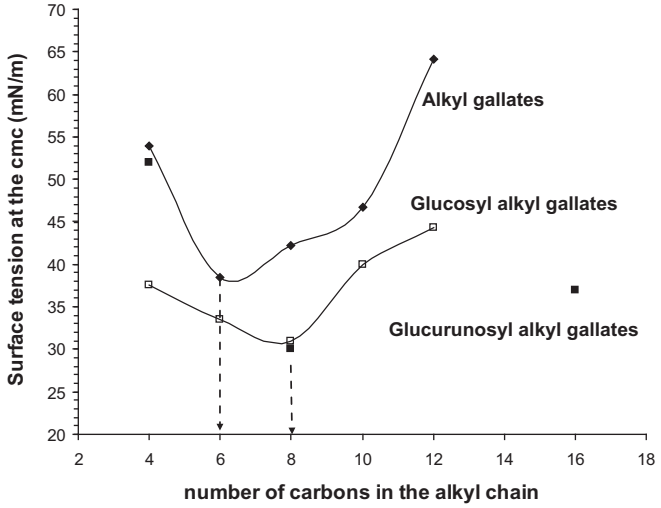


Fig. 8. Surface tension versus log of the concentration plots for the series of alkyl gallates **4**–**8**, glucosyl- and glucuronosyl alkyl gallates **11**–**15** and **18**–**20**, respectively.

good surfactants when the appropriate hydrophilic–lipophilic balance (HLB) is attained. The introduction of a neutral or a charged monosaccharide in the polar head of the alkyl gallates results in a series of compounds, glycosyl alkyl gallates **11**–**20**, that display even better surfactant properties, in some cases similar to other commonly used surfactants.

2.3. Antioxidant capacity of alkyl gallates 4–10 and glycosyl alkyl gallates 11–20

The DPPH radical scavenging assay and the FRAP reducing power tests were carried out to evaluate the antioxidant activity of alkyl gallates **4**–**10** and glycosyl alkyl gallates **11**–**20** (see Tables 3 and 4). Gallic acid, hydroxytyrosol and hydroxytyrosol octanoate were included as controls. The results obtained in the radical scavenging experiment showed very similar radical scavenging efficiency for all the alkyl gallates (**4**–**10**) and the control gallic acid. When a sugar moiety is introduced in the scaffold of the alkyl gallate (compounds **11**–**20**), the radical scavenging efficiency decreases being, in general terms, lower for the glucuronosyl alkyl gallates than for the glucosyl alkyl gallates. The lost of a phenolic hydroxyl group in compounds **11**–**20** with respect to the alkyl gallates must be the most important factor affecting radical scavenging activity.

Table 3
Radical scavenging and reducing power of alkyl gallates **4**–**10** and controls hydroxytyrosol **1**, hydroxytyrosol octanoate **2** and gallic acid **3**

Compound	DPPH EC_{50}	FRAP
Hydroxytyrosol (**1**)	0.720±0.000	1.144±0.095
Hydroxytyrosol octanoate (**2**)	0.686±0.033	1.128±0.120
Gallic acid (**3**)	0.205±0.001	4.411±0.121
Butyl gallate (**4**)	0.227±0.002	2.827±0.092
Hexyl gallate (**5**)	0.253±0.004	2.552±0.060
Octyl gallate (**6**)	0.264±0.001	1.643±0.072
Decyl gallate (**7**)	0.255±0.001	1.417±0.089
Dodecyl gallate (**8**)	0.238±0.002	1.565±0.025
Hexadecyl gallate (**9**)	0.261±0.001	1.136±0.053
Octadecyl gallate (**10**)	0.258±0.001	0.965±0.082

Concerning the ferric reducing ability measured with the FRAP assay, the number of donated electrons decreases as the length chain increases in the three series, alkyl gallates (**4**–**10**), glucosyl alkyl gallates (**11**–**17**) and glucuronosyl alkyl gallates (**18**–**20**). Once again, the FRAP values of compounds **11**–**20** were lower than those obtained for the corresponding alkyl gallates **4**–**10**. Nevertheless,

Table 4
Radical scavenging and reducing power of glycosyl alkyl gallates **11**–**20**

Compounds	DPPH EC_{50}	FRAP
Glc-butyl gallate (**11**)	0.479±0.000	2.436±0.078
Glc-hexyl gallate (**12**)	0.458±0.001	1.863±0.025
Glc-octyl gallate (**13**)	0.614±0.009	1.388±0.111
Glc-decyl gallate (**14**)	0.496±0.004	1.496±0.087
Glc-dodecyl gallate (**15**)	0.490±0.009	1.144±0.063
Glc-hexadecyl gallate (**16**)	0.674±0.006	0.250±0.056
Glc-octadecyl gallate (**17**)	0.500±0.002	0.232±0.048
GlcA-butyl gallate (**18**)	0.590±0.0101	3.785±0.10
GlcA-octyl gallate (**19**)	0.661±0.0026	1.252±0.075
GlcA-hexadecyl gallate (**20**)	0.466±0.0134	0.224±0.062

the radical scavenging and reducing power values obtained for the new antioxidants seem to be satisfactory to display an optimum antioxidant activity in different matrices. In fact, the DPPH and FRAP values obtained for the glycosyl alkyl gallates **11**–**20** are better, for example, than those reported for hydroxytyrosol **1** and hydroxytyrosol octanoate **2** (see Table 2) and these phenolic antioxidants have proved to be excellent antioxidants in oils and oil-in-water systems, respectively.

It is well-known that gallic acid and alkyl gallates are very potent antioxidants. Based on our previous results with tyrosol and hydroxytyrysol fatty acid esters[30] and due to the amphiphilic character of alkyl gallates **4**–**10**, it could be envisaged that they could display surfactant properties. Now, it is clear that they can be considered as surfactant antioxidants. It is important to mention that surfactant antioxidants could find important applications in the food and cosmetic industries.[52–54] Scarce examples of antioxidants with surface active character have been described so far, such as alkanoyl-6-*O*-ascorbic acid esters,[55] alkyl ammonium ascorbate salts,[56] tocopheryl polyethylene glycol succinate[57] and BHT alkyl ammonium salts.[58] At the same time, the only examples where the polar head is a phenol group are the butyl and dodecyl esters of *p*-hydroxyphenylacetic acid (HPA) that are able to slightly decrease the surface tension in a water-hexadecane interface[39] and tyrosol and hydroxytyrysol fatty acid esters as our group recently demonstrated.[30]

The new glycosyl alkyl gallates **11**–**20** present slightly worse antioxidant capacity than their corresponding alkyl gallates as could be expected due to the lost of one of phenolic hydroxyl groups. In contrast, the sugar–phenolic hybrid polar head makes them display better surfactant effectiveness than the corresponding alkyl gallates. This aspect may compensate their actual antioxidant potency when tested in emulsified systems or as antioxidants to prevent oxidative stress in cells.

3. Conclusion

Alkyl gallates **4**–**10**, commonly used antioxidants have presented notable surface active properties in aqueous solutions. This finding may partially explain their high antioxidant efficiency in emulsified systems. In the search of even better antioxidant surfactants, glucosyl- and glucuronosyl alkyl gallates **11**–**20** have been prepared by a short synthetic route. The new antioxidants have shown better surface-active efficiency that their corresponding alkyl gallates and in some cases their surfactant effectiveness is as good as for universal surfactants, such as Brij-30 or Tween-20. The antioxidant activity of glycosyl alkyl gallates was somewhat lower with respect to their parent alkyl gallates most probably due to the lost of one of the phenolic hydroxyl groups. However, their radical scavenging capacity and reducing power were even better than for other excellent phenolic antioxidants, such as hydroxytyrosol and hydroxytyrosol fatty acid esters. Experiments to investigate the potential applications in the food, pharmaceutical and cosmetic industries of the new glycosyl alkyl gallates are in progress.

4. Experimental

4.1. General

All chemicals were obtained either from Aldrich Chemicals or TCI and used without further purification, unless otherwise noted. All reactions were monitored by TLC on precoated Silica-Gel 60 plates F_{254} (Merck), and detected by heating with Mostain (500 mL of 10% H_2SO_4, 25 g of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1 g $Ce(SO_4)_2\cdot 4H_2O$). Products were purified by flash chromatography with Merck Silica-gel 60 (200–400 mesh). High resolution FAB (+) mass spectral analyses was obtained on a Micromass AutoSpec-Q spectrometer. NMR spectra were recorded on either a Bruker AVANCE 300 or ARX 400 or Bruker Advance DRX 500 MHz, 300 or 400 MHz (^{1}H), 75 or 100 (^{13}C), at room temperature for solutions in $CDCl_3$, D_2O or CD_3OD. Chemical shifts are referred to the solvent signal. ^{2}D experiments (COSY, TOCSY, and HMQC) were done when necessary to assign the oligosaccharide. Chemical shifts are in parts per million with respect to acetone signal, which was used as an external reference using a volume of 1 μL. In all experiments the ^{1}H carrier frequency was kept at the water resonance. Data were processed using manufacturer software, raw data were multiplied by shifted exponential window function prior to Fourier transform, and the baseline was corrected using polynomial fitting.

4.2. General procedure for acetal formation

All alkyl gallates were protected with isopropylydene acetal. The corresponding alkyl gallate and camphor sulfonic acid in catalytic amounts were dissolved in dry chloroform, 2,2-dimethoxypropane was then added and the reaction mixture was stirred for 16 h at 60 °C. NEt_3 was then added in order to neutralize. Solvents were removed in vacuo and the crude was purified by flash chromatography with hexane/ethyl acetate by using different polarities depending on the alkyl group. Reactions yields rated from 40 to 60%.

4.3. General procedure for glycosylation

Acceptors **21**–**27** (1 equiv) and glucosyl/glucuronosyl trichloroacetimidate **28** or **29** (1.2–1.5 equiv) were dissolved in dry CH_2Cl_2 (1 mL for each 100 mg); $BF_3\cdot OEt_2$ (0.1–0.15 equiv) was then added. The reaction mixture was stirred for 30–60 min and NEt_3 was then added. Solvents were removed and the crude was purified by flash chromatography with hexane/ethyl acetate affording the corresponding glycosyl/glucurunosyl derivatives with high yields (75–95%).

4.3.1. Butyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***30***. Glucosyl trichloroacetimidate **28** (2.2 g, 5.05 mmol) and butyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **21** (896 mg, 3.36 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **30** (1.78 g, 89%) as a white glassy solid. $[\alpha]_D^{22}$ −21.6 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.16 (d, 1H, *J*=1.4 Hz, H_{arom}), 5.21 (m, 4H, H-1, H-2, H-3, H-4), 4.26 (m, 3H, H-6, $COOCH_2$), 4.10 (dd, 1H, *J*=12.2, 2.1 Hz, H-6′), 3.81 (ddd, 1H, *J*=9.7, 4.9, 2.3 Hz, H-5), 2.03 (m, 12H, $COOCH_3$), 1.69 (m, 8H, $C(CH_3)_2$, CH_2), 1.43 (m, 2H, CH_2), 0.94 (t, 3H, *J*=7.4 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.3, 169.4, 169.3, 165.7 (C=O), 149.0, 140.6 (Cq_{arom}), 139.37, 124.32 (C_{arom}), 120.33 (C_{ip}), 115.33 (C_{arom}), 105.60 (C_{arom}), 99.9 (C-1), 72.7, 72.2, 71.2, 68.3, 64.9 ($COOCH_2R$),

61.9 (C-6), 30.8 (CH_2), 25.9 (CH_{3ip}), 25.9 (CH_{3ip}), 20.7, 20.65 ($COOCH_3$), 19.34 (CH_2), 13.82 (CH_3).

4.3.2. Hexyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***31***. Glucosyl trichloroacetimidate **28** (1.15 g, 2.66 mmol) and hexyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **22** (556 mg, 1.9 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **31** (896 g, 76%) as glassy solid. $[\alpha]_D^{22}$ −19.0 (*c* 1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, 1H, *J*=1.4 Hz, H_{arom}), 7.16 (d, 1H, *J*=1.4 Hz, H_{arom}), 5.21 (m, 4H, H-1, H-2, H-3, H-4), 4.25 (m, 3H, H-6, $COOCH_2R$), 4.10 (dd, 1H, *J*=12.2, 2.1 Hz, H-6), 3.81 (ddd, 1H, *J*=9.7, 4.9, 2.3 Hz, H-5), 2.04 (m, 12H, $COOCH_3$), 1.68 (m, 8H, CH_{3ip}, $OCOCH_2CH_2R$), 1.34 (m, 10H, 5× CH_2), 0.87 (t, 3H, *J*=6.7 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 170.3, 169.4, 169.3 (C=O), 165.7 (C=O), 148.9 (Cq_{arom}), 140.6 (Cq_{arom}), 139.3 (C_{arom}), 124.3 (C_{arom}), 120.3 (C_{ip}), 115.2 (C_{arom}), 105.6 (C_{arom}), 99.9 (C-1), 72.7, 72.2, 71.1, 68.3, 65.2 ($COOCH_2R$), 61.91 (C-6), 31.5 (CH_2), 28.7 (CH_2), 25.9 (CH_{3ip}), 25.9 (CH_{3ip}), 25.76 (CH_2), 22.62 (CH_2), 20.7, 20.6, 20.5 ($COOCH_3$), 14.09 (CH_3).

4.3.3. Octyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***32***. Glucosyl trichloroacetimidate **28** (324 mg, 0.74 mmol) and octyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **23** (200 mg, 0.62 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **32** (320 g, 79%) as glassy solid. $[\alpha]_D^{22}$ −12.0 (*c* 1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.14 (d, 1H, *J*=1.5 Hz, H_{arom}), 5.30–5.01 (m, 4H, H-1, H-2, H-3, H-4), 4.24 (m, 3H, H-6, OCH_2R), 4.09 (m, 1H, H-6′), 3.84–3.78 (m, 1H, H-5), 2.01 (m, 12H, $COOCH_3$), 1.66 (m, 8H, CH_{3ip}, OCH_2CH_2R), 1.28 (m, 10H, 5× CH_2), 0.83 (t, 3H, *J*=6.7 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 107.6, 107.3, 107.2, 169.4 (C=O), 148.8 (C_{arom}), 140.5 (C_{arom}), 139.3 (C_{arom}), 124.2 (C_{arom}), 120.3 (C_{ip}), 115.1 (CH_{arom}), 105.5 (CH_{arom}), 99.8 (C-1), 72.6, 72.1, 71.1, 68.2, 65.2 ($COOCH_2R$), 61.8 (C-6), 31.8 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 28.7 (CH_2), 26.0 (CH_{3ip}), 25.9 (CH_{3ip}), 22.6 (CH_2), 20.6 ($COOCH_3$), 14.10 (CH_3). HRMS (ES^+) calcd for $C_{32}H_{44}O_{14}Na$ ($M+Na^+$) 675.2629. Found: 675.2638.

4.3.4. Decyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***33***. Glucosyl trichloroacetimidate **28** (2.7 g, 5.57 mmol) and decyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **24** (1.3 g, 3.71 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **33** (2.32 g, 93%) as a white glassy solid; $[\alpha]_D^{22}$ −17.5 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.42 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.14 (d, 1H, *J*=1.5 Hz, H_{arom}), 5.42–5.34 (m, 2H, H-3, H-1), 5.18 (dd, 1H, *J*=8.0 and 9.5 Hz, H-2), 5.13 (t, 1H, *J*=9.5 Hz, H-4), 4.33 (dd, 1H, *J*=5.0 and 12.3 Hz, H-6), 4.26 (t, 2H, CH_2), 4.14 (dd, 1H, *J*=2.1 and 12.2 Hz, H-6′), 4.09–4.05 (m, 1H, H-5), 2.08, 2.07, 2.05, 2.02 (4 s, 12H, CH_3CO), 1.77–1.72 (m, 8H, $C(CH_3)_2$, CH_2), 1.31–1.30 (m, 14H, 7× CH_2), 0.90 (t, 3H, *J*=6.5 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 170.9, 170.2, 169.8, 169.6 (C=O), 165.7 ($O=C_{benzoate}$), 148.9, 140.7, 139.5, 120.5 (Cq_{arom}), 123.8 ($C(CH_3)_2$), 114.8, 104.7 (CH_{arom}), 99.5 (C-1), 72.6 (C-3), 71.8 (C-5), 71.2 (C-2), 68.3 (C-4), 64.9 (CH_2O), 61.7 (C-6), 31.7, 29.3, 29.0, 28.9, 25.8, 24.6, 24.5, 22.3, 19.3, 19.2, 13.1 (CH_3). HRMS (ES^+) calcd for $C_{34}H_{48}NaO_{14}$ ($M+Na^+$) 703.2942. Found: 703.2975.

4.3.5. Dodecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***34***. Glucosyl trichloroacetimidate **28** (1.9 g, 4.4 mmol) and dodecyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **25** (1.12 g, 3.0 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **34** (1.8 g, 86%) as a glassy solid; $[\alpha]_D^{22}$ −6.4 (*c* 1 in $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 7.37 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.15 (d, 1H, *J*=1.5 Hz, H_{arom}), 5.31–5.11 (m, 4H, H-3, H-1, H-2, H-4), 4.29 (dd, 1H, *J*=5.0 and 12.3 Hz, H-6), 4.22 (t, 2H, *J*=7.0 Hz, OCH_2), 4.12–4.05 (m, 1H, H-6′), 3.85–3.79 (m, 1H, H-5), 2.05, 2.02, 2.01 (3 s, 12H, CH_3CO), 1.68 (m, 6H, $C(CH_3)_2$), 1.28–1.20 (m, 20H, 10× CH_2), 0.86 (t, 3H, *J*=6.5 Hz, CH_3); δ ^{13}C (62.5 MHz, $CDCl_3$) 170.7, 170.3, 169.4, 169.3, 169.6 (C=O), 165.7 ($O=C_{benzoate}$), 148.9, 140.5, 139.5, 124.2 (Cq_{arom}), 120.3 ($C(CH_3)_2$), 115.1, 105.5 (CH_{arom}), 99.5 (C-1), 72.6 (C-3), 72.1 (C-5), 71.1 (C-2), 68.2 (C-4), 65.2 (CH_2O), 61.8 (C-6), 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 28.7, 26.1, 26.0, 25.9, 22.7, 20.7, 20.6, 14.1 (CH_3). HRMS (ES^+) calcd for $C_{36}H_{52}O_{14}Na$ ($M+Na^+$) 731.3255. Found: 731.3260.

4.3.6. Hexadecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***35***. Glucosyl trichloroacetimidate **28** (1.3 g, 3.0 mmol) and hexadecyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **26** (1.01 g, 2.34 mmol) were submitted a glycosylation conditions following general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **35** (1.4 g, 79%) as a glassy solid; $[\alpha]_D^{22}$ −12.2 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, 1H, *J*=1.3 Hz, H_{arom}), 7.17 (d, 1H, *J*=1.3 Hz, H_{arom}), 5.21 (m, 4H, H-1, H-2, H-3, H-4), 4.26 (m, 3H, H-6, OCH_2R), 4.11 (dd, 1H *J*=12.3, 2.2 Hz, H-6), 3.82 (ddd, 1H, *J*=9.9, 5.0, 2.3 Hz, H-5), 2.06 (m, 12H, $COOCH_3$), 1.70 (m, 8H, CH_{3ip}, OCH_2CH_2R), 1.33 (m, 26H, 13× CH_2), 0.86 (t, 3H, *J*=6.8 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.4, 169.5, 169.4 (C=O), 165.8 (C=O), 149.0, 140.6, 139.4, 124.3 (Cq_{arom}), 120.3 (C_{ip}), 115.3 (CH_{arom}), 105.6 (CH_{arom}), 99.9 (C-1), 72.7 (C-3), 72.3 (C-5), 71.2 (C-2), 68.3 (C-4), 65.3 (OCH_2), 61.9 (C-6), 32.0 (CH_2), 29.8 (CH_2), 29.78 (CH_2), 29.76 (CH_2), 29.72 (CH_2), 29.66 (CH_2), 29.47 (CH_2), 29.41 (CH_2), 28.85 (CH_2), 26.13 (CH_2), 26.00(CH_{3ip}), 25.96(CH_{3ip}), 22.79 (CH_2), 20.7, 20.6, 20.5 ($COOCH_3$), 14.2 (CH_3). HRMS (ES^+) calcd for $C_{40}H_{60}O_{14}Na$ ($M+Na^+$) 787.3881. Found: 787.3931.

4.3.7. Octadecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-O-isopropylidene-benzoate ***36***. Glucosyl trichloroacetimidate **28** (1.7 g, 4.35 mmol) and octadecyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **27** (1.4 g, 2.34 mmol) were submitted a glycosylation conditions following general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **36** (1.6 g, 67%) as a glassy solid; $[\alpha]_D^{22}$ −9.0 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.16 (d, 1H, *J*=1.5 Hz, H_{arom}), 5.20 (m, 4H, H-1, H-2, H-3, H-4), 4.24 (m, 3H, H-6, $COOCH_2R$), 4.10 (m, 1H, H-6), 3.81 (ddd, 1H, *J*=9.9, 5.0, 2.4 Hz, H-5), 2.03 (m, 12H, $COOCH_3$), 1.68 (m, 8H, CH_{3ip}, $COOCH_2CH_2R$), 1.23 (m, 30H, 15× CH_2), 0.85 (t, 3H, *J*=6.8 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.3, 169.4, 169.3 (C=O), 165.7 (C=O), 149.0 (C_{arom}), 140.5 (C_{arom}), 139.3 (C_{arom}), 124.3 (C_{arom}), 120.3 (C_{ip}), 115.2 (CH_{arom}), 105.5 (CH_{arom}), 99.9 (C-1), 72.7 (C-3), 72.3 (C-5), 71.2 (C-2), 68.3 (C-4), 65.2 (OCH_2R), 61.9 (C-6), 33.0 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 28.8 (CH_2), 26.1 (CH_2), 25.9 (CH_{3ip}), 25.9 (CH_{3ip}), 22.8 (CH_2), 20.8, 20.7, 20.6 ($COOCH_3$), 14.2 (CH_3).

4.3.8. Butyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-O-isopropylidene-benzoate ***44***. Glucuronopyranosyl trichloroacetimidate **29** (590 mg, 1.32 mmol) and butyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **21** (235 mg, 0.88 mmol) were submitted to glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 1:1) to afford **44** (254 mg, 42%) as a glassy solid. $[\alpha]_D^{22}$ +14.8 (*c* 1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.11 (d, 1H, *J*=1.5 Hz, H_{arom}), 5.28–5.18 (m, 4H, H-1, H-2, H-3, H-4), 4.19 (t, 2H, *J*=6.6 Hz, $COOCH_2$), 4.05 (d, 1H, *J*=9.6 Hz, H-5),

3.66 (s, 3H, $COOCH_3$), 2.00, 1.98, 1.97 (3 s, 12H, O=CCH_3), 1.66–1.59 (m, 8H, $C(CH_3)_2$, CH_2), 1.42–1.36 (m, 2H, CH_2), 0.89 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 169.3, 169.2, 166.7, 165.6 (C=O), 149.0, 140.3, 138.8, 124.3 (C_{arom}), 120.2 (C_{ip}), 115.6 (C_{arom}), 105.6 (C_{arom}), 99.5 (C-1), 72.7 (C-5), 71.9, 70.9, 69.2 (C-2, C-3, C-4), 64.8 ($COOCH_2R$), 52.9 (OCH_3), 30.7 (CH_2), 25.8, 25.7 (CH_{3ip}), 20.6, 20.5 ($COOCH_3$), 19.2 (CH_2), 13.7 (CH_3). HRMS (ES^+) calcd for $C_{27}H_{34}NaO_{14}$ ($M+Na^+$) 605.1846. Found: 605.1850.

4.3.9. Octyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-O-isopropylidene-benzoate ***45***. Glucuronopyranosyl trichloroacetimidate **29** (310 g, 0.69 mmol) and octyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **23** (185 mg, 0.58 mmol) were submitted a glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 2:1) to afford **45** (194 mg, 53%) as a glassy solid. $[\alpha]_D^{22}$ −21.5 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H, H_{arom}), 7.16 (s, 1H, H_{arom}), 5.33–5.23 (m, 4H, H-1, H-2, H-3, H-4), 4.22 (t, 2H, J=6.6 Hz, $COOCH_2$), 4.10 (d, 1H, J=9.6 Hz, H-5), 3.71 (s, 3H, $COOCH_3$), 2.05, 2.03, 2.01 (3 s, 12H, O=CCH_3), 1.69–1.66 (m, 8H, $C(CH_3)_2$, CH_2), 1.37–1.23 (m, 10H, 5× CH_2), 0.86 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 169.3, 169.2, 166.7, 165.6 (C=O), 149.0, 140.3, 138.8, 124.3 (C_{arom}), 120.2 (C_{ip}), 115.6 (C_{arom}), 105.5 (C_{arom}), 99.5 (C-1), 72.7 (C-5), 71.9, 70.9, 69.2 (C-2, C-3, C-4), 65.2 ($COOCH_2R$), 52.9 (OCH_3), 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2 (CH_2), 26.0, 25.8, 25.7 (CH_{3ip}), 22.6, 20.6, 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+) calcd for $C_{31}H_{42}NaO_{14}$ ($M+Na^+$) 661.2472. Found: 661.2474.

4.3.10. Hexadecyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-O-isopropylidene-benzoate ***46***. Glucuronopyranosyl trichloroacetimidate **29** (1.8 g, 4.0 mmol) and hexadecyl 3-hydroxy-4,5-*O*-isopropylidene benzoate **26** (874 mg, 2.0 mmol) were submitted a glycosylation conditions following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 3:1 to 5:2) to afford **46** (960 mg, 63%) as a glassy solid. $[\alpha]_D^{22}$ −7.4 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H, H_{arom}), 7.16 (s, 1H, H_{arom}), 5.36–5.24 (m, 4H, H-1, H-2, H-3, H-4), 4.22 (t, 2H, J=6.6 Hz, $COOCH_2$), 4.12 (d, 1H, J=9.6 Hz, H-5), 3.71 (s, 3H, $COOCH_3$), 2.06, 2.04, 2.02 (3 s, 12H, O=CCH_3), 1.69–1.67 (m, 8H, $C(CH_3)_2$, CH_2), 1.40–1.25 (m, 26H, 13× CH_2), 0.86 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 169.3, 169.2, 166.7, 165.6 (C=O), 149.0, 140.3, 138.8, 124.2 (C_{arom}), 120.2 (C_{ip}), 115.6 (C_{arom}), 105.6 (C_{arom}), 99.5 (C-1), 72.7 (C-5), 71.9, 70.9, 69.2 (C-2, C-3, C-4), 65.2 ($COOCH_2R$), 52.9 (OCH_3), 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2 (CH_2), 26.0, 25.8, 25.7 (CH_{3ip}), 22.6, 20.6, 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+) calcd for $C_{39}H_{58}NaO_{14}$ ($M+Na^+$) 773.3724. Found: 773.3745.

4.4. General procedure for acetal deprotection

Removal of the isopropylidene group was carried out by dissolving compounds **30**–**36** and **44**–**46** in pure trifluoroacetic acid (1 mL per each 100 mg) and reaction mixture was stirred at room temperature for 24 h. Solvent was then removed and coevaporated with toluene 2 or three times. Crude was purified by flash chromatography with hexane/ethyl acetate affording compounds 15–21 with high yields (65–85%).

4.4.1. Butyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***37***. Compound **30** (1.53 g, 1.35 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **37** (1.1 g, 78%); $[\alpha]_D^{22}$ −8.4 (*c* 1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, 1H, J=1.8 Hz, H_{arom}), 7.26 (d, 1H, J=1.8 Hz, H_{Ar}), 5.28 (dt, 2H, J=19.1, 9.5 Hz, H-2, H-4), 5.14 (t, 1H, J=9.4 Hz, H-3), 5.02 (d, 1H, J=7.4 Hz, H-1), 4.32–4.07 (m, 4H, H-6, H-6′, OCH_2R), 3.88 (ddd, 1H, J=9.9, 5.4, 2.2 Hz, H-5), 2.06 (m, 12H, $COOCH_3$), 1.70 (m, 2H, $COOCH_2CH_2R$), 1.43 (m, 2H, CH_2), 0.95 (t, 3H, J=6.4 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 169.6 (C=O), 166.02 (C=O), 144.8, 143.9, 139.1, 122.5 (Cq_{arom}), 113.3 (CH_{arom}), 111.1 (CH_{arom}), 101.3 (C-1), 72.5 (C-3), 72.2 (C-5), 71.4 (C-2), 68.1 (C-4), 65.0 (OCH_2R), 61.6 (C-6), 30.8 (CH_2), 20.8, 20.7, 20.6 ($COOCH_3$), 19.3 (CH_2), 13.8 (CH_3). HRMS (ES^+) calcd for $C_{25}H_{32}NaO_{14}$ ($M+Na^+$) 579.1690. Found: 579.1697.

4.4.2. Hexyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***38***. Compound **31** (1.00 g, 1.42 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 1:1 to 1:2) affording compound **38** (770 g, 78%); $[\alpha]_D^{22}$ −9.5 (*c* 1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, 1H, J=1.8 Hz, H_{arom}), 7.26 (d, 1H, J=1.8 Hz, H_{arom}), 6.62, 5.89 (2br s, 2H, OH), 5.34–5.25 (m, 2H, H-2, H-4), 5.14 (t, 1H, J=9.4 Hz, H-3), 5.00 (d, 1H, J=7.5 Hz, H-1), 4.30–4.19 (m, 4H, H-6, H-6′, OCH_2R), 3.88 (ddd, 1H, J=9.9, 5.4, 2.2 Hz, H-5), 2.10, 2.08, 2.04, 2.03 (4s, 12H, $COOCH_3$), 1.71 (m, 2H, $COOCH_2CH_2R$), 1.39–1.21 (m, 6H, CH_2), 0.95 (t, 3H, J=6.4 Hz, CH_3). ^{13}C NMR (62 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 169.6 (C=O), 166.02 (C=O), 144.8, 143.9, 139.1, 122.6 (Cq_{arom}), 113.3 (CH_{arom}), 111.1 (CH_{arom}), 101.4 (C-1), 72.5 (C-3), 72.2 (C-5), 71.5 (C-2), 68.1 (C-4), 65.3 (OCH_2R), 61.7 (C-6), 331.5, 28.8, 25.8, 22.7, 20.9, 20.8, 20.7 20.6 ($COOCH_3$), 14.2 (CH_3). HRMS (ES^+) calcd for $C_{27}H_{36}NaO_{14}$ ($M+Na^+$) 607.2003. Found: 607.2017.

4.4.3. Octyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***39***. Compound **32** (78 mg, 0.12 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:1) affording compound **39** (53 mg, 73%); $[\alpha]_D^{22}$ −5.4 (*c* 1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H, H_{arom}), 7.26 (s, 1H, H_{arom}), 5.29 (dt, 2H, J=17.2, 9.5 Hz, H-2, H-4), 5.14 (t, 1H, J=9.5 Hz, H-3), 5.02 (d, 1H, J=7.6 Hz, H-1), 4.25 (m, 4H, H-6, H-6′, OCH_2R), 3.88 (dd, 1H, J=7.8, 5.7 Hz, H-5), 2.06 (m, 12H, $COOCH_3$), 1.72 (m, 2H, OCH_2CH_2R), 1.32 (m, 10H, 5× CH_2), 0.87 (t, 3H, J=6.3 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 169.6 (C=O), 166.0 (C=O), 144.8, 143.9, 139.1, 122.7 (Cq_{arom}), 113.3 (CH_{arom}), 111.8 (CH_{arom}), 101.4 (C-1), 72.6 (C-3), 72.2 (C-5), 71.5 (C-2), 68.1 (C-4), 65.3 (OCH_2R), 61.7 (C-6), 32.0 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 26.1 (CH_2), 22.8 (CH_2), 20.9, 20.7, 20.6, 20.5 ($COOCH_3$), 14.20 (CH_3).

4.4.4. Decyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***40***. Compound **33** (920 mg, 1.35 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **40** (605 mg, 70%); $[\alpha]_D^{22}$ −11.5 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.36 (d, 1H, J=1.5 Hz, H_{arom}), 7.28 (d, 1H, J=1.5 Hz, H_{arom}), 5.40 (t, 1H, J=9.5 Hz, H-3), 5.28–5.22 (m, 2H, H-1, H-2), 5.14 (t, 1H, J=9.5 Hz, H-4), 4.33 (dd, 1H, J=6.0 and 12.5 Hz, H-6), 4.26 (t, 2H, J=6.5 Hz, OCH_2), 4.14 (dd, 1H, J=2.0 and 12.5 Hz, H-6′), 4.07–4.04 (m, 1H, H-5), 2.08, 2.07, 2.05, 2.01 (4 s, 12H, CH_3CO), 1.77–1.72 (m, 2H, CH_2), 1.45–1.43 (m, 2H, CH_2), 1.38–1.31 (m, 12H, 6× CH_2), 0.90 (t, 3H, J=6.5 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 170.9, 170.2, 170.1, 169.8 (C=O), 166.5 (O=$C_{benzoate}$), 145.7, 144.7, 141.0, 120.5 (Cq_{arom}), 112.0, 111.2 (CH_{arom}), 100.2 (C-1), 72.8 (C-3), 71.8 (C-5), 71.5 (C-2), 68.3 (C-4), 64.6 (CH_2O), 61.7 (C-6), 31.7, 29.3, 29.1, 29.0, 28.5, 25.8, 24.6, 22.3, 19.4, 19.3, 19.2, 13.1 (CH_3). HRMS (ES^+) calcd for $C_{31}H_{44}NaO_{14}$ ($M+Na^+$) 663.2629. Found: 663.2629.

4.4.5. Dodecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***41***. Compound **34** (264 mg, 0.37 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **41** (132 mg, 53%); $[\alpha]_D^{22}$ −6.1 (*c* 1 in

$CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (s, 1H, H_{arom}), 7.23 (s, 1H, H_{arom}), 5.28 (m, 2H, H-2, H-4), 5.13 (t, 1H, J=9.4 Hz, H-3), 5.03 (d, 1H, J=7.4 Hz, H-1), 4.18 (m, 4H, H-6, H-6′, OCH_2R), 3.87 (dd, 1H, J=7.8, 5.6 Hz, H-5), 2.05 (m, 12H, $COOCH_3$), 1.69 (dd, 2H, J=13.9, 6.7 Hz, OCH_2CH_2R), 1.32 (m, 16H, 8× CH_2), 0.85 (t, 3H, J=6.4 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 169.6 (C=O), 166.0 (C=O), 144.8, 143.9139.1, 122.4 (Cq_{arom}), 113.2 (CH_{arom}), 111.0 (CH_{arom}), 101.2 (C-1), 72.5 (C-3), 72.2 (C-5), 71.4 (C-2), 68.1 (C-4), 65.3 (OCH_2R), 61.7 (C-6), 31.9 (CH_2), 29.7 (CH_2), 29.68 (CH_2), 29.61 (CH_2), 29.40 (CH_2), 29.37 (CH_2), 28.79 (CH_2), 26.09 (CH_2), 22.74 (CH_2), 20.8, 20.7, 20.6 ($COOCH_3$), 14.17 (CH_3). HRMS (ES^+) calcd for $C_{33}H_{48}O_{14}Na$, 691.2942. Found; 691.2925.

4.4.6. Hexadecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***42***. Compound **35** (222 mg, 0.30 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **42** (169 mg, 80%); $[\alpha]_D^{22}$ −2.0 (*c* 1 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (s,1H, H_{arom}), 7.26 (s, 1H, H_{arom}), 5.28 (m, 2H, H-2, H-4), 5.14 (t, 1H, J=9.4 Hz, H-3), 5.04 (d, 1H, J=7.5 Hz, H-1), 4.23 (m, 4H, H-6, H-6′, OCH_2R), 4.89 (m, 1H, H-5), 2.05 (m, 12H, $COOCH_3$), 1.70 (m, 2H, OCH_2CH_2R), 1.33 (m, 26H, 13× CH_2), 0.85 (t, 3H, J=6.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.3, 170.1, 169.5 (C=O), 166.0 (C=O), 144.7, 143.8, 139.1, 122.4 (Cq_{arom}), 113.2 (CH_{arom}), 111.2 (CH_{arom}), 101.2 (C-1), 72.4 (C-3), 72.1 (C-5), 71.4 (C-2), 68.0 (C-4), 65.2 (OCH_2R), 61.6 (C-6), 31.9, 29.8, 29.7, 29.5, 29.4, 29.3, 29.2, 28.9, 26.0, 22.7 (CH_2), 20.9, 20.7, 20.6, 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+): mass calculated for $C_{37}H_{56}O_{14}Na$ 747.3568. Found; 747.3622.

4.4.7. Octadecyl 3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-4,5-dihydroxybenzoate ***43***. Compound **36** (200 mg, 0.25 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:1) affording compound **43** (158 mg, 83%); $[\alpha]_D^{22}$+0.2 (*c* 1 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (s, 1H, H_{arom}), 7.24 (s, 1H, H_{arom}) 5.28 (m, 2H, H-2, H-4), 5.13 (t, 1H, J=9.4 Hz, H-3), 5.03 (d, 1H, J=7.4 Hz, H-1), 4.21 (m, 4H, H-6, H-6′, $COOCH_2R$), 3.88 (m, 1H, H-5), 2.05 (m, 12H, $COOCH_3$), 1.70 (m, 2H, $COOCH_2CH_2R$), 1.32 (m, 30H, CH_2), 0.85 (t, 3H, J=6.6 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 169.6 (C=O), 166.1 (C=O), 144.8, 143.9, 139.1, 122.4 (Cq_{arom}), 113.2 (CH_{arom}), 111.0 (CH_{arom}), 101.19 (C-1), 72.5 (C-3), 72.3 (C-5), 71.4 (C-2), 68.1 (C-4), 65.3 (OCH_2R), 61.7 (C-6), 32.0 (CH_2), 29.76 (CH_2), 29.73 (CH_2), 29.69 (CH_2), 29.64 (CH_2), 29.42 (CH_2), 29.39 (CH_2), 28.80 (CH_2), 26.10 (CH_2), 22.75 (CH_2), 20.64, 20.61, 20.60, 20.58 ($COOCH_3$), 14.18 (CH_3). HRMS (ES^+): mass calculated for $C_{39}H_{60}O_{14}Na$ (M+Na); 775.3881. Found; 775.3942.

4.4.8. Butyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***47***. Compound **44** (242 mg, 0.41 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **47** (180 mg, 81%); $[\alpha]_D^{22}$ −17.0 (*c* 1 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (s, 1H, H_{arom}), 7.20 (s, 1H, H_{arom}), 7.06, 5.87 (2br s, 2H, OH), 5.31–5.19 (m, 3H, H-2, H-3, H-4), 5.03 (d, 1H, J=7.47 Hz, H-1), 4.19 (t, 2H, J=6.5 Hz, $COOCH_2$), 4.13 (d, 1H, J=9.0 Hz, H-5), 3.68 (s, 3H, $COOCH_3$), 2.05, 1.99 (s s, 9H, O=CCH_3), 1.67–1.60 (m, 2H, CH_2), 1.41–1.30 (m, 2H, CH_2), 0.89 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 170.0, 169.6, 167.1, 166.0 (C=O), 145.1, 143.7, 139.7, 122.3 (C_{arom}), 113.4, 111.8 (C_{arom}), 101.2 (C-1), 72.3 (C-5), 71.3, 71.1, 68.9 (C-2, C-3, C-4), 64.9 ($COOCH_2R$), 53.2 (OCH_3), 30.7 (CH_2), 20.6, 20.5 20.4 ($COOCH_3$), 19.2 (CH_2), 13.7 (CH_3). HRMS (ES^+) calcd for C24$H_{30}NaO_{14}$ (M+Na^+) 565.1533. Found: 565.1539.

4.4.9. Octyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***48***. Compound **45** (72 mg, 0.11 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:2) affording compound **48** as an oil (44 mg, 65%); $[\alpha]_D^{22}$ −12.5 (*c* 1 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 1H, J=1.8 Hz, H_{arom}), 7.16 (d, 1H, J=1.8 Hz, H_{arom}), 7.11, 5.77 (2br s, 2H, OH), 5.41–5.31 (m, 3H, H-2, H-3, H-4), 5.10 (d, 1H, J=7.12 Hz, H-1), 4.26 (t, 2H, J=6.6 Hz, $COOCH_2$), 4.20 (d, 1H, J=9.6 Hz, H-5), 3.78 (s, 3H, $COOCH_3$), 2.15, 2.08, 2.07 (3 s, 12H, O=CCH_3), 1.78–1.71 (m, 2H, CH_2), 1.46–1.25 (m, 10H, 5× CH_2), 0.90 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 169.9, 169.5, 167.0, 165.9 (C=O), 145.1, 143.6, 139.6, 122.6 (C_{arom}), 113.4, 112.2 (C_{arom}), 101.6 (C-1), 72.4 (C-5), 71.2, 71.1, 68.9 (C-2, C-3, C-4), 65.2 ($COOCH_2R$), 53.2 (OCH_3), 31.8, 29.3, 29.2, 28.7, 26.0, 22.6 (CH_2) 20.7, 20.6 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+) calcd for $C_{28}H_{38}NaO_{14}$ (M+Na^+) 621.2159. Found: 621.2140.

4.4.10. Hexadecyl 3-O-(methyl-2,3,4-tri-O-acetyl-β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***49***. Compound **46** (337 mg, 0.45 mmol) was deprotected by following the general procedure. The reaction crude was purified by flash chromatography (hexane/ethyl acetate from 2:1 to 1:1) affording compound **49** as an oil (200 mg, 62%); $[\alpha]_D^{22}$ −9.4 (*c* 1 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (s, 1H, H_{arom}), 7.05 (s, 1H, H_{arom}), 6.92, 5.77 (2br s, OH), 5.18–5.04 (m, 3H, H-2, H-3, H-4), 4.89 (d, 1H, J=7.5 Hz, H-1), 4.04–3.97 (m, 3H, H-5, OCH_2), 3.52 (s, 3H, $COOCH_3$), 1.90, 1.83, 1.82 (3 s, 12H, O=CCH_3), 1.52–1.45 (m, 2H, CH_2), 1.23–1.00 (m, 26H, 13× CH_2), 0.65 (t, 3H, J=7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 169.9, 169.5, 167.0, 165.9 (C=O), 145.0, 143.7, 139.6, 122.5 (C_{arom}), 113.4, 112.0 (C_{arom}), 101.4 (C-1), 72.3 (C-5), 71.3, 71.1, 68.9 (C-2, C-3, C-4), 65.2 ($COOCH_2R$), 53.2 (OCH_3), 31.9, 29.7, 29.6, 29.5, 29.45, 29.4, 29.3, 29.2 28.7, 26.0, 22.7(CH_2), 20.6, 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+) calcd for $C_{36}H_{54}NaO_{14}$ (M+Na^+) 733.3411. Found: 773.3398.

4.5. General procedure for acetyl deprotection

Compounds **37**–**43** and **47**–**49** were dissolved in methanol (2 mL for each 100 mg) and Na_2CO_3 (0.3 equiv) was then added. The reaction mixture was stirred for 1 h and when starting material had disappeared, IR-120 was then added until pH=7. The reaction mixture was then filtered and solvents removed to afford compounds **11**–**20** in high yields.

4.5.1. Butyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***11***. Compound **37** (289 mg, 0.52 mmol) was deprotected by following the general procedure affording compound **11** (200 mg, quantitative); $[\alpha]_D^{22}$ −53.0 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.19 (d, 1H, J=1.9 Hz, H_{arom}), 7.02 (d, 1H, J=1.9 Hz, H_{arom}), 4.61 (d, 1H, J=6.6 Hz, H-1), 4.08 (t, 2H, J=6.6 Hz, OCH_2), 3.70 (m, 1H, H-6), 3.57 (dd, 1H, J=4 and 12.3 Hz, H-6′), 3.32–3.25 (m, 3H, H-2, H-3, H-4), 3.09–3.08 (m, 1H, H-5), 1.52–1.43 (m, 2H, CH_2), 1.27–1.19 (m, 2H, CH_2), 0.75 (t, 3H, J=7.35 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 166.8 (O=$C_{benzoate}$), 145.4, 145.3, 140.2, 120.6, 111.8, 110.3 (C_{arom}), 102.6 (C-1), 76.8 (C-3), 76.1 (C-5), 73.4 (C-2), 69.6 (C-4), 64.4 (CH_2O), 60.7 (C-6), 30.5, 18.9 (CH_2), 12.8 (CH_3). HRMS (ES^+) calcd for $C_{17}H_{24}NaO_{10}$ (M+Na^+) 411.1267. Found: 411.1263.

4.5.2. Hexyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***12***. Compound **38** (293 mg, 0.52 mmol) was deprotected by following the general procedure affording compound **12** (200 mg, 96%); $[\alpha]_D^{22}$ −53.6 (*c* 1 in MeOH); δ_H (400 MHz, MeOD) 7.44 (d, 1H, J=2.0 Hz, H_{arom}), 7.25 (d, 1H, J=2.0 Hz, H_{arom}), 4.84 (d, 1H, J=6.6 Hz, H-1), 4.24 (t, 2H, J=6.6 Hz, OCH_2), 3.91 (dd, 1H, J=2.2 ans 12.2 Hz, H-6), 3.79 (dd, 1H, J=4.48 and 12.2 Hz, H-6′), 3.55–3.45 (m, 3H, H-2, H-3, H-4), 3.34–3.32 (m, 1H, H-5), 1.77–1.70 (m, 2H, CH_2), 1.48–1.33 (m, 6H, 3× CH_2), 0.92 (t, 3H, J=6.88 Hz, CH_3); δ ^{13}C

(100 MHz, MeOD) 166.8 (O=$C_{benzoate}$), 145.4, 145.4, 140.3, 120.6, 111.8, 110.4 (C_{arom}), 102.9 (C-1), 76.8 (C-3), 76.2 (C-5), 73.4 (C-2), 69.6 (C-4), 64.7 (CH_2O), 60.8 (C-6), 31.3, 31.2, 28.4, 25.5, 22.3 (CH_2), 13.0 (CH_3). HRMS (ES^+) calcd for $C_{19}H_{28}NaO_{10}$ ($M+Na^+$) 439.1580. Found: 439.1589.

4.5.3. Octyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***13***. Compound **39** (53 mg, 0.09 mmol) was deprotected by following the general procedure affording compound **13** (38 mg, quantitative); $[\alpha]_D^{22}$ −53.8 (*c* 1 in MeOH); δ_H (400 MHz, MeOD) 7.44 (d, 1H, *J*=2.0 Hz, H_{arom}), 7.25 (d, 1H, *J*=2.0 Hz, H_{arom}), 4.87 (br s, 1H, H-1), 4.25 (t, 2H, *J*=6.6 Hz, OCH_2), 3.92−3.80 (m, 2H, H-6, H-6′), 3.52−3.45 (m, 4H, H-2, H-3, H-4, H-5), 1.76−1.73 (m, 2H, CH_2), 1.45−1.32 (m, 10H, 5× CH_2), 0.90 (t, 3H, *J*=6.88 Hz, CH_3); δ ^{13}C (100 MHz, MeOD) 166.1 (O=$C_{benzoate}$), 146.9, 146.8, 141.6, 122.0, 113.2, 111.8 (C_{arom}), 104.3 (C-1), 78.2 (C-3), 77.5 (C-5), 74.8 (C-2), 70.9 (C-4), 66.0 (CH_2O), 62.1 (C-6), 32.9, 30.4, 30.3, 29.8, 27.2, 23.7 (CH_2), 14.4 (CH_3). HRMS (ES^+) calcd for $C_{21}H_{32}NaO_{10}$ ($M+Na^+$) 467.1893. Found: 467.1922.

4.5.4. Decyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***14***. Compound **40** (320 mg, 0.5 mmol) was deprotected by following the general procedure affording compound **14** (175 mg, 75%); $[\alpha]_D^{22}$ −33.3 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.25 (d, 1H, *J*=1.5 Hz, H_{arom}), 7.05 (d, 1H, *J*=1.5 Hz, H_{arom}), 4.58 (d, 1H, *J*=6.6 Hz, H-1), 4.08 (t, 2H, *J*=6.6 Hz, OCH_2), 3.80 (m, 1H, H-6), 3.65 (dd, 1H, *J*=3.9 and 12.0 Hz, H-6′), 3.36−3.25 (m, 4H, H-2, H-3, H-4, H-5), 1.65−1.58 (m, 2H, CH_2), 1.33−1.20 (m, 14H, 7× CH_2), 0.90 (t, 3H, *J*=6.5 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 166.8 (O=$C_{benzoate}$), 145.4, 111.8, 110.5 (C_{arom}), 102.9 (C-1), 76.9 (C-3), 76.2 (C-5), 73.4 (C-2), 69.6 (C-4), 64.6 (CH_2O), 60.8 (C-6), 31.7, 29.3, 29.1, 29.0, 28.4, 25.8, 22.3, 13.1 (CH_3). HRMS (ES^+) calcd for $C_{23}H_{36}NaO_{10}$ ($M+Na^+$) 495.2206. Found: 495.2216.

4.5.5. Dodecyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***15***. Compound **41** (111 mg, 0.16 mmol) was deprotected by following the general procedure affording compound **15** (83 mg, quantitative); $[\alpha]_D^{22}$ −8.0 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.20 (d, 1H, *J*=1.8 Hz, H_{arom}), 7.02 (d, 1H, *J*=1.8 Hz, H_{arom}), 4.60 (d, 1H, *J*=6.9 Hz, H-1), 4.01 (t, 2H, *J*=6.8 Hz, OCH_2), 3.69−3.58 (m, 1H, H-6), 3.56 (dd, 1H, *J*=4.1 and 12.0 Hz, H-6′), 3.33−3.24 (m, 4H, H-2, H-3, H-4, H-5), 1.54−1.47 (m, 2H, CH_2), 1.27−1.01 (m, 20H, 10× CH_2), 0.67 (t, 3H, *J*=6.2 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 166.8 (O=$C_{benzoate}$), 145.5, 140.2, 120.6, 111.8, 110.4 (C_{arom}), 102.9 (C-1), 76.8 (C-3), 76.2 (C-5), 73.4 (C-2), 69.6 (C-4), 64.6 (CH_2O), 60.8 (C-6), 31.7, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.4, 25.8, 22.3 (CH_2), 13.1 (CH_3). HRMS (ES^+) calcd for $C_{25}H_{40}NaO_{10}$ ($M+Na^+$) 523.2519. Found: 523.2484.

4.5.6. Hexadecyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***16***. Compound **42** (180 mg, 0.20 mmol) was deprotected by following the general procedure affording compound **16** (111 mg, quantitative); $[\alpha]_D^{22}$ −25.9 (*c* 1 in MeOH); δ_H (300 MHz, MeOD) 7.43 (d, 1H, *J*=1.92 Hz, H_{arom}), 7.26 (d, 1H, *J*=1.92 Hz, H_{arom}), 4.90 (br s, 1H, H-1), 4.24 (t, 2H, *J*=6.4 Hz, OCH_2), 3.93−3.84 (m, 1H, H-6), 3.80 (dd, 1H, *J*=4.0 and 12.0 Hz, H-6′), 3.57−3.42 (m, 4H, H-2, H-3, H-4, H-5), 1.80−1.73 (m, 2H, CH_2), 1.49−1.23 (m, 26H, 13× CH_2), 0.90 (t, 3H, *J*=6.2 Hz, CH_3); δ ^{13}C (62.5 MHz, MeOD) 166.8 (O=$C_{benzoate}$), 145.5, 145.4, 140.2, 120.6, 111.8, 110.4 (C_{arom}), 102.9 (C-1), 76.8 (C-3), 76.1 (C-5), 73.4 (C-2), 69.6 (C-4), 64.6 (CH_2O), 60.7 (C-6), 31.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.4, 25.8, 22.3 (CH_2), 13.1 (CH_3). HRMS (ES^+) calcd for $C_{29}H_{48}NaO_{10}$ ($M+Na^+$) 579.3145. Found: 579.3142.

4.5.7. Octadecyl 3-O-(β-D-glucopyranosyl)-4,5-dihydroxybenzoate ***17***. Compound **43** (147 mg, 0.19 mmol) was deprotected by the following general procedure affording compound **17** (112 mg, 98%); δ_H (300 MHz, MeOD) 7.44 (s, 1H, H_{arom}), 7.26 (s, 1H, H_{arom}), 4.87 (br s, 1H, H-1), 4.24 (m, 2H, OCH_2), 3.90−3.80 (m, 2H, H-6, H-6′), 3.57−3.45 (m, 4H, H-2, H-3, H-4, H-5), 1.76 (m, 2H, CH_2), 1.46−1.15 (m, 30H, 15× CH_2), 0.90 (m, 3H, CH_3); δ ^{13}C (75 MHz, $CDCl_3$) 166.8 (O=$C_{benzoate}$), 145.5, 145.4, 140.2, 120.6, 111.8, 110.4 (C_{arom}), 103.0 (C-1), 76.9 (C-3), 76.2 (C-5), 73.4 (C-2), 69.6 (C-4), 64.6 (CH_2O), 60.8 (C-6), 31.7, 29.4, 29.5, 29.3, 29.2, 29.1, 29.0, 28.5, 25.8, 22.3 (CH_2), 13.0 (CH_3). HRMS (ES^+) calcd for $C_{31}H_{52}NaO_{10}$ ($M+Na^+$) 607.3458. Found: 607.3455.

4.5.8. Butyl 3-O-(β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***18***. Compound **47** (150 mg, 0.22 mmol) was deprotected by the following the general procedure. Reaction crude was purified by RP-C18 with MeOH/H_2O affording compound **18** (65 mg, 74%); $[\alpha]_D^{22}$ −85.0 (*c* 1 in MeOH); ^{1}H NMR (300 MHz, MeOD) δ 7.28 (s, 1H, H_{arom}), 7.17 (s, 1H, H_{arom}), 4.87 (d, 1H, *J*=7.0 Hz, H-1), 4.17 (t, 2H, *J*=6.5 Hz, OCH_2), 3.79 (m, 1H, H-5), 3.57−3.52 (m, 3H, H-2, H-4, H-3), 1.66−1.57 (m, 2H, CH_2), 1.37−1.30 (m, 2H, CH_2), 0.82 (t, 3H, *J*=7.2 Hz, CH_3). ^{13}C NMR (101 MHz, MeOD) δ 175.5, 169.5 (C=O), 146.6, 112.2, 111.4, 110.8 (C_{arom}), 102.0 (C-1), 761, 75.2, 72.7, 71.7, 65.2 (OCH_2R), 30.0 (CH_2), 18.7 (CH_2), 13.0 (CH_3). HRMS (ES^+) calcd for $C_{17}H_{22}NaO_{11}$ ($M+Na^+$) 425.1060. Found: 425.1065.

4.5.9. Octyl 3-O-(β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***19***. Compound **48** (101 mg, 0.17 mmol) was deprotected by following the general procedure affording compound **19** (81 mg, 88%); $[\alpha]_D^{22}$ −16.0 (*c* 1 in MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.22 (d, 1H, *J*=2.0 Hz, H_{arom}), 7.09 (d, 1H, *J*=2.0 Hz, H_{arom}), 4.73 (d, 1H, *J*=7.6 Hz, H-1), 4.06 (t, 2H, *J*=6.5 Hz, OCH_2), 3.83 (d, 1H, *J*=9.6 Hz, H-5), 3.51−3.35 (m, 3H, H-2, H-3, H-4), 1.60−1.53 (m, 2H, CH_2), 1.32−1.10 (m, 10H, 5× CH_2), 0.72 (t, 3H, *J*=7.0 Hz, CH_3). ^{13}C NMR (101 MHz, MeOD) δ 172.0, 168.0 (C=O), 146.9, 146.5, 141.7, 122.0, 113.4, 111.8 (C_{arom}), 104.3 (C-1), 76.9, 76.7, 74.4, 72.9 (C-5, C-2, C-3, C-4), 66.2 (OH_2R), 32.9, 30.2, 29.7, 29.6, 27.0, 23.6 (CH_2), 14.4 (CH_3). HRMS (ES^+) calcd for $C_{21}H_{30}NaO_{11}$ ($M+Na^+$) 481.1686. Found: 481.1695.

4.5.10. Hexadecyl 3-O-(β-D-glucopyranosyluronate)-4,5-dihydroxybenzoate ***20***. Compound **49** (164 mg, 0.23 mmol) was deprotected by following the general procedure to afford compound **20** (105 mg, 79%); $[\alpha]_D^{22}$ −3.3 (*c* 1 in MeOH/$CHCl_3$ 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (s, 1H, H_{arom}), 7.05 (s, 1H, H_{arom}), 6.92, 5.77 (2 br s, OH), 5.18−5.04 (m, 3H, H-2, H-3, H-4), 4.89 (d, 1H, *J*=7.5 Hz, H-1), 4.04−3.97 (m, 3H, H-5, OCH_2), 3.52 (s, 3H, $COOCH_3$), 1.90, 1.83, 1.82 (3 s, 12H, O=CCH_3), 1.52−1.45 (m, 2H, CH_2), 1.23−1.00 (m, 26H, 13× CH_2), 0.65 (t, 3H, *J*=7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 169.9, 169.5, 167.0, 165.9 (C=O), 145.0, 143.7, 139.6, 122.5 (C_{arom}), 113.4, 112.0 (C_{arom}), 101.4 (C-1), 72.3 (C-5), 71.3, 71.1, 68.9 (C-2, C-3, C-4), 65.2 ($COOCH_2R$), 53.2 (OCH_3), 31.9, 29.7, 29.6, 29.5, 29.45, 29.4, 29.3, 29.2 28.7, 26.0, 22.7(CH_2), 20.6, 20.5 ($COOCH_3$), 14.1 (CH_3). HRMS (ES^+) calcd for $C_{29}H_{46}NaO_{11}$ ($M+Na^+$) 593.2938. Found: 593.2945.

4.6. Surface tension and CMC determination

Surface tension measurements were performed at 23 °C by means of the Wilhelmy plate method in a Krüss K12 tensiometer. Samples were prepared by successive dilutions of an initial concentrated solution. Prior to each surface tension measurement, samples were left 30 min in repose to attain the equilibrium. The possible aggregation properties of the gallate derivatives were evidenced from the adsorption isotherms obtained when surface tension is plotted graphically against the logarithm of the concentration. The typical surfactant profile consists of a linear decrease of the surface tension when the compound concentration increases, followed by a surface tension stabilization when the

concentration corresponding to the saturation of the interface is attained. The intersection of the two linear portions in the graph determines the CMC.

4.7. Determination of HLB values

The HLB values were calculated following the equation described by Griffin[59] for non-ionic surfactants. HLB=20(hydrophilic group molecular weight)/(surfactant molecular weight).

4.8. Calculation of aggregation parameters

The area occupied per molecule adsorbed at the saturated water-air interface (in $Å^2$) can be obtained from the equation: $A=10^{16}/N_A\,\Gamma_{max}$, where N_A is the Avogadro's number and Γ_{max} is the adsorption at the saturated interface expressed in mol/cm^2, calculated according to the Gibbs equation: $\Gamma_{max}=-(\Delta\gamma/\Delta\log C)/2.303nRT$, where n is the number of molecular species in solution (n=1 for non-ionic compounds as in our case) and ($\Delta\gamma/\Delta\log C$) is the slope of the linear portion of the graph before the CMC.

4.9. DPPH• radical scavenging assay

Measurement of DPPH• radical scavenging activity was performed according to reported recommendations.[60] Conditions consist in approximately 20 min reaction period and a molar ratio between DPPH• and antioxidant that permits 60–80% radical scavenging activity for the most potent antioxidant. Briefly, 2,2-diphenyl-1-picrylhydrazyl (DPPH•) in ethanol (250 μM, 2 mL) was added to 2 mL of the test compounds at different concentrations in ethanol. The final concentrations of the test compounds in the reaction mixtures were 0.5, 5, 10, 25 and 50 μM. Each mixture was then shaken vigorously and held for 30 min at room temperature in the dark. The decrease in absorbance of DPPH• at 517 nm was measured. Ethanol was used as a blank solution. DPPH• ethanol solution (2 mL) served as the control. All tests were performed in triplicate. A dose–response curve was obtained for each compound. ED50 corresponds to either micrograms or micromoles of product able to consume half the amount of free radical divided by micromoles of initial DPPH•. The results are expressed as antiradical power (ARP), or 1/ED50.

4.10. Reducing power of the phenolic Compounds

FRAP (Ferric Reducing/Antioxidant Power) method was used by adaptation of the procedure of Benzie and Strain.[61] The FRAP reagent was prepared daily by mixing sodium acetate buffer 300 mM (pH 3.6), 2,4,6-tripyridyl-*s*-triazine (TPTZ) 10 mM and ferric chloride 20 mM, in the ratio 10:1:1, respectively. TPTZ solution was prepared in HCl 40 mM. 1.5 mL of FRAP reagent were incubated for 10 min at 37 °C. Then, 150 μL of water and 50 μL of phenolic solution (0.2–4 mg/L) were added and the absorbance was measured at 593 nm after 4 min. The standard curve was built with ferrous chloride. The number of donated electrons was calculated from the slopes of the lineal adjustments between the phenolic concentration and the FRAP activity.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.07.046.

References and notes

1. Beckman, K. B.; Ames, B. N. *Physiol. Rev.* **1998**, *78*, 547–581.
2. Halliwell, B.; Gutteridge, J. M. C. In *Free radicals in Biology and Medicine*; Press, C., Ed.: Oxford, 1989; pp 416–494.
3. Regnstrom, J.; Nilsson, J.; Tornvall, P.; Hamsten, A.; Landou, C. *Lancet* **1992**, *339*, 1183–1186.
4. Schapira, A. H.; Olanow, C. W. *JAMA* **2004**, *291*, 358–364.
5. Zafrilla, P.; Mulero, J.; Xandri, J. M.; Santo, E.; Caravaca, G.; Morillas, J. M. *Curr. Med. Chem.* **2006**, *13*, 1075–1083.
6. Block, G. *Nutr. Rev.* **1992**, *50*, 207–213.
7. Rice-Evans, C. A.; Diplock, A. T. *Free Radical Biol. Med.* **1993**, *15*, 77–96.
8. Willcox, B. J.; Curb, J. D.; Rodriguez, B. L. *Am. J. Cardiol.* **2008**, *101*, S75–S86.
9. Zern, T. L.; Fernandez, M. L. *J. Nutr.* **2005**, *135*, 2291–2294.
10. Yang, C. S.; Wang, X.; Lu, G.; Picinich, S. C. *Nat. Rev. Cancer* **2009**, *9*, 429–439.
11. Rossi, L.; Mazzitelli, S.; Arciello, M.; Capo, C. R.; Rotilio, G. *Neurochem. Res.* **2008**, *33*, 2390–2400.
12. Andres-Lacueva, C.; Shukitt-Hale, B.; Galli, R.; Jauregui, O.; Lamuela-Raventos, R.; Joseph, J. *Nutr. Neurosci.* **2005**, *8*, 111–120.
13. Krikorian, R.; Shidler, M. D.; Nash, T. A.; Kalt, W.; Vinqvist-Tymchuk, M. R.; Shukitt-Hale, B.; Joseph, J. A. *J. Agric. Food Chem.* **2010**, *58*, 3996–4000.
14. González-Santiago, M.; Martín-Bautista, E.; Carrero, J. J.; Fonollá, J.; Baró, L.; Bartolomé, M. V.; Gil-Loyzaga, P.; López-Huertas, E. *Atherosclerosis* **2006**, *188*, 35–42.
15. Benavente-García, O.; Castillo, J.; Lorente, J.; Ortuño, A.; Del Rio, J. A. *Food Chem.* **2000**, *68*, 457–462.
16. Hras, A. R.; Hadolin, M.; Knez, Z.; Bauman, D. *Food Chem.* **2000**, *71*, 229–233.
17. Mateos, R.; Dominguez, M. M.; Espartero, J. L.; Cert, A. *J. Agric. Food Chem.* **2003**, *51*, 7170–7175.
18. Pazos, M.; Alonso, A.; Sanchez, I.; Medina, I. *J. Agric. Food Chem.* **2008**, *56*, 3334–3340.
19. Torres de Pinedo, A.; Peñalver, P.; Morales, J. C. *Food Chem.* **2007**, *103*, 55–61.
20. Torres de Pinedo, A.; Peñalver, P.; Pérez-Victoria, I.; Rondón, D.; Morales, J. C. *Food Chem.* **2007**, *105*, 657–665.
21. Torres de Pinedo, A.; Peñalver, P.; Rondón, D.; Morales, J. C. *Tetrahedron* **2005**, *61*, 7654–7660.
22. Grasso, S.; Siracusa, L.; Spatafora, C.; Renis, M.; Tringali, C. *Bioorg. Chem.* **2007**, *35*, 137–152.
23. Mateos, R.; Trujillo, M.; Pereira-Caro, G.; Madrona, A.; Cert, A.; Espartero, J. L. *J. Agric. Food Chem.* **2008**, *56*, 10960–10966.
24. Trujillo, M.; Mateos, R.; Collantes de Teran, L.; Espartero, J. L.; Cert, R.; Jover, M.; Alcudia, F.; Bautista, J.; Cert, A.; Parrado, J. *J. Agric. Food Chem.* **2006**, *54*, 3779–3785.
25. Laguerre, M.; López Giraldo, L. J.; Lecomte, J.; Figueroa-Espinoza, M.-C.; Baréa, B.; Weiss, J.; Decker, E. A.; Villeneuve, P. *J. Agric. Food Chem.* **2010**, *58*, 2869–2876.
26. Medina, I.; Lois, S.; Alcántara, D.; Lucas, R.; Morales, J. C. *J. Agric. Food Chem.* **2009**, *57*, 9773–9779.
27. Laguerre, M.; López Giraldo, L. J.; Lecomte, J.; Figueroa-Espinoza, M.-C.; Baréa, B.; Weiss, J.; Decker, E. A.; Villeneuve, P. *J. Agric. Food Chem.* **2009**, *57*, 11335–11342.
28. Sasaki, K.; Alamed, J.; Weiss, J.; Villeneuve, P.; López Giraldo, L. J.; Lecomte, J.; Figueroa-Espinoza, M.-C.; Decker, E. A. *Food Chem.* **2010**, *118*, 830–835.
29. Laguerre, M.; Wrutniak-Cabello, C.; Chabi, B.; López Giraldo, L. J.; Lecomte, J.; Villeneuve, P.; Cabello, G. *J. Pharm. Pharmacol.* **2011**, *63*, 531–540.
30. Lucas, R.; Comelles, F.; Alcántara, D.; Maldonado, O. S.; Curcuroze, M.; Parra, J. L.; Morales, J. C. *J. Agric. Food Chem.* **2010**, *58*, 8021–8026.
31. Palozza, P.; Simone, R.; Picci, N.; Buzzoni, L.; Ciliberti, N.; Natangelo, A.; Manfredini, S.; Vertuani, S. *Free Radical Biol. Med.* **2008**, *44*, 1452–1464.
32. Masaki, H.; Okamoto, N.; Sasaki, S.; Sakurai, H. *Biol. Pharm. Bull.* **1997**, *20*, 304–308.
33. Serrano, A.; Palacios, C.; Roy, G.; Cespón, C.; Villar, M. L.; Nocito, M.; González-Porqué, P. *Arch. Biochem. Biophys.* **1998**, *350*, 49–54.
34. Locatelli, C.; Rosso, R.; Santos-Silva, M. C.; de Souza, C. A.; Licinio, M. A.; Leal, P.; Bazzo, M. L.; Yunes, R. A.; Creczynski-Pasa, T. B. *Bioorg. Med. Chem.* **2008**, *16*, 3791–3799.
35. Dufour, C.; da Silva, E.; Potier, P.; Queneau, Y.; Dangles, O. *J. Agric. Food Chem.* **2002**, *50*, 3425–3430.
36. He, L.; Galland, S.; Dufour, C.; Chen, G.-R.; Dangles, O.; Fenet, B.; Praly, J.-P. *Eur. J. Org. Chem.* **2008**, *2008*, 1869–1883.
37. Shindo, K.; Asagi, E.; Sano, A.; Hotta, E.; Minemura, N.; Mikami, K.; Tamesada, E.; Misawa, N.; Maoka, T. *J. Antibiot.* **2008**, *61*, 185–191.
38. Shindo, K.; Endo, M.; Miyake, Y.; Wakasugi, K.; Morritt, D.; Bramley, P. M.; Fraser, P. D.; Kasai, H.; Misawa, N. *J. Antibiot.* **2008**, *61*, 729–735.
39. Yuji, H.; Weiss, J.; Villeneuve, P.; Lopez Giraldo, L. J.; Figueroa-Espinoza, M. C.; Decker, E. A. *J. Agric. Food Chem.* **2007**, *55*, 11052–11056.
40. Nicolaou, K. C.; Mitchell, H. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1576–1624.
41. Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21–123.
42. Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 78–84.

43. Bollenback, G. N.; Long, J. W.; Benjamin, D. G.; Lindquist, J. A. *J. Am. Chem. Soc.* **1955**, *77*, 3310–3315.
44. Excoffier, G.; Gagnaire, D.; Utille, J.-P. *Carbohydr. Res.* **1975**, *39*, 368–373.
45. Fischer, B.; Nudelman, A.; Ruse, M.; Herzig, J.; Gottlieb, H. E.; Keinan, E. *J. Org. Chem.* **1984**, *49*, 4988–4993.
46. Harding, J. R.; King, C. D.; Perrie, J. A.; Sinnott, D.; Stachulski, A. V. *Org. Biomol. Chem.* **2005**, *3*, 1501–1507.
47. Schmidt, R. R.; Michel, J.; Roos, M. *Liebigs Ann. Chem.* **1984**, *1984*, 1343–1357.
48. Heins, A.; Garamus, V. M.; Steffen, B.; Stöckmann, H.; Schwarz, K. *FOBI* **2007**, *1*, 189–201.
49. Rosen, M. J. *Surfactant and Interfacial Phenomena*; Wiley: New York, NY, 1978.
50. Niño, M.; Patino, J. *J. Am. Oil Chem. Soc.* **1998**, *75*, 1241–1248.
51. Schich, M. J. *Nonionic Surfactants*; Marcel Dekker: New York, NY, 1987.
52. Kawanishi, K.; Hashimoto, Y.; JP63246350, 1988.
53. Mu, L.; Feng, S. S. *J. Controlled Release* **2002**, *80*, 129–144.
54. Thommy, C.; EP182934, 1986.
55. Palma, S.; Manzo, R. H.; Allemandi, D.; Fratoni, L.; Lo Nostro, P. *Colloids Surf., A* **2003**, *212*, 163–173.
56. Mounanga, T. K.; Gérardin, P.; Poaty, B.; Perrin, D.; Gérardin, C. *Colloids Surf., A* **2008**, *318*, 134–140.
57. Yan, A.; Von Dem Bussche, A.; Kane, A. B.; Hurt, R. H. *Carbon* **2007**, *45*, 2463–2470.
58. Przestalski, S.; Hladyszowski, J.; Kuczera, J.; Rózycka-Roszak, B.; Trela, Z.; Chojnacki, H.; Witek, S.; Fisicaro, E. *Biophys. J.* **1996**, *70*, 2203–2211.
59. Griffin, W. C. *J. Soc. Cosmet. Chem.* **1954**, *5*, 259–267.
60. Nenadis, N.; Tsimidou, M. *J. Am. Oil Chem. Soc.* **2002**, *79*, 1191–1195.
61. Benzie, I. F.; Strain, J. J. *Anal. Biochem.* **1996**, *239*, 70–76.