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C-D-Glucopyranosyl Derivatives of Tocopherols – Synthesis and Evaluation as Amphiphilic Antioxidants

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Treatment of dimethylhydroquinone dimethyl ethers (*ortho* and *meta* isomers) with glycopyranose pentaacetates (D-*gluco*, D-*galacto*) in the presence of $SnCl_4$ and F_3CCO_2Ag selectively afforded the corresponding *C*-β-D-glycosyl derivatives by aromatic electrophilic substitution. Oxidation of the dimethoxybenzene moiety with ceric ammonium nitrate delivered *C*-β-D-glycosyl-dimethylbenzoquinones, which were reduced with $Na_2S_2O_4$ to the corresponding *C*-β-D-glycosyl-dimethylhydroquinones. $ZnCl_2$-catalyzed cyclization either with methylbut-2-en-1-ol (prenyl alcohol) or with all-racemic phytol led to acetyl-protected *C*-β-D-glycosyl chromanols or *C*-β-D-glycosyl tocopherols, the sugar residues of which were deacetylated under base catalysis conditions. These new molecules were evaluated as antioxidants in terms of their ability to inhibit the peroxidation of linoleic acid in SDS micelles. The position of the *C*-glucosyl moiety on the phenolic nucleus emerges as the critical structural determinant of their activity.

Introduction

Vitamin E constitutes a family of eight related molecules, in which a chromanol ring bears either a saturated $C_{16}H_{33}$ phytyl chain (tocopherols) or an unsaturated isoprenoid chain (tocotrienols). The chromanol ring displays one to three methyl groups with different substitution patterns, denoted by the lettering α, β, γ or δ. The four tocopherols have asymmetric carbons at positions 2, 4′ and 8′ (Scheme 1), while in the case of the four tocotrienols only one chiral centre – at C2 – exists. Such naturally occurring lipophilic molecules, practically insoluble in aqueous media, have long been known as antioxidants, primarily as a function of the reducing properties of the phenolic nucleus. Among them, α-tocopherol is the most abundant, and also the most biologically active. Recent progress has shed more light on the mechanisms of its biological activity.[1] Natural α-tocopherol, with three methyl groups on the ring and three (*R*)-configured chiral centres, is recognized well by α-tocopherol transfer protein (α-TTP) the binding pocket of which can accommodate α-tocopherol with a U-shaped phytyl chain. Vitamin E was originally claimed to be the fertility vitamin, after it was demonstrated that the embryos of α-TTP–/– female mice died at mid-gestation, while an α-tocopherol-supplemented diet allowed full-term pregnancy. Nowadays, the roles of vitamin E in humans, animals and plants are all better understood, and they appear quite diverse and complex in view of the fact that these dietary molecules have both antioxidant and pro-oxidant properties and may be involved in the prevention of atherogenesis and cancers.[2,3] A lot of experimental or theoretical work has thus recently been devoted to investigating the activity of phenolic antioxidants and the possible influence of co-antioxidants.[4,5] While the beneficial effects of supplementation with vitamin E have fuelled many debates and stimulated intensive academic and industrial investigations, how the protective antioxidants act in vivo has raised many ques-

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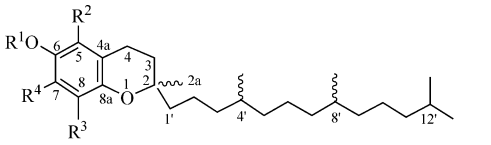
tions, in particular with regard to the exact location and orientation of antioxidant molecules at the molecular level. For instance, it is presumed that the regeneration of α-tocopherol by vitamin C (ascorbate) is made possible by the location of the tocopheroxyl radical adjacent to the interface, so as to abstract a hydrogen atom or an electron from ascorbate.[6]



	R^1	R^2	R^3	R^4
α-tocopherol	H	Me	Me	Me
***O*-glucoside**	β-D-*Glc*p	Me	Me	Me
***C*-glucoside**	H	β-D-*Glc*p	Me	Me
***C*-glucoside**	H	Me	β-D-*Glc*p	Me
***C*-glucoside**	H	Me	Me	β-D-*Glc*p

Scheme 1. Racemic α-tocopherol and glucosylated derivatives.

In this context, the chemical synthesis of antioxidants, possibly with improved properties, is an active field. The easily available tocopheryl bromide, for example, has recently been converted into the corresponding phosphonium salt, further elaborated into various furotocopheryl derivatives or coupled onto modified polystyrene to provide a new vitamin-E-loaded resin.[7] In other approaches, the 5a-azido-tocopheryl derivative, also prepared from tocopheryl bromide,[8] and its 5a-nitro analogue[9] have provided access to tocopheryl-1,2,3-triazoles or -isoxazolines through cycloaddition reactions. Interestingly, the tocopheryl-1,2,3-triazoles might undergo base-induced cleavage of the tocopheryl moiety, with potential applications in drug-delivery systems. Condensation of trimethylhydroquinone with aldehydes provided 3-oxachromanol-type antioxidants,[10] which were comparatively studied with α-tocopherol and pentamethylchromanol, as well as with ubichromanol, ubichromenol and twin-chromanol. The last of these was found to be a promising new candidate as an artificial antioxidant in biological systems.[11] all-*rac*-α-Selenotocopherol has been synthesized and found to be a slightly less potent antioxidant than α-tocopherol, in keeping with the value of the OH bond dissociation energy, which was found to be approximately 1 kcal mol^{-1} higher than that of α-tocopherol.[12] Moreover, phenolic compounds with one or two nitrogen atoms in the aromatic ring (e.g., 3-pyridinols,[13] 6-amino-3-pyridinols,[13] 5-pyrimidinols[14] and analogues) are extremely effective chain-breaking antioxidants in homogeneous organic solutions, a tetrahydro-1,8-naphthyridin-3-ol being almost 30 times more effective than α-tocopherol at inhibiting lipid peroxidation.[13,15] Chemical modifications of the alkyl chain have also been considered, as shown by the synthesis of tocopherol fatty alcohols as microglial activation modulators,[16] or the preparation of new chroman/catechol hybrids, evaluated against oxidative stress-induced cellular damage and as neuroprotectants.[17]

It is worth mentioning ongoing efforts being made towards the synthesis and evaluation of novel compounds designed as inhibitors of lipid peroxidation with protective effects against myocardial ischemia-reperfusion damage.[18] From a series of molecules containing lipoic acid and trolox connected through spacers[19] and examined for their antioxidant activity and their protective effects against reperfusion arrhythmias, it was found that the 2- and the 5-substituted chromanols exhibited the better cardioprotective activity.[20] Other 5-substituted analogues were also synthesized by connecting the chromanol ring to methylsulfonylaminophenyl residues through tertiary amine moieties (a combination of pharmacophores identified for the most active class III antiarrhythmics), so as to obtain new compounds that were evaluated with regard to their antiarrhythmic and antioxidant activity.[21] In an extension of this approach, novel hybrids combining the pharmacophoric redox moieties of vitamin E and motifs responsible for the antiarrhythmic properties of the class I antiarrhythmics procainamide and lidocaine were prepared and evaluated. The tests suggested that the efficacy of the new compounds in preventing reperfusion arrhythmias could be attributed to their combined effects involving inhibition of free-radical-mediated damage coupled to antiarrhythmic properties.[22]

Because ascorbic acid and tocopherols are hydrophilic and lipophilic molecules, respectively, modified amphiphilic antioxidants have been synthesized with the goal of improving their accessibility towards various media.[23] While novel ascorbic acid derivatives (6-*O*-acyl-2-*O*-α-D-glucopyranosyl-L-ascorbic acids) have been evaluated as lipophilic topical prodrugs of ascorbic acid (with transdermal activity in a human living skin equivalent model),[24] other studies, following an opposite strategy, have involved the modification of lipophilic chromanols and tocopherols for the preparation of water-soluble molecules with antioxidant activities in aqueous media [e.g., the commercially available trolox (COOH-substituted chromanol) or its reduced derivative (CH_2OH-substituted chromanol)]. After glycosylation, the latter compound afforded a water-soluble *O*-alkyl glycoside[25] showing radical scavenging properties comparable to those of tocopherol, trolox and ascorbic acid, or even higher under specific conditions.[26] Oligosaccharides of tocopherols (*O*-aryl glycoside type; see Scheme 1) represent another class of water-soluble derivatives, the biological applicability of which, however, is dependent on deglycosidation in vivo as the free phenoxyl group is essential for the redox properties of tocopherols. Their synthesis was achieved in good yield by glycosidation between oligosaccharide peracetates and tocopherol with BF_3·etherate as catalyst.[27] Hence, all-*rac*-α-tocopheryl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside was obtained in 66% yield and was then deacetylated (97% yield). From benzyl-protected α-D-glucopyranose trichloroacetimidate as glucosyl donor, the two-step synthesis was achieved in 67% overall yield.[28] All the deacetylated tocopheryl oligosaccharides prepared were soluble in DMSO or pyridine, while their solubilities in CH_2Cl_2, MeOH or H_2O depended on the size of the sugar resi-

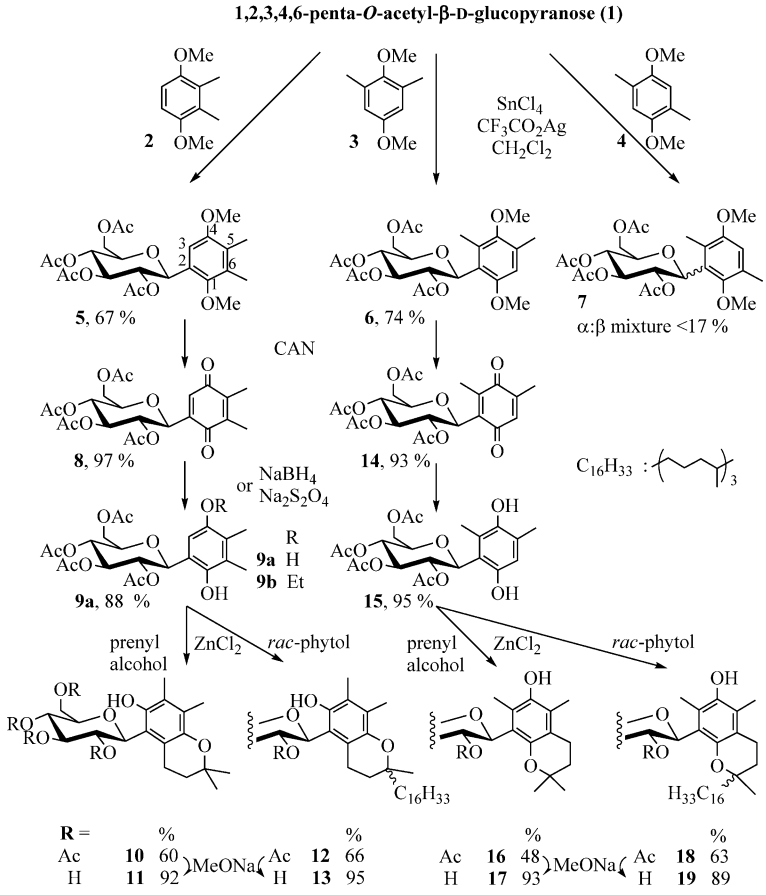
due.[27a] Glycosidation of α-tocopherol and analogues by cultured plant cells has also been investigated.[29]

This account reports on synthetic routes to *C*-(β-D-glycopyranosyl)chromanols and *C*-(β-D-glycopyranosyl)tocopherols (D-*gluco*, D-*galacto* series) with acetylated or deacetylated sugar moieties. These new *C*-glucosylated analogues of vitamin E are then evaluated for their ability to inhibit the peroxidation of linoleic acid within SDS micelles.

Results and Discussion

1. Synthetic Results

C-Glycosyl arenes (also frequently termed aryl-*C*-glycosides; see Scheme 1)[30] and *C*-glycosyl flavonoids[31] are continuously attracting attention, because many of them are bioactive natural compounds. This has stimulated interest with regard to their biosynthesis and their chemical synthesis.[32,33] Our recent synthesis of *C*-glycopyranosyl-hydro- and -benzoquinones[34] via the known *C*-glycopyranosyl-1,4-dimethoxybenzenes[35] highlighted a poorly known route[36] to small molecules that have not received much attention, although their stabilities and polyfunctional structures should convey interesting chemical and biological properties, in view also of the diverse bioactivities of quinoid compounds.[37] In particular, we found that *C*-glucopyranosyl-hydro- and -benzoquinones were modest inhibitors of glycogen phosphorylase, as shown by enzymatic and crystallographic studies.[34b] This study provided a basis for further elaboration of a new scaffold for obtaining more effective inhibitors of the enzyme, while nitration of 2-(tetra-*O*-acetyl-β-D-glycopyranosyl)-1,4-dimethoxybenzenes led, after reduction and acylation of the resulting amino groups, to a series of 5-*N*-amido derivatives.[38] After preliminary attempts at cyclization between *C*-β-D-galactopyranosyl-hydroquinone and all-racemic phytol had afforded low yields of regioisomers related to *C*-D-galactopyranosyl tocopherol (see Supporting Information), we considered *C*-glycopyranosyl-dimethylhydroquinones (*o*-, *m*- and *p* isomers) as appropriate building blocks for preparing *C*-glycosyl-chromanols and *C*-glycosyl-tocopherols upon annelation with 3-methylbut-2-en-1-ol (prenyl alcohol) or all-racemic phytol. In line with our previous syntheses,[34] electrophilic substitution reactions between dimethyl-substituted 1,4-dimethoxybenzenes (*o*, *m*, or *p* isomers, **2**–**4**; Scheme 2) and appropriate glycosyl donors were considered a key step



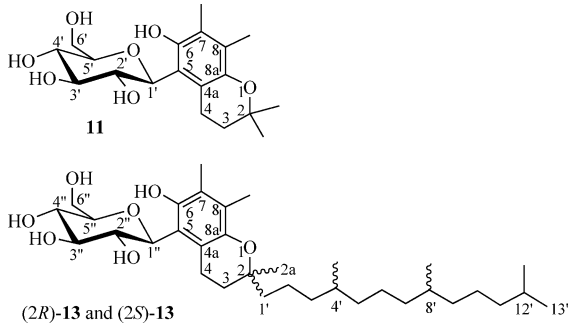
Scheme 2. Synthesis of *C*-β-D-glucosyl-chromanols and *C*-β-D-glucosyl-tocopherols.

towards the desired D-glycosylated dimethyl-substituted chromanols and tocopherols. Methylation of commercially available 2,3-dimethyl-hydroquinone easily afforded the *o*-dimethyl isomer **2**. The dimethyl-substituted 1,4-dimethoxybenzenes **3**[39] and **4**[40] were prepared in three steps (Fremy's salt oxidation, reduction, methylation) from 2,6-dimethyl- and 2,5-dimethylanisole by adaptation of reported methods.

Electrophilic substitution of the dimethyl-substituted 1,4-dimethoxybenzenes **2**–**4** with β-D-glucopyranose peracetate (for the D-*galacto* analogues, see Supporting Information) was accomplished on stirring the reaction mixture containing $SnCl_4$ and silver trifluoroacetate in CH_2Cl_2 at ca 28 °C for 4/5 h, as reported.[34] Although differing significantly, the yields recorded for the *C*-glucosyl compounds **5**–**7** could be interpreted on the basis of minimized steric interactions in the substitution transition states (**2**, less hindered than **3** and **4**), and on the contributions of the methyl groups in stabilizing the cationic Wheland intermediates (best stabilized for **3**, relative to **2** and **4**). The reaction with **4** (higher hindrance, lower reactivity) produced an α/β mixture in modest yield (10%), which was increased to ca. 17% with **4** in larger excess (4 equiv.). Because of its lack of reactivity and stereoselectivity, this last sequence was abandoned. With β-D-galactopyranose pentaacetate (see Supporting Information), the yield was 76% for the coupling to **2** [72% for the desired D-*galacto* analogue of **5**, together with 4% of 1,4-dimethoxy-2,3-dimethyl-5-(3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)benzene], while **5** (D-*gluco*) was obtained in 67% yield. This again showed the influence of the glycosyl donor configuration on the outcome of the electrophilic aromatic substitution, with a higher selectivity in the D-*galacto* series than in the D-*gluco* series.[34,35]

When condensation of **9a** with racemic phytol was first attempted with $ZnCl_2$ in $CHCl_3$ containing EtOH as stabilizer (0.6%), the expected product **12** was formed in a somewhat lower yield (61% instead of the 66% optimized yield) because of the formation of 1-ethoxy-4-hydroxy-2,3-dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene(**9b**) in 27% yield. This is reminiscent of the formation of a methoxy derivative upon acid-catalyzed deacetylation of (tetra-*O*-acetyl-β-D-glucopyranosyl)benzoquinone in MeOH acidified with AcCl.[34b] Anhydrous ethanol-free $CHCl_3$ was therefore used for preparing the glycosyl-chromanols and glycosyl-tocopherols from **9a** and **15** upon annelation with prenyl alcohol or racemic phytol, with anhydrous $ZnCl_2$ as catalyst.

NMR spectroscopy provided a basis for assigning the structures of the prepared compounds, in which the carbon atoms were numbered as shown in Scheme 2 and Scheme 3. In the *ortho*-dimethyl series derived from **2**, all compounds gave well-resolved NMR spectra at room temperature in $CDCl_3$ (acetylated molecules) or [D_6]acetone (deacetylated structures). For (2*R*)-**13** and (2*S*)-**13**, each of which features a hydrophilic sugar residue and a lipophilic chain, use of $CDCl_3$ led to badly resolved spectra, as already noted for a *O*-glucoside,[27a] but [D_6]acetone was found to be a suitable solvent at ambient temperature, showing smaller signals corresponding to the (4′*RS*,8′*RS*) diastereoisomers present in (2*R*)-**13** and (2*S*)-**13**. Similar observations relating to the choice of solvent were made about α-tocopheryl oligosaccharides when investigated by NMR, since CD_3OD or [D_6]DMSO appeared to be suitable, in contrast to D_2O, perhaps due to the existence of supramolecular structures as micelles.[27a] Indeed, various sugar-based motifs can be found among amphiphilic molecules that produce nanotube architectures.[41] However, well resolved spectra can be interpreted in terms either of the presence of rotamers in fast equilibrium (free rotation) or, for the chromanols **10**–**13**, of the existence of a major conformer with possible intramolecular H-bonding. In the γ-tocopherol derivatives **12** and **13**, the minimum-energy conformers should, for steric reasons, have the anomeric hydrogen in a staggered position with respect to the C4 methylene of chromanol. This arrangement, which was supported by strong NOESY and CROESY correlations between the anomeric hydrogen and H4a and H4b, should place the phenoxyl group and the ring oxygen at a short distance and favour their intramolecular H-bonding. For compounds **13**, the configuration at C2 was tentatively assigned[34a] from the measured optical rotations, found to be +42.4 [(2*R*)-**13**] and +28.5 [(2*S*)-**13**].



Scheme 3. Structures of compounds **11** and **13** with NMR numbering.

In the *meta*-dimethyl series, only the acetylated benzoquinone **14** and the hydroquinone **15** gave well-resolved spectra in $CDCl_3$ at ambient temperature. The other compounds required heating in [D_6]DMSO (**6**/90 °C; **16** and **18**/120 °C, **19**/90 °C – spectra not quite clear) or [D_6]DMSO + D_2O (**17**/90 °C). In relation to **5** (see above), restricted rotation about the glycosidic bond due to steric hindrance could explain the need for heating above the coalescence temperature in order to record well resolved spectra for **6** and **7** (*para*-dimethyl). The sterically less demanding structure of **14**, in relation to **6**, might account for the quality of its spectra in $CDCl_3$ at ambient temperature (free rotation), while for **15**, an intramolecularly H-bonded atropoisomer can be envisaged. While the eight chromanol derivatives appear to be sterically hindered, it is difficult to classify them in terms of hindrance based on a simple analysis. It seems reasonable to assume that their conformations also depend

on intramolecular H-bonding between the sugar and chromanol moieties. Obviously, H-bonding between the phenolic OH and the pyran oxygen is possible only for **10**–**13**. Natural tocopherols display a methyl group at C8 and either a methyl group or hydrogen atom at C5 and C7, being classified as α (Me at C5 and C7), β (Me at C5, H at C7), γ (H at C5, Me at C7) or δ (H at C5 and C7). Because **18** and **19** have two methyl substituents adjacent to the phenolic hydroxy group in a nonclassical arrangement that can be denoted ε, we propose to regard these compounds as derivatives of ε-tocopherol.

Initiation:	$R–N=N–R + 2\ O_2 \rightarrow 2\ ROO^{\bullet} + N_2$	R_i
	$ROO^{\bullet} + LH + O_2 \rightarrow ROOH + LOO^{\bullet}$	k_1
Propagation:	$LOO^{\bullet} + LH + O_2 \rightarrow LOOH + LOO^{\bullet}$	k_2
Inhibition of initiation:	$ROO^{\bullet} + AH \rightarrow ROOH + A^{\bullet}$	k_{a1}
Inhibition of propagation:	$LOO^{\bullet} + AH \rightarrow LOOH + A^{\bullet}$	k_{a2}
Termination:	$2\ LOO^{\bullet} \rightarrow$ nonradical products	k_t

Scheme 4. Mechanism of the peroxidation of linoleic acid (LH) induced by a diazo compound (R–N=N–R) in the presence of an antioxidant (AH).

2. Evaluation as Antioxidants

Polyunsaturated fatty lipids are sensitive to oxidation in food during processing, storage or domestic treatments, this phenomenon being responsible for a loss of sensorial and nutritional quality.[42,43] Polyunsaturated fatty lipids are also important targets of oxidative stress in living tissues.[44–49] Their oxidation products, in particular hydroperoxides and aldehydes, are potentially toxic and involved in chemical modifications of proteins and nucleic acids that may initiate events in the development of cancers and artherosclerosis. In addition, lipid peroxidation is particularly pernicious, since it takes place by a radical-chain mechanism in which a single initiating species can trigger the accumulation of several equivalents of hydroperoxides upon repetition of the propagation step. The inhibition of lipid peroxidation is therefore a major concern in food and health research and forms the basis of common antioxidant tests. In particular, antioxidant tests dealing with biphasic systems (micelles, liposomes, emulsions) aimed at modelling of cell membranes or food emulsions afford the opportunity to compare antioxidants with similar H-donating or electron-donating capacities (e.g., the tocopherol analogues synthesized in this work) but with distinct hydrophilic–lipophilic balances and thus expected to partition differently between the aqueous and lipid phases.

In this work, α-tocopherol and its *C*-glucosyl analogues were investigated for their abilities to inhibit the peroxidation of linoleic acid (LH, H refers to one of the labile bisallylic H-atoms) within SDS micelles in a neutral phosphate buffer and under a constant flow (chemical rate R_i) of initiating peroxyl radicals ($ROO^{\bullet}$) formed by the thermal decomposition of the water-soluble diazo compound AAPH [R–N=N–R, R = $Me_2C–C(=NH_2^+)–NH_2$]. The mechanism of lipid peroxidation and its inhibition by antioxidants is shown in Scheme 4. The antioxidant (AH) can act by two distinct mechanisms.[50,51]

– It can compete with LH for the initiating radicals. This process is called inhibition of initiation and must take place in the aqueous phase or at the interface. Its efficiency is measured by $AE_1 = k_{a1}/k_1$.

– It can compete with LH for the propagating lipid peroxyl radicals ($LOO^{\bullet}$). This process is called inhibition of propagation and must take place in the lipid phase. Its efficiency is measured by $AE_2 = k_{a2}/k_2$.

Chain-breaking antioxidants such as α-tocopherol efficiently inhibit propagation. Consequently, the curves featuring the accumulation of lipid hydroperoxides (LOOH, spectroscopic monitoring at 234 nm through the conjugated 1,3-dienyl moiety) display a well-defined lag phase during which the peroxidation is very slow before sharply resuming once the antioxidant has been consumed. In contrast, polyphenols, although possibly better radical scavengers than α-tocopherol (both in terms of rate constant and stoichiometry), inhibit the peroxidation of linoleic acid without a lag phase. This observation was quantitatively interpreted by assuming that polyphenols essentially act as initiation inhibitors.[50]

From the time dependence of the LOOH concentration, it is clear that the tocopherol analogues in which the *C*-glycosyl moiety is *meta* to the phenolic OH group (**16**–**19**) inhibit the peroxidation of linoleic acid with a lag phase, whereas no significant lag phase is apparent with the tocopherol analogues in which the *C*-glycosyl moiety is *ortho* to the phenolic OH group (**10**–**13**; Figure 1). Consistently, when the ratio of the initial rate of inhibited peroxidation (R_p) to the constant rate of uninhibited peroxidation (R_p^0) is plotted vs. the total antioxidant concentration, a much sharper decrease is observed with **16**–**19** (Figure 2). From those curves, IC_{50} values (antioxidant concentration giving $R_p/R_p^0 = 1/2$) can be extracted (Table 1).

Tocopherol analogues **16**–**19** are better inhibitors (i.e., giving lower IC_{50} values than **10**–**13**). Rather unexpectedly, the relative positions of the *C*-glucosyl and OH groups on the aromatic ring emerge as the critical determinant of the antioxidant activity, whereas the presence or absence of the phytyl chain plays only a minor role. As a general trend, acetylation of the glucosyl moiety slightly enhances the inhibitory capacity.

For a more quantitative analysis aimed at estimating AE_1 and AE_2, the following strategy was devised.

– For chain-breaking antioxidants (α-tocopherol, **16**–**19**) at low concentrations, the A(234 nm) vs. time curves display well-defined lag phases and are amenable to kinetic analysis with AE_2, R_i and the antioxidant stoichiometry (n = number of peroxyl radicals trapped per antioxidant molecule) as the adjustable parameters [see Equations (1), (2) and (3); C_{LH} = total lipid concentration, (AH) = nC, C = total antioxidant concentration)].[51]

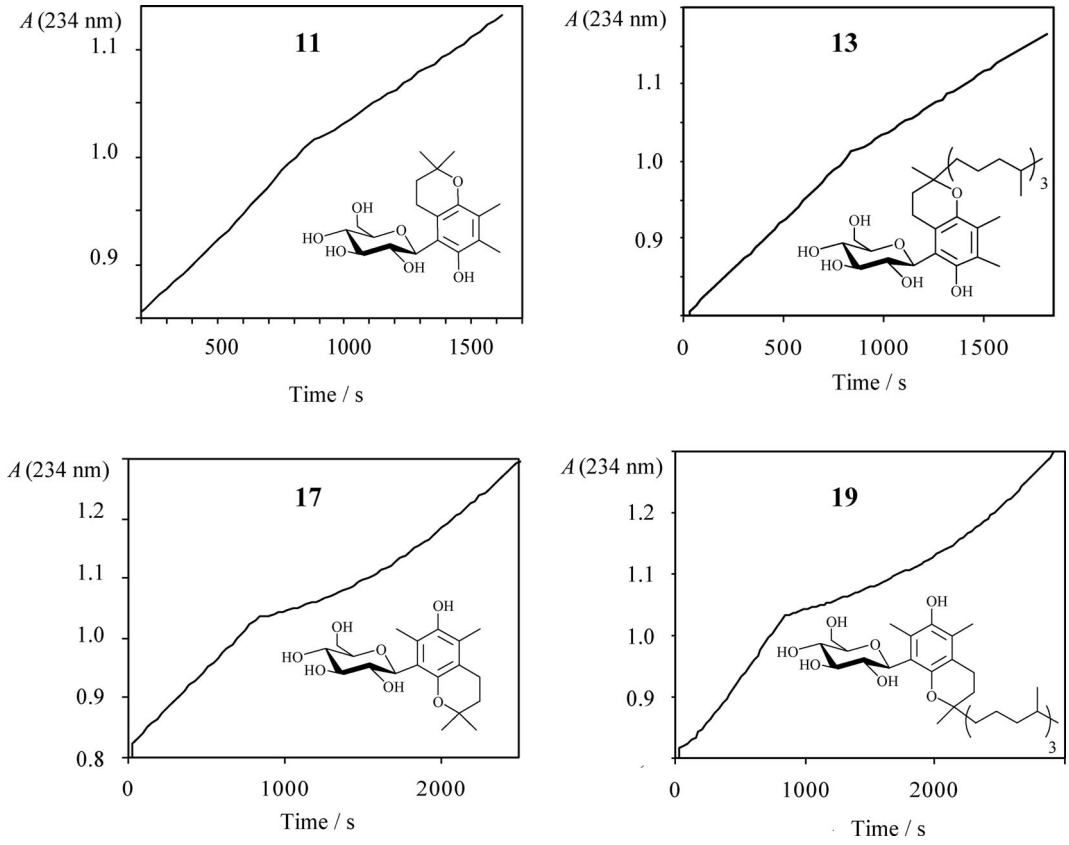


Figure 1. Time dependence of the LOOH concentration during uninhibited and inhibited peroxidation of linoleic acid. The concentration of antioxidant (added at $t \approx 800$ s) was about 0.8 μM.

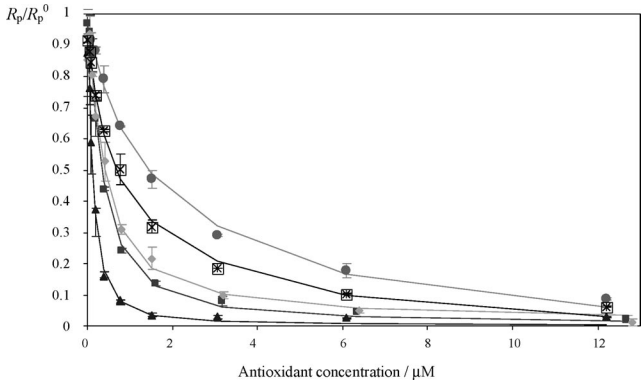


Figure 2. Plots of R_p/R_p^0 vs. total antioxidant concentration ($n = 3$ for each experimental point). The solid lines are the result of the curve-fitting procedures (see text); ▲ α-tocopherol, * **10**, ● **11**, ♦ **18**, ■ **19**.

Table 1. IC_{50} values of the antioxidants as inhibitors of the AAPH-induced peroxidation of linoleic acid.

Antioxidant	α-Toc.	**10**	**11**	**12**	**13**	**16**	**17**	**18**	**19**
IC_{50} [μM]	0.14	0.76	1.40	1.10	1.30	0.32	0.55	0.45	0.35

At low antioxidant concentrations, the inhibition of initiation was neglected (AE_1 set at 0). With α-tocopherol, n can be safely set at 2 on the basis of the oxidation products it forms during the scavenging of the $LOO^{\cdot}$ radicals.[52] Thus, AE_2 and R_i can be estimated (Table 2). An average R_i value of 740 pM s^{-1} was then used in all calculations. With **16**–**19**, the curve-fittings yielded optimized values of AE_2 and n.

– The R_p/R_p^0 ratio can be expressed as a function of AE_1, AE_2, R_i and (AH) = nC [Equations (4) and (5)].[50]

$$R_p = \frac{d}{dt}(\text{LOOH}) = k_q(\text{AH})^2 (1 + \frac{C_{LH}}{AE_2(\text{AH})})[(1 + \frac{2R_i}{k_q(\text{AH})^2})^{1/2} - 1] \quad (1)$$

$$R_a = -\frac{d}{dt}(\text{AH}) = k_q(\text{AH})^2 [(1 + \frac{2R_i}{k_q(\text{AH})^2})^{1/2} - 1] \quad (2)$$

$$k_q = \frac{1}{2R_i}(\frac{AE_2 R_p^0}{C_{LH}})^2 \quad (3)$$

$$\frac{R_p}{R_p^0} = (\frac{k_q}{2R_i})^{1/2}(AH)(1 + AE_2\frac{(\text{AH})}{C_{LH}})[(1 + \frac{2f_1R_i}{k_q(\text{AH})^2})^{1/2} - 1] \quad (4)$$

$$f_1 = \frac{1}{1 + AE_1(\text{AH})/C_{LH}} \quad (5)$$

Table 2. Inhibition of the AAPH-induced peroxidation of linoleic acid. Kinetic analysis of the A(234 nm) vs. time curves for the chain-breaking antioxidants ($r > 0.999$).

Antioxidant	C/nM	R_p^0 /nM s^{-1}	R_i /pM s^{-1}, n	AE_2
α-Tocopherol[a]	191	10.1	737 (±7)	3010 (±100)
		8.7	716 (±4)	4120 (±140)
	381	10.0	728 (±5)	3390 (±100)
		11.7	713 (±7)	3350 (±150)
		11.5	802 (±3)	4100 (±120)
16[b]	193	11.5	2.22 (±0.03)	1030 (±30)
	387	13.0	1.61 (±0.01)	1170 (±30)
		15.4	2.47 (±0.05)	400 (±20)
	774	13.2	1.37 (±0.01)	1180 (±10)
		13.2	1.38 (±0.01)	1650 (±30)
17[b]	191	10.3	1.65 (±0.03)	670 (±30)
	381	11.1	1.67 (±0.03)	410 (±20)
		10.1	1.15 (±0.01)	1140 (±40)
	762	11.3	1.02 (±0.01)	1080 (±40)
		10.0	1.02 (±0.01)	1060 (±30)
18[b]	200	13.4	2.12 (±0.03)	520 (±10)
		12.5	2.34 (±0.02)	450 (±10)
	400	16.1	0.83 (±0.01)	650 (±10)
		13.8	1.05 (±0.01)	970 (±20)
	800	15.3	1.83 (±0.02)	390 (±10)
		12.9	1.22 (±0.04)	810 (±40)
19[b]	198	10.9	2.37 (±0.05)	940 (±50)
	396	11.1	1.89 (±0.02)	890 (±30)
		11.1	1.85 (±0.02)	850 (±30)
	793	10.6	1.78 (±0.01)	810 (±10)
		10.4	1.83 (±0.01)	840 (±10)
	1524	10.6	1.57 (±0.01)	880 (±10)

[a] n set at 2. [b] R_i set at 740 pM s^{-1}.

For chain-breaking antioxidants (α-tocopherol, **16**–**19**), the R_p/R_p^0 vs. C curves were analyzed so as to extract AE_1 and n (Table 3), AE_2 being set at a constant average value deduced from Table 2. The low stoichiometries (in the 0.5–1.0 range) probably point to the antioxidants being only partially oxidized during the early stage of the peroxidation process. For antioxidants believed (from the absence of lag phase) to act mainly as initiation inhibitors (i.e., **10**–**13**), AE_1 and AE_2 were selected as the adjustable parameters, n being set constant at 0.75 (Table 3). As expected, the AE_2 values thus estimated are quite low ($AE_2 < 20$).

Table 3. Inhibition of the AAPH-induced peroxidation of linoleic acid. Mathematical analysis of the R_p/R_p^0 vs. total antioxidant concentration plots (R_i set at 740 pM s^{-1}).

Antioxidant	R_p^0 /nM s^{-1}	AE_1	AE_2	r	n
α-Tocopherol	10.3	8400 (±6400)	3600[a]	0.997	0.55 (±0.11)
10	12.1	14100 (±1300)	10 (±4)	0.998	0.75[b]
11	9.2	5800 (±500)	18 (±5)	0.998	0.75[b]
12	10.9	9700 (±1200)	10 (±5)	0.995	0.75[b]
13	10.2	7200 (±500)	7 (±2)	0.998	0.75[b]
16	13.0	1270 (±990)	1090[a]	0.990	0.75[b]
17	10.7	460 (±410)	870[a]	0.997	0.65 (±0.08)
18	13.3	270 (±370)	630[a]	0.993	0.92 (±0.13)
19	10.0	1320 (±740)	870[a]	0.999	0.89 (±0.11)

[a] Mean value from Table 2. [b] Set constant.

From Table 2, it can be noted that the chain length of uninhibited peroxidation (R_p^0/R_i) lies in the 10–20 range: that is, on average, each LOO$^\cdot$ can react with 10–20 LH molecules before it recombines with another LOO$^\cdot$ to terminate the chain. Moreover, under our conditions (C_{SDS} = 0.1 M, C_{LH} = 2.55 mM), each micelle contains approximately N = 60 SDS molecules[53] and 1–2 LH molecules. Taking a CMC value of 7 mM for SDS,[54] the micelle concentration (C_M) can also be estimated: $C_M = (C_{SDS} - CMC)/N \approx 1$–2 mM. Under such conditions, LOO$^\cdot$ must rapidly diffuse from one micelle to another so as to propagate the radical chain efficiently. Similar considerations apply to the antioxidants themselves.

Indeed, Figure 2 shows that efficient chain-breaking antioxidants at concentrations as low as 1–5 μM (i.e., at least 200 times lower than the micelle concentration) can reduce the peroxidation rate by a factor of 10. Part of this efficiency might reflect their ability to search micelles for the propagating lipid peroxyl radicals. Hence, intermicellar diffusion of the antioxidants and lipid peroxyl radicals might be a crucial factor in the overall process of radical scavenging.[55] For instance, the efficiency of α-tocopherol in inhibiting the peroxidation of linoleic acid in SDS micelles is higher than that of trolox, which essentially partitions in the aqueous phase, but lower than that of trolox methyl ester, which is mainly located in the micellar phase like α-tocopherol, but displays the additional advantage of diffusing more rapidly from one micelle to another.[55] The main parameters governing the relative abilities of antioxidants to inhibit lipid peroxidation in micelles are therefore: the intrinsic reactivity of the antioxidants (H-donating or electron-donating capacity), their ability to enter the micellar pseudo-phase with a correct orientation relative to the lipid peroxyl radicals, and their intermicellar mobility.

With regard to the antioxidants studied in this work, the following remarks can be made.

– From their structural similarity, it seems reasonable to assume that the antioxidants should display similar H-donating capacities. In fact, the *C*-glucosyl group is likely to deactivate the phenolic nucleus slightly through a conjunction of steric and electronic effects including the electron-withdrawing effect of the O atoms and acetyl groups. In **10**–**13** (Glc *ortho* to the phenolic OH), an additional deactivating effect could arise from the possible formation of an intramolecular H-bond with the pyran O atom of Glc (six-membered ring), which would be likely to enhance the bond dissociation energy (BDE) of the phenolic OH.[56] However, calculations on a series of simplified structures suggest that the replacement of a methyl group by a *C*-glycosyl group, either acetylated or not and either *ortho* or *meta* to the OH group, induces only minor changes in the BDE value (Table 4).

– The AE_2 values of chain-breaking antioxidants (**16**–**19**) show that these vitamin E analogues react less rapidly than α-tocopherol with the lipid peroxyl radicals (Table 2). For the more hydrophilic **17** and **19** (deacetylated Glc), this

Table 4. Bond dissociation energies (BDEs) of the phenolic OH groups in compounds **20**–**22**.

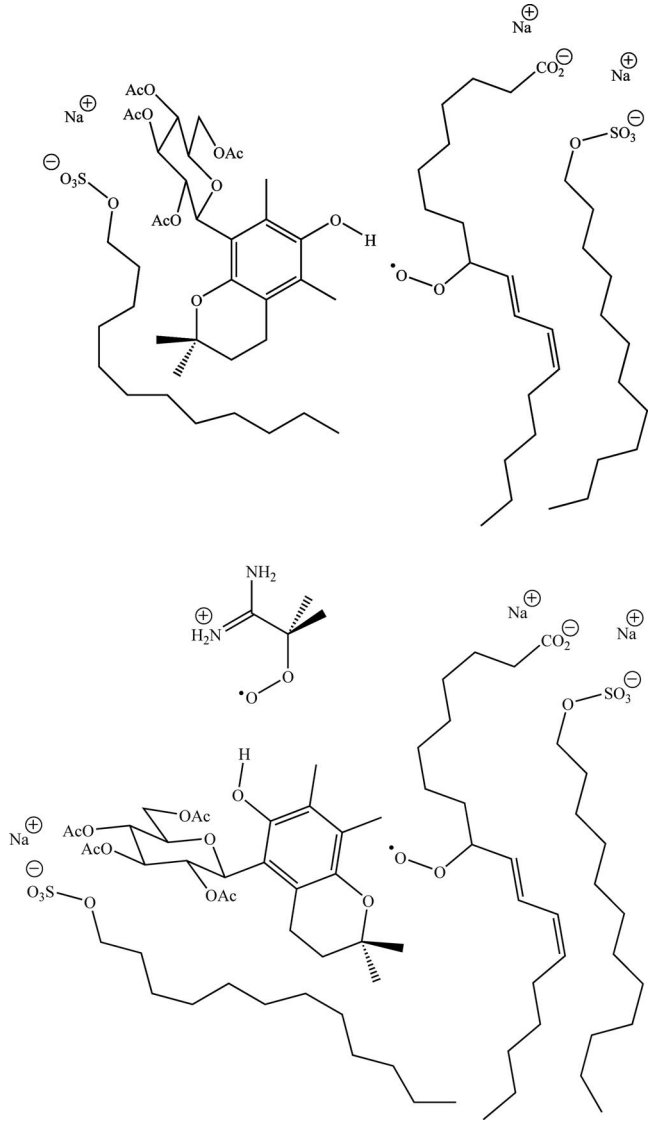
Compound[a]	α/°[b]	*BDE*/kcal mol^{-1}
20	45.0[c]	74.1
21	57.6	73.8
20b (peracetylated Glc)	43.1[c]	74.6
21b (peracetylated Glc)	63.0	73.1
22	–	73.9

[a] 2-β-D-glucopyranosyl-4-methoxy-3,5,6-trimethylphenol (**20**), 3-β-D-glucopyranosyl-4-methoxy-2,5,6-trimethylphenol (**21**), 4-methoxy-2,3,5,6-tetramethylphenol (**22**). [b] Dihedral angle about the glycosidic bond (from O-5(pyran) to C(OR), R = H or Me). [c] H-bonded conformers, between O-5(pyran) and the phenolic OH, d = 0.182 nm.

could reflect a less favourable partitioning in the micelles. More generally, the steric hindrance brought about by the *C*-glycosyl moiety, whether acetylated or not, might significantly decrease the rate constant for LOO$^{\cdot}$ scavenging (k_{a2}). The additional activity of **16**–**19** as initiation inhibitors cannot be precisely assessed, as evidenced by the high standard deviations in the AE_1 parameter (Table 3). We may mention, however, that there is no indication that the *C*-glycosyl moiety of **17** and **19**, which would be likely to favour their location in the aqueous phase, increases their potency as initiation inhibitors in relation to α-tocopherol. However, since the initiating peroxyl radicals are positively charged and the micelle surface negatively charged, the interface could be the privileged site for inhibition of initiation. Overall, **16** and **19** emerge as the most efficient antioxidants after α-tocopherol. Remarkably, **16** (no phytyl chain, acetylated Glc) and **19** (phytyl chain, deacetylated Glc) can be considered intermediate antioxidants in terms of hydrophilic–lipophilic balance. This character might favour their localization at the micelle surface. In the same series (Glc *meta* to the phenolic OH), the most hydrophilic antioxidant **17** (no phytyl chain, deacetylated Glc) and the most lipophilic one **18** (phytyl chain, acetylated Glc) appear to be less efficient. The observation that **19** is better than **17**, due to a higher AE_1 value for the former, is consistent with the inhibition of initiation taking place predominantly at the interface. When the *C*-glycosyl group is acetylated, the presence of the phytyl chain might be considered unfavourable (**16** better than **18**). It can be proposed that the highly hydrophobic antioxidant **18** is strongly bound to the micelles and thus less prone to intermicellar diffusion.

– Although poorer antioxidants than **16**–**19**, compounds **10**–**13** (Glc *ortho* to the phenolic OH) can be regarded as efficient scavengers of the hydrophilic initiating radicals (Table 3). In the series, **10** (no phytyl chain, acetylated Glc) emerges as the most active antioxidant. In particular, it reacts with ROO$^{\cdot}$ more rapidly than the corresponding deacetylated analogue **11**, once more suggesting that inhibition of initiation (like initiation itself) is an interfacial phenomenon.

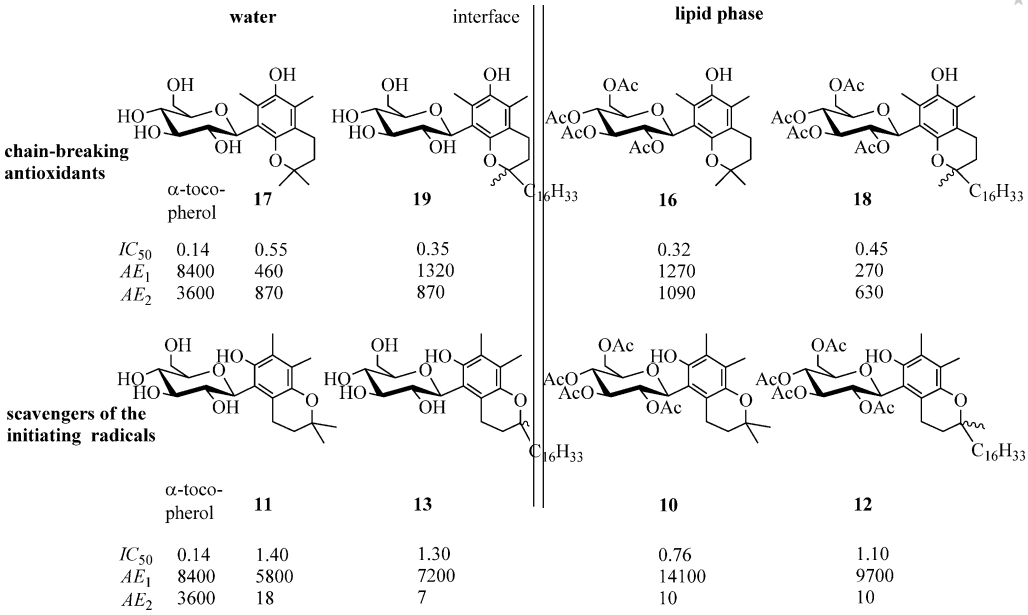
Overall, the quantitative analysis confirms that the *ortho* vs. *meta* position of Glc relative to the phenolic OH of the antioxidants determines the mechanism of inhibition. Since **10**–**13** appear to be effective at scavenging the initiating radicals, it is likely that their lower overall inhibitory activities do not reflect lower H-donating activities but rather less favourable positioning with respect to the lipid peroxyl radicals. A possible positioning of the best antioxidants in each series (i.e., **10** and **16**) in the SDS micelles is proposed in Scheme 5. Finally, the antioxidant activities displayed by the different vitamin E analogues are summarized in Scheme 6.



Scheme 5. Hypothetical positioning of **10** and **16** in the SDS micelles.

Conclusions

In this work, simple and efficient synthetic routes to β-*C*-glycosyl analogues of tocopherols and chromanol are described. The *C*-glycosidation of phenolic antioxidants could be a means to improve water solubility while preserving the



Scheme 6. Antioxidant activities of the vitamin E analogues.

phenolic OH, which is critical to the antioxidant activity. It could also help deliver antioxidants to specific cells through binding to glucose transporters or lectins. Moreover, *C*-glycosylated antioxidants would be expected to be metabolically more stable than their *O*-glycosylated counterparts. The antioxidants synthesized in this work inhibit the peroxidation of linoleic acid through two distinct mechanisms, depending on the position of the *C*-glucosyl moiety (whether acetylated or not). In the series in which the *C*-glucosyl moiety lies *ortho* to the phenolic OH group, the antioxidants essentially scavenge the hydrophilic peroxyl radicals derived from the diazo initiator and are only moderately effective ($IC_{50} > 0.7$ μM). In the series in which the *C*-glucosyl moiety lies *meta* to the phenolic OH group, the antioxidants also scavenge the lipophilic peroxyl radicals derived from the lipid and are significantly more effective ($IC_{50} < 0.6$ μM). Overall, the best antioxidants in each series display intermediate hydrophilic–lipophilic balances either with an acetylated glucosyl moiety or with a phytyl chain.

Experimental Section

General Methods: Dichloromethane and chloroform were washed three times with water before drying over $CaCl_2$ and distillation over CaH_2. Dry methanol was obtained by distillation from magnesium methoxide. Acetonitrile was distilled from CaH_2 and stored over molecular sieves (3 Å). Other solvents were of commercial analytical grade quality and were used without further purification. Organic solutions were dried with anhydrous $MgSO_4$ and concentrated in vacuo at 40–50 °C (bath temperature). TLC was performed on DC-Alurolle Kieselgel 60 F_{254} (Merck), and the plates were visualized by gentle heating and/or were inspected under UV light: depending on the absorbance of the molecule present, the spots visible under different wavelengths (254, 312 nm) might differ in colour and/or intensity. When inspected with 312 nm wavelength, most compounds were visible as violet spots, unless stated otherwise. For column chromatography, Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. Melting points were measured in open capillary tubes with a Büchi apparatus or on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at room temperature. NMR spectra were recorded with Bruker AC 200 (200/50 MHz for $^1H/^{13}C$), Bruker DRX 300/Avance 300 (300/75 MHz for $^1H/^{13}C$) or Bruker DRX 500 (500/125 MHz for $^1H/^{13}C$) spectrometers. Chemical shifts are referenced to Me_4Si (^1H), or to the residual solvent signals (^{13}C). NMR solvents were purchased from Euriso-Top (Saint Aubin, France). The following abbreviations are used to indicate the observed multiplicities: s singlet, d doublet, dd doublet of doublet, t triplet, q quadruplet, m multiplet, br. broad. Assignments of signals marked with asterisks (*) are uncertain. HRMS (LSIMS) mass spectra were recorded in the positive mode (unless stated otherwise) with a Thermo Finnigan Mat 95 XL spectrometer. MS (ESI) mass spectra were recorded in the positive mode with a Thermo Finnigan LCQ spectrometer. Elemental analyses were performed at the Service Central d'Analyses du CNRS (Vernaison, France).

1,4-Dimethoxy-2,3-dimethylbenzene (2): Commercially available 2,3-dimethylhydroquinone (1.38 g) dissolved in DMSO (8 mL) was methylated as described[57] to afford 1,4-dimethoxy-2,3-dimethylbenzene (1.52 g, 92% yield) as white crystals, m.p. 73–75 °C (PE/CH_2Cl_2) (ref.[57] 74–75 °C).

1,4-Dimethoxy-2,6-dimethylbenzene (3): 1,4-Dimethoxy-2,6-dimethylbenzene was prepared from 2,6-dimethylphenol in three steps (oxidation with Fremy's salt, 89%; reduction in ca. 1:1 (v/v) $H_2O/CHCl_3$ with 4 equiv. $Na_2S_2O_4$, 88%; methylation with KOH, CH_3I in DMSO, 84%), as adapted from ref.[39] The physical data of the 2,6-dimethylbenzoquinone, -hydroquinone and -hydroquinone dimethyl ether were in accordance with ref.[39]

1,4-Dimethoxy-2,5-dimethylbenzene (4): 1,4-Dimethoxy-2,5-dimethylbenzene was prepared from 2,5-dimethylphenol in three steps (oxidation with Fremy's salt, 94%; reduction in ca. 1:1 (v/v) $H_2O/CHCl_3$ with 4 equiv. $Na_2S_2O_4$, 93%; methylation with KOH, CH_3I in DMSO, 91%), as adapted from ref.[39] The physical data for the 2,5-dimethylbenzoquinone, -hydroquinone, and -hydroqui-

none dimethyl ether were in accordance with those reported in ref.[40]

1,4-Dimethoxy-2,3-dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene (5): Compounds **1** (985 mg, 2.5 mmol) and **2** (830 mg, 5.0 mmol, 2 equiv.) were dissolved in anhydrous dichloromethane (6 mL). Silver trifluoroacetate (831 mg, 3.75 mmol, 1.5 equiv.) was added, and the mixture was stirred at about 28 °C under argon, protected from light with aluminium foil. A solution of $SnCl_4$ in CH_2Cl_2 (1 M, 7.5 mL, 7.5 mmol, 3 equiv.) was added dropwise to the mixture with stirring. After 3 h, TLC showed completion of the reaction, with **1**, R_f = 0.36 (EtOAc/PE, 1:2), having been converted into several products, R_f = 0.43, 0.31, 0.26, 0.24 (EtOAc/PE, 1:2). Saturated aq. $NaHCO_3$ (40 mL) was added. After stirring for 15 min, the mixture was filtered through a bed of celite, which was rinsed with CH_2Cl_2 (3 × 25 mL). The filtrate was washed with a satd. NaCl solution (30 mL) and then with water (30 mL), then dried with $MgSO_4$. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc/PE, 1:2) to afford compound **5**, which was recrystallized from CH_2Cl_2/PE (825 mg, 66.5% yield). White crystals, m.p. 89.5–91 °C; R_f = 0.43 (EtOAc/PE, 1:2). $[\alpha]_D^{22}$ = –20.8 (c = 0.76 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.71 (s, 1 H, Ar-H), 5.52 (t, $J_{2',3'}$ = 9.1 Hz, 1 H, $H_{2'}$), 5.38 (t, $J_{3',4'}$ = 9.1 Hz, 1 H, $H_{3'}$), 5.24 (t, $J_{4',5'}$ = 9.7 Hz, 1 H, $H_{4'}$), 4.90 (d, $J_{1',2'}$ = 10 Hz, 1 H, $H_{1'}$), 4.24 (dd, $J_{5',6a'}$ = 5.0, $J_{6a',6b'}$ = 12.3 Hz, 1 H, $H_{6a'}$), 4.12 (dd, $J_{5',6b'}$ = 2.3 Hz, 1 H, $H_{6b'}$), 3.90 (ddd, 1 H, $H_{5'}$), 3.81 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 2.21, 2.12, 2.07, 2.04, 2.03, 1.80 (6 s, 18 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.7, 170.4, 169.6, 169.3 (C=O, acetyl), 154.0, 151.2 (C_2, C_5),* 131.0, 128.1, 125.3 (C_1, C_4, C_6),* 106.6 (C_3), 76.2, 74.9, 74.5, 70.8, 68.9 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 62.7 ($C_{6'}$), 62.0, 55.8 (OCH_3), 20.8, 20.7, 20.7, 20.6 (CH_3, acetyl), 12.8, 12.2 (CH_3, Ar) ppm. $C_{24}H_{32}O_{11}$ (496.19): C 58.06, H 6.50, O 35.45; found C 57.90, H 6.54, O 34.90.

1,4-Dimethoxy-3,5-dimethyl-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene (6): By the preceding procedure for the production of **5**, compounds **1** (985 mg, 2.5 mmol) and **3** (830 mg, 5.0 mmol, 2 equiv.) reacted within 3 h to afford product **6** (916.6 mg, 73.9% yield) after workup and chromatography (mobile phase: EtOAc/PE, 1:2). White foam, $[\alpha]_D^{22}$ = –10.1 (c = 0.86 in CH_2Cl_2); R_f = 0.40 (EtOAc/PE, 1:2). ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90 °C): δ = 6.69 (s, 1 H, Ar-H), 5.54 (t, $J_{2',3'}$ = 9.3 Hz, 1 H, $H_{2'}$), 5.30 (t, $J_{3',4'}$ = 9.5 Hz, 1 H, $H_{3'}$), 5.10 (d, $J_{1',2'}$ = 9.3 Hz, 1 H, $H_{1'}$), 5.05 (t, $J_{4',5'}$ = 10.0 Hz, 1 H, $H_{4'}$), 4.16 (dd, $J_{5',6a'}$ = 3.4, $J_{6a',6b'}$ = 12.4 Hz, 1 H, $H_{6a'}$), 4.11 (dd, $J_{5',6b'}$ = 4.1 Hz, 1 H, $H_{6b'}$), 4.00 (m, 1 H, $H_{5'}$), 3.76 (s, 3 H, OMe), 3.58 (s, 3 H, OMe), 2.33, 2.22, 2.03, 2.01, 1.95, 1.69 (6 s, 18 H, CH_3) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz, 90 °C): δ = 170.1, 169.7, 169.5, 168.7 (C=O, acetyl), 154.6, 151.3 (C_1, C_4),* 131.8, 131.7, 121.7 (C_2, C_3, C_5),* 112.9 (C_6), 75.4, 74.7, 73.6, 70.6, 69.2 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 62.5 ($C_{6'}$), 59.8, 56.9 (OCH_3), 20.6, 20.6, 20.5, 20.2 (CH_3, acetyl), 16.4, 12.5 (CH_3, Ar) ppm. $C_{24}H_{32}O_{11}$ (496.19): calcd. C 58.06, H 6.50, O 35.45; found C 57.76, H 6.46, O 35.95.

1,4-Dimethoxy-2,5-dimethyl-3-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene (7): By the preceding procedure for the production of **5** or **6**, compounds **1** (585 mg, 1.5 mmol) and **4** (996 mg, 6.0 mmol, 4 equiv.; twice as much as usual), dissolved in anhydrous dichloromethane (7 mL), were stirred at ca 28 °C after addition of silver trifluoroacetate (495 mg, 2.25 mmol, 1.5 equiv.) and a solution of $SnCl_4$ in CH_2Cl_2 (1 M, 4.5 mL, 4.5 mmol, 3 equiv.). After 1 day, TLC showed the almost complete conversion of **1**, R_f = 0.43 (EtOAc/PE, 2:3) into two major products, R_f = 0.55, 0.18 (EtOAc/PE, 2:3). After workup and concentration, the residue was applied to a column (mobile phase: EtOAc/PE, 1:2) to afford compound **7** (128 mg, 17% yield) as a 3:7 α/β anomeric mixture (NMR). R_f = 0.55 (EtOAc/PE, 2:3). α-Anomer: ^{1}H NMR ([D$_6$]DMSO, 500 MHz, 120 °C): δ = 6.76 (s, 1 H, Ar-H), 5.70 (d, $J_{1',2'}$ = 2.8 Hz, 1 H, $H_{1'}$), 5.21 (t, J = 5 Hz, 1 H), 5.13 (t, J = 5.3 Hz, 1 H), 5.10 (1 H, hidden signal revealed by integral), 4.49 (dd, $J_{5',6a'}$ = 8.0, $J_{6a',6b'}$ = 13.1 Hz, 1 H, $H_{6a'}$), 4.26 (m, 2 H, $H_{5'}$, $H_{6b'}$), 3.75, 3.70 (2 s, 6 H, OMe), 2.32, 2.23 (2 s, 6 H, CH_3-arom.), 2.11, 2.09, 2.00, 1.81 (4 s, 12 H, acetyl) ppm. ^{13}C NMR ([D$_6$]DMSO, 125 MHz, 120 °C): δ = 170.7, 170.0, 169.5, 169.3 (C=O, acetyl), 154.9, 151.0 (C_1, C_4),* 129.2, 128.2, 126.6 (C_2, C_3, C_6),* 115.2 (C_5), 75.1, 72.3, 71.1, 69.3, 68.0 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 62.5 ($C_{6'}$), 61.2, 57.1 (OCH_3), 21.1, 21.0, 21.0, 20.8 (CH_3, acetyl), 16.8, 13.4 (CH_3, Ar) ppm. β-Anomer: ^{1}H NMR ([D$_6$]DMSO, 500 MHz, 120 °C): δ = 6.79 (s, 1 H, Ar-H), 5.60 (t, $J_{2',3'}$ = 9.6 Hz, 1 H, $H_{2'}$), 5.32 (t, $J_{3',4'}$ = 9.3 Hz, 1 H, $H_{3'}$), 5.10 (t, $J_{4',5'}$ = 9.7 Hz, 1 H, $H_{4'}$), 5.08 (d, $J_{1',2'}$ = 9.8 Hz, 1 H, $H_{1'}$), 4.18 (d, J = 3.2 Hz, 2 H, $H_{6a'}$, $H_{6b'}$), 4.04 (dt, J = 3.6, J = 3.6, J = 9.7 Hz, 1 H, $H_{5'}$), 3.75, 3.70 (2 s, 6 H, OMe), 2.26, 2.23 (2 s, 6 H, CH_3-arom.), 2.03, 1.99, 1.95, 1.68 (4 s, 12 H, acetyl) ppm. ^{13}C NMR ([D$_6$]DMSO, 125 MHz, 120 °C): δ = 170.5, 170.2, 170.0, 169.1 (C=O, acetyl), 154.5, 152.7 (C_1, C_4),* 129.0, 128.8, 125.6 (C_2, C_3, C_6),* 115.8 (C_5), 76.3, 75.6, 74.1, 71.4, 69.9 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 63.1 ($C_{6'}$), 61.9, 57.1 (OCH_3), 21.0, 21.0, 20.9, 20.6 (CH_3, acetyl), 16.7, 12.4 (CH_3, Ar) ppm. MS (ESI, positive mode): m/z (%) = 519.1 (100) $[M + Na]^+$.

2,3-Dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,4-benzoquinone (8): Compound **5** (1120 mg, 2.26 mmol), dissolved in acetonitrile (4 mL), was oxidized with ceric ammonium nitrate (CAN, 3717 mg, 6.78 mmol, 3 equiv.) dissolved in water (5 mL) at room temperature with stirring. After 25 min, TLC showed that the reaction was complete, compound **5**, R_f = 0.43 (EtOAc/PE, 1:2), having been converted into a single new product with R_f = 0.45 (EtOAc/PE, 1:2). The reaction mixture was extracted with CH_2Cl_2 (3 × 25 mL), washed with brine (40 mL) and then dried with $MgSO_4$. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc/PE, 1:2) to afford compound **8** (1028 mg, 97.6% yield). Yellow needles, m.p. 119–120 °C (CH_2Cl_2/PE); R_f = 0.45 (EtOAc/PE, 1:2, violet under UV 312 nm, dark spot at 254 nm). $[\alpha]_D^{22}$ = –1.2 (c = 0.8 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.80 (d, $J_{1',3}$ = 0.8 Hz, 1 H, Ar), 5.34 (t, $J_{3',4'}$ = 9.4 Hz, 1 H, $H_{3'}$), 5.11 (t, $J_{4',5'}$ = 10.0 Hz, 1 H, $H_{4'}$), 4.97 (t, $J_{2',3'}$ = 9.2 Hz, 1 H, $H_{2'}$), 4.66 (dd, $J_{1',2'}$ = 9.7, $J_{1',3}$ = 0.8 Hz, 1 H, $H_{1'}$), 4.20 (dd, $J_{5',6a'}$ = 4.7, $J_{6a',6b'}$ = 12.4 Hz, 1 H, $H_{6a'}$), 4.10 (dd, $J_{5',6b'}$ = 2.3 Hz, 1 H, $H_{6b'}$), 3.79 (ddd, 1 H, $H_{5'}$), 2.06, 2.02, 1.99, 1.99, 1.98, 1.87 (6 s, 18 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 186.9, 185.7 (C=O, benzoquinone), 170.6, 170.1, 169.7, 169.5 (C=O, acetyl), 143.4, 141.0, 140.9 (C_2, C_5, C_6),* 133.4 (C_3), 76.2, 73.8, 72.3, 72.2, 68.3 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$), 62.0 ($C_{6'}$), 20.8, 20.6, 20.6, 20.5 (CH_3, acetyl), 12.4, 12.2 (benzoquinone CH_3) ppm. IR (KBr): $\tilde{\nu}$ = 1760 (C=O, acetyl), 1650 (C=O, benzoquinone) cm^{-1}. $C_{22}H_{26}O_{11}$ (466.15): calcd. C 56.65, H 5.62, O 37.73; found C 56.56, H 5.97, O 36.77.

2,3-Dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,4-hydroquinone (9a): A solution of $Na_2S_2O_4$ (2052 mg, 12 mmol, 6 equiv.) in water (7 mL) was added to compound **8** (932 mg, 2 mmol), dissolved in $CHCl_3$ (6 mL). The reaction mixture was stirred vigorously at room temperature for 12 min, whereupon the yellow colour of the organic layer disappeared. TLC showed that compound **8**, R_f = 0.51 (CH_2Cl_2/EtOAc, 8:1), had changed into a more polar compound. The reaction mixture was washed with water (3 × 25 mL) and dried with $MgSO_4$. After filtration and concentration, the residue was applied to a column (mobile phase: CH_2Cl_2/EtOAc, 8:1) to afford compound **9a** (820 mg, 1.752 mmol,

87.6% yield). White crystals, m.p. 192–193 °C (CH_2Cl_2/PE); R_f = 0.21 (CH_2Cl_2/EtOAc, 8:1). $[\alpha]_D^{25}$ = –37 (c = 0.8 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.49 (s, 1 H, OH, Ar), 6.35 (s, 1 H, Ar-H), 5.37–5.23 (m, 3 H, $H_{2'}$, $H_{3'}$, $H_{4'}$), 4.87 (s, 1 H, OH, Ar), 4.52 (br. d, $J_{1',2'}$ = 8.0 Hz, 1 H, $H_{1'}$), 4.32 (dd, $J_{5',6a'}$ = 3.8, $J_{6a',6b'}$ = 12.4 Hz, 1 H, $H_{6a'}$), 4.16 (d, $J_{6a',6b'}$ = 12.4 Hz, 1 H, $H_{6b'}$), 3.89 (m, 1 H, $H_{5'}$), 2.16, 2.13, 2.12, 2.06, 2.01, 1.86 (6 s, 18 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.8, 170.5, 169.5, 169.0 (C=O, acetyl), 146.8, 146.8 (C_1, C_4, Ar), 126.6, 125.1, 117.6 (C_2, C_5 and C_6, Ar), 111.7 (C_3, Ar), 80.0, 76.1, 73.9, 70.7, 68.0 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 61.7 ($C_{6'}$), 20.7, 20.7, 20.6, 20.5 (CH_3, acetyl), 12.2, 12.1 (Ar-*C*H_3) ppm. $C_{22}H_{28}O_{11}$ (468.16): calcd. C 56.41, H 6.02, O 37.57; found C 56.15, H 6.22, O 37.26.

1-Ethoxy-4-hydroxy-2,3-dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene (9b): Compound **9b** was formed in 27% yield as a by-product from **9a** (98 mg, 0.209 mmol) and all-racemic phytol (0.07 mL, 0.195 mmol, 0.93 equiv.) on treatment at reflux for 1 day in $CHCl_3$ (3 mL, commercial grade, stabilized with ca. 0.6% ethanol) in the presence of anhydrous $ZnCl_2$ (106 mg, 0.778 mmol, 6 equiv.) in which **12** was obtained as a diastereoisomeric mixture (90 mg, 0.12 mmol, 61.5% yield based on phytol). **9b**: White crystals, m.p. 161–162.5 °C (CH_2Cl_2/PE); R_f = 0.24 (PE/EtOAc, 3:1); $[\alpha]_D^{22}$ = –24.9 (c = 1.2 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.53 (s, 1 H, Ar-OH, exchanged with D_2O), 6.37 (s, 1 H, Ar-H), 5.36–5.28 (m, 3 H, $H_{2'}$, $H_{3'}$ and $H_{4'}$), 4.54 (d, $J_{1',2'}$ = 9.2 Hz, 1 H, $H_{1'}$), 4.31 (dd, $J_{5',6a'}$ = 3.8, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6'a}$), 4.17 (dd, $J_{5',6b'}$ = 2.1 Hz, 1 H, $H_{6'b}$), 3.87 (m, 1 H, $H_{5'}$), 3.86 (m, 2 H, superimposed signals, OCH_2CH$_3$), 2.16, 2.13, 2.12, 2.05, 2.01, 1.84 (6 s, 18 H, 2 CH_3, 4 OAc), 1.38 (t, J = 6.9 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.0, 170.8, 169.7, 169.1 (C=O, acetyl), 150.5 (C_4), 147.6 (C_1), 128.8 (C_5), 127.1 (C_6), 117.1 (C_2), 110.4 (C_3), 81.0 ($C_{1'}$), 76.5 ($C_{5'}$), 74.3 ($C_{3'}$), 70.9 ($C_{2'}$), 68.3 ($C_{4'}$), 65.4 (O*C*H$_2$CH$_3$), 62.0 ($C_{6'}$), 21.1, 21.0, 21.0, 20.9 (CH_3, acetyl), 15.5 (OCH$_2$*C*H$_3$), 12.6, 12.5 (Ar-CH_3) ppm. MS (ESI, +C): *m*/*z* (%) = 519.2 (100) $[M + Na]^+$, 514.2 (35) $[M + NH_4]^+$.

6-Hydroxy-2,2,7,8-tetramethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)chroman (10): Anhydrous $ZnCl_2$ (979 mg, 7.2 mmol, 6 equiv.) was added to compound **9a** (560 mg, 1.2 mmol) and 3-methylbut-2-en-1-ol (prenyl alcohol, 0.123 mL, 1.19 mmol) dissolved in dry $CHCl_3$ (6 mL) and the mixture was heated at reflux under argon for 20 h while being stirred and protected from light. TLC showed that the reaction was almost complete, with **9a**, R_f = 0.08 (EtOAc/PE, 1:2), still being slightly visible, while 3-methylbut-2-en-1-ol, R_f = 0.56–0.53 (EtOAc/PE, 1:2) had disappeared, with formation of a more polar product, R_f = 0.23 (EtOAc/PE, 1:2). After cooling and filtration, the organic phase was washed with H_2O (40 mL), saturated aq. $NaHCO_3$ (40 mL) and brine (40 mL), and was then dried with $MgSO_4$. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc/PE, 1:2) to afford **10** (384 mg, 0.716 mmol, 60% yield), which was recrystallized from CH_2Cl_2/PE. White crystals, m.p. 205–206.5 °C (CH_2Cl_2/PE); R_f = 0.23 (EtOAc/PE, 1:2). $[\alpha]_D^{22}$ = –4.4 (c = 0.9 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.93 (s, 1 H, Ar-OH), 5.58 (t, $J_{2',3'}$ = 9.3 Hz, 1 H, $H_{2'}$), 5.35–5.31 (m, 2 H, $H_{3'}$, $H_{4'}$), 4.86 (d, $J_{1',2'}$ = 10.0 Hz, 1 H, $H_{1'}$), 4.33 (dd, $J_{5',6a'}$ = 3.14, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6a'}$), 4.14 (dd, $J_{5',6b'}$ = 2.0 Hz, 1 H, $H_{6b'}$), 3.86 (m, 1 H, $H_{5'}$), 2.72 (t, J = 6.7 Hz, 2 H, 2 H_4), 2.14, 2.14 2.07, 2.06, 2.01, 1.81 (6 s, 18 H, 4 Ac, Me_{7a}, Me_{8b}), 1.75 (2 H, overlapped, 2 H_3), 1.29, 1.23 (2 s, 6 H, Me_{2a}, Me_{2b}) ppm. ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ = 170.7, 170.5, 169.3, 168.4 (C=O, acetyl), 146.9, 145.0 (C_6, C_{8a}, Ar),* 127.6, 124.9, 115.4, 114.9 (C_5, C_7, C_8, C_{4a}, Ar),* 76.2, 76.2, 74.2, 70.3, 67.7 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 72.4 (C_2), 61.4 ($C_{6'}$), 33.1, 20.8 (C_3, C_4),* 26.9, 26.3 (C_{2a}, C_{2b}), 20.7, 20.7, 20.6, 20.4 (CH_3, acetyl), 12.2, 11.9 (Me_{7a}, Me_{8b}) ppm. $C_{27}H_{36}O_{11}$ (536.23): calcd. C 60.44, H 6.76, O 32.80; found C 59.98, H 6.74, O 33.75.

5-(β-D-Glucopyranosyl)-6-hydroxy-2,2,7,8-tetramethylchroman (11): A solution of sodium methoxide in methanol (4 mL, 0.1 M) was poured into a flask containing compound **10** (268 mg, 0.5 mmol). After the mixture had been stirred at room temperature for 2 h, TLC showed that compound **10** had changed into a more polar compound, R_f = 0.23 (EtOAc). Then a slight excess of IR 120 was added (pH paper for monitoring) and stirring of the mixture was continued for 20 min. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc) to afford compound **11** (168.4 mg, 91.5% yield). White solid, m.p. 135–137 °C (EtOAc/Et_2O); R_f = 0.23 (EtOAc). $[\alpha]_D^{22}$ = +48.2 (c = 0.7 in acetone). ^{1}H NMR ([D_6]acetone, 500 MHz): δ = 7.75 (s, 1 H, Ar-OH), 4.74 (d, $J_{1',2'}$ = 9.5 Hz, 1 H, $H_{1'}$), 4.43, 4.39, 4.09 (3 br. signals, 3 H, sugar OH), 3.90–3.84 (m, 2 H, $H_{6a'}$, $H_{6b'}$), 3.76 (t, $J_{2',3'}$ = 9.1 Hz, 1 H, $H_{2'}$), 3.69 (t, $J_{3',4'}$ = 9.1, $J_{4',5'}$ = 9.5 Hz, 1 H, $H_{4'}$), 3.58 (t, $J_{2',3'}$ = 9.1, $J_{3',4'}$ = 8.8 Hz, 1 H, $H_{3'}$), 3.50 (dt, $J_{4',5'}$ = 9.5, $J_{5',6a'}$ = $J_{5',6b'}$ = 3.1 Hz, 1 H, $H_{5'}$), 2.98 (m, overlapping signals, sugar OH, 2 H, H_{4a}), 2.68 (dt, J_{gem} = 16.4, J = 6.6 Hz, 1 H, H_{4b}), 2.07, 2.05 (2 s, 6 H, Me_{7a}, Me_{8b}), 1.74 (m, 2 H, $H_{3a,b}$), 1.28, 1.25 (2 s, 6 H, Me_{2a}, Me_{2b}) ppm. ^{13}C NMR ([D_6]acetone, 125 MHz): δ = 147.3 (C_6), 145.0 (C_{8a}), 125.1 (C_8), 123.1 (C_7), 119.0 (C_5), 117.5 (C_{4a}), 81.3 ($C_{5'}$), 79.0 ($C_{3'}$), 78.4 ($C_{1'}$), 73.4 ($C_{2'}$), 72.5 (C_2), 70.2 ($C_{4'}$), 61.3 ($C_{6'}$), 33.3 (C_3), 26.8, 26.2 (C_{2a}, C_{2b}),* 21.1 (C_4), 11.7, 11.5 (C_{7a}, C_{8b}) ppm. MS (ESI, positive mode): *m*/*z* (%): 759.0 (100) $[2M + Na]^+$, 391.1 (15) $[M + Na]^+$, 369.0 (10) $[M + H]^+$. MS (ESI, negative mode): *m*/*z* (%) = 770.7 (10) $[2M + Cl]^-$, 402.8 (100) $[M + Cl]^-$, 367.0 (85) $[M - H]^-$.

5-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-γ-tocopherol (12): Compound **9a** (270 mg, 0.577 mmol), dissolved in $CHCl_3$ (5 mL), was mixed with all-racemic phytol (0.2 mL, 0.556 mmol, 0.96 equiv.) and anhydrous $ZnCl_2$ (453.7 mg, 3.336 mmol, 6 equiv.). The mixture was stirred under argon at reflux for 24 h, protected from light. TLC showed that the reaction was almost complete, with **9a**, R_f = 0.05 (EtOAc/PE, 1:3), still being visible under UV 312 nm, while phytol, R_f = 0.52–0.48 (EtOAc/PE, 1:3), was hardly visible, in contrast to the desired products, visible on TLC as two spots, R_f = 0.20 and 0.19 (EtOAc/PE, 1:3). The mixture was cooled to room temperature and filtered. The filtrate was washed with saturated aq. $NaHCO_3$ (40 mL) and brine (40 mL) and H_2O (40 mL), and was then dried with $MgSO_4$. After filtration and concentration, the residue was applied to a column (mobile phase: PE/EtOAc, 3:1) to afford compound **12** as a diastereoisomeric mixture (272 mg, 0.365 mmol, 65.6% yield, based on phytol), which was recrystallized from CH_2Cl_2/PE. In other experiments using larger amounts of phytol (2, 3, or 4 equiv.), the reaction mixture was more complex, and the desired product **12**, obtained in ca. 60% yield, was contaminated with impurities. Hence, use of minimized amounts of phytol appeared more suitable. Use of $CHCl_3$ stabilized with EtOH (ca. 0.6% EtOH) afforded **12** in lower yield (61.5%, based on phytol), due to the formation of **9b** (27% yield) as a by-product (see above). Compound **12** (2*RS*,4′*RS*,8′*RS* mixture): white crystals, m.p. 144–146 °C (CH_2Cl_2/PE); R_f = 0.20 (EtOAc/PE, 1:3). $[\alpha]_D^{22}$ = –0.227 (c = 0.88 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.93, 6.90 (2 s, exchangeable with D_2O, 1 H, Ar-OH), 5.58 (t, $J_{1'',2''}$ = 9.9, $J_{2'',3''}$ = 7.9 Hz, 1 H, $H_{2''}$), 5.35–5.30 (m, 2 H, $H_{3''}$, $H_{4''}$), 4.86 (d, $J_{1'',2''}$ = 9.9 Hz, 1 H, $H_{1''}$), 4.33 (dd, $J_{5'',6a''}$ = 2.9, $J_{6a'',6b''}$ = 12.4 Hz, 1 H, $H_{6a''}$), 4.15 (d, $J_{6a'',6b''}$ = 12.4 Hz, 1 H, $H_{6b''}$), 3.89 (m, 1 H, $H_{5''}$), 2.70 (t, J = 6.5 Hz, 2 H, $H_{4a,b}$), 2.14, 2.14, 2.08, 2.06, 2.01, 1.82 (6 s, 18 H, CH_3), 1.75 (2 H, overlapped, $H_{3a,b}$), 1.60–1.0 (m, 24 H, $H_{1'-12'}$ and H_{2a}), 0.89–

0.86 (m, 12 H, $Me_{13',4'a,8'a,12'a}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.7, 170.5, 169.3, 168.4 (C=O, acetyl), 146.8, 144.9 (C_6, C_{8a}), 127.6, 124.9, 115.6, 114.9 (C_5, C_7, C_8, C_{4a}), 76.2, 76.2, 74.2, 70.3, 67.8 ($C_{1''}$, $C_{2''}$, $C_{3''}$, $C_{4''}$, $C_{5''}$), 74.4 (C_2), 61.4 ($C_{6''}$), 39.4, 39.4, 37.4, 37.4, 37.3, 31.7, 24.8, 24.5, 21.0, 20.6, 20.6 (methylene: C_3, C_4, $C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{5'}$, $C_{6'}$, $C_{7'}$, $C_{9'}$, $C_{10'}$, $C_{11'}$), 32.8, 28.0, 23.5, 22.8, 22.6, 20.4, 19.8, 19.7 ($C_{4'}$, $C_{8'}$, $C_{12'}$, $C_{13'}$, $C_{4'a}$, $C_{8'a}$, $C_{12'a}$, C_{2a}), 20.7, 20.7, 20.6, 20.6 (CH_3, acetyl), 12.2, 11.9 (C_{7a}, C_{8b}) ppm. $C_{42}H_{66}O_{11}$ (746.46): calcd. C 67.53, H 8.91, O 23.56; found C 67.56, H 8.83, O 22.67.

5-(β-D-Glucopyranosyl)-γ-tocopherol [(2*R*)-13 and (2*S*)-13]: A solution of sodium methoxide in methanol (5 mL, 0.1 M) was poured into a flask containing compound **12** (405 mg, 0.54 mmol). After the mixture had been stirred at room temperature for 2 h, TLC showed the conversion of **12** into polar products visible as two spots on the plates. A slight excess of IR 120 H^+ was added (pH paper for monitoring), and stirring of the mixture was continued for 20 min. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc/CH_2Cl_2 2:1, then 4:1, then 8:1, at last pure EtOAc) to afford three fractions: compound (2*S*)-**13** (70.4 mg), a mixture of compounds (2*S*)-**13** and (2*R*)-**13** (125.5 mg, the proportion of (2*S*)-**13** and (2*R*)-**13** being about 2:3 according to the ^1H NMR spectrum), and compound (2*R*)-**13** (100.6 mg), with combined total yield of 95%. The ratio of (2*S*)-**13** and (2*R*)-**13** can be estimated as ca. 2:3.

Compound (2*S*)-13: Pale yellow amorphous solid, $[a]_D^{22}$ = +28.5 (*c* = 1 in acetone); R_f = 0.50 (EtOAc). ^1H NMR ([D_6]acetone, 500 MHz): δ = 7.76 (s, 1 H, Ar-OH), 4.73 (d, $J_{1'',2''}$ = 9.5 Hz, 1 H, $H_{1''}$), 4.72, 4.47, 4.26, 3.13 (4 br. signals, 4 H, sugar OH), 3.90–3.83 (m, 2 H, $H_{6a''}$, $H_{6b''}$), 3.77 (t, $J_{1'',2''}$ = 9.5, $J_{2'',3''}$ = 8.8 Hz, 1 H, $H_{2''}$), 3.71 (t, $J_{3'',4''}$ = 8.8, $J_{4'',5''}$ = 9.2 Hz, 1 H, $H_{4''}$), 3.60 (t, $J_{2'',3''}$ = $J_{3'',4''}$ = 8.8 Hz, 1 H, $H_{3''}$), 3.49 (br. d, $J_{4'',5''}$ = 9.2 Hz, 1 H, $H_{5''}$), 3.00 (m, 1 H, H_{4a}), 2.65 (m, 1 H, H_{4b}), 2.07, 2.07 (2 s, 6 H, Me_{7a}, Me_{8b}), 1.75 (m, 2 H, $H_{3a,b}$), 1.59–1.13 (m, 21 H, $H_{1'-12'}$), 1.22 (s, 3 H, H_{2a}), 0.91–0.89 (m, 12 H, $H_{13'}$, $H_{4'a}$, $H_{8'a}$, $H_{12'a}$) ppm. ^{13}C NMR ([D_6]acetone, 125 MHz): δ = 147.2 (C_6), 144.8 (C_{8a}), 125.1 (C_8), 123.1 (C_7), 119.0 (C_5), 117.7 (C_{4a}), 81.3 ($C_{5''}$), 78.8 ($C_{3''}$), 78.3 ($C_{1''}$), 74.5 (C_2), 73.3 ($C_{2''}$), 70.0 ($C_{4''}$), 61.2 ($C_{6''}$), 31.9,[a] 31.8[a] (C_3), 20.7 (C_4), 40.3,[a] 40.1,[a] 39.6, 38.0,[a] 37.9,[a] 37.9,[a] 37.9,[a] 37.7,[a] 37.7, 37.6, 25.1, 24.7, 21.4,[a] 21.3,[a] 20.7 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{5'}$, $C_{6'}$, $C_{7'}$, $C_{9'}$, $C_{10'}$, $C_{11'}$), 33.1, 33.0,[a] 32.9,[a] 28.2, 23.6, 22.6, 22.5, 19.7,[a] 19.7,[a] 19.6, 19.5[a] ($C_{4'}$, $C_{8'}$, $C_{12'}$, $C_{13'}$, $C_{4'a}$, $C_{8'a}$, $C_{12'a}$, C_{2a}), 11.8, 11.6 (C_{7a}, C_{8b}) ppm. At 125 MHz, the (4′*RS*,8′*RS*) stereoisomers present gave additional small signals, labelled with the superscript [a]. MS (ESI +C): *m*/*z* (%) = 1179.3 (100) [2 M + Na]$^+$, 578.3 (30) [M]$^+$. MS (ESI –C): *m*/*z* (%) = 190.8 (40) [2 M + Cl]$^-$, 613.2 (100) [M + Cl]$^-$, 577.2 (20) [M – H]$^-$.

Compound (2*R*)-13: Pale yellow amorphous solid, $[a]_D^{22}$ = +42.4 (*c* = 1 in acetone); R_f = 0.43 (EtOAc). ^1H NMR ([D_6]acetone, 500 MHz): δ = 7.79 (s, 1 H, Ar-OH), 4.73 (d, $J_{1'',2''}$ = 9.5 Hz, 1 H, $H_{1''}$), 4.62, 4.47, 4.19, 3.01 (4 s, exchanged with D_2O, 4 H, sugar OH), 3.89–3.83 (m, 2 H, $H_{6a''}$, $H_{6b''}$), 3.75 (t, $J_{1'',2''}$ = 9.5, $J_{2'',3''}$ = 8.8 Hz, 1 H, $H_{2''}$), 3.70 (t, $J_{3'',4''}$ = 8.8, $J_{4'',5''}$ = 9.8 Hz, 1 H, $H_{4''}$), 3.58 (t, $J_{2'',3''}$ = $J_{3'',4''}$ = 8.8 Hz, 1 H, $H_{3''}$), 3.49 (br. d, *J* = 9.5 Hz, 1 H, $H_{5''}$), 2.96 (m, 1 H, H_{4a}), 2.68 (dt, *J* = 6.3, *J* = 6.6, J_{gem} = 16.4 Hz, 1 H, H_{4b}), 2.07, 2.07 (s, 6 H, Me_{7a}, Me_{8b}), 1.74 (t, *J* = 6.6 Hz, 2 H, $H_{3a,b}$), 1.62–1.11 (m, 21 H, $H_{1'-12'}$), 1.22 (s, 3 H, H_{2a}), 0.90–0.88 (m, 12 H, $H_{13'}$, $H_{4'a}$, $H_{8'a}$, $H_{12'a}$) ppm. ^{13}C NMR ([D_6]acetone, 50 MHz): δ = 148.2 (C_6), 145.9 (C_{8a}), 126.2 (C_8), 124.2 (C_7), 120.2 (C_5), 118.8 (C_{4a}), 82.5 ($C_{5''}$), 80.0 ($C_{3''}$), 79.5 ($C_{1''}$), 75.6 (C_2), 74.5 ($C_{2''}$), 71.3 ($C_{4''}$), 62.4 ($C_{6''}$), 33.1 (C_3), 21.9 (C_4), 41.4, 40.7, 39.1, 38.8, 38.6, 26.2, 26.2, 25.8, 22.4 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{5'}$, $C_{6'}$, $C_{7'}$, $C_{9'}$, $C_{10'}$, $C_{11'}$), 33.0, 32.9, 28.2, 23.6, 22.6, 22.5, 19.7, 19.6 ($C_{4'}$, $C_{8'}$, $C_{12'}$, $C_{13'}$, $C_{4'a}$, $C_{8'a}$, $C_{12'a}$, C_{2a}), 11.8, 11.6 (Me_{7a}, Me_{8b}) ppm. MS (ESI, +C): *m*/*z* (%) = 1179.3 (65) [2 M + Na]$^+$, 578.3 (100) [M]$^+$. MS (ESI, –C): *m*/*z* (%) = 1190.9 (65) [2 M + Cl]$^-$, 613.2 (100) [M + Cl]$^-$, 577.3 (65) [M – H]$^-$.

3,5-Dimethyl-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,4-benzoquinone (14): As described for the synthesis of **8**, compound **6** (306 mg, 0.617 mmol), dissolved in acetonitrile (2 mL), was treated with CAN (1.01 g, 1.85 mmol, 3 equiv.) dissolved in water (2 mL) with stirring for 25 min at room temperature. TLC showed that the reaction was over, with **6**, R_f = 0.40 (EtOAc/PE, 1:2), having been converted into a single new product, R_f = 0.43 (EtOAc/PE, 1:2). After workup, purification by column chromatography (mobile phase: EtOAc/PE, 1:2) afforded compound **14** (268 mg, 0.575 mmol, 93.2% yield). Yellow crystals, m.p. 149–150.5 °C (CH_2Cl_2/EP); R_f = 0.43 (EtOAc/PE, 1:2, violet under UV 312 nm, dark spot under 254 nm). $[a]_D^{22}$ = –63 (*c* = 0.7 in CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 6.56 (d, $J_{6,5\text{-Me}}$ = 1.4 Hz, 1 H, Ar-H), 5.43 (t, $J_{1',2'}$ = 9.9, $J_{2',3'}$ = 9.1 Hz, 1 H, $H_{2'}$), 5.31 (t, $J_{2',3'}$ = 9.1, $J_{3',4'}$ = 9.7 Hz, 1 H, $H_{3'}$), 5.20 (t, $J_{3',4'}$ = $J_{4',5'}$ = 9.7 Hz, 1 H, $H_{4'}$), 4.96 (d, $J_{1',2'}$ = 9.9 Hz, 1 H, $H_{1'}$), 4.20 (dd, $J_{5',6a'}$ = 2.6, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6a'}$), 4.17 (dd, $J_{5',6b'}$ = 4.0, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6b'}$), 3.76 (dq, 1 H, $H_{5'}$), 2.27, 2.08, 2.06, 2.01, 1.87 (5 s, 15 H, CH_3 at position 3, and acetyl), 2.04 (d, 3 H, *J* = 1.5 Hz, Me at position 5) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 187.7, 185.3 (C=O, benzoquinone), 170.6, 170.1, 169.6, 169.5 (C=O, acetyl), 145.9, 145.8, 136.8 (C_2, C_3, C_5),* 133.0 (C_6), 76.3, 74.2, 71.9, 70.2, 68.3 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$),* 61.9 ($C_{6'}$), 20.7, 20.6, 20.6, 20.4 (CH_3, acetyl), 16.0, 12.7 (benzoquinone CH_3) ppm. IR (KBr): $\tilde{\nu}$ = 1750 (C=O, acetyl), 1650 (C=O, benzoquinone) cm^{-1}. $C_{22}H_{26}O_{11}$ (466.15): calcd. C 56.65, H 5.62, O 37.73; found C 56.57, H 5.61, O 37.50.

3,5-Dimethyl-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,4-hydroquinone (15): As described for the synthesis of **9a**, compound **14** (268 mg, 0.575 mmol), dissolved in $CHCl_3$ (4 mL), was reduced with $Na_2S_2O_4$ (600 mg, 3.45 mmol, 6 equiv.) in water (4 mL). The mixture was stirred vigorously at room temperature for 12 min. TLC showed that compound **14**, R_f = 0.55 (CH_2Cl_2/EtOAc, 8:1), had changed into a more polar compound, R_f = 0.17 (CH_2Cl_2/EtOAc, 8:1). After workup and concentration, the residue was applied to a column (mobile phase: CH_2Cl_2/EtOAc, 8:1) to afford compound **15** (256 mg, 0.547 mmol, 95.1% yield). White crystals, m.p. 198.5–200 °C (CH_2Cl_2/PE); R_f = 0.17 (CH_2Cl_2/EtOAc, 8:1). $[a]_D^{25}$ = –23.9 (*c* = 0.8 in $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.95 (s, exchangeable, 1 H, OH), 6.58 (s, 1 H, H_6), 5.50 (t, $J_{1',2'}$ = $J_{2',3'}$ = 9.5 Hz, 1 H, $H_{2'}$), 5.37–5.30 (2 overlapping triplets, 2 H, $H_{3'}$ and $H_{4'}$), 4.91 (d, $J_{1',2'}$ = 9.9 Hz, 1 H, $H_{1'}$), 4.32 (dd, $J_{5',6a'}$ = 2.3, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6a'}$), 4.25 (s, exchangeable, 1 H, OH), 4.15 (dd, $J_{5',6b'}$ = 1.4, $J_{6a',6b'}$ = 12.5 Hz, 1 H, $H_{6b'}$), 3.88 (m, 1 H, $H_{5'}$), 2.21, 2.17, 2.12, 2.06, 2.01, 1.81 (6 s, 18 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.7, 170.4, 169.4, 168.6 (C=O, acetyl), 149.4, 145.5 (C_1, C_4), 125.3, 125.3, 122.3 (C_2, C_3, C_5, Ar), 117.6 (C_6), 77.0, 76.1, 73.9, 70.4, 67.8 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$), 61.4 ($C_{6'}$), 20.7, 20.7, 20.6, 20.3 (CH_3, acetyl), 16.3, 12.3 (Ar-CH_3) ppm. $C_{22}H_{28}O_{11}$ (468.16): calcd. C 56.41, H 6.02, O 37.57; found C 56.03, H 6.21, O 37.51.

6-Hydroxy-2,2,5,7-tetramethyl-8-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)chroman (16): By the procedure optimized for the *ortho*-dimethyl series, compound **15** (500 mg, 1.068 mmol), dissolved in anhydrous $CHCl_3$ (6 mL), was mixed with prenyl alcohol (0.11 mL, 1.06 mmol) and anhydrous $ZnCl_2$ (878 mg, 6.41 mmol, 6 equiv.). The mixture, protected from light with aluminium foil, was stirred at reflux under argon for 20 h. TLC showed that the reaction was

almost complete, with **15**, R_f = 0.08 (EtOAc/PE, 1:2) still being visible under UV 312 nm, while 3-methylbut-2-en-1-ol, R_f = 0.56–0.53 (EtOAc/PE, 1:2) had disappeared, with formation of a new product, R_f = 0.21 (EtOAc/PE, 1:2). After workup and concentration, the residue was applied to a column (mobile phase: EtOAc/PE, 1:2) to afford **16** (320.7 mg, 0.6 mmol, 48.2% yield) as a white foam. R_f = 0.21 (EtOAc/PE, 1:2). $[\alpha]_D^{25}$ = –1.1 (c = 0.8 in CH_2Cl_2). ^{1}H NMR ([D$_6$]DMSO): recording of the spectra at room temp., 50, 90 °C (300 MHz) and 120 °C (500 MHz) resulted in improved resolution, although H$_{1'}$ and H$_{2'}$ still gave broad signals. ^{1}H NMR ([D$_6$]DMSO, 120 °C, 500 MHz): δ = 7.00 (s, 1 H, Ar-OH), 5.65 (br triplet, 1 H, H$_{2'}$), 5.24 (t, $J_{2',3'}$ = 9.1, $J_{3',4'}$ = 9.5 Hz, 1 H, H$_{3'}$), 5.11 (br d, 1 H, H$_{1'}$), 5.07 (t, $J_{3',4'}$ = 9.5, $J_{4',5'}$ = 9.8 Hz, 1 H, H$_{4'}$), 4.14 (d, J = 3.5 Hz, 2 H, H$_{6a'}$, H$_{6b'}$), 3.91 (dt, $J_{4',5'}$ = 9.8, $J_{5',6a'}$ = $J_{5',6b'}$ = 3.8 Hz, 1 H, H$_{5'}$), 2.58 (t, J = 6.9 Hz, 2 H, H$_{4ab}$), 2.27, 2.08 (2 s, 6 H, Me$_{5a}$, Me$_{7a}$), 2.03, 2.00, 1.95, 1.71 (4 s, 12 H, 4 Ac), 1.77 (t, J = 6.9, J = 6.6 Hz, 2 H, H$_{3ab}$), 1.33, 1.29 (2 s, 6 H, Me$_{2a}$, Me$_{2b}$) ppm. ^{13}C NMR ([D$_6$]DMSO, 120 °C, 125 MHz): δ = 170.5, 170.2, 169.9, 169.2 (C=O, acetyl), 146.8, 146.5 (C$_6$, C$_{8a}$, Ar),* 125.3, 125.1, 120.4, 118.3 (C$_5$, C$_7$, C$_8$, C$_{4a}$, Ar),* 76.0, 76.0, 74.5, 71.7, 70.0 (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$),* 73.5 (C$_2$), 63.4 (C$_{6'}$), 33.6, 21.4 (C$_3$, C$_4$),* 27.6, 27.0 (C$_{2a}$, C$_{2b}$), 21.4, 21.0, 21.0, 20.8 (CH$_3$, acetyl), 13.3, 12.6 (Me$_{7a}$, Me$_{8b}$) ppm. $C_{27}H_{36}O_{11}$ (536.23): calcd. C 60.44, H 6.76, O 32.80; found C 60.92, H 7.05, O 31.23.

8-(β-D-Glucopyranosyl)-6-hydroxy-2,2,5,7-tetramethylchroman (17): A solution of sodium methoxide in methanol (4 mL, 0.1 M) was poured into a flask containing compound **16** (302 mg, 0.563 mmol), which was stirred at room temperature for 2 h, after which a more polar compound had been formed. A slight excess of Amberlyst resin IR 120 H$^+$ was added, and stirring of the mixture was continued for 20 min. After filtration and concentration, the residue was applied to a column (mobile phase: EtOAc) to afford **17** (192.6 mg, 93% yield) as a white amorphous solid; R_f = 0.19 (EtOAc). $[\alpha]_D^{25}$ = +18.3 (c = 0.6 in CH_3OH). ^{1}H NMR ([D$_6$]-DMSO + D$_2$O, 90 °C, 500 MHz): δ = 4.68 (br. signal, 1 H, H$_{1'}$), 3.86 (br. signal, 1 H, H$_{2'}$), 3.71 (dd, $J_{5',6'a}$ = 2.3, $J_{6'a,6'b}$ = 11.7 Hz, 1 H, H$_{6'a}$), 3.50 (dd, $J_{5',6'b}$ = 5.1, $J_{6'a,6'b}$ = 11.7 Hz, 1 H, H$_{6'b}$), 3.30–3.20 (m, 3 H, H$_{3'}$, H$_{4'}$, H$_{5'}$), 2.56 (t, J = 6.6, J = 6.3 Hz, 2 H, H$_{4a,b}$), 2.22, 2.06 (2 s, 6 H, Me$_{5a}$, Me$_{7a}$), 1.74 (t, J = 6.6, J = 6.0 Hz, 2 H, H$_{3a,b}$), 1.25, 1.21 (2 s, 6 H, Me$_{2a}$, Me$_{2b}$) ppm. ^{13}C NMR ([D$_6$]-DMSO + D$_2$O, 90°, 125 MHz): δ = 147.0, 146.4 (C$_6$, C$_{8a}$), 124.9, 123.9, 123.8, 118.2 (C$_{4a}$, C$_5$, C$_7$, C$_8$), 81.6, 80.0, 72.9, 71.8, 71.8 (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$), 73.2 (C$_2$), 62.9 (C$_{6'}$), 33.6 (C$_3$), 27.7, 26.7 (C$_{2a}$, C$_{2b}$), 21.5 (C$_4$), 13.8, 12.6 (C$_{5a}$, C$_{7a}$) ppm. MS (ESI, +C): m/z (%) = = 759.0 (100) [2 M + Na]$^+$, 391.1 (27) [M + Na]$^+$.

8-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-ε-tocopherol (18): Compound **15** (300 mg, 0.64 mmol) dissolved in $CHCl_3$ (5 mL) was mixed with racemic phytol (0.23 mL, 0.64 mmol, 1 equiv.) and anhydrous $ZnCl_2$ (520 mg, 3.84 mmol, 6 equiv.). The mixture was stirred at reflux under argon for 24 h with protection against light (aluminium foil). TLC showed that the reaction was almost complete, with compound **15**, R_f = 0.06 (EtOAc/PE, 1:3) still being visible under UV light (λ = 312 nm), while phytol, R_f = 0.52–0.48 (EtOAc/PE, 1:3) was hardly visible, in contrast to the desired product, R_f = 0.26 (EtOAc/PE, 1:3). Workup and purification as described above for **12** yielded compound **18** as a mixture of diastereoisomers (300.4 mg, 0.40 mmol, 62.7% yield). Brown-red syrup, R_f = 0.26 (EtOAc/PE, 1:3). $[\alpha]_D^{25}$ = +4.66 (c = 0.88 in CH_2Cl_2). ^{1}H NMR ([D$_6$]DMSO, 120 °C, 500 MHz): δ = 7.26 (s, 1 H, Ar-OH, more visible when the spectra was recorded at 90 °C), 5.64 (br. signal, 1 H, H$_{2''}$), 5.234 and 5.227 (2 t, J = 9.5, J = 9.1 Hz, 1 H, H$_{3''}$), 5.11 (br. signal, 1 H, H$_{1''}$), 5.10–5.04 (m, 1 H, complex H$_{4''}$), 4.16 (dd, $J_{5'',6''a}$ = 3.2, $J_{6''a,6''b}$ = 12 Hz, 1 H, H$_{6''a}$), 4.11 (dd, $J_{5'',6''b}$ = 4.5, $J_{6''a,6''b}$ = 12 Hz, 1 H, H$_{6''b}$), 3.86 (m, 1 H, H$_{5''}$), 2.57 (m, 2 H, H$_{4a}$, H$_{4b}$), 2.27, 2.08, 2.02, 2.00, 1.94 (5 s, 15 H, 2 ArCH$_3$, 3 OAc), 1.74 (m, 2 H, H$_{3a}$, H$_{3b}$), 1.71 (2 s, 3 H, acetyl at C$_{2''}$), 1.61–1.12 (m, 24 H, H$_{1'-12'}$ and Me$_{2a}$), 0.93–0.87 (m, 12 H, Me$_{13',4'a,8'a,12'a}$) ppm. ^{13}C NMR ([D$_6$]DMSO, 120 °C, 125 MHz): δ = 170.4, 170.15, 170.1, 169.9, 169.8, 169.1 (C=O, acetyl), 146.5, 125.3, 125.3, 125.2, 125.1, 120.4, 120.2, 118.5, 118.4 (C$_6$, C$_{8a}$, C$_5$, C$_7$, C$_8$, C$_{4a}$), 76.3, 76.0, 71.6, 70.2, 70.1 (C$_{1''}$, C$_{2''}$, C$_{3''}$, C$_{4''}$, C$_{5''}$), 75.7, 75.6 (C$_2$), 63.5, 63.4 (C$_{6''}$), 41.5, 39.8, 38.2, 37.8, 37.7, 37.6, 31.9, 24.9, 24.7, 21.5, 21.1 (methylene: C$_3$, C$_4$, C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{5'}$, C$_{6'}$, C$_{7'}$, C$_{9'}$, C$_{10'}$, C$_{11'}$), 33.1, 28.2, 24.0, 23.7, 23.1, 23.1, 21.0, 21.0, 20.7, 20.4, 20.3 (C$_{4'}$, C$_{8'}$, C$_{12'}$, C$_{13'}$, C$_{4'a}$, C$_{8'a}$, C$_{12'a}$, C$_{2a}$), 20.4, 20.3, 20.3, 20.3 (CH$_3$, acetyl), 13.3, 12.6 (C$_{7a}$, C$_{8b}$) ppm. MS (ESI, positive mode): m/z (%): 1515.6 (55) [2 M + Na]$^+$, 769.4 (100) [M + Na]$^+$, 764.1 (40) [M + NH$_4$]$^+$, 747.1 (45) [M + H]$^+$. HRMS (FAB, nitrobenzyl alcohol) calcd. for $C_{42}H_{67}O_{11}$ [M + H]$^+$: 747.4683, found: 747.46790.

8-(β-D-Glucopyranosyl)-ε-tocopherol (19): A solution of sodium methoxide in methanol (3 mL, 0.1 M) was poured into a flask containing compound **18** (212 mg, 0.284 mmol). After the mixture had been stirred at room temperature for 2 h, TLC showed that compound **18**, R_f = 0.26 (EtOAc/PE, 1:3) had changed into a more polar compound, R_f = 0.60 (EtOAc). After neutralization (Amberlyst resin IR 120 H$^+$), filtration and concentration, the residue was applied to a column (mobile phase: EtOAc) to afford compound **19** (146 mg, 89% yield) as a brown-red amorphous solid, R_f = 0.60 (EtOAc). $[\alpha]_D^{25}$ = +18.8 (c = 0.74 in acetone); ^{1}H NMR ([D$_6$]-DMSO, 90 °C, 500 MHz): diastereoisomeric mixture giving a complex and uninformative spectrum for the sugar part, while the chain and chroman protons were visible. MS (ESI, positive mode): m/z (%): 1179.4 (100) [2 M + Na]$^+$, 601.4 (45) [M + Na]$^+$; (ESI, negative mode): m/z (%): 1191.2 (60) [2 M + Cl]$^-$, 623.1 (100) [M + HCOO]$^-$, 577.3 (45) [M – H]$^-$.

Evaluation of Antioxidant Properties

Chemicals: (±) α-Tocopherol, linoleic acid, AAPH [2,2′-azo-bis(2-methylpropionamidine) dihydrochloride] and SDS (sodium dodecylsulfate) were purchased from Sigma–Aldrich (L'Isle d'Abeau, France). All reagents were of the highest purity available (95–99%) and were used without purification. All solvents used were analytical grade. The phosphate buffer (pH 7.4, 50 mM NaH_2PO_4) was prepared with Millipore Q-Plus water and eluted on a chelating resin (chelex 100, 0.4 milliequiv. mL^{-1}, Bio-Rad) to remove contaminating metal traces.

UV/Vis Spectroscopy: UV/Vis spectra were recorded on a Hewlett–Packard 8453 diode array spectrometer fitted with a magnetically stirred cell (optical pathlength: 1 cm). The temperature in the cell was maintained by means of a water thermostatted bath.

Inhibition of Linoleic Acid Peroxidation: A freshly prepared solution of linoleic acid (2.55 mM, 2 mL) in a phosphate buffer (pH 7.4) containing SDS (0.1 M) was placed in the spectrometer cell at 37 °C. At time zero, a freshly prepared solution of AAPH (80 mM, 25 μL) in the same buffer was added, followed ca. 800 s later by an antioxidant solution in MeOH (25 μL). The experiments were repeated with different antioxidant concentrations (1 mM and lower). The initial level of hydroperoxides (molar absorption coefficient at 234 nm was 26100 M^{-1} cm^{-1}) was below 2% in all experiments. The uninhibited and inhibited peroxidation rates were calculated from the slope of the A(234 nm) vs. time lines before and after antioxidant addition with fixed time intervals. Each experimental point was the mean of two to three measurements. Errors were lower than 10%.

Data Analysis: The Scientist program (MicroMath, Salt Lake City, USA) was used for all curve-fitting procedures. Details on the calculations [see Equations (1)–(5)] have already been published.[50,51] Standard deviations and correlation coefficients are reported.

Molecular Modelling: All calculations were performed in the gas phase with use of Hyperchem software (Autodesk, Sausalito, USA). Firstly, the search for the most stable conformation about the glycosidic bond was achieved by molecular mechanics (MM+ force field). Then, the most stable conformation was further optimized by semiempirical quantum mechanics calculations (PM3 parametrization, UHF mode) for each phenol and the corresponding aryloxyl radical. Intramolecular H-bonding was allowed within the *C*-glycosyl moiety and, when possible, between the phenolic OH and the *C*-glycosyl moiety (O-5).

Supporting Information (see also the footnote on the first page of this article): a) Description of the $ZnCl_2$-catalyzed reaction between 2-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-hydroquinone and all-racemic phytol. b) Experimental details for the coupling reaction between 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose and 1,4-dimethoxy-2,3-dimethylbenzene as a route to 5-*C*-β-D-galactopyranosyl-7,8-dimethylchroman-6-ols and *C*-β-D-galactopyranosyl-γ-tocopherols. c) Evaluation of the solubilities of the prepared acetylated and deacetylated *C*-β-D-glycosylchroman-6-ols and *C*-β-D-glycosyltocopherols (D-*gluco*, D-*galacto* series). d) Miscellaneous bioactivities.

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