Synthesis and crystal structure determination of model compounds for the dibenzodioxocine structure occurring in wood lignins

Pirkko Karhunen, Petteri Rummakko, Aarne Pajunen and Gösta Brunow *

Department of Chemistry, PO Box 55, FIN-00014, University of Helsinki, Finland

Model compounds for the dibenzodioxocine structure, a new structural unit recently discovered in wood lignins, have been synthesised by two different methods. In one route, the 8-membered ring is formed by ring closure of an arylglycerol β-aryl ether with a 5,5′-biphenyl structure in the aryl ether moiety. The other, which gave better yields, involves a biomimetic oxidative phenol coupling. Crystal structures have been obtained for one β-aryl ether and of two dibenzodioxocine isomers, as well as of a product of acid hydrolysis containing a 7-membered ring structure.

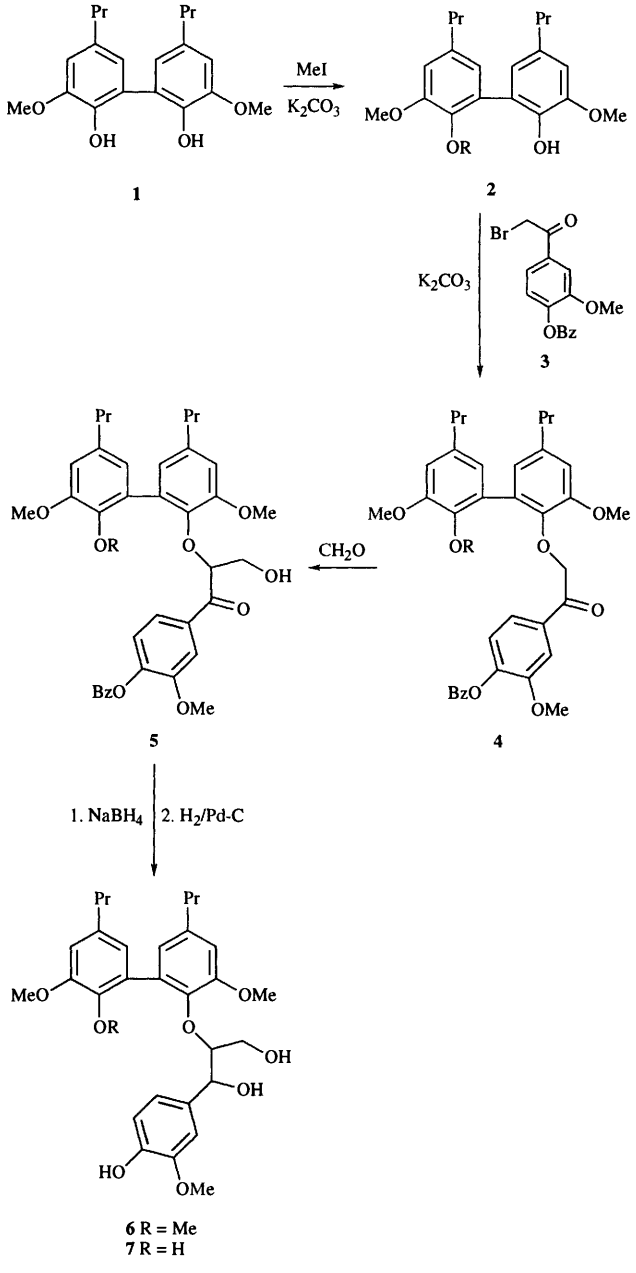
An important feature of the chemical structure of wood lignins is the *o*,*o*-dihydroxybiphenyl structures that are especially prominent in softwood lignins. We have recently [1] discovered that a large part of these structures is, in fact, connected by ether bonds to phenylpropane units in the lignin, forming 8-membered ring structures. The discovery of these dibenzodioxocine structures may have important consequences for the understanding of lignin reactivity both in pulping processes and in the biodegradation of wood. For the purpose of obtaining data for the spectroscopic determination of such structures and for studying their reactivity, we have explored two synthetic routes to the dibenzodioxocine structure. In the first, we built an arylglycerol β-aryl ether with a 5,5′-biphenyl in the aryl ether moiety, using conventional methods.[2] The *threo* isomer of this novel β-ether structure crystallised in a form that allowed crystal structure determination (Fig. 1). Although a quinomethane methide generated from this phenolic benzyl alcohol (Scheme 1) did form the expected 8-membered ring it was in low yield, the main product being a 7-membered ring diphenylmethane structure formed by acid catalysis. A second route [3] using a biomimetic oxidative phenol coupling proved more useful for the preparation of these dibenzodioxocines. The dibenzodioxocines are formed as a mixture two diastereoisomers. The crystal structures of two such isomers have been obtained (Figs. 2 and 4).

The synthesis of the β-aryl ethers

The starting material was propylguaiacol (made from commercial isoeugenol by hydrogenation) which was dimerised to the biphenyl **1**. In a first approach, compound **1** was monomethylated to **2** (R = Me) and treated with the α-bromo ketone **3** to give **4** (R = Me) (Scheme 1). Reaction with formaldehyde, borohydride reduction and debenzylation afforded crystalline compound **6**, the structure of which was determined by X-ray crystallography and shown to have a *threo* configuration (Fig. 1). The reduction with sodium borohydride seems to be strongly *threo* selective in this case. We then found that the β-aryl ether could be prepared without protecting one of the phenolic groups in **1**. Reaction of **1** with the bromo ketone **3** gave a nearly quantitative yield of **4** (R = H), reaction of which with formaldehyde followed by borohydride reduction and debenzylation gave in this case a 1 : 1 mixture of *erythro* and *threo* isomers of **7**.

The ring closure

To test whether an 8-membered ring structure could be formed *via* a quinomethane (Scheme 2) ketone **4** (R = H) was reduced to **8** and treated with trimethylsilyl bromide, followed



Scheme 1

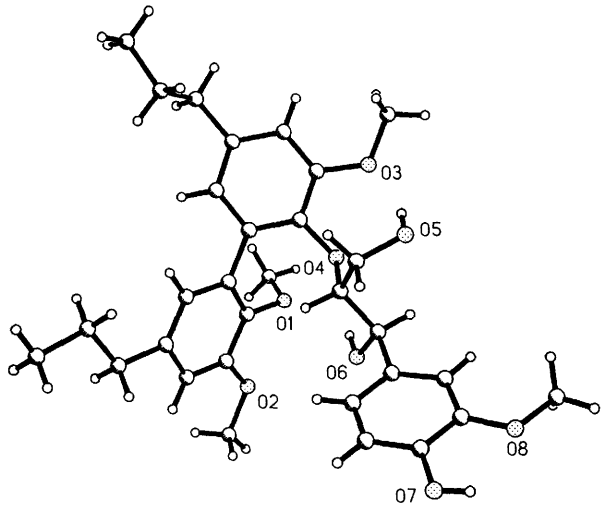
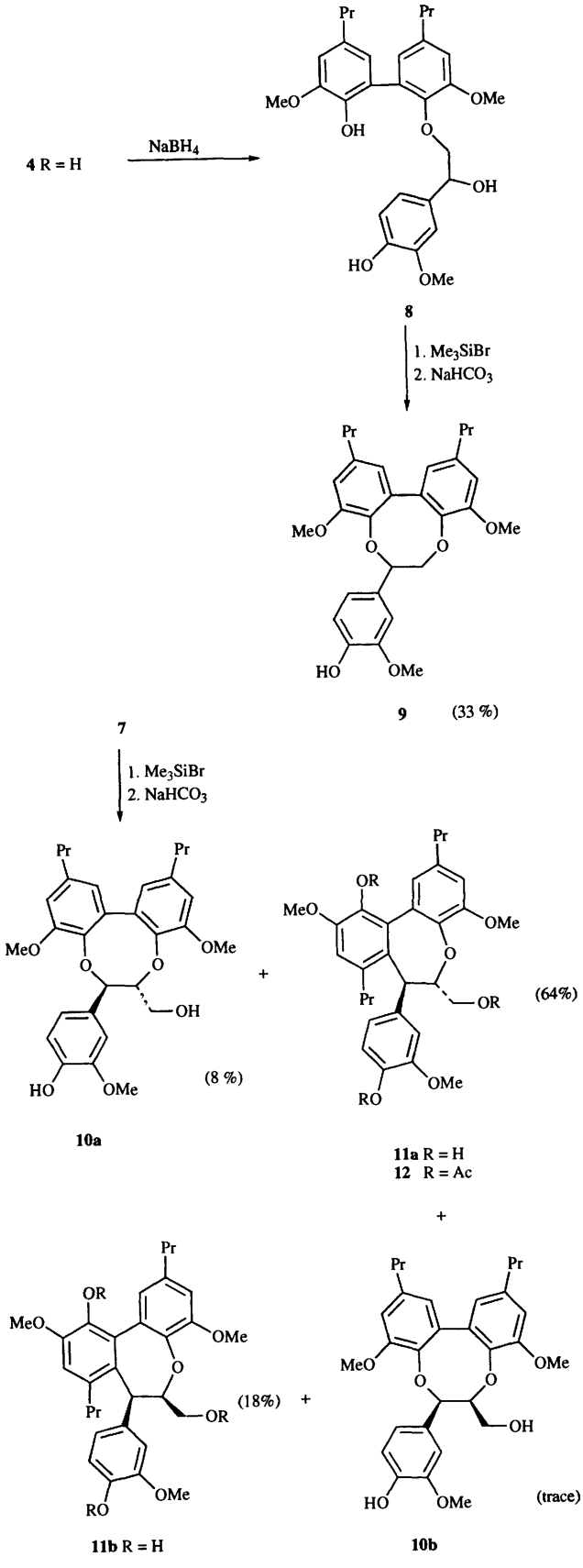


Fig. 1 The crystal structure of compound **6**

by sodium hydrogen carbonate. The solution was evaporated to dryness and acetylated. Chromatographic work-up yielded crystalline **9** (33%). This demonstrates that ring closure can occur *via* a quinomethane. When compound **7** was treated in the same way as **8**, the corresponding dibenzodioxocine derivative **10a** was isolated in 8% yield. The main product (82% yield) in the latter reaction was a mixture of two diastereoisomers **11a** and **11b** (64 and 18%, respectively); the peracetate of the more abundant isomer, obtained in crystalline form, was subjected to X-ray analysis and shown to have the 7-membered ring structure **12** (Fig. 3). The formation of this product probably occurs under the acidic conditions of the TMSBr treatment: treatment of **7** with toluene-*p*-sulfonic acid in dioxane yielded a similar mixture of products **10** and **11**. A benzyl cation is probably formed more readily from **7** than from **8**, and reacts with an adjacent aromatic ring forming the diphenylmethane structure in **11**.

The oxidative coupling

In the phenol oxidation method a practical problem is the optimisation of the conditions for the cross-coupling of the *o*,*o*-dihydroxybiphenyl compound with coniferyl alcohol (Scheme 3). The concentrations of phenoxyl radicals from the two species have to be of the same magnitude for the cross-coupling to occur. The best results were obtained when compound **1** was oxidised in the presence of an excess of coniferyl alcohol with silver oxide in dichloromethane. Flash chromatography of the crude mixture yielded **10a** (34%). A diastereoisomer **10b** was obtained in 19% yield, bringing the total cyclisation products to 53%. Oxidations with H_2O_2–HRP were less satisfactory. Oxidation of **1** in aqueous dioxane (pH 6) and with gradual addition of coniferyl alcohol and oxidant gave *ca.* 3% of **10a** and **10b**. A similar oxidation with dehydrodivanillyl alcohol **13** as the biphenyl component, gave *ca.* 18% of a dibenzodioxocine. The crystalline peracetate was shown by X-ray analysis to have structure **14** (Fig. 4). An important by-product in this case (*ca.* 30%) is a tetrameric dioxepine **15**, similar to the one obtained by Pew and Connors.[4]



Scheme 2

Experimental

General

Melting points, determined in open-capillary tubes with an electrothermal apparatus, are uncorrected. Horse-radish peroxidase (HRP) (EC 1.11.1.7) was from Serva, activity 277 U mg^{-1} (purpurogallin method). Hydrogen peroxide (a 30% solution, Merck) was diluted to give a 3% solution before use. Analytical TLC was performed on silica gel 60 F_{254} plates (Merck) and flash chromatography on silica gel 60, 230–400 mesh (Merck). NMR spectra were recorded on Varian Unity 500 and Varian Gemini 200 spectrometers with tetramethylsilane as internal standard. Mass spectra were obtained with a JEOL JMS-01SG-2 instrument.

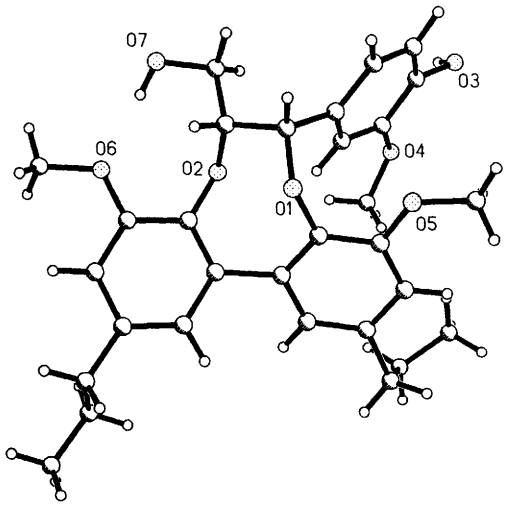


Fig. 2 The crystal structure of compound **10b**

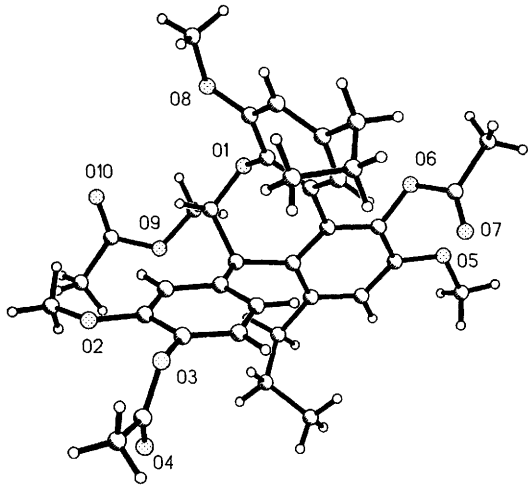


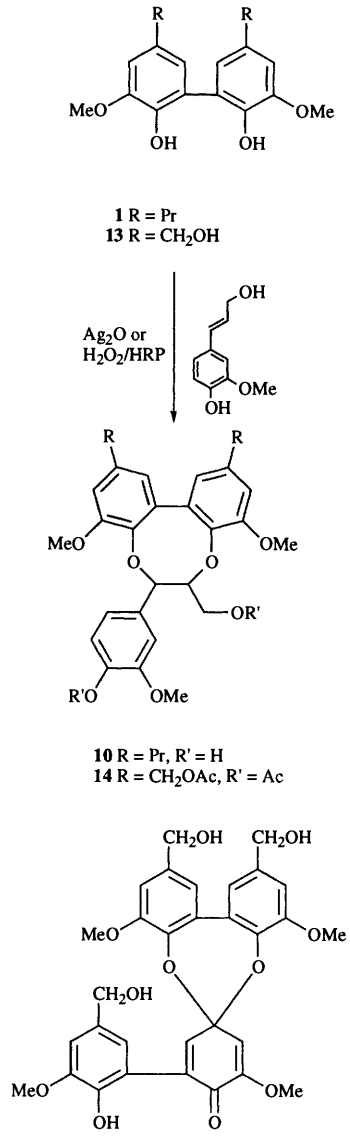
Fig. 3 The crystal structure of compound **12**

6,6′-Dihydroxy-5,5′-dimethoxy-3,3′-dipropylbiphenyl 1 (dehydrodipropylguaiacol)

The compound was made from propylguaiacol (from isoeugenol by catalytic hydrogenation) by oxidation with hexacyanoferrate(III)[5] in acetate buffer at neutral pH; yield 47%, mp 149–151 °C (lit.,[6,7] 152 °C); δ_H(200 MHz; $CDCl_3$) 0.96 (6 H, t, CH_3), 1.63 (4 H, m, CH_2), 2.58 (4 H, t, CH_2), 3.91 (6 H, s, OMe), 6.04 (2 H, s, OH) and 6.75 (4 H, m, ArH); δ_C 13.9 (CH_3), 24.8 (CH_2), 37.9 (CH_2), 56.1 (OCH_3), 110.6, 122.9, 124.4, 134.7, 140.5 and 147.1 (C arom).

Monomethylated dehydrodipropylguaiacol 2 (R = Me)[8]

Biphenyl **1** (2.8 g, 8.5 mmol) in dimethylformamide (20 ml) and potassium carbonate (7 g) was methylated with methyl iodide (1.2 g, 8.4 mmol) in dimethylformamide (2 ml) under an inert (Ar) atmosphere, the progress of the reaction being followed by TLC (eluent ethyl acetate–toluene 1:2). Work-up consisted of pouring the reaction mixture into water (40 ml) followed by extraction with ethyl acetate. The organic phase was washed with water and brine and then evaporated. The crude product was purified with flash chromatography (eluent ethyl acetate–hexane, 1:3), to give a yellowish oil (1.6 g, 55%); δ_H(200 MHz; $CDCl_3$) 0.96 (6 H, m, CH_3), 1.67 (4 H, m, CH_2), 2.55 (4 H, m, CH_2), 3.64 (3 H, s, OMe), 3.89 (3 H, s, OMe), 3.93 (3 H, s, OMe), 6.52 (1 H, s, OH) and 6.74 (4 H, m, ArH); δ_C 14.3, 14.6 (CH_3), 25.0, 25.2 (CH_2), 38.2, 38.5 (CH_2), 56.3, 56.4, 61.6 (OCH_3), 111.4, 112.3, 123.2, 123.7, 125.9, 132.4, 134.7, 141.5, 144.1, 148.4 and 152.7 (C arom).



Scheme 3

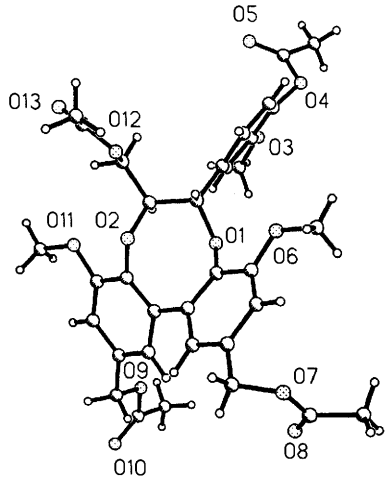


Fig. 4 The crystal structure of compound **14**

Bromination of 4-benzyloxy-3-methoxyacetophenone

The benzylated ketone[9] (40.7 g, 0.16 mol) was dissolved in 99% warm ethanol and the solution was cooled to room temperature with a stream of nitrogen. The nitrogen flow was stopped and bromine (31.2 ml, 0.2 mol) was added in one portion. Passage of

nitrogen was then resumed and the mixture was stirred. After *ca.* 30 min a white precipitate began to form at the same time as the bromine colour disappeared. The nitrogen stream was maintained for 2 h after which the mixture was cooled in a refrigerator to give crystalline compound **3**. This was filtered off and recrystallised from ethanol (49.7 g 74%), mp 104–106 °C (lit.,[10] 102.5–103 °C).

1-(4-Benzyloxy-3-methoxyphenyl)-2-(5,5′-dipropyl-3,3′-dimethoxy-2′-hydroxy-1,1′-biphenyl-2-yloxy)ethanone 4 (R = H) and 1-(4-benzyloxy-3-methoxyphenyl)-2-(5,5′-dipropyl-2,3,3′-trimethoxy-1,1′-biphenyl-2-yloxy)ethanone 4 (R = Me)

The biphenyl component (*ca.* 5 mmol) was dissolved in acetone to which dry potassium carbonate (10 mmol) and the bromo ketone **3** (5 mmol) were then added. The mixture was stirred vigorously for *ca.* 4 h at room temperature after which the carbonate was filtered off and the filtrate evaporated to give a chromatographically homogeneous oil (98%); for **4** (R = H): δ_H(200 MHz; $CDCl_3$) 0.93 (6 H, q, CH_3), 1.61 (4 H, m, CH_2), 2.50 (4 H, m, CH_2), 3.77 (3 H, s, OMe), 3.83 (3 H, s, OMe), 3.89 (3 H, s, OMe), 5.11 (2 H, s, α-CH_2), 5.22 (2 H, s, CH_2Ph), 6.18 (1 H, s, OH), 6.60–6.82 (5 H, m, ArH) and 7.32–7.49 (7 H, m, ArH); *m/z* 584 (M^+, 18%), 341 (18), 325 (100) and 91 (55) (Found: M^+, 584.2793. $C_{36}H_{40}O_7$ requires *M*, 584.2774); and for **4** (R = Me): δ_H(200 MHz; $CDCl_3$) 0.92 (6 H, q, CH_3), 1.61 (4 H, m, CH_2), 2.52 (4 H, m, CH_2), 3.62 (3 H, s, OMe), 3.79 (3 H, s, OMe), 3.83 (3 H, s, OMe), 3.89 (3 H, s, OMe), 4.93 (2 H, s, α-CH_2), 5.21 (2 H, s, CH_2Ph), 6.62 (5 H, m, ArH) and 7.35–7.51 (7 H, m, ArH).

2-(5,5′-Dipropyl-2′,3,3′-trimethoxy-1,1′-biphenyl-2-yloxy)-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol 6 and 2-(5,5′-dipropyl-2′-hydroxy-3,3′-dimethoxy-1,1′-biphenyl-2-yloxy)-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol 7

The starting ketones (*ca.* 5 g) were dissolved in absolute ethanol (70 ml) to which dry potassium carbonate (6 g) and 37% aqueous formaldehyde were added. The mixture was stirred vigorously for *ca.* 5 h to give the ketols **5** (55–67%) on evaporation of the filtered reaction mixture and recrystallisation from ethyl acetate. For **5** (R = H): mp 138–139 °C; δ_H(200 MHz; $CDCl_3$) 0.94 (6 H, m, CH_3), 1.61 (4 H, m, CH_2), 2.41 (2 H, t, CH_2), 2.56 (2 H, t, CH_2), 3.22 (1 H, t, OH), 3.68–3.80 (2 H, m, γ-CH_2), 3.72 (3 H, s, OMe), 3.76 (3 H, s, OMe), 3.90 (3 H, s, OMe), 5.17 (1 H, m, β-CH), 5.22 (2 H, s, CH_2Ph), 5.92 (1 H, s, Ar-OH), 6.45 (1 H, d, ArH), 6.62–6.86 (6 H, m, ArH) and 7.30–7.50 (5 H, m, ArH); *m/z* 614 (M^+, 7%), 596 (8), 584 (22), 355 (93), 325 (100) 301 (21), 241 (18) and 91 (52) (Found: M^+, 614.2900. $C_{37}H_{42}O_8$ requires *M*, 614.2879). Both ketols **5** were reduced with sodium borohydride in ethanol and the products were debenzylated by catalytic hydrogenation (10% Pd–C). Flash chromatography (ethyl acetate–hexane) yielded compounds **6** (67%) and **7** (79%) as diastereoisomeric mixtures. Compound **6** was crystalline mp 124–126 °C. Crystals for X-ray analysis were grown from ethanol–light petroleum. NMR data (200 MHz; $CDCl_3$) for *threo*-**6**: δ_H 0.96 (6 H, t, CH_3), 1.67 (4 H, m, CH_2), 2.59 (4 H, m, CH_2), 2.93 (1 H, t, OH), 3.29 and 3.54 (1 H, m, γ-CH, overlapping with methoxy signals), 3.68, 3.82, 3.90 and 3.97 (3 H, s, OMe), 3.80–3.95 (1 H, m, β-CH, overlapping with methoxy signals), 4.90 (1 H, d, *J* 9.0, α-CH), 5.59 (1 H, s, ArOH) and 6.65–6.83 (7 H, m, ArH); *m/z* 540 (M^+, 5%), 522 (20), 492 (77), 370 (18), 355 (68), 344 (95) and 315 (35) (Found: M^+, 540.2738. $C_{31}H_{40}O_8$ requires *M*, 540.2723); and for *threo*-**7**: δ_H 0.96 (6 H, m, CH_3), 1.65 (4 H, m, CH_2), 2.58 (4 H, m, CH_2), 2.92 (1 H, t, OH), 3.30 (1 H, m, γ-CH), 3.55 (1 H, m, γ-CH), 3.79, 3.91, and 3.94 (3 H, s, OMe), 3.75–4.00 (1 H, m, β-CH, overlapping with methoxy signals), 4.93 (1 H, d, *J* 9.1, α-CH), 5.73 (1 H, s, ArOH), 5.89 (1 H, s, ArOH) and 6.63–6.87 (7 H, m, ArH); *m/z* 526 (M^+, 5%), 508 (52), 490 (47), 479 (46), 356 (35), 341 (47), 330 (100), 301 (50), 285 (20) and 137 (17) (Found: M^+, 526.2559. $C_{30}H_{38}O_8$ requires *M*, 526.2567). NMR data (200 MHz; $CDCl_3$) for *erythro*-**6**; δ_H 0.97 (6 H, t, CH_3), 1.66 (4 H, m, CH_2), 2.58 (4 H, m, CH_2), 3.04–3.65 (3 H, m, γ-CH_2 and OH), 3.68–4.00 (1 H, m, β-CH, overlapping with methoxy signals), 3.71, 3.83, 3.89, 3.98 (3 H_2, s, OMe), 5.00 (1 H, d, α-CH), 5.70 (1 H, s, ArOH), 6.71–6.99 (7 H, m, ArH); and for *erythro*-**7**; 0.96 (6 H, m, CH_3), 1.65 (4 H, m, CH_2), 2.58 (4 H, m, CH_2), 3.08–3.75 (3 H, m, γ-CH_2 and OH), 3.81, 3.87 and 3.94 (3 H, s, OMe), 4.22 (1 H, m, β-CH), 5.01 (1 H, d, *J* 2.8, α-CH), 5.74 (1 H, s, ArOH), 5.92 (1 H, s, ArOH) and 6.70–7.00 (7 H, m, ArH).

Ring closure

Trimethylsilyl bromide (3 mmol) was added to a solution of the β-ether (1 mmol) in chloroform (25 ml) with vigorous stirring under an argon stream. After *ca.* 1 min the solution was washed with saturated aq. sodium hydrogen carbonate (2 × 15 ml) and with brine (15 ml), dried (Na_2SO_4) and evaporated. The residue was analysed by flash chromatography (eluent ethyl acetate–toluene 1:2). Compound **7** yielded *trans*-6,7-dihydro-7-(4-hydroxy-3-methoxyphenyl)-4,9-dimethoxy-2,11-dipropyldibenzo[*e*,*g*][1,4]dioxocin-6-ylmethanol **10a** as an oil (8%), which slowly crystallised, mp 167–170 °C; δ_H(200 MHz, $CDCl_3$), 0.99 (3 H, t, CH_3), 1.02 (3 H, t, CH_3), 1.71 (4 H, m, CH_2), 2.62 (4 H, m, CH_2), 3.34–3.70 (2 H, m, γ-CH_2), 3.74, 3.88, 3.92 (3 H, s, OMe), 4.14 (1 H, m, β-H), 4.54 (1 H, d, *J* 10.0, α-H), 5.70 (1 H, s, ArOH) and 6.74–6.92 (7 H, m, ArH); δ_C 13.9, 14.0 (CH_3), 24.6 (CH_2), 38.1 (CH_2), 55.7, 55.9 (OCH_3), 63.0 (γ-CH_2), 85.0 (α-CH), 87.0 (β-CH), 109.5, 111.3, 112.2, 114.4, 120.9, 121.3, 121.6, 130.1, 132.1, 133.3, 139.1, 139.5, 143.5, 144.8, 145.9, 146.8, 151.3 and 151.8 (C arom.); *m/z* 509 (30%), 508 (M^+, 88), 491 (35), 490 (M − H_2O, 100), 478 (57), 447 (38), 341 (30), 330 (60), 329 (30), 328 (55), 301 (25), 299 (30), 297 (23), 285 (43) and 137 (18); λ_{max}(95% EtOH)/nm 220, 255 and 284. Spectral data for acetylated **10a** are given in ref. 3. The main product was a stereoisomeric mixture of 11-hydroxy 7-(4-hydroxy-3-methoxyphenyl)-6-hydroxymethyl-4,10-dimethoxy-2,8-dipropyl-6,7-dihydrodibenzo[*b*,*d*]oxepine **11** (82%). Data for **11a**: (*trans*-isomer) (64%) viscous oil; δ_H(200 MHz; $CDCl_3$), 0.75 (3 H, t, CH_3), 0.95 (3 H, t, CH_3), 1.30–1.70 (4 H, overlapping multiplets, CH_2), 2.30–2.80 (4 H, overlapping multiplets, CH_2), 3.62 (3 H, s, OMe), 3.80 (3 H, s, OMe), 3.93 (3 H, s, OMe), 3.65–4.00 (2 H, m, β-CH, γ-CH overlapping with methoxy signals), 4.36 (1 H, br s, α-CH), 5.20 (1 H, m, γ-CH), 5.26 (1 H, s, ArOH), 5.69 (1 H, s, ArOH), 6.25–6.78 (6 H, m, ArH). The crystalline peracetate **12** of this fraction, mp 149–150 °C, was recrystallised for X-ray analysis (Fig. 3). Spectral data for **12**: δ_H(400 MHz; $CDCl_3$) 0.78 (3 H, t, CH_3), 0.98 (3 H, t, CH_3), 1.38 (2 H, m, CH_2), 1.62 (2 H, m, CH_2), 2.11, 2.13, 2.23 (3 × 3 H, s, $COCH_3$), 2.31 (2 H, t, CH_2), 2.56 (1 H, m, CH), 2.76 (1 H, m, CH), 3.61 (3 H, s, OMe), 3.81 (3 H, s, OMe), 3.91 (3 H, s, OMe), 4.07 (1 H, dd, H_γ, J_1 11.0, J_2 8.0), 4.48 (1 H, dd, H_β, J_1 11.0, J_2 5.4), 4.70 (1 H, br s, H_α), 5.44 (1 H, dd, H_γ, J_1 8.0, J_2 5.4) and 6.26–6.89 (6 H, m, ArH); δ_C 13.6, 14.5 (CH_3), 20.7, 21.0 ($COCH_3$), 24.5, 24.6 (CH_2), 36.6, 37.9 (CH_2), 43.7 (α-CH), 55.7, 56.1, 56.2 (OCH_3), 64.8 (γ-CH_2), 83.9 (β-CH), 110.7, 112.3, 112.6, 118.7, 121.6, 121.9, 128.2, 131.5, 132.7, 136.0, 137.2, 138.8, 140.2, 140.3, 141.5, 149.9, 150.7, 151.7 (C arom.), 169.0, 170.5 ($COCH_3$). Data for **11b** (*cis*-isomer) (18%) viscous oil; δ_H(200 MHz; $CDCl_3$) 1.00 (6 H, m, CH_3), 1.66 (4 H, m, CH_2), 2.46–2.88 (4 H, m, CH_2), 3.38–3.94 (3 H, m, β-CH, γ-CH_2 overlapping with methoxy signals), 3.55 (3 H, s, OMe), 3.88 (3 H, s, OMe), 3.93 (3 H, s, OMe), 4.65 (1 H, d, *J* 7.4, α-CH), 4.95 (1 H, q, γ-CH), 5.35 (1 H, s, ArOH), 5.79 (1 H, s, ArOH) and 6.13–6.92 (6 H, m, ArH); *m/z* 508 (M^+, 100%), 477 (15), 405 (10) and 341 (83) (Found: M^+, 508.2449, $C_{30}H_{36}O_7$ requires *M*, 508.2461).

Compound **8** was obtained from **4** by reduction with $NaBH_4$ and debenzylation. For **8**: δ_H(200 MHz; $CDCl_3$) 0.95 (6 H, m, CH_3), 1.65 (4 H, m, CH_2), 2.57 (4 H, m, CH_2), 3.50–3.85 (2 H, m), 3.82 (3 H, s, OMe), 3.89 (3 H, s, OMe), 3.92 (3

H, s, OMe), 4.69 (1 H, m), 5.59 (1 H, s, ArOH), 6.00 (1 H, s, ArOH) and 6.62–6.85 (7 H, m, ArH); *m/z* 478 (M − H_2O, no molecular ion, 100%), 341 (27), 331 (25), 301 (18), 285 (11) and 137 (10). Compound **8** yielded 33% of compound **9**, which was purified as the peracetate, mp 189–190 °C; δ_H(500 MHz; $CDCl_3$) 1.00, 1.02 (6 H, overlapping triplets, CH_3), 1.71 (4 H, m, CH_2), 2.32 (3 H, s, $COCH_3$), 2.63 (4 H, q, CH_2), 3.76 (3 H, s, OMe), 3.84 (3 H, s, OMe), 3.89 (3 H, s, OMe), 3.82–3.91 (1 H, m, H_β), 4.52 (1 H, dd, J_1 3.4 and J_2 11.6, H_β), 5.04 (1 H, dd, J_1 3.4 and J_2 11.6, H_α) and 6.75–7.21 (7 H, m, ArH); δ_C 13.9, 14.0 (CH_3), 20.7 ($COCH_3$), 24.6 (CH_2), 38.1, 38.2 (CH_2), 55.9, 56.0 (OCH_3), 76.3 (β-CH), 82.7 (α-CH), 110.8, 111.8, 112.2, 118.5, 121.1, 121.4, 122.3, 132.7, 132.8, 137.2, 139.1, 144.8, 145.0, 151.0, 151.8, 152.1 (C arom.), 169.0 (C=O); *m/z* 520 (M^+, 90%), 478 (100), 341 (27) and 299 (14) (Found: M^+, 520.2463. $C_{31}H_{36}O_7$ requires *M*, 520.2461).

Oxidative coupling of dehydrodipropylguaiacol 1 and coniferyl alcohol with silver(I) oxide

Dehydrodipropylguaiacol **1** (0.66 g, 2 mmol) and coniferyl alcohol (0.72 g, 4 mmol) were dissolved in dichloromethane (50 ml) and silver oxide (0.70 g, 3 mmol) was added to the solution which was then stirred for 45 h at room temp. After filtration (Celite) and evaporation of the mixture the product was fractionated by flash chromatography (acetic acid–diethyl ether–CH_2Cl_2 1:10:100) to give the dibenzodioxocine **10a** (*trans*-isomer) (34%).

The *cis*-isomer of the dibenzodioxocine, **10b** was isolated (19%) and had mp 136–138 °C; δ_H(200 MHz; $CDCl_3$) 1.00 (6 H, m, CH_3), 1.68 (4 H, m, CH_2), 2.60 (4 H, m, CH_2), 3.12 (3 H, br s, OMe), 3.31 (3 H, br s, OMe), 3.84 (1 H, m, γ-H), 3.95 (3 H, s, OMe), 4.20 (1 H, d, γ-H, *J* 9), 4.46 (1 H, m, β-H), 5.14 (1 H, d, α-H, *J* 2.9), 5.61 (1 H, s, ArOH), 6.38 (1 H, s, ArH) and 6.65–7.00 (6 H, m, ArH); δ_C 13.9, 24.7, 38.1, 55.0, 55.4, 55.9, 63.4, 80.3 (α-C), 89.2 (β-C), 111.0, 111.4, 112.6, 112.8, 121.7, 123.1, 125.4, 126.8, 133.9, 134.1, 139.2, 139.5, 144.2, 144.5, 145.7, 151.0 and 153.6 (C arom.). The product was recrystallised for X-ray analysis (Fig. 2).

Oxidative coupling of dehydrodipropylguaiacol 1 and coniferyl alcohol in aqueous dioxane

Compound **1** (0.43 g, 1.3 mmol) was dissolved in a mixture of dioxane (400 ml) and citrate–phosphate buffer solution (400 ml; 0.005 M, pH 6) to which HRP (20 mg) was then added. Coniferyl alcohol (0.40 g, 2.2 mmol) was dissolved in 5 ml of dioxane buffer solution mixture (1:1) and hydrogen peroxide (2.2 mmol) was diluted to 5 ml with dioxane–buffer solution. The coniferyl alcohol and hydrogen peroxide solutions were then injected simultaneously during 3.5 h into the reaction mixture. After being stirred overnight at room temperature, the mixture was extracted twice with ethyl acetate and the extract dried (Na_2SO_4) and evaporated. The resulting product (740 mg) was acetylated and with acetic anhydride–pyridine (1:1) and purified by flash chromatography (EtOAc–toluene, 1:3) to yield the dibenzodioxocine **10a** (diacetate) (3% calculated on coniferyl alcohol); spectral data given in ref. 3.

Oxidative coupling of dehydrodivanillyl alcohol 13 and coniferyl alcohol in aqueous dioxane

Dehydrodivanillyl alcohol[11] **13** (1 g, 3.3 mmol) was dissolved in dioxane (27 ml) to which citrate–phosphate buffer solution (27 ml; 0.005 M, pH 6) and HRP (20 mg) were then added. Coniferyl alcohol (0.5 g, 2.8 mmol) was dissolved in dioxane–buffer solution (1:1); 5 ml. Hydrogen peroxide (2.8 mmol) was diluted to 5 ml with dioxane–buffer solution. The reaction and the work-up were carried out as described above. The acetylated product (1.65 g) was fractionated by flash chromatography (EtOAc–toluene 1:2) to give 7-(4-acetyloxy-3-methoxyphenyl)-2,6,11-tris(acetyloxymethyl)-*trans*-6,7-dihydro-4,9-dimethoxydibenzo[*e,g*][1,4]dioxocine **14** (18% calculated on coniferyl alcohol), mp 130–131 °C; for spectral data see ref. 3. Crystals for X-ray analysis were grown from toluene–heptane; the crystal structure is shown in Fig. 4. A dimerisation product of **13**, 6,9-bis(hydroxymethyl)-3′,4,11-trimethoxy-5′-(2″-hydroxy-5″-hydroxymethyl-3″-methoxyphenyl)dibenzo[*d,f*]-dioxepine-2-spiro-4′-cyclohexa-2′,5′-dienone **15** was isolated (29%),[12] mp 200–202 °C (decomp.); δ_H(200 MHz; [$^2H_6$]DMSO) 3.63 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.89 (s, 6 H, 2 × OMe), 4.45 (d, 2 H, CH_2), 4.60 (d, 4 H, 2 × CH_2), 5.10 (t, 1 H, OH), 5.37 (t, 2 H, OH), 5.88 (d, 1 H, =CH), 6.58 (d, 1 H, =CH), 6.68 (d, 1 H, ArH), 6.95 (d, 1 H, ArH), 7.15 (s, 4 H, ArH) and 8.70 (s, 1 H, ArOH); δ_C 59.2, 59.6, 59.8, 66.8, 66.9, 112.7, 113.4, 114.3, 114.6, 121.5, 123.9, 126.0, 137.1, 137.5, 140.8, 141.0, 143.7, 145.1, 147.1, 151.1, 154.4, 156.6 and 181.9.

X-Ray crystallography

Data were collected on a Rikagu AFC7S diffractometer at −80 °C using graphite monochromated Mo-Kα radiation (λ = 0.710 73 Å). Three standard reflections monitored throughout the data collection showed no loss in intensity with time. The data were corrected for Lorentz and polarisation effects, no absorption corrections being applied. The structures were solved by direct methods and the non hydrogen atoms were refined anisotropically by full-matrix least-squares on F^2. The hydrogen atoms were placed at calculated positions and the atoms assigned isotropic thermal parameters, U(H) = 1.2 U_{eq}(CH,CH_2), U(H) = 1.5 U_{eq}(CH_3), and allowed to ride on their parent carbon atoms. Computations were carried out using the SHELXTL-PC[13] and SHELX93[14] program systems. Atomic coordinates, bond lengths, angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. For details see *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request for this information should be accompanied by a full bibliographic citation together with the reference number 207/36.

Crystal data for compound 6. $C_{31}H_{40}O_8$, M = 540.63. Monoclinic, space group $C2/c$, a = 37.214(7), b = 11.045(2), c = 14.087(3) Å, β = 99.16(3)°, V = 5716 Å^3, Z = 8, D_c = 1.256 g cm^{-3}, μ(Mo-Kα) = 0.090 mm^{-1}, F(000) = 2320. Colourless block, 0.45 × 0.35 × 0.30 mm. Full-matrix least squares refinement on 353 parameters for 2333 independent reflections in the range 5.5 < 2θ < 48° gave R_1 = 0.0782 [1112 $I > 2\sigma(I)$ reflections] and wR_2 = 0.176 for all data. The final electron difference map was featureless with largest peak 0.25 e Å^{-3}.

Crystal data for compound 10b. $C_{30}H_{36}O_7$, M = 508.59. Monoclinic, space group $P2_1/c$, a = 9.846(2), b = 13.041(3), c = 20.868(4) Å, β = 100.26(3)°, V = 2636 Å^3, Z = 4, D_c = 1.281 g cm^{-3}, μ(Mo-Kα) = 0.090 mm^{-1}, F(000) = 1088. Colourless block, 0.45 × 0.30 × 0.30 mm. Full-matrix least squares refinement on 335 parameters for 3351 independent reflections in the range 5.0 < 2θ < 50° gave R_1 = 0.0490 [1157 $I > 2\sigma(I)$ reflections] and wR_2 = 0.205 for all data. The final electron difference map was featureless with the largest peak 0.15 e Å^{-3}.

Crystal data for compound 12. $C_{36}H_{42}O_{10}$ M = 634.70. Monoclinic, $P2_1/n$ (alt. $P2_1/c$, No. 14), a = 13.372(10), b = 9.672(9), c = 26.038(14) Å, β = 101.32(6)°, V = 3302 Å^3, Z = 4, D_c = 1.277 g cm^{-3}, μ(Mo-Kα) = 0.093 mm^{-1}, F(000) = 1352. Colourless prism, 0.35 × 0.35 × 0.20 mm. Full-matrix least-squares refinement on 415 parameters for 4855 independent reflections in the range 5.16 < 2θ < 47° gave R_1 = 0.0820 [3364 $I > 2\sigma(I)$ reflections] and wR_2 = 0.2479 for all data. The final electron difference map was featureless with largest peak 0.36 e Å^{-3}.

Crystal data for compound 14. $C_{34}H_{36}O_{13}$, M = 652.63. Monoclinic, space group $C2/c$, a = 27.410(5), b = 11.604(2),

$c = 23.065(5)$ Å, $\beta = 117.06(3)°$, $Z = 8$, $D_c = 1.327$ g cm^{-3}, $\mu = 0.102$ mm^{-1}, $F(000) = 2752$. Colourless block, 0.40 × 0.35 × 0.15 mm. Full-matrix least-squares refinement on 424 parameters for 4549 independent reflections in the range $4.96 < 2\theta < 46°$ gave $R_1 = 0.119$ [1540 $I > 2\sigma(I)$ reflections] and $wR_2 = 0.374$ for all data. The poor quality and the weak diffraction power of the crystals resulted in a rather high R value. The final electron difference map was featureless with the largest peak 0.38 e Å^{-3}.

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