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Received (in Cambridge) 30th June 1998, Accepted 22nd July 1998

The preparation of β-O-4 oligomeric compounds that mimic the lignin structure is pertinent to the study of the mechanism of action of lignin-degrading enzymes. A strategy for the synthesis of racemic oligomers β-O-4 phenolic models of lignin is reported here. The procedure is quite general with respect to the number of linked units. It starts from simple building blocks that are prepared in a few conventional steps from commercially available starting materials. The building blocks can be classified as three different units, an initiating **3**, a repeating **4** and a terminating unit **5**. The combination of these units by aldol-type reactions allows the synthesis of oligomeric materials containing the β-O-4 structure. The procedure allows the determination of the relative configurations of the stereocenters generated in the aldol-type reactions that provide the β-O-4 skeleton. The synthesis procedure reported here for the trimer **6** and tetramer **7** can be easily extended to higher oligomers and it is suitable also for automated synthesis.

Introduction

Lignin contains a large part (about 25%) of the total carbon fixed by photosynthesis. It is the second most abundant natural polymer, after cellulose, as a source of renewable carbon.[1] Therefore it represents a huge deposit of renewable raw material for production of new materials. Lignin is an amorphous, water-insoluble polymer of phenylpropanoid units, linked together by a variety of carbon–carbon and carbon–oxygen bonds and assembled in a non-repeating motif.[1–3] Therefore, lignin biosynthesis and biodegradation must differ from that of other biological polymers where identical subunits are linked by a single type of bond.[4,5] The predominant bond type in lignin is the aryl glycerol β-aryl ether (β-O-4) which is shown in Fig. 1.

Lignin protects cellulose from most forms of microbial attack and gives rigidity to plants. As it is present in wood in large amounts, lignin is the major waste product of the pulp and paper industry.[6] Due to its aromatic nature, its biodegradation can be difficult and produces environmental pollution. On the other hand, degradation of lignin in biocompatible products, which could serve as starting materials in synthesis and have low environmental impact, is of great interest for researchers. *In vivo*, the degradation of lignin represents the starting step for utilization of cellulose.[7] It is essentially performed by lignin-degrading fungi, which are able in some cases to degrade lignin to CO_2, while most of the lignin is degraded to humic material.[8] Degradation of lignin by filamentous fungi is initiated by extracellular peroxidases,[9] which are responsible for oxidative depolymerization of lignin. Peroxidases are enzymes where the prosthetic group is the heme moiety containing, in the resting state, a five coordinate high spin iron(III). The enzyme reacts with hydrogen peroxide to form a two electron oxidized form of peroxidases.[10] This form then oxidizes the substrate in two one-electron steps. The structural properties of some fungal peroxidases are well characterized both in the crystal[11] and in solution.[12] Although it is now 15 years since the discovery of these enzymes in the extracellular fluids of the lignin-degrading fungi,[13] no commercial processes utilizing these fungi or their enzymes are in use. One of the main problems to be overcome is the full comprehension of the biochemical process. In this respect, it is of great importance to understand the correlation between enzymatic efficiency and properties of substrates, *i.e.* the nature of the units constituting

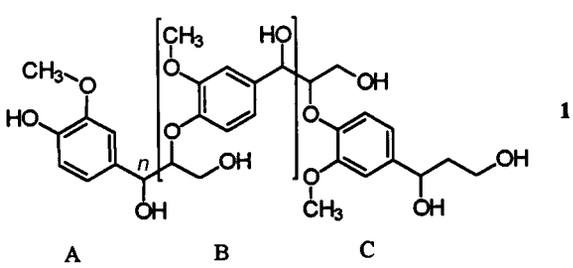

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Fig. 1

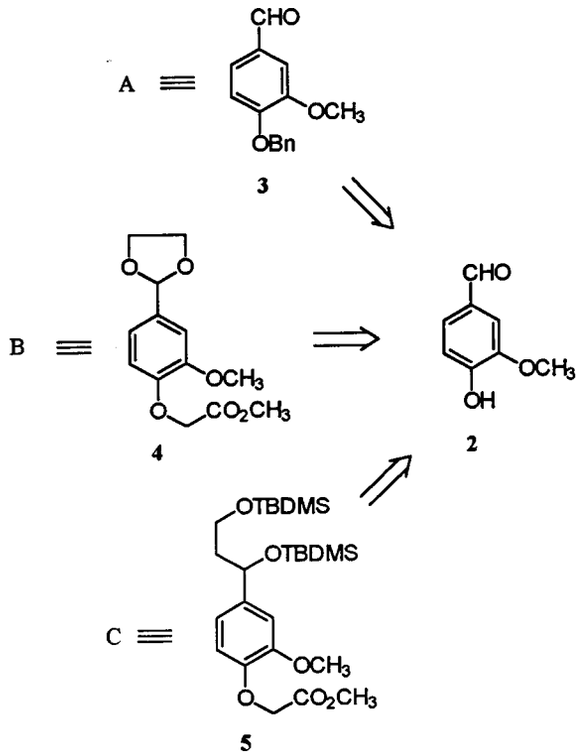
them and the types of linkages between the units. Therefore the availability of molecules with a single type of linkage is useful to understand specific aspects of the enzymatic degradation.

Since the aryl glycerol β-aryl ether bond is the major intermonomer linkage in lignin,[5] syntheses of models containing only β-O-4 are very important for the study of the biodegradation of lignin. Syntheses of the dimeric and trimeric lignin β-O-4 models have already been reported,[14,15] together with some trimeric compounds containing structurally different monomeric units and types of bonds.[16] Oligomeric structures are expected to be more appropriate mimics of the lignin structure than dimeric and trimeric compounds and also our model, containing a propane-1,3-diol terminating unit, appears to be a more appropriate model of the polymeric β-O-4 structure of lignin. Furthermore, none of the syntheses reported was fully designed for an iterative process leading to the synthesis of oligomers.

The goal of this work is to develop a general procedure for the preparation of β-O-4 oligomeric compounds which mimic the lignin structure, by using simple building blocks synthesized from commercially available starting materials. The procedure we developed can be expanded in principle to as many units as required, with reasonably good yields.

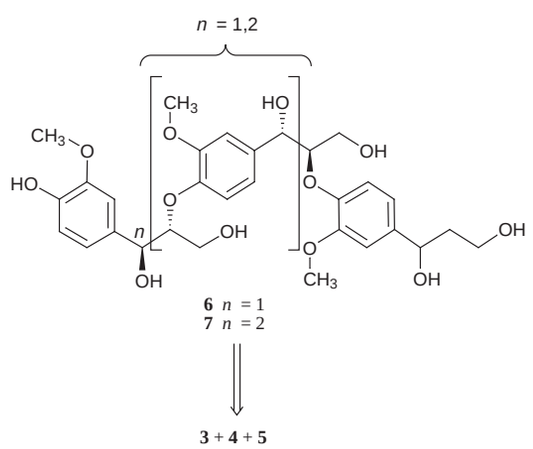
The structure of an oligomeric β-O-4 compound like **1** (Fig. 1) consists of three types of units: (i) an initiating unit A; (ii) a repeating unit B; (iii) a terminating unit C.

Our aldol-type synthetic approach uses vanillin **2** (Scheme 1) as starting material from which synthetic equivalents of the B and C units can be obtained by simple transformations, while the A unit (compound **3**) is commercially available.



Scheme 1

The repeating and terminating units **4** and **5** should bear a subunit responsible for the C–C bond formation. The phenoxyacetate function of compounds **4** and **5** was chosen to serve as the joining element through a carbanion-promoted aldol reaction with the vanillin molecule. The synthesis of racemic trimeric and tetrameric phenolic compounds **6** and **7**, according to this strategy, is reported in this paper (Scheme 2).



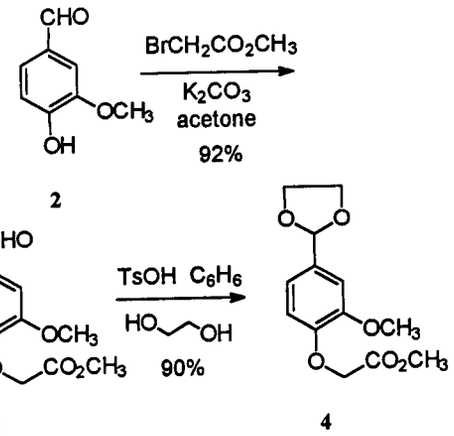
Scheme 2

Results and discussion

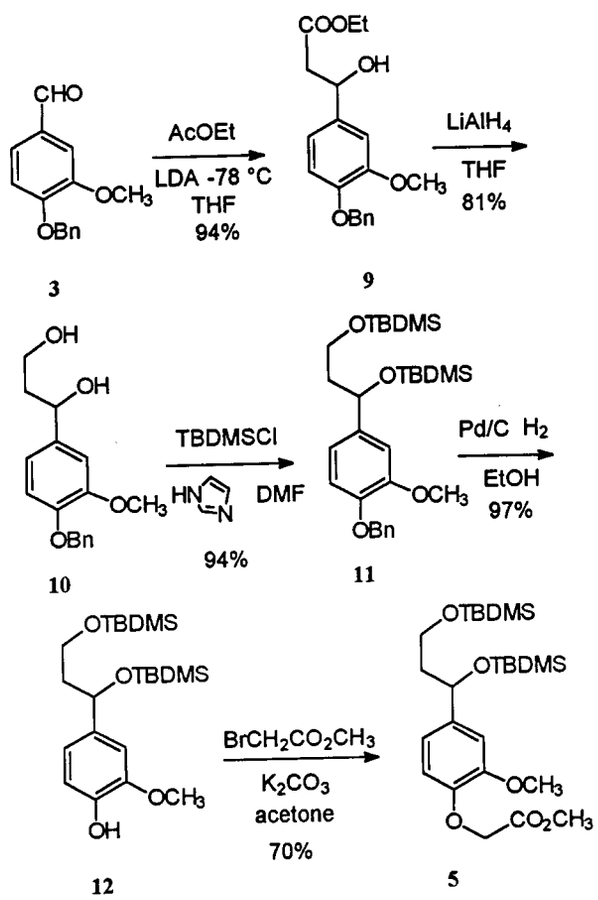
Synthesis of the building blocks 4 and 5

Compound **4** was obtained in high overall yield (83%) from vanillin in two steps consisting of a nucleophilic substitution with methyl α-bromoacetate and protection of the aldehydic group in **8** as a dioxolane (Scheme 3).

The terminating unit **5** was obtained in good overall yield (48%) in five steps (Scheme 4). Aldol reaction between benzylvanillin **3** and the lithium enolate of ethyl acetate in anhydrous THF at −78 °C gave the hydroxypropionate **9** in high yield. Compound **9** was reduced with $LiAlH_4$ to the diol **10**, which was protected as the bis(*tert*-butyldimethylsilyl) (TBDMS)

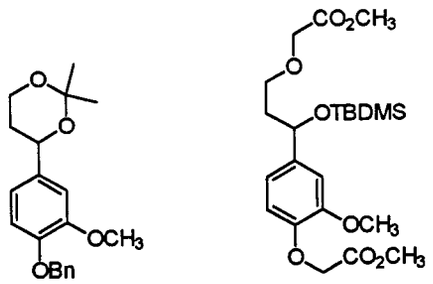


Scheme 3



Scheme 4

ether. Hydrogenolysis of the benzylic group followed by nucleophilic substitution with methyl α-bromoacetate gave the terminating unit **5**. The protection of diol **10** with the more convenient dimethyl ketal protecting group as in **13** gave some problems of selectivity during the hydrogenolysis step. In fact, the hydrogenolysis of **13** also led to compounds originating from the cleavage of the dioxane benzylic C–O bond. An attempt to avoid this problem, by performing the hydrogenolysis before the diol protection, gave poorer overall yields because of problems encountered during purification of the phenolic ketal. The TBDMS protecting group was found to be a satisfactory solution to overcome these problems. The yield of the final alkylation step to obtain **5** was lowered by the formation of the by-product **14** which was formed by the partial deprotection of the primary TBDMS ether in **12** followed by double nucleophilic substitution of methyl α-bromoacetate.



13 14

Synthesis of the trimeric and tetrameric units

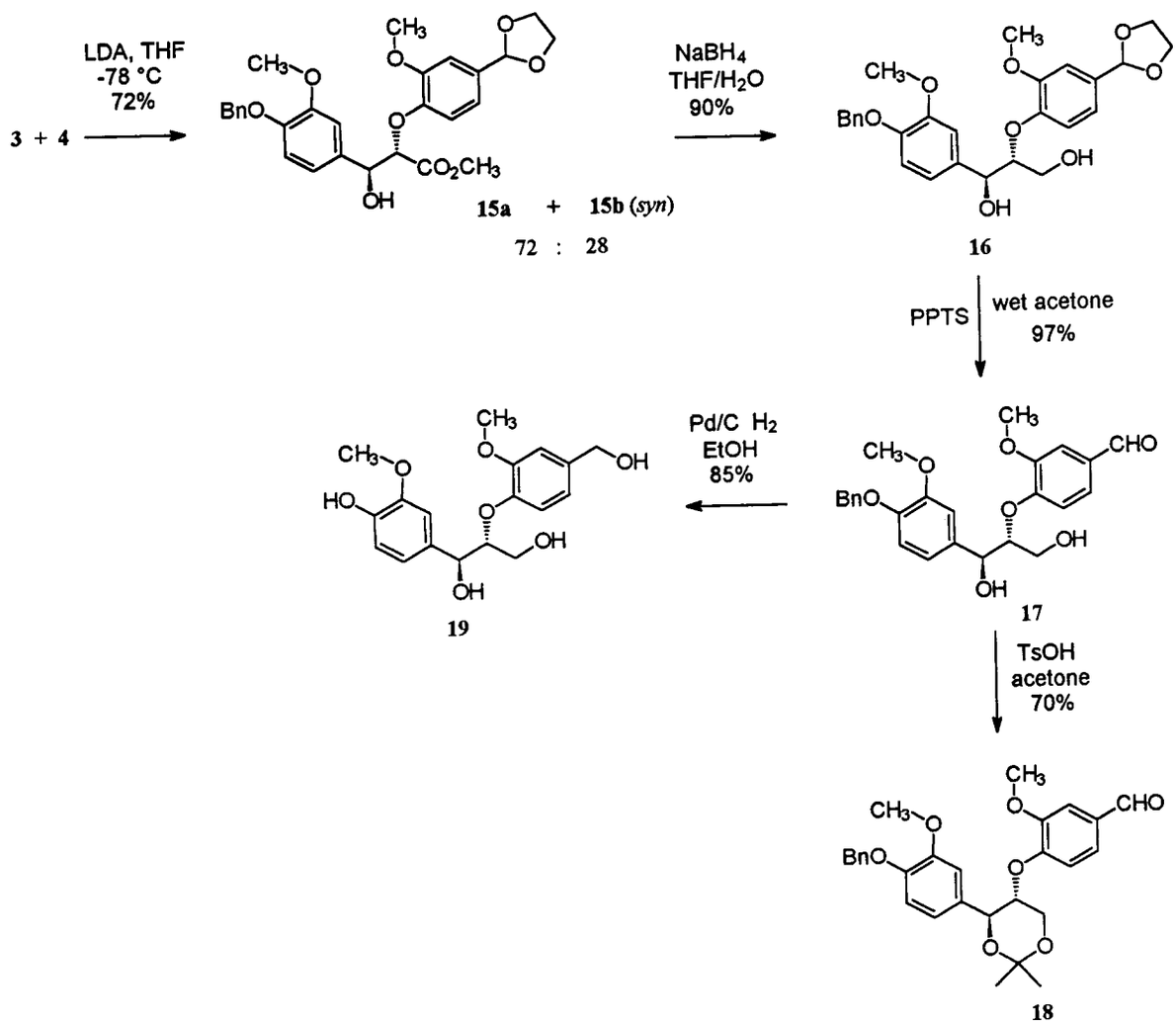
The assembly of the units for the production of oligomeric compounds was carried out in a stepwise manner which started with the synthesis of the already known dimeric compound **18**[16d] (Scheme 5), which was synthesized in a slightly different manner. Addition of the lithium enolate of B unit **4** to benzylvanillin **3** at −78 °C in dry THF gave a mixture of two diastereomeric adducts **15a** and **15b**, in 72:28 diastereomeric ratio as estimated from the ^{1}H NMR spectrum, which were separated by flash chromatography on silica gel.

Unequivocal assignment of the stereochemistry in the diastereomers **15a**,**b** was only possible at a later stage of the synthesis. The major diastereomer **15a** was reduced to the diol **16** by $NaBH_4$ at room temperature, which gave the aldehyde by treatment with pyridinium toluene-*p*-sulfonate (PPTS). The use of 2,2-dimethoxypropane and PPTS to form dioxane **18** led also to the undesired protection of the aldehydic group of **17** as the dimethyl acetal. To avoid this, dry acetone and catalytic amounts of TsOH were used, even though the yield was somewhat lower.[17] Compound **18** allowed us to determine the relative configuration of the two stereocenters of the cyclic ketal in the major diastereomer. The ^{13}C NMR spectrum of **18** showed an axial methyl group at 19.58 ppm, an equatorial methyl group at 28.40 ppm and a C(2) acetal carbon at 99.63 ppm (Scheme 6), values which suggested that the 1,3-dioxolane **18** exists in a well defined chair conformation.[18] Then, the coupling constants of protons H_a and H_b, measured from the splitting of the H_α ^{1}H NMR signal ($J_{a,b} = 9.15$ Hz) indicated a *trans* diequatorial relationship of the C(4) and C(5) substituents in **18** (Scheme 6). Therefore, condensation of the *E*-lithium enolate (**a**) of **4**, formed in these reaction conditions,[19] with benzylvanillin must proceed preferentially through a six membered transition state in which the C(4) and C(5) substituents are in the most favorable *trans* diequatorial orientation as shown in Scheme 6, to give the *anti* product **15a** preferentially.

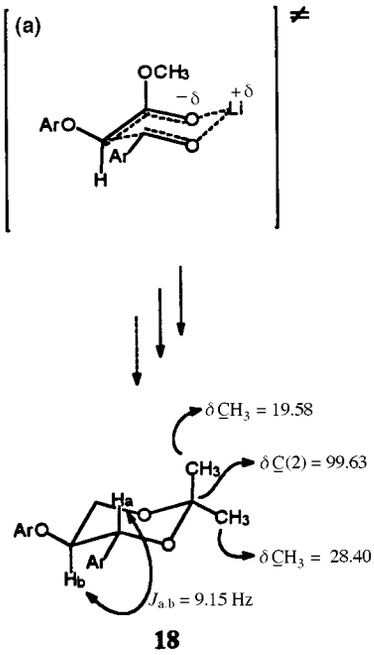
At this stage of the synthesis it was also possible to synthesize a dimeric phenolic β-O-4 model **19** in 85% yield by submitting the aldehyde **17** to hydrogenation conditions (Scheme 5).

The synthesis of the phenolic trimeric β-O-4 compound **6** has been performed through the five steps as depicted in Scheme 7.

The addition of the C unit **5** to the aldehyde **18** was performed through the lithium enolate of **5** generated at −78 °C

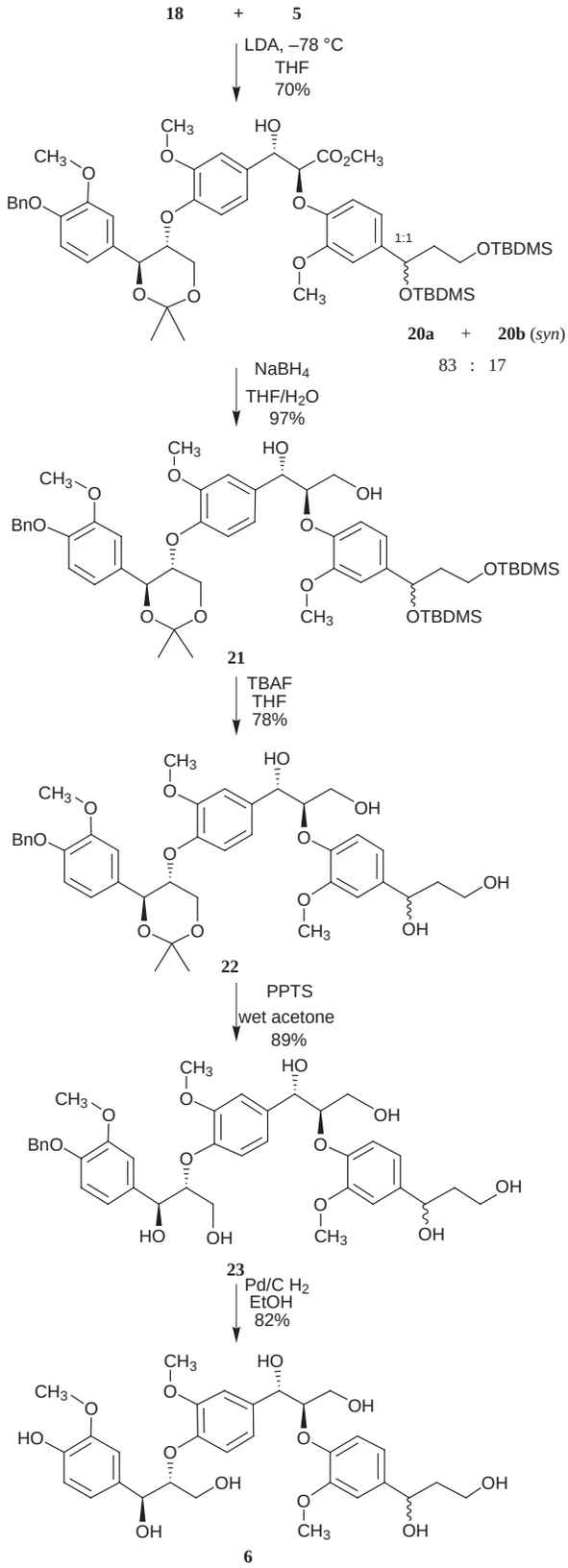


Scheme 5



18

Scheme 6



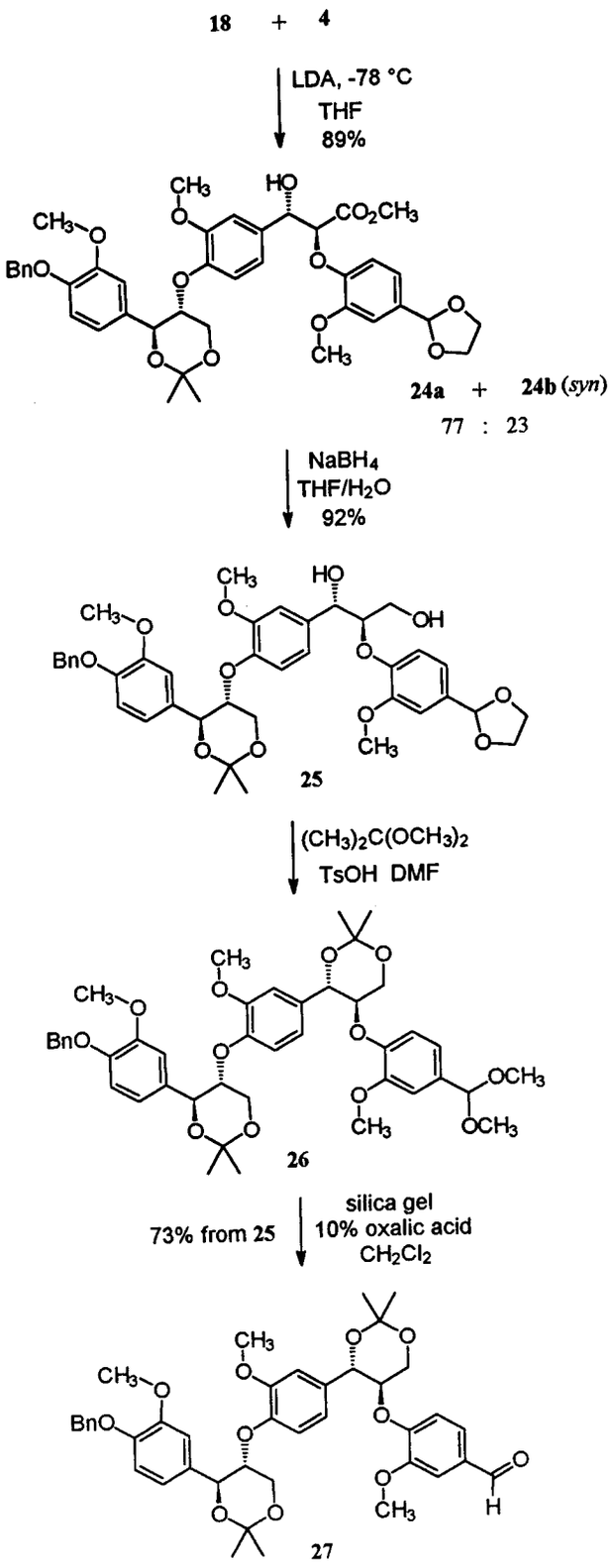
Scheme 7

in dry THF yielding a mixture of four diastereomers. Slightly higher selectivity was observed in the addition of the enolate to **18**, as the *anti*:*syn* ratio was 83:17. Each *anti* and *syn* diastereomer is present as a 1:1 mixture of isomers deriving from the added stereocenter of unit C. The 1:1 stereomeric couple of the major diastereomer can be separated and assigned the *anti* configuration on the basis of the ^{1}H NMR spectrum. The reduction of the methyl ester function of **20a** with $NaBH_4$ at room temperature afforded the final protected trimeric β-O-4 structure in quantitative yields. The protecting groups were removed selectively, first using tetrabutylammonium fluoride (TBAF) in THF to remove the two TBDMS groups and then PPTS in wet acetone to remove the dimethyl ketal. It was important to use this order of deprotection in order to obtain a better overall yield and a simpler purification process. Finally, the benzylic group was removed by hydrogenolysis on Pd/C in EtOH at room temperature to give the phenolic trimeric β-O-4 lignin model compound **6**.

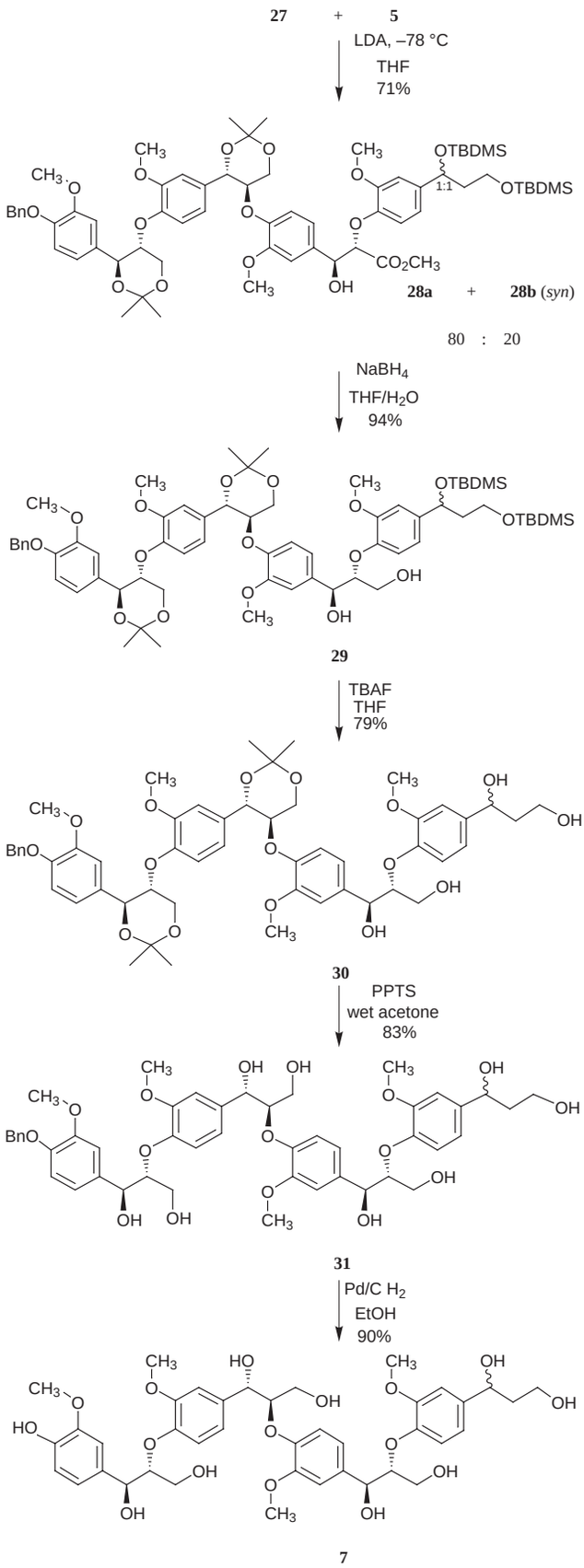
The synthesis of a similar β-O-4 trimer has been already reported.[15a] However, the latter adduct contained as substituent in the terminal aromatic ring the CH_2OH group instead of the CHO. This prevents the addition of further units to the trimer and therefore the formation of a further β-O-4 bond, because of the presence of the CH_2OH group on the terminal aromatic ring instead of the aldehydic group necessary for the following aldolic condensation.

The synthesis of a tetrameric compound **7** required a second addition of the repeating unit **4** to the aldehyde **18**, before the terminating unit **5** was introduced. However, the synthetic sequence required the solution of several problems related to protecting groups. The second addition of **4** was carried out under the same reaction conditions as used for the synthesis of **18**; *i.e.* with addition of the lithium enolate of **4** generated at −78 °C in dry THF (Scheme 8). The two diastereomeric adducts **24a** and **24b** were now obtained in a 77:23 diastereomeric ratio, as estimated from the ^{1}H NMR spectrum and the major *anti*-diastereomer **24a** was separated by flash chromatography. After reduction of the ester function with $NaBH_4$ at room temperature, the hydroxylic functions of **25** were protected with 2,2-dimethoxypropane in the presence of a catalytic amount of TsOH.[17] Under these conditions, we also induced a transacetalization of the aldehyde functionality, from the dioxolane **25** to the dimethyl acetal **26**, which should allow an easier, more selective deprotection of the aldehydic group. The dimethyl acetal group of **26** was in fact selectively removed by using silica gel as a mild agent in the presence of a small amount of an aqueous solution of 10% oxalic acid,[20] to afford the aldehyde **27** in 73% yield from **25**.

The addition of the terminating unit **5** to the trimeric aldehyde **27** was carried out through the lithium enolate of **5**



Scheme 8



Scheme 9

generated at −78 °C in dry THF (Scheme 9). The aldol-type reaction gave a mixture of four diastereomers, analogously to what was previously observed in the same addition to **18**. The *anti*:*syn* ratio was determined to be 80:20 from the ^{1}H NMR spectrum and the 1:1 stereomeric couple of the major diastereomer can be separated as described before for the preparation of the trimeric species. Reduction of the ester function in **28a** and deprotection of the functional groups as performed for trimer **6** gave the tetrameric lignin model **7** in 55% yield from **28a**. A tetrameric compound could be in principle obtained by condensation of two dimeric units. However this procedure yielded very low amounts of products.

Conclusion

A trimeric and a tetrameric model of lignin with the β-O-4 moiety were synthesized in 17% (9 step) and 10% (13 step) yield,

respectively, starting from vanillin. The synthetic strategy uses an aldol-type reaction that provides the *anti* diol as the major diastereomer. The synthesis can be of general application and is designed to be extended to the synthesis of oligomeric phenolic or non-phenolic materials. A repeating unit and a terminating unit were synthesized from vanillin in a few conventional steps and the combination of these building blocks, as shown in the synthesis of the trimer **6** and tetramer **7**, could be suitably designed for an automated synthesis. This procedure makes available a number of molecules with desired length and type of repeating units which can be used for systematic kinetic studies on peroxidases. These studies will shed light on the mechanism of degradation of lignin.

Experimental

All the reactions which required dry conditions were run under a nitrogen atmosphere using anhydrous solvents. Melting points (mp) were measured with a Leits Wetzlar hot-plate apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra (in $CDCl_3$ solution, unless otherwise stated) were recorded on a Bruker MSL 200, DRX 500 and Avance 600 spectrometers with coupling constants (*J*) given in Hz. Notations s, d, t, q, m and br indicate singlet, doublet, triplet, quartet, multiplet and broad, respectively. Mass spectra (MS) were recorded on a QMD 1000 Carlo Erba instrument by GC or direct inlet (EI, 70 eV) and on an HP 1100 MSD instrument with electron spray (ES) ionization mode in negative polarity (Vcap 4000 V). Elemental analyses were performed with a Carlo Erba 1106 instrument.

Methyl (4-formyl-2-methoxyphenoxy)acetate 8

To a solution of vanillin (3 g, 19.7 mmol) in dry acetone (33 cm^3), methyl α-bromoacetate (4.5 g, 29.5 mmol) and anhydrous K_2CO_3 (4.08 g, 29.5 mmol) were added at room temperature. The mixture was heated at reflux for 2 h, then filtered, washed with AcOEt and the filtrate was concentrated to give a yellowish solid. The solid was recrystallized from EtOH to give pure **8** (4.1 g, 18.12 mmol, yield 92%), mp 94.5–95.5 °C (Found: C, 58.7; H, 5.5. $C_{11}H_{12}O_5$ requires C, 58.9; H, 5.4%); δ_H(200 MHz) 3.82 (3 H, s, CO_2CH_3), 3.96 (3 H, s, OCH_3), 4.80 (s, 2 H, $CH_2CO_2CH_3$), 6.90 (1 H, d, *J* 8.1, Ar), 7.43 (1 H, d, *J* 8.1, Ar), 7.45 (1 H, s, Ar), 9.87 (1 H, s, CHO); δ_C 52.4 (q, CO_2CH_3), 56.1 (q, OCH_3), 65.8 (t, $CH_2CO_2CH_3$), 109.8 (d, Ar), 112.3 (d, Ar), 126.1 (d, Ar), 131.2 (s, Ar), 150.0 (2 s, Ar), 168.5 (s, CO_2CH_3), 190.8 (d, CHO); *m*/*z* 224 (M$^+$, 100%), 209 (3), 165 (32), 151 (65), 150 (36), 137 (21), 119 (23), 105 (18), 95 (69), 79 (49), 77 (86), 65 (36), 63 (42).

Methyl [4-(1,3-dioxolan-2-yl)-2-methoxyphenoxy]acetate 4

To a solution of **8** (3.167 g, 14.1 mmol) in 56 cm^3 of benzene, ethanediol (1.18 cm^3, 21.1 mmol) and a catalytic amount of TsOH (0.05%) were added at room temperature. The solution was heated at reflux for 2 h using a Dean-Stark apparatus to distil off the azeotrope benzene–H_2O. The reaction mixture was then washed with water, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give **4** as a white solid that was recrystallized from EtOH (3.4 g, 12.7 mmol, yield 90%), mp 92–94 °C (Found: C, 58.3; H, 6.0. $C_{13}H_{16}O_6$ requires C, 58.6; H, 5.7%); δ_H(200 MHz) 3.78 (3 H, s, CO_2CH_3), 3.90 (3 H, s, OCH_3), 3.97–4.18 (4 H, m, CH_2CH_2), 4.70 (2 H, s, $CH_2CO_2CH_3$), 5.75 (1 H, s, CHO_2), 6.81 (1 H, d, *J* 8.1, Ar), 6.95–7.07 (2 H, m, Ar); δ_C 52.2 (q, CO_2CH_3), 55.9 (q, OCH_3), 65.2 (2 t, CH_2CH_2), 66.4 (t, $CH_2CO_2CH_3$), 103.4 (d, CHO_2), 109.9 (d, Ar), 113.7 (d, Ar), 119.1 (d, Ar), 132.1 (s, Ar), 147.9 (s, Ar), 149.6 (s, Ar), 169.3 (s, CO_2CH_3); *m*/*z* 268 (M$^+$, 1%), 254 (7), 224 (100), 165 (26), 149 (26), 137 (24), 119 (32), 105 (17), 95 (53), 79 (38), 77 (53), 65 (24), 63 (28).

1-(4-Benzyloxy-3-methoxyphenyl)propane-1,3-diol 10

n-Butyllithium (10.32 cm^3 of a 1.6 M solution in hexanes, 15.48 mmol) was added to a solution of diisopropylamine (2.17 cm^3, 15.48 mmol) in dry THF (20 cm^3) at 0 °C. After 20 min at 0 °C, AcOEt (1.21 cm^3, 12.4 mmol) was added dropwise at −78 °C and after 10 min a solution of benzylvanillin (2.5 g, 10.31 mmol) in dry THF was added. After 30 min at −78 °C, the reaction was quenched with saturated aqueous NH_4Cl (30 cm^3) and extracted with Et_2O (3 × 30 cm^3). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the product **9** sufficiently pure to be used for the following step (9.69 mmol, 3.2 g, yield 94%): δ_H(200 MHz) 1.27 (3 H, t, *J* 7.2, CH_2CH_3), 2.60–2.80 (2 H, m, CH_2CHOH), 3.30 (1 H, br s, OH), 3.90 (3 H, s, OCH_3), 4.19 (2 H, q, *J* 7.2, CH_2CH_3), 5.05 (1 H, dd, *J* 8.5 and 3.9, CHOH), 5.15 (2 H, s, CH_2Ph), 6.80–6.84 (2 H, m, Ar), 6.98 (1 H, s, Ar), 7.28–7.43 (5 H, m, Ph).

A solution of **9** (940 mg, 2.84 mmol) in 5 cm^3 of dry THF was added to a suspension of $LiAlH_4$ (323 mg, 8.52 mmol) in 15 cm^3 of dry THF. The solution was stirred at room temp. for 1 h, then THF–H_2O 1:1 was slowly added at 0 °C to eliminate the excess of $LiAlH_4$. After addition of 5% HCl, the organic layer was separated, washed with brine and dried over Na_2SO_4. After filtration and concentration, the crude product was purified by flash chromatography on silica gel (eluent AcOEt–light petroleum 80:20) to give pure **10** as a white solid (663 mg, 2.3 mmol, yield 81%), mp 89–90 °C (Found: C, 70.5; H, 7.1. $C_{16}H_{18}O_4$ requires C, 70.8; H, 7.0%); δ_H(200 MHz) 1.80–2.10 (2 H, m, CH_2CH_2OH), 2.28 (1 H, br s, OH), 2.63 (1 H, br s, OH), 3.82 (2 H, t, *J* 5.6, CH_2CH_2OH), 3.88 (3 H, s, OCH_3), 4.86 (1 H, dd, *J* 8.5 and 3.8, CHOH), 5.13 (2 H, s, CH_2Ph), 6.78–6.85 (2 H, m, Ar), 6.94 (1 H, d, *J* 1.6, Ar), 7.28–7.43 (5 H, m, Ph); δ_C 40.4 (t, CH_2CH_2OH), 56.0 (q, OCH_3), 61.4 (t, CH_2CH_2OH), 71.1 (t, CH_2Ph), 74.1 (d, CHOH), 109.4 (d, Ar), 113.9 (d, Ar), 117.8 (d, Ar), 127.3 (2 d, Ph), 127.9 (d, Ph), 128.6 (2 d, Ph), 132.2 (s, Ar), 137.7 (s, Ar), 147.5 (s, Ar), 149.7 (s, Ar); *m*/*z* 288 (M$^+$, 15%), 270 (4), 243 (10), 180 (5), 149 (13), 123 (18), 95 (24), 91 (100), 77 (27), 73 (53), 65 (85).

Methyl {4-[1,3-bis(*tert*-butyldimethylsilyloxy)propyl]-2-methoxyphenoxy}acetate 5

To a solution of **10** (2.66 g, 9.23 mmol) and imidazole (6.28 g, 9.23 mmol) in dry DMF (9.2 cm^3) *tert*-butyldimethylsilyl chloride (6.96 g, 46.16 mmol) was added portionwise at room temp. and the mixture was stirred for 1 h. After addition of water and extraction with light petroleum (3 × 50 cm^3), the organic layer was washed with brine, dried and concentrated to give **11** as a colourless solid (4.46 g, 8.62 mmol, yield 94%), sufficiently pure to be used for the following step: δ_H(200 MHz) −0.14 (3 H, s, $SiCH_3$), 0.02 (3 H, s, $SiCH_3$), 0.04 (6 H, s, 2 × $SiCH_3$), 0.88 (9 H, s, Bu^t), 0.91 (9 H, s, Bu^t), 1.65–1.98 (2 H, m, CH_2CH_2OSi), 3.50–3.80 (2 H, m, CH_2CH_2OSi), 3.88 (3 H, s, OCH_3), 4.77 (1 H, dd, *J* 8.0 and 5.0, CHOSi), 5.14 (2 H, s, CH_2Ph), 6.70–6.84 (2 H, m, Ar), 6.93 (1 H, d, *J* 1.9, Ar), 7.28–7.47 (5 H, m, Ph).

A solution of **11** (4.46 g, 8.63 mmol) in EtOH (172 cm^3) was added to 10% Pd/C (274 mg) and hydrogenated at atmospheric pressure and 20 °C for 1 h and 30 min. The solution was filtered over Celite and concentrated to give the phenolic compound **12** (3.57 g, 8.37 mmol, yield 97%), sufficiently pure to be used for the following step: δ_H(200 MHz) −0.14 (3 H, s, $SiCH_3$), 0.015 (3 H, s, $SiCH_3$), 0.03 (6 H, s, 2 × $SiCH_3$), 0.87 (9 H, s, Bu^t), 0.90 (9 H, s, Bu^t), 1.64–1.98 (2 H, m, CH_2CH_2OSi), 3.50–3.80 (2 H, m, CH_2CH_2OSi), 3.87 (3 H, s, OCH_3), 4.76 (1 H, dd, *J* 7.9 and 5.0, CHOSi), 5.51 (1 H, br s, OH), 6.70–6.88 (3 H, m, Ar).

To a solution of **12** (3.57 g, 8.37 mmol) in dry acetone (14 cm^3) methyl α-bromoacetate (2.36 cm^3, 25.1 mmol) and anhydrous K_2CO_3 (3.47 g, 25.1 mmol) were added at room temperature. The mixture was heated at reflux for 40 h, then filtered

and washed with AcOEt and the filtrate concentrated to give a yellow oil. The oil was dissolved in AcOEt, washed with brine and the organic layer dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel (eluent AcOEt–light petroleum 10:90) to give **5** (2.90 g, 5.81 mmol, yield 70%) (Found: C, 60.3; H, 9.6. $C_{25}H_{46}O_6Si_2$ requires C, 60.2; H, 9.9%); δ_H(200 MHz) −0.15 (3 H, s, $SiCH_3$), 0.01 (3 H, s, $SiCH_3$), 0.03 (6 H, s, 2 × $SiCH_3$), 0.86 (9 H, s, Bu^t), 0.89 (9 H, s, Bu^t), 1.70–1.96 (2 H, m, C$H_2$$CH_2$OSi), 3.50–3.77 (2 H, m, CH_2CH_2OSi), 3.79 (3 H, s, CO_2CH_3), 3.86 (3 H, s, OCH_3), 4.67 (2 H, s, CH_2OAr), 4.76 (1 H, dd, *J* 7.8 and 4.9, CHOSi), 6.74 (2 H, s, Ar), 6.92 (1 H, s, Ar); δ_C −5.3 (2 q, 2 × $SiCH_3$), −5.1 (q, $SiCH_3$), −4.7 (q, $SiCH_3$), 18.1 (2 s, 2 × SiC), 25.8 (3 q, Bu^t), 25.9 (3 q, Bu^t), 44.0 (t, *C*$H_2$$CH_2$OSi), 52.1 (q, CO_2*C*H_3), 55.7 (q, OCH_3), 59.5 (t, CH_2*C*H_2OSi), 66.6 (t, *C*H_2OAr), 71.3 (d, CHOSi), 109.6 (d, Ar), 113.8 (d, Ar), 117.8 (d, Ar), 140.3 (s, Ar), 146.0 (s, Ar), 149.4 (s, Ar), 169.7 (s, *C*O_2CH_3); *m*/*z* 483 (M^+ −15, 2%), 413 (55), 339 (47), 325 (35), 235 (53), 189 (65), 147 (100), 131 (77), 91 (62), 89 (71), 73 (100).

(2*R**,3*R**)- and (2*R**,3*S**)-Methyl 3-(4-benzyloxy-3-methoxyphenyl)-2-[4-(1,3-dioxolan-2-yl)-2-methoxyphenoxy]-3-hydroxypropionate 15a,b

n-Butyllithium (4.55 cm^3 of a 1.6 M solution in hexanes, 7.28 mmol) was added at 0 °C to a solution of diisopropylamine (1.0 cm^3, 7.28 mmol) in dry THF (12 cm^3). After 20 min at 0 °C, a solution of **4** (1.74 g, 6.07 mmol) in dry THF (10 cm^3) was added dropwise at −78 °C and followed, after 10 min, by a solution of benzylvanillin (1.47 g, 6.07 mmol) in dry THF (5 cm^3). After 40 min at −78 °C, the reaction was quenched with saturated aqueous NH_4Cl (20 cm^3) and extracted with AcOEt (3 × 25 cm^3). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a viscous oil that contained the two diastereomers **15a** and **15b** in 72:28 diastereomeric ratio. Purification by flash chromatography on silica gel (eluent AcOEt–light petroleum 60:40) allowed the separation of the two diastereomers **15a** (R_f = 0.23, 1.59 g) and **15b** (R_f = 0.16, 0.63 g) in 72% overall yield.

Compound **15a** (Found: C, 64.9; H, 6.1. $C_{28}H_{30}O_9{\cdot}\frac{1}{2}H_2O$ requires C, 64.7; H, 6.0%); δ_H(200 MHz) 3.64 (3 H, s, CO_2CH_3), 3.70 (1 H, br d, *J* 5.0, OH), 3.83 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 3.96–4.18 (4 H, m, CH_2CH_2), 4.70 (1 H, d, *J* 5.2, C*H*CO_2CH_3), 5.13 (2 H, s, CH_2Ph), 5.14 (1 H, t, *J* 5.2, C*H*OH), 5.71 (1 H, s, CHO_2), 6.78–7.08 (6 H, m, Ar), 7.26–7.43 (5 H, m, Ph); δ_C 51.6 (q, CO_2*C*H_3), 55.4 (2 q, OCH_3), 64.7 (2 t, CH_2CH_2), 70.4 (t, CH_2Ph), 73.3 (d, *C*HCO_2CH_3), 82.9 (d, *C*HOH), 102.9 (d, CHO_2), 110.3 (d, Ar), 109.9 (d, Ar), 113.1 (d, Ar), 116.7 (d, Ar), 118.7 (d, Ar), 118.9 (d, Ar), 126.9 (2 d, Ph), 127.4 (d, Ph), 128.1 (2 d, Ph), 132.3 (s, Ar), 132.6 (s, Ar), 136.8 (s, Ar), 147.39 (s, Ar), 147.44 (s, Ar), 148.9 (s, Ar), 149.8 (s, Ar), 169.6 (s, *C*O_2CH_3); *m*/*z* 401 (M^+ − 91 − 18, 5%), 268 (19), 243 (20), 209 (96), 91 (100), 77 (5), 73 (33), 65 (5).

Compound **15b**: δ_H(200 MHz) 3.54 (3 H, s, CO_2CH_3), 3.85 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 3.96–4.18 (4 H, m, CH_2CH_2), 4.52 (1 H, d, *J* 6.5, C*H*CO_2CH_3), 5.05 (1 H, d, *J* 6.4, C*H*OH), 5.12 (2 H, s, CH_2Ph), 5.71 (1 H, s, CHO_2), 6.80–7.08 (6 H, m, Ar), 7.26–7.43 (5 H, m, Ph); δ_C 51.9 (q, CO_2*C*H_3), 55.6 (q, OCH_3), 55.7 (q, OCH_3), 65.0 (2 t, CH_2CH_2), 70.7 (t, CH_2Ph), 74.5 (d, *C*HCO_2CH_3), 84.5 (d, CHOH), 103.1 (d, CHO_2), 110.0 (d, Ar), 110.2 (d, Ar), 113.4 (d, Ar), 116.7 (d, Ar), 119.0 (d, Ar), 119.1 (d, Ar), 127.1 (2 d, Ph), 127.6 (d, Ph), 128.3 (2 d, Ph), 131.2 (s, Ar), 133.0 (s, Ar), 136.9 (s, Ar), 147.7 (s, Ar), 147.9 (s, Ar), 149.5 (s, Ar), 150.0 (s, Ar), 169.6 (s, Ar).

(1*R**,2*S**)-4-[1-(4-Benzyloxy-3-methoxyphenyl)-1,3-dihydroxypropan-2-yloxy]-3-methoxybenzaldehyde 17

$NaBH_4$ (1.39 g, 36.8 mmol) was added at room temp. portionwise in 6 h to a solution of **15a** (1.881 g, 3.68 mmol) in THF–H_2O 3:1 (36.8 cm^3). After 10 h at room temp., water (20 cm^3) was added, the aqueous solution extracted with Et_2O (3 × 50 cm^3) and the combined organic extracts washed, dried over Na_2SO_4, filtered and concentrated to give the product **16** (1.6 g, 3.31 mmol, yield 90%), sufficiently pure to be used for the next reaction: δ_H(200 MHz) 2.70 (1 H, br s, OH), 3.47 (1 H, br s, OH), 3.60–3.81 (2 H, m, CH_2OH), 3.87 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.00–4.20 (5 H, m, CH_2CH_2, C*H*CH_2OH), 4.93 (1 H, d, *J* 4.4, C*H*OH), 5.12 (2 H, s, CH_2Ph), 5.73 (1 H, s, CHO_2), 6.80–7.10 (6 H, m, Ar), 7.28–7.44 (5 H, m, Ph); δ_C 55.8 (q, OCH_3), 55.9 (q, OCH_3), 60.8 (t, CH_2OH), 65.2 (2 t, CH_2CH_2), 70.9 (t, CH_2Ph), 72.8 (d, *C*HCH_2OH), 86.2 (d, *C*HOH), 103.3 (d, CHO_2), 110.1 (d, Ar), 110.2 (d, Ar), 113.8 (d, Ar), 118.7 (d, Ar), 119.1 (d, Ar), 119.8 (d, Ar), 127.3 (2 d, Ph), 127.8 (d, Ph), 128.5 (2 d, Ph), 132.9 (s, Ar), 133.9 (s, Ar), 137.2 (s, Ar), 147.5 (s, Ar), 147.9 (s, Ar), 149.6 (s, Ar), 150.9 (s, Ar).

To a solution of **16** (347 mg, 0.72 mmol) in acetone–H_2O 4:1 (8.2 cm^3), PPTS (54 mg, 0.215 mmol) was added at room temp. and the mixture was heated at reflux for 4 h. After distillation of acetone, saturated aqueous $NaHCO_3$ was added and the aqueous solution extracted with Et_2O (3 × 10 cm^3). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated to give **17**, sufficiently pure to be used for the next reaction (306 mg, 0.698 mmol, yield 97%). Chromatography on silica gel (eluent AcOEt–light petroleum 70:30) gave an analytically pure sample of **17** (Found: C, 67.2; H, 6.2. $C_{25}H_{26}O_7{\cdot}\frac{1}{2}H_2O$ requires C, 67.1; H, 6.1%); δ_H(200 MHz) 2.4 (1 H, br s, OH), 3.2 (1 H, br s, OH), 3.79 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 3.78–3.98 (2 H, m, CH_2OH), 4.39 (1 H, dt, *J* 4.7 and 3.3, C*H*CH_2OH), 4.94 (1 H, d, *J* 4.7, C*H*OH), 5.08 (2 H, s, CH_2Ph), 6.79–7.00 (4 H, m, Ar), 7.27–7.43 (7 H, m, Ar, Ph), 9.77 (1 H, d, *J* 1, CHO); δ_C 55.7 (2 q, 2 × OCH_3), 60.3 (t, CH_2OH), 70.7 (t, CH_2Ph), 73.1 (d, *C*HCH_2OH), 84.3 (d, *C*HOH), 109.8 (d, Ar), 110.2 (d, Ar), 113.6 (d, Ar), 115.0 (d, Ar), 118.0 (d, Ar), 126.2 (d, Ar), 127.1 (2 d, Ph), 127.7 (d, Ph), 128.3 (2 d, Ph), 131.0 (s, Ar), 133.0 (s, Ar), 136.8 (s, Ar), 147.7 (s, Ar), 149.4 (s, Ar), 150.5 (s, Ar), 152.6 (s, Ar), 190.8 (d, CHO); *m*/*z* 438 (M^+, 2%), 299 (2), 242 (48), 178 (24), 151 (42), 123 (16), 91 (100), 77 (20), 65 (33).

(4*R**,5*S**)-4-[4-(4-Benzyloxy-3-methoxyphenyl)-2,2-dimethyl-1,3-dioxan-5-yloxy]-3-methoxybenzaldehyde 18 [16d]

To a solution of **17** (1.35 g, 3.08 mmol) in dry acetone (40 cm^3) anhydrous TsOH (59 mg, 0.308 mmol) was added at room temperature. After 1 h, molecular sieves 4 Å were added and the solution stirred vigorously for one more hour, followed by anhydrous Na_2CO_3 to quench the acidity. The solvent was then evaporated and the residue dissolved in Et_2O, washed with water, dried over Na_2SO_4, filtered and concentrated to leave a mixture of **18** and **17** in 70:30 ratio. Compound **18** was separated by flash chromatography on silica gel (eluent AcOEt–light petroleum 30:70) to give a white solid (895 mg, 1.87 mmol, conversion yield 61%, yield 70%), mp 140–141 °C (Found: C, 70.1; H, 6.4. $C_{28}H_{30}O_7$ requires C, 70.3; H, 6.3%); δ_H(200 MHz) 1.53 (3 H, s, CCH_3), 1.64 (3 H, s, CCH_3), 3.84 (6 H, s, 2 × OCH_3), 3.96–4.22 (2 H, m, CH_2OC), 4.33 (1 H, dt, *J* 9.1 and 5.3, C*H*CH_2O), 4.93 (1 H, d, *J* 9.1, CHOC), 5.11 (2 H, s, CH_2Ph), 6.60 (1 H, d, *J* 8.1, Ar), 6.79 (1 H, d, *J* 8.5, Ar), 6.94–7.04 (2 H, m, Ar), 7.19–7.40 (7 H, m, Ar, Ph), 9.78 (1 H, s, CHO); δ_C 19.6 (q, C*C*H_3), 28.4 (q, C*C*H_3), 55.8 (2 q, 2 × OCH_3), 62.3 (t, *C*H_2OC), 70.8 (t, CH_2Ph), 74.0 (d, *C*HCH_2O), 76.3 (d, *C*HOC), 99.6 [s, *C*$(CH_3)_2$], 109.77 (d, Ar), 110.8 (d, Ar), 113.7 (d, Ar), 114.4 (d, Ar), 119.3 (d, Ar), 126.0 (d, Ar), 127.1 (2 d, Ph), 127.7 (d, Ph), 128.4 (2 d, Ph), 130.8 (s, Ar), 131.8 (s, Ar), 137.0 (s, Ar), 147.9 (s, Ar), 149.4 (s, Ar), 150.4 (s, Ar), 153.4 (s, Ar), 190.7 (d, CHO); *m*/*z* 478 (M^+, 1%), 242 (49), 178 (31), 149 (18), 91 (100), 65 (15).

(1*R,2*S**)-1-(4-Hydroxy-3-methoxyphenyl)-2-(4-hydroxymethyl-2-methoxyphenoxy)propane-1,3-diol 19**

A solution of dimer **17** (460 mg, 1.05 mmol) in EtOH (21 cm^3) was added to 10% Pd/C (55.6 mg) and hydrogenated at atmospheric pressure and 20 °C for 4 h. The solution was filtered over Celite and concentrated to give quantitatively phenolic dimer **19** as a yellowish oil. The oil was purified by flash chromatography on silica gel (AcOEt–light petroleum 90:10) to obtain pure colourless **19** (312 mg, 0.89 mmol, yield 85%) (Found: C, 60.5; H, 6.8. $C_{18}H_{22}O_7\cdot\frac{1}{2}H_2O$ requires C, 60.2; H, 6.45%); δ_H(200 MHz) 3.40–3.72 (2 H, m, CHCH_2OH), 3.88 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.08–4.18 (1 H, m, CHCH$_2$OH), 4.65 (2 H, s, ArCH_2OH), 4.97 (1 H, d, *J* 4.4, CHOH), 5.62 (1 H, br s, ArOH), 6.79–7.00 (6 H, m, Ar); *m*/*z* 350 (M^+, 1%), 180 (100), 154 (28), 153 (38), 137 (46), 93 (51), 91 (16), 77 (22), 65 (41).

(2*R,3*R**,4′*R**,5′*S**,1″*R** and 1″*S**) and (2*R**,3*S**,4′*R**,5′*S**,1″*R** and 1″*S**)-Methyl 3-{4-[4′-(4-benzyloxy-3-methoxyphenyl)-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy]-3-methoxyphenyl}-2-{4-[1″,3″-bis(*tert*-butyldimethylsilyloxy)propyl]-2-methoxyphenoxy}-3-hydroxypropionate 20a,b**

n-Butyllithium (1.5 cm^3 of a 1.6 M solution in hexanes, 2.4 mmol) was added at 0 °C to a solution of diisopropylamine (0.34 cm^3, 2.4 mmol) in dry THF (5 cm^3). After 20 min at 0 °C, a solution of **5** (1.20 g, 2.4 mmol) in dry THF (5 cm^3) was added at −78 °C followed, after 10 min, by a solution of **18** (765 mg, 1.6 mmol) in dry THF (5 cm^3). After 30 min at −78 °C, saturated aqueous NH_4Cl (20 cm^3) was added and the mixture extracted with AcOEt (3 × 20 cm^3). The combined extracts were dried over Na_2SO_4, filtered and concentrated to give a viscous oil consisting of a mixture of the four possible diastereomeric compounds in 83:17 ratio of *anti* **20a**:*syn* **20b** (1.091 g, 1.12 mmol, yield after purification 70%) (Found: C, 64.9; H, 7.7. $C_{53}H_{76}O_{13}Si_2$ requires C, 65.1; H, 7.8%). By flash chromatography on silica gel (eluent AcOEt–light petroleum 20:80) it was possible to collect enriched fractions of the two inseparable *anti*-diastereomers **20a** which were used in the following steps for the synthesis of **6**.

Compound **20a**: (R_f = 0.07); δ_H(200 MHz), signals of the two *anti* major diastereomers, −0.16 (3 H, s, $SiCH_3$), 0.00 (3 H, s, $SiCH_3$), 0.03 (6 H, s, 2 × $SiCH_3$), 0.86 (9 H, s, Bu^t), 0.89 (9 H, s, Bu^t), 1.49 (3 H, s, CCH_3), 1.62 (3 H, s, CCH_3), 1.60–1.98 (2 H, m, CH_2CH$_2$OSi), 3.50–3.70 (2 H, m, CH$_2$CH_2OSi), 3.62 (3 H, s, CO_2CH_3), 3.73 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.97–4.19 (3 H, m, CHCH_2OC), 4.68 (1 H, d, *J* 4.4, CHCO$_2$CH$_3$), 4.76 (1 H, dd, *J* 7.2 and 5.0, CHOSi), 4.88 (1 H, d, *J* 8.4, CHOC), 5.05 (1 H, d, *J* 4.4, CHOH), 5.12 (2 H, s, CH$_2$Ph), 6.43 (1 H, dd, *J* 8.2 and 1.6, Ar), 6.65–7.05 (8 H, m, Ar), 7.26–7.43 (5 H, m, Ph); δ_C [signals of the two (*a*, *b*) *anti* major diastereomers] 5.4 (2 q, 2 × $SiCH_3$), −5.2 (q, $SiCH_3$), −4.7 (q, $SiCH_3$), 18.1 [2 s, 2 × $C(CH_3)_3$], 19.6 (q, CCH_3), 25.7 (3 q, Bu^t), 25.8 (3 q, Bu^t), 28.4 (q, CCH_3), 44.0 (t, CH_2CH_2OSi), 52.0 (q, CO_2CH_3), 55.7 (2 q, 2 × OCH_3), 55.9 (q, OCH_3), 59.4 (t, CH_2OSi), 62.8 (t, CH_2OC), 70.9 (t, CH_2Ph), 71.2 (d, CHOSi), 73.6 (d, $CHCO_2CH_3$), 74.4 (d, $CHCH_2O$), 77.2 (d, CHOC), 84.12 (d, *b*, CHOH), 84.17 (d, *a*, CHOH), 99.4 [s, $C(CH_3)_2$], 109.7 (d, Ar), 110.79 (d, *b*, Ar), 110.84 (d, *a*, Ar), 111.1 (d, Ar), 113.8 (d, Ar), 116.87 (d, *b*, Ar), 116.92 (d, *a*, Ar), 118.2 (d, Ar), 118.5 (d, Ar), 119.09 (d, *b*, Ar), 119.15 (d, *a*, Ar), 119.6 (d, Ar), 127.1 (2 d, Ph), 127.7 (d, Ph), 128.4 (2 d, Ph), 132.3 (s, Ar), 133.6 (s, Ar), 137.2 (s, Ar), 142.01 (s, *b*, Ar), 142.05 (s, *a*, Ar), 145.78 (s, *b*, Ar), 145.82 (s, *a*, Ar), 146.8 (s, Ar), 147.9 (s, Ar), 149.4 (s, Ar), 150.2 (s, Ar), 150.28 (s, *b*, Ar), 150.32 (s, *a*, Ar), 169.7 (s, CO_2CH_3).

Compound **20b**: (R_f = 0.05); δ_H(200 MHz) (detectable signals of the two *syn* minor diastereomers) 4.41 (1 H, d, *J* 7.2, CHCO$_2$CH$_3$), 4.99 (1 H, d, *J* 7.2, CHOH); δ_C [detectable signals of the two (*a*, *b*) *syn* minor diastereomers] 74.6 (d, $CHCO_2CH_3$), 85.32 (d, *b*, CHOH), 85.44 (d, *a*, CHOH), 169.8 (s, CO_2CH_3).

(1*R,2*S**,1′*R**,2′*S**,1″*S** and 1″*R**)-1-(4-Benzyloxy-3-methoxyphenyl)-2-(4-{2′-[4-(1″,3″-dihydroxypropyl)-2-methoxyphenoxy]-1′,3′-dihydroxypropyl}-2-methoxyphenoxy)propane-1,3-diol 23**

To a solution of **20a** (328 mg, 0.34 mmol) in THF–H_2O 3:1 (4 cm^3), $NaBH_4$ (39 mg, 1.02 mmol) was added at room temp. portionwise over a period of 3 h. After 24 h at room temperature, water (3 cm^3) was added, the aqueous solution extracted with Et_2O (3 × 10 cm^3), the combined extracts washed with water, dried over Na_2SO_4, filtered and concentrated to give the crude product **21** (313 mg, 0.33 mmol, yield 97%), which was used for the next reaction step without purification. Compound **21**: δ_H(200 MHz) 0.15 (3 H, s, $SiCH_3$), 0.015 (3 H, s, $SiCH_3$), 0.04 (6 H, s, 2 × $SiCH_3$), 0.87 (9 H, s, Bu^t), 0.89 (9 H, s, Bu^t), 1.49 (3 H, s, CCH_3), 1.62 (3 H, s, CCH_3), 1.63–1.90 (2 H, m, CH_2CH$_2$OSi), 2.70 (1 H, br s, OH), 3.40–3.90 (4 H, m, CH$_2$CH_2OSi, CH_2OH), 3.73 (3 H, s, OCH_3), 3.84 (6 H, s, 2 × OCH_3), 3.96–4.10 (4 H, m, CHCH$_2$OH, CHCH_2OC), 4.79 (1 H, dd, *J* 7.3 and 4.7, CHOSi), 4.84–4.92 (2 H, m, CHOH, CHOC), 5.12 (2 H, s, CH_2Ph), 6.41 (1 H, dd, *J* 8.2 and 1.6, Ar), 6.65 (1 H, d, *J* 8.2, Ar), 6.76–7.05 (7 H, m, Ar), 7.26–7.42 (5 H, m, Ph).

To a solution of **21** (313 mg, 0.33 mmol) in 3.3 cm^3 of dry THF, TBAF (0.82 cm^3 of a 1 M solution in THF, 0.82 mmol) was added at 0 °C and after 10 min the mixture was left at room temp. for 28 h. The solvent was removed *in vacuo*, the residue dissolved in AcOEt, washed with water, dried over Na_2SO_4, filtered and concentrated to give crude **22**. Purification by elution on a short pad of silica gel (AcOEt with 2% EtOH) afforded **22** as a yellowish viscous oil (187 mg, 0.26 mmol, yield 78%). Compound **22**: δ_H(200 MHz) 1.51 (3 H, s, CCH_3), 1.63 (3 H, s, CCH_3), 1.85–2.04 (2 H, m, CH_2CH$_2$OH), 3.40–3.72 (2 H, m, CH$_2$CH_2OH), 3.72 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.80–3.90 (2 H, m, CH_2OH), 4.03–4.18 (4 H, m, CHCH$_2$OH, CHCH_2OC), 4.85–4.94 (3 H, m, 2 × CHOH, CHOC), 5.13 (2 H, s, CH_2Ph), 6.41 (1 H, d, *J* 8.2, Ar), 6.65 (1 H, d, *J* 8.2, Ar), 6.78–6.88 (4 H, m, Ar), 6.95–7.03 (3 H, m, Ar), 7.26–7.43 (5 H, m, Ph).

To a solution of **22** (187 mg, 0.26 mmol) in acetone–H_2O 3:2 (5.2 cm^3), PPTS (33 mg, 0.13 mmol) was added at room temp. and the mixture was heated at reflux for 24 h. Acetone was removed *in vacuo*, saturated aqueous $NaHCO_3$ added and extracted with AcOEt (3 × 10 cm^3). The organic solution was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a crude oil, which was purified by flash chromatography on silica gel (eluent AcOEt with 5% EtOH) to give colourless **23** (158 mg, 0.23 mmol, yield 89%) (Found: C, 63.6; H, 6.6. $C_{37}H_{44}O_{12}\cdot H_2O$ requires C, 63.6; H, 6.6%); δ_H(200 MHz) 1.80–2.03 (2 H, m, CH_2CH$_2$OH), 2.34 (1 H, br s, OH), 2.80 (2 H, br s, 2 × OH), 3.18 (1 H, br s, OH), 3.53 (1 H, br s, OH), 3.60–3.80 (2 H, m, CH$_2$CH_2OH), 3.81–4.00 (4 H, m, 2 × CH_2OH), 3.86 (3 H, s, OCH_3), 3.88 (6 H, s, 2 × OCH_3), 4.04–4.27 (2 H, m, 2 × CHCH$_2$OH), 4.80–5.02 (3 H, m, 3 × CHOH), 5.15 (2 H, s, CH_2Ph), 6.80–7.03 (9 H, m, Ar), 7.27–7.43 (5 H, m, Ph); *m*/*z* (ES) 679.7 (M − H^-, 40%), 393.4 (100), 345.3 (20), 197.2 (41), 149.3 (9).

(1*R,2*S**,1′*R**,2′*S**,1″*S** and 1″*R**)-2-(4-{2′-[4-(1″,3″-Dihydroxypropyl)-2-methoxyphenoxy]-1′,3′-dihydroxypropyl}-2-methoxyphenoxy)-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol 6**

A solution of **23** (108 mg, 0.158 mmol) in EtOH (3.2 cm^3) was added to 10% Pd/C (10 mg) and hydrogenated at atmospheric pressure and 20 °C for 1 h. The solution was filtered over Celite,

concentrated and the residue purified by flash chromatography (gradient eluent AcOEt with 2% EtOH, AcOEt with 5% EtOH) to give the pure colourless trimeric compound **6** (77 mg, 0.13 mmol, yield 82%). The spectroscopic analysis of **6** (particularly ^{13}C NMR) shows the presence of many possible conformational equilibria in solution. Compound **6**: (Found: C, 59.1; H, 6.7. $C_{30}H_{38}O_{12}\cdot H_2O$ requires C, 59.2; H, 6.6%); δ_H(D_2O, 500 MHz) 1.69–1.80 (1 H, m, $\frac{1}{2}\times CH_2CH_2OH$), 1.81–1.90 (1 H, m, $\frac{1}{2}\times CH_2CH_2OH$), 3.38–3.75 (11 H, m, $3\times OCH_3$, CH_2OH), 3.77–3.93 (4 H, m, $2\times CH_2OH$), 4.35–4.48 (2 H, m, $2\times CHCH_2OH$), 4.53–4.68 (3 H, m, $3\times CHOH$), 6.55–6.90 (9 H, m, Ar); *m*/*z* (ES) 589.5 ($M-H^-$, 100%) 541.5 (68), 393.4 (34), 391.4 (44), 345.3 (28), 343.3 (62), 197.3 (28), 195.3 (71), 149.2 (20).

(2*R**,3*R**,4′*R**,5′*S**) and (2*R**,3*S**,4′*R**,5′*S**)-Methyl 3-{4-[4′-(4-Benzyloxy-3-methoxyphenyl)-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy]-3-methoxyphenyl}-2-[4-(1,3-dioxolan-2-yl)-2-methoxyphenoxy]-3-hydroxypropionate 24a,b

n-Butyllithium (5.33 cm^3 of a 1.6 M solution in hexanes, 8.53 mmol) was added to a solution of diisopropylamine (1.90 cm^3, 8.53 mmol) in dry THF (30 cm^3) at 0 °C. After 15 min at 0 °C, compound **4** (2.44 g, 8.53 mmol) in 25 cm^3 of dry THF was added dropwise at −78 °C. Compound **18** (2.72 g, 5.68 mmol) in dry THF (40 cm^3) was then added at −78 °C and after 1 h the reaction was quenched with saturated aqueous NH_4Cl. The mixture was extracted with Et_2O (3×100 cm^3), washed with brine and the organic layer dried over Na_2SO_4, filtered and concentrated to give a residue that consisted of the two diastereomers **24a** and **24b** in 77 : 23 ratio. Purification by flash chromatography on silica gel (eluent AcOEt–light petroleum 1 : 1) afforded diastereomers **24a** (2.92 g, $R_f = 0.24$) and **24b** (0.87 g, $R_f = 0.17$) as colourless oils in 89% overall yield.

Compound **24a** (Found: C, 64.05; H, 6.2. $C_{41}H_{46}O_{13}\cdot H_2O$ requires C, 64.4; H, 6.3%); δ_H(200 MHz) 1.51 (3 H, s, CCH_3), 1.63 (3 H, s, CCH_3), 3.58 (1 H, br d, *J* 5, OH), 3.64 (3 H, s, CO_2CH_3), 3.73 (3 H, s, OCH_3), 3.85 (6 H, s, $2\times OCH_3$), 4.00–4.20 (7 H, m, CH_2CH_2, $CHCH_2OC$), 4.68 (1 H, d, *J* 4.9, $CHCO_2CH_3$), 4.90 (1 H, d, *J* 8.4, CHOC), 5.06 (1 H, t, *J* 4.9, CHOH), 5.13 (2 H, s, CH_2Ph), 5.73 (1 H, s, CHO_2), 6.42 (1 H, dd, *J* 8.2 and 1.9, Ar), 6.74 (1 H, dt, *J* 8.2 and 2.2, Ar), 6.80–6.88 (2 H, m, Ar), 6.90–7.05 (5 H, m, Ar), 7.26–7.43 (5 H, m, Ph); δ_C 19.3 (q, CCH_3), 27.9 (q, CCH_3), 51.6 (q, CO_2CH_3), 55.2 (q, OCH_3), 55.3 (q, OCH_3), 55.4 (q, OCH_3), 62.3 (t, CH_2OC), 64.7 (2 t, CH_2CH_2), 70.4 (t, CH_2Ph), 73.2 (d, $CHCH_2O$), 74.0 (d, $CHCO_2CH_3$), 76.7 (d, CHOC), 82.8 (d, CHOH), 99.0 [s, $C(CH_3)_2$], 102.8 (d, CHO_2), 109.8 (d, Ar), 110.5 (d, Ar), 110.8 (d, Ar), 113.3 (d, Ar), 116.3 (d, Ar), 116.7 (d, Ar), 118.7 (d, Ar), 118.9 (d, Ar), 119.3 (d, Ar), 126.8 (2 d, Ph), 127.3 (d, Ph), 128.0 (2 d, Ph), 132.0 (s, Ar), 132.7 (s, Ar), 133.8 (s, Ar), 136.8 (s, Ar), 146.3 (s, Ar), 147.3 (s, Ar), 147.5 (s, Ar), 148.9 (s, Ar), 149.6 (s, Ar), 149.8 (s, Ar), 169.4 (s, CO_2CH_3).

Compound **24b**: δ_H(200 MHz) 1.51 (3 H, s, CCH_3), 1.63 (3 H, s, CCH_3), 3.54 (3 H, s, CO_2CH_3), 3.72 (3 H, s, OCH_3), 3.85 (6 H, s, $2\times OCH_3$), 3.98–4.20 (7 H, m, CH_2CH_2, $CHCH_2OC$), 4.46 (1 H, d, *J* 6.5, $CHCO_2CH_3$), 4.88 (1 H, d, *J* 8.3, CHOC), 5.00 (1 H, d, *J* 6.5, CHOH), 5.13 (2 H, s, CH_2Ph), 5.73 (1 H, s, CHO_2), 6.42 (1 H, d, *J* 8.3, Ar), 6.70 (1 H, d, *J* 8.4, Ar), 6.80–7.05 (7 H, m, Ar), 7.27–7.43 (5 H, m, Ph); δ_C 19.6 (q, CCH_3), 28.3 (q, CCH_3), 52.0 (q, CO_2CH_3), 55.6 (2 q, $2\times OCH_3$), 55.8 (q, OCH_3), 62.7 (t, CH_2OC), 65.1 (2 t, CH_2CH_2), 70.8 (t, CH_2Ph), 74.4 (2 d, $CHCO_2CH_3$, $CHCH_2O$), 77.1 (d, CHOC), 84.6 (d, CHOH), 99.4 [s, $C(CH_3)_2$], 103.2 (d, CHO_2), 110.0 (d, Ar), 110.5 (d, Ar), 111.0 (d, Ar), 113.6 (d, Ar), 116.8 (d, Ar), 118.9 (d, Ar), 119.2 (d, Ar), 119.3 (d, Ar), 119.5 (d, Ar), 127.1 (2 d, Ph), 127.7 (d, Ph), 128.4 (2 d, Ar), 132.2 (s, Ar), 132.7 (s, Ar), 133.3 (s, Ar), 137.1 (s, Ar), 146.9 (s, Ar), 147.7 (s, Ar), 147.8 (s, Ar), 149.3 (s, Ar), 150.1 (s, Ar), 150.3 (s, Ar), 169.6 (s, CO_2CH_3).

(1*R**,2*S**,4′*R**,5′*S**)-1-{4-[4′-(4-Benzyloxy-3-methoxyphenyl)-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy]-3-methoxyphenyl}-2-[4-(1,3-dioxolan-2-yl)-2-methoxyphenoxy]propane-1,3-diol 25

To a solution of **24a** (3 g, 3.92 mmol) in 39 cm^3 of THF–H_2O 3 : 1, $NaBH_4$ (1.04 g, 27.44 mmol) was added at room temp. portionwise over a period of 5 h. After 20 h at room temperature, water was added, the aqueous solution was extracted with Et_2O (3×40 cm^3) and the combined extracts washed with water, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give **25** (2.60 g, 3.62 mmol, yield 92%), sufficiently pure to be used for the next reaction (Found: C, 64.9; H, 6.3. $C_{40}H_{46}O_{12}\cdot H_2O$ requires C, 65.2; H, 6.6%); δ_H(200 MHz) 1.50 (3 H, s, CCH_3), 1.63 (3 H, s, CCH_3), 3.55 (2 H, m, CH_2OH), 3.72 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.00–4.19 (8 H, m, CH_2CH_2, $CHCH_2OH$, $CHCH_2OC$), 4.88 (2 H, d, *J* 4.8, CHOH, CHOC), 5.12 (2 H, s, CH_2Ph), 5.75 (1 H, s, CHO_2), 6.42 (1 H, d, *J* 8.2, Ar), 6.63 (1 H, d, *J* 8.4, Ar), 6.79–6.87 (2 H, m, Ar), 6.90–7.08 (5 H, m, Ar), 7.27–7.43 (5 H, m, Ph); δ_C 19.6 (q, CCH_3), 28.5 (q, CCH_3), 55.8 (q, OCH_3), 55.9 (2 q, $2\times OCH_3$), 60.6 (t, CH_2OH), 62.8 (t, CH_2OC), 65.3 (2 t, CH_2CH_2), 70.9 (t, CH_2Ph), 72.5 (d, $CHCH_2OC$), 74.6 (d, $CHCH_2OH$), 77.2 (d, CHOC), 87.4 (d, CHOH), 99.5 (s, $C(CH_3)_2$), 103.3 (d, CHO_2), 109.9 (d, Ar), 110.0 (d, Ar), 111.1 (d, Ar), 113.8 (d, Ar), 117.4 (d, Ar), 118.2 (d, Ar), 119.8 (d, Ar), 120.0 (d, Ar), 120.7 (d, Ar), 127.2 (2 d, Ph), 127.8 (d, Ph), 128.5 (2 d, Ph), 132.3 (s, Ar), 133.9 (s, Ar), 134.3 (s, Ar), 137.2 (s, Ar), 146.5 (s, Ar), 147.5 (s, Ar), 147.9 (s, Ar), 149.4 (s, Ar), 150.5 (s, Ar), 151.6 (s, Ar).

(4*R**,5*S**,4′*R**,5′*S**)-4-(4′-{4-[4″-(4-Benzyloxy-3-methoxyphenyl)-2″,2″-dimethyl-1″,3″-dioxan-5″-yloxy]-3-methoxyphenyl}-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy)-3-methoxybenzaldehyde 27

A solution of **25** (2.56 g, 3.56 mmol), 2,2-dimethoxypropane (1.75 cm^3, 14.24 mmol) and a catalytic amount of TsOH (27 mg) in dry DMF (4.75 cm^3) were stirred at room temp. for 2 h. Saturated aqueous $NaHCO_3$ (5 cm^3) was added, the aqueous layer extracted with AcOEt (3×10 cm^3), dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the crude compound **26** (2.64 g): δ_H(200 MHz) 1.49 (6 H, s, $2\times CCH_3$), 1.61 (6 H, s, $2\times CCH_3$), 3.28 (6 H, s, $2\times OCH_3$), 3.69 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.96–4.20 (6 H, m, $2\times CH_2OC$, $2\times CHCH_2OC$), 4.86 (2 H, t, *J* 7.3, $2\times CHOC$), 5.13 (2 H, s, CH_2Ph), 5.23 [1 H, s, $CH(OCH_3)_2$], 6.40–6.48 (2 H, m, Ar), 6.74–7.05 (7 H, m, Ar), 7.27–7.42 (5 H, m, Ph).

An aqueous solution of 10% oxalic acid (0.79 g, 29 drops) was added with continuous magnetic stirring to a suspension of silica gel (7.92 g, silica gel 60, Merck, for column chromatography, 70–230 mesh) in CH_2Cl_2 (10.6 cm^3). After 5 min, the water phase disappeared due to the absorption on the silica gel surface. The crude compound **26** (2.64 g, 3.47 mmol) was added and stirring was continued at room temp. for 1 h. After neutralization with $NaHCO_3$, the solid phase was separated by suction filtration and the solid was washed several times with CH_2Cl_2. Evaporation of the solvent under reduced pressure gave compound **27**, which was purified by flash chromatography on silica gel (eluent AcOEt–light petroleum 1 : 1) to afford the pure aldehyde **27** (1.86 g, 2.60 mmol, yield from **25** 73%) (Found: C, 68.6; H, 6.65. $C_{41}H_{46}O_{11}$ requires C, 68.9; H, 6.5%); δ_H(200 MHz) 1.49 (3 H, s, CCH_3), 1.52 (3 H, s, CCH_3), 1.61 (3 H, s, CCH_3), 1.62 (3 H, s, CCH_3), 3.68 (3 H, s, OCH_3), 3.83 (6 H, s, $2\times OCH_3$), 3.92–4.38 (6 H, m, $2\times CH_2OC$, $2\times CHCH_2OC$), 4.87 (1 H, d, *J* 8.4, CHOC), 4.89 (1 H, d, *J* 8.7, CHOC), 5.13 (2 H, s, CH_2Ph), 6.40 (1 H, dd, *J* 8.2 and 3.1, Ar), 6.58 (1 H, dd, *J* 8.2 and 2.7, Ar), 6.79–7.04 (5 H, m, Ar), 7.21 (1 H, dt, *J* 8.1 and 1.9, Ar), 7.27–7.43 (6 H, m, Ph, Ar), 9.77 (1 H, d, *J* 1.8,

CHO); δ_C 19.6 (2 q, 2 × CCH_3), 28.2 (q, CCH_3), 28.4 (q, CCH_3), 55.6 (q, OCH_3), 55.8 (2 q, 2 × OCH_3), 62.2 (t, CH_2OC), 62.7 (t, CH_2OC), 70.9 (t, CH_2Ph), 73.8 (d, $CHCH_2OC$), 74.3 (d, $CHCH_2OC$), 76.2 (d, *C*HOC), 77.2 (d, *C*HOC), 99.4 [s, $C(CH_3)_2$], 99.7 [s, $C(CH_3)_2$], 109.7 (d, Ar), 111.1 (d, Ar), 113.8 (d, Ar), 114.3 (d, Ar), 117.0 (d, Ar), 117.1 (d, Ar), 119.3 (d, Ar), 119.5 (d, Ar), 126.0 (d, Ar), 127.2 (2 d, Ph), 127.7 (d, Ph), 128.5 (2 d, Ph), 130.9 (s, Ar), 132.4 (s, Ar), 133.3 (s, Ar), 137.2 (s, Ar), 146.9 (s, Ar), 147.8 (s, Ar), 149.4 (s, Ar), 150.1 (s, Ar), 150.3 (s, Ar), 152. 3 (s, Ar), 190.7 (d, CHO).

(2*R**,3*R**,4′*R**,5′*S**,4″*R**,5″*S**,1‴*S** and 1‴*R**) and (2*R**,3*S**,4′*R**,5′*S**,4″*R**,5″*S**,1‴*S** and 1‴*R**)-Methyl 3-[4-(4′-{4-[4″-(4-benzyloxy-3-methoxyphenyl)-2″,2″-dimethyl-1″,3″-dioxan-5″-yloxy]-3-methoxyphenyl}-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy)-3-methoxyphenyl]-2-{4-[1‴,3‴-bis(*tert*-butyldimethylsilyloxy)propyl]-2-methoxyphenoxy}-3-hydroxypropionate 28a,b

n-Butyllithium (2 cm³ of a 1.6 M solution in hexanes, 3.19 mmol) was added at 0 °C to a solution of diisopropylamine (0.45 cm³, 3.19 mmol) in dry THF (5 cm³). After 20 min at 0 °C, a solution of **5** (1.21 g, 2.39 mmol) in dry THF (7 cm³) was added at −78 °C followed after 10 min by a solution of **27** (1.14 g, 1.59 mmol) in dry THF (8 cm³). After 30 min at −78 °C, saturated aqueous NH_4Cl (20 cm³) was added to the mixture and then extracted with Et_2O (3 × 30 cm³). The combined extracts were dried over Na_2SO_4, filtered and concentrated to give a viscous oil consisting of a mixture of the four possible diastereomeric tetrameric compounds in 80:20 ratio of *anti* **28a**:*syn* **28b** (1.36 g, 1.12 mmol, yield after purification 71%) (Found: C, 65.1; H, 7.7. $C_{66}H_{92}O_{17}Si_2$ requires C, 65.3, H, 7.6%). By flash chromatography on silica gel (eluent AcOEt–light petroleum 40:60) it was possible to collect the enriched fractions of the two *anti*-diastereomers **28a**, which were used in the following steps for the synthesis of **7**.

Compound **28a** (R_f = 0.38); δ_H(600 MHz) (signals of the two *anti* major diastereomers) −0.15 (3 H, s, $SiCH_3$), 0.02 (3 H, s, $SiCH_3$), 0.038 (3 H, s, $SiCH_3$), 0.044 (3 H, s, $SiCH_3$), 0.88 (9 H, s, Bu^t), 0.90 (9 H, s, Bu^t), 1.50 (6 H, s, 2 × CCH_3), 1.61 (3 H, s, CCH_3), 1.62 (3 H, s, CCH_3), 1.68–1.75 (1 H, m, $\frac{1}{2}CH_2CH_2OSi$), 1.83–1.89 (1 H, m, $\frac{1}{2}CH_2CH_2OSi$), 3.65–3.77 (2 H, m, CH_2CH_2OSi), 3.64 (3 H, s, OCH_3), 3.68 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.91–4.17 (6 H, m, 2 × CH_2OC, 2 × $CHCH_2OC$), 4.65 (1 H, m, $CHCO_2CH_3$), 4.77 (1 H, dd, *J* 7.7 and 4.7, CHOSi), 4.83 (1 H, d, *J* 9.0, CHOC), 4.87 (1 H, d, *J* 9.1, CHOC), 5.04 (1 H, m, *C*HOH), 5.14 (2 H, s, CH_2Ph), 6.38–6.45 (2 H, m, Ar), 6.69–6.77 (3 H, m, Ar), 6.83–7.01 (6 H, m, Ar), 7.06 (1 H, s, Ar), 7.29 (1 H, d, *J* 7.5, Ph), 7.34 (2 H, t, *J* 7.7, Ph), 7.41 (2 H, d, *J* 7.9, Ph); δ_C(200 MHz) [only detectable signals of the two (*a*, *b*) *anti* major diastereomers] −5.4 (2 q, 2 × $SiCH_3$), −5.1 (q, $SiCH_3$), −4.7 (q, $SiCH_3$), 18.1 [2 s, $C(CH_3)_3$], 19.6 (2 q, 2 × CCH_3), 25.8 (3 q, Bu^t), 25.9 (3 q, Bu^t), 28.4 (2 q, 2 × CCH_3), 44.0 (t, CH_2CH_2OSi), 52.0 (q, CO_2CH_3), 55.7 (3 q, 3 × OCH_3), 55.9 (q, OCH_3), 59.4 (t, CH_2OSi), 62.7 (2 t, 2 × CH_2OC), 70.9 (t, CH_2Ph), 71.2 (d, CHOSi), 73.5 (d, $CHCO_2CH_3$), 74.4 (2 d, 2 × $CHCH_2OC$), 76.79 (d, *b*, CHOC), 76.78 (d, *a*, CHOC), 77.41 (d, *b*, CHOC), 77.42 (d, *a*, CHOC), 84.0 (d, CHOH), 99.4 [2 s, 2 × $C(CH_3)_2$], 109.7 (d, Ar), 111.1 (d, Ar), 113.8 (d, Ar), 118.2 (d, Ar), 119.6 (d, Ar), 127.2 (2 d, Ph), 127.7 (d, Ph), 128.5 (2 d, Ph), 132.4 (s, Ar), 133.9 (s, Ar), 134.0 (s, Ar), 137.2 (s, Ar), 141.8 (s, Ar), 145.8 (s, Ar), 146.5 (s, Ar), 146.7 (s, Ar), 147.9 (s, Ar), 149.4 (s, Ar), 150.2 (s, Ar), 169.9 (s, CO_2CH_3).

Compound **28b** (R_f = 0.34); δ_H(600 MHz) (detectable signals of the two *syn* minor diastereomers) 4.43 (1 H, m, $CHCO_2CH_3$), 5.00 (1 H, m, *C*HOH); δ_C, detectable signal of the *syn* minor diastereomers, 85.1 (d, CHOH).

(1*R**,2*S**,4′*R**,5′*S**,4″*R**,5″*S**,1‴*S** and 1‴*R**)-1-[4-(4′-{4-[4″-(4-Benzyloxy-3-methoxyphenyl)-2″,2″-dimethyl-1″,3″-dioxan-5″-yloxy]-3-methoxyphenyl}-2′,2′-dimethyl-1′,3′-dioxan-5′-yloxy)-3-methoxyphenyl]-2-{4-[1‴,3‴-bis(*tert*-butyldimethylsilyloxy)-propyl]-2-methoxyphenoxy}propane-1,3-diol 29

To a solution of **28a** (400 mg, 0.33 mmol) in 3.3 cm³ of THF–H_2O 3:1, $NaBH_4$ (85 mg, 2.31 mmol) was added portionwise at room temp. over a period of 5 h. After 24 h at room temperature, water was added and the aqueous solution was extracted with AcOEt (3 × 5 cm³). The combined extracts were washed with water, dried over Na_2SO_4, filtered and concentrated *in vacuo* to give **29** (367 mg, 0.31 mmol, yield 94%), sufficiently pure to be used for the next reaction (Found: C, 64.9; H, 7.8. $C_{65}H_{92}O_{16}Si_2 \cdot H_2O$ requires C, 64.9; H, 7.7%); δ_H(200 MHz) −0.14 (3 H, s, $SiCH_3$), 0.03 (3 H, s, $SiCH_3$), 0.05 (6 H, s, 2 × $SiCH_3$), 0.88 (9 H, s, Bu^t), 0.91 (9 H, s, Bu^t), 1.49 (6 H, s, 2 × CCH_3), 1.61 (6 H, s, 2 × CCH_3), 1.70–1.98 (2 H, m, CH_2CH_2OSi), 2.84 (1 H, br s, OH), 3.64–3.50 (2 H, m, CH_2OSi), 3.65–3.80 (2 H, m, CH_2OH), 3.68 (3 H, s, OCH_3), 3.71 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.92–4.17 (7 H, m, 2 × $CHCH_2OC$, $CHCH_2OH$), 4.78–4.89 (4 H, m, 2 × *C*HOC, *C*HOH, *C*HOSi), 5.13 (2 H, s, CH_2Ph), 6.38–6.46 (2 H, m, Ar), 6.60–7.06 (10 H, m, Ar), 7.27–7.43 (5 H, m, Ph); δ_C [only detectable signals of the two (*a*, *b*) *anti* diastereomers] −5.4 (2 q, 2 × $SiCH_3$), −5.2 (q, $SiCH_3$), −4.8 (q, $SiCH_3$), 18.1 [2 s, 2 × $C(CH_3)_3$], 19.5 (2 q, 2 × CCH_3), 25.7 (3 q, Bu^t), 25.8 (3 q, Bu^t), 28.3 (2 q, 2 × CCH_3), 43.9 (t, CH_2CH_2OSi), 55.6 (3 q, 3 × OCH_3), 55.8 (q, OCH_3), 59.4 (t, CH_2OSi), 60.6 (t, CH_2OH), 62.7 (2 t, 2 × CH_2OC), 70.8 (t, CH_2Ph), 71.1 (d, CHOSi), 72.4 (d, $CHCH_2OH$), 74.3 (d, $CHCH_2OC$), 74.4 (d, $CHCH_2OC$), 76.71 (d, *b*, CHOC), 76.77 (d, *a*, CHOC), 77.2 (d, *b*, CHOC), 77.3 (d, *a*, CHOC), 87.0 (d, CHOH), 99.4 [2 s, 2 × $C(CH_3)_2$], 109.5 (d, Ar), 111.0 (d, Ar), 113.7 (d, Ar), 118.6 (d, Ar), 119.6 (d, Ar), 127.1 (2 d, Ph), 127.6 (d, Ph), 128.4 (2 d, Ph), 132.3 (s, Ar), 133.8 (s, Ar), 133.9 (s, Ar), 134.8 (s, Ar), 137.1 (s, Ar), 142.0 (s, Ar), 145.4 (s, Ar), 146.1 (s, Ar), 146.7 (s, Ar), 147.8 (s, Ar), 149.3 (s, Ar), 150.1 (s, Ar), 151.1 (s, Ar).

(1*R**,2*S**,1′*R**,2′*S**,1″*R**,2″*S**,1‴*S** and 1‴*R**)-1-(4-Benzyloxy-3-methoxyphenyl)-2-{4-[2′-(4-{2″-[4-(1‴,3‴-dihydroxypropyl)-2-methoxyphenoxy]-1″,3″-dihydroxypropyl}-2-methoxyphenoxy)-1′,3′-dihydroxypropyl]-2-methoxyphenoxy}propane-1,3-diol 31

To a solution of **29** (340 mg, 0.29 mmol) in 1 cm³ of dry THF, TBAF (1.16 cm³ of a 1 M solution in THF, 1.16 mmol) was added at 0 °C and after 10 min the mixture was stirred at room temp. for 20 h. The solvent was then evaporated and the residue dissolved in AcOEt. The organic layer was washed with water, dried over Na_2SO_4, filtered and concentrated to give an oil, which was purified by elution on a short pad of silica gel (AcOEt with 3% EtOH) to afford **30** (220 mg, 0.23 mmol, yield 79%): δ_H(200 MHz) 1.49 (6 H, s, 2 × CCH_3), 1.61 (6 H, s, 2 × CCH_3), 1.80–1.96 (2 H, m, CH_2CH_2OH), 3.00 (4 H, br s, 4 × OH), 3.45–3.81 (4 H, m, 2 × CH_2OH), 3.68 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 3.82 (6 H, s, 2 × OCH_3), 3.90–4.10 (7 H, m, 2 × $CHCH_2OC$, 2 × $CHCH_2OH$), 4.79–4.90 (4 H, m, 2 × *C*HOH, 2 × *C*HOC), 5.11 (2 H, s, CH_2Ph), 6.36–6.43 (2 H, m, Ar), 6.60–7.04 (10 H, m, Ar), 7.27–7.43 (5 H, m, Ph).

To a solution of **30** (220 mg, 0.23 mmol) in acetone–H_2O 1:1 (2.3 cm³), PPTS (28 mg, 0.11 mmol) was added at room temp. and the mixture was heated at reflux for 20 h. Acetone was removed *in vacuo* to give an oil which was purified by flash chromatography on silica gel (eluent AcOEt with 10% EtOH) to give pure **31** (166 mg, 0.19 mmol, yield 83%) (Found: C, 61.6; H, 6.4. $C_{47}H_{56}O_{16} \cdot 2H_2O$ requires C, 61.8; H, 6.6%); δ_H(200 MHz) 1.80–2.08 (2 H, m, CH_2CH_2OH), 3.60–3.76 (2 H, m, CH_2CH_2OH), 3.79–4.00 (6 H, m, 3 × CH_2OH), 3.86 (3 H, s, OCH_3), 3.88 (9 H, s, 3 × OCH_3), 4.12–4.19 (3 H, m, 3 ×

C*H*CH_2OH), 4.92 (4 H, br s, 4 × C*H*OH), 5.14 (2 H, s, CH_2Ph), 6.75–7.03 (12 H, m, Ar), 7.27–7.45 (5 H, m, Ph); *m*/*z* (ES) 875.9 ($M - H^-$, 100%), 677.7 (10), 589.5 (35), 393.4 (37), 197.2 (11).

(1*R,2*S**,1′*R**,2′*S**,1″*R**,2″*S**,1‴*S** and 1‴*R**)-2-{4-[2′-(4-{2″-[4-(1‴,3‴-Dihydroxypropyl)-2-methoxyphenoxy]-1″,3″-dihydroxypropyl}-2-methoxyphenoxy)-1′,3′-dihydroxypropyl]-2-methoxyphenoxy}-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol 7**

A solution of **31** (98 mg, 0.112 mmol) in EtOH (2.2 cm^3) was added to 10% Pd/C (12 mg) and hydrogenated at atmospheric pressure and 20 °C for 1.5 h. The solution was filtered over Celite, concentrated to give a viscous oil, which was purified by flash chromatography (gradient eluent AcOEt with 10% EtOH, AcOEt with 15% EtOH and 2% NH_3) to give pure colourless tetramer **7** (79 mg, 0.10 mmol, yield 90%). The spectroscopic analysis of **6** (particularly ^{13}C NMR) shows the presence of many possible conformational equilibria in solution. Compound **7** (Found: C, 59.1; H, 6.6. $C_{40}H_{50}O_{16}\cdot 1.5H_2O$ requires C, 59.0; H, 6.6%); δ_H(D_2O, 500 MHz) 1.67–1.80 (1 H, m, ½ × C*H*$_2$$CH_2OH$), 1.81–1.91 (1 H, m, ½ × C*H*$_2$$CH_2OH$), 3.32–3.62 (14 H, m, 4 × OCH_3, CH_2C*H*$_2$OH), 3.74–3.94 (6 H, m, 3 × C*H*$_2$OH), 4.32–4.48 (3 H, m, 3 × C*H*CH_2OH), 4.50–4.69 (4 H, m, 4 × C*H*OH), 6.50–6.88 (12 H, m, Ar); *m*/*z* (ES) 785.7 ($M - H^-$, 100%) 379.1 (33), 363.1 (14), 285.1 (37), 269.1 (13), 191.1 (23).

Acknowledgements

We would like to thank Professor I. Bertini for helpful discussions. Valuable suggestions on the synthetic procedure from Professor G. Brunow and Professor B. Rindone are warmly acknowledged. Discussions with Professor M. Tien on the mechanism of peroxidases have been fruitful. The study has been carried out with financial support from the Commission of the European Communities, Agriculture and Fisheries (FAIR) specific RTD programme, CT95-0805, "OXEPI". It does not necessarily reflect its views and in no way anticipates the Commission's future policy in this area. We thank also Professor G. Moneti (Centro interdipartimentale di Spettrometria di Massa) for performing the MS-ES experiments and Mr S. Papaleo for MS experiments.

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