A highly stereoselective synthesis of 3-hydroxy-1-aryltetralin lignans based on the stereoselective hydroxylation of α,β-dibenzyl-γ-butyrolactones: the first synthesis of (±)-cycloolivil

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Lignans of the 3-hydroxy-1-aryltetralin series 1 and 2 have been synthesised in good yields in a highly diastereoselective manner. The stereochemistry at C-1, C-2 and C-3 of 1 and 2 was completely controlled by an electrophilic addition of oxodiperoxymolybdenum(pyridine)hexamethylphosphoric triamide (MoOPH) to the metal enolates of α,β-disubstituted γ-butyrolactones 4 and the Friedel–Crafts type intramolecular cyclisation of 3. This method was applied to the stereoselective synthesis of (±)-cycloolivil 1e.

Introduction

Currently, lignans[1] of the 3-hydroxy-1-aryltetralin series **1** and **2** are of considerable interest because some of them, including cycloolivil **1e**, have been isolated from the stem bark of *Olea europaea* L.,[2] *Stereospermum kunthianum* Cham,[3] which shows intriguing biological activity (*e.g.* diuretic, antiseptic, antifebrile and antirheumatic). In spite of the significance of this biological activity, there is but a single reported synthesis of this series of lignans, in which trachelogenin diacetate was oxidised with lead tetraacetate to α-acetoxy-trachelogenin diacetate, a compound which was then converted into the corresponding 3-hydroxy-1-aryltetralin derivative by a Friedel–Crafts type cyclisation and subsequent reduction.[4] This method, however, is applicable only to a limited range of the compounds, since α-hydroxy-α,β-dibenzyl lactones[5] are not easily accessible. In connection with our interest in new compounds from lignan derivatives having interesting biological activity,[6–8] we have studied the synthesis of this series of lignans. Here, we report our results for the first stereoselective synthesis of 3-hydroxy-1-aryltetralin lignans **1** and **2**.

Results and discussion

Synthetic strategy

Scheme 1 illustrates the main features of our synthetic strategy involving: the three-component reaction of **5**, **6** and but-2-enolide, the stereoselective electrophilic addition of MoOPH to the metal enolate of **4** and conversion of the resulting intermediate into the desired products **1** and **2**. We have already reported that electrophilic attack on the metal enolate of β-substituted α-benzyl-γ-butyrolactone took place predominantly from the upper face to afford the *trans*-product in spite of the presence of the β-substituent; the shielding of the bottom face by the phenyl moiety of the α-benzyl group, as a result of conformational rigidity induced by 1,3-allylic strain, would be effective in allowing preferential attack of an electrophile from the upper face.[9,10] We envisaged that electrophilic attack on the metal enolate of **4** would occur in the same manner from the upper face in spite of the presence of the β-substituent (Fig. 1 in Scheme 1). Thus, the relative stereochemistry of the contiguous carbon centres of **3**, C-2 and C-3,

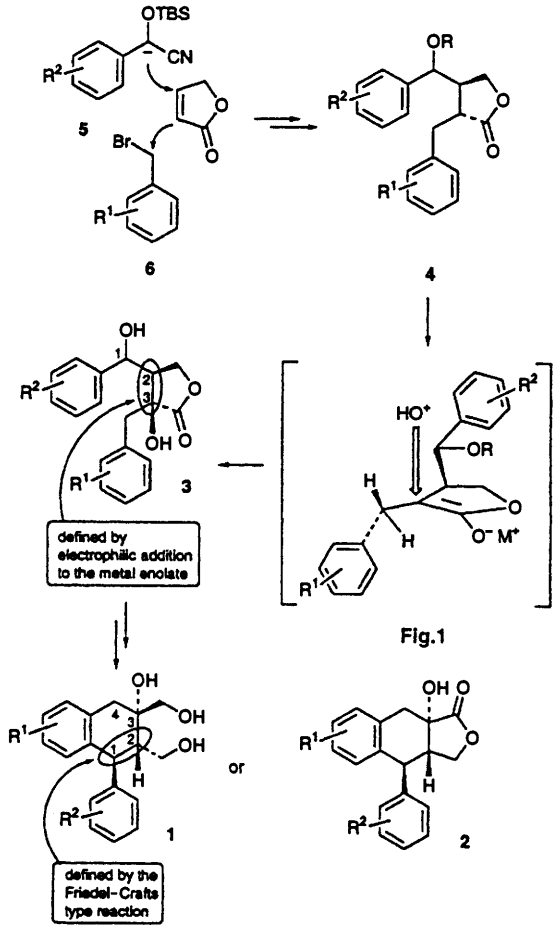
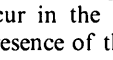


Fig.1

a R^1 = 6,7-OCH_2O; R^2 = 3,4-$(OMe)_2$

b R^1 = 6,7,8-$(OMe)_3$; R^2 = 3,4-OCH_2O

c R^1 = 6,7-OCH_2O; 

d R^1 = 6-OMe, 7-OCH_2Ph; R^2 = 3-OMe, 4-OCH_2Ph

e R^1 = 6-OMe, 7-OH; R^2 = 3-OMe, 4-OH

Scheme 1

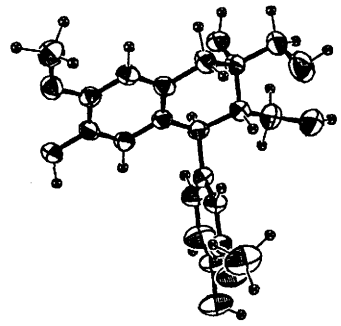


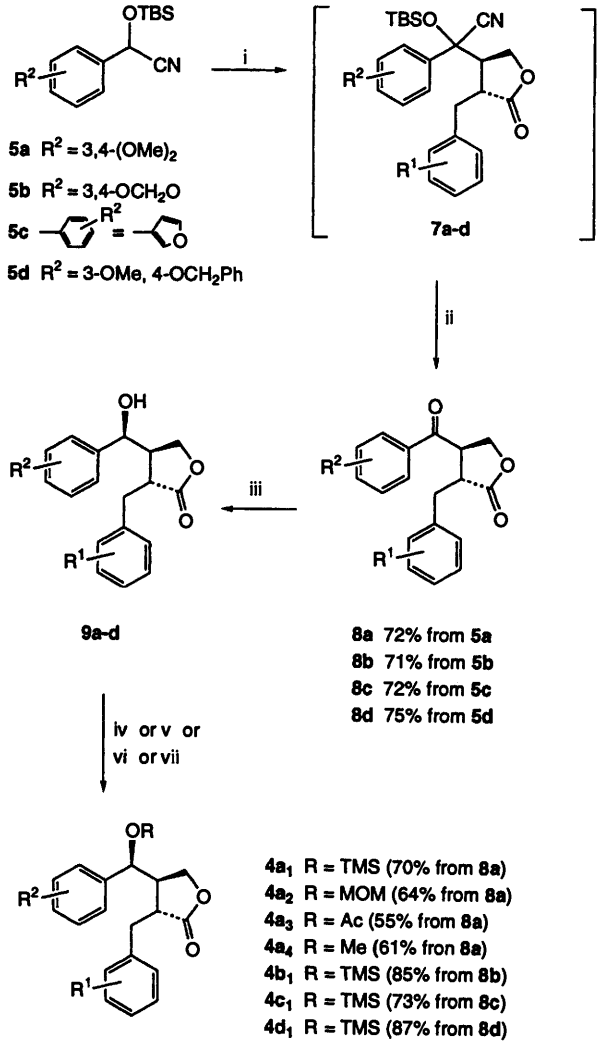
Fig. 2 X-Ray crystal structure of **1e**

would be defined by the electrophilic attack on the metal enolate of **4** to furnish a predominance of the *trans*-product **3**; the stereoselectivity and chemical yield would be affected by the protecting group introduced for the α-hydroxy group. The relative stereochemistry of the C-1 and C-2 carbon centres of **1** and **2** would be defined by the Friedel–Crafts type intramolecular cyclisation of **3**.[11]

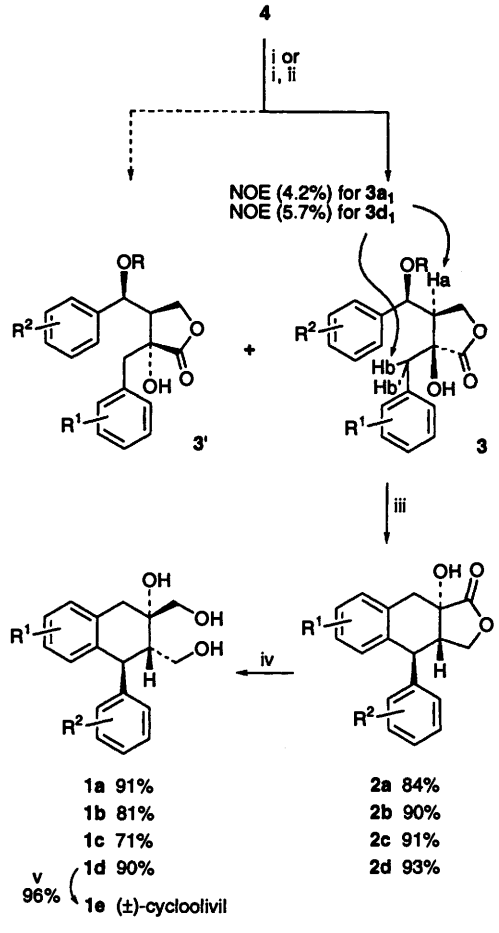
Synthesis of 3-hydroxy-1-aryltetralin lignans 1 and 2

Following the above strategy, we initially synthesised the requisite substrate **4** from *O*-silylated cyanohydrin **5** (Scheme 2). The conjugate addition of the lithium salt of **5a**, prepared by reaction of **5a** with lithium diisopropylamide (LDA), to but-2-enolide in THF at −78 °C, followed by trapping of the resulting enolate with 3,4-methylenedioxybenzyl bromide gave **7a**. Without isolation of **7a**, the mixture was treated with tetrabutylammonium fluoride (Bu_4NF) to afford the *trans*-γ-butyrolactone **8a** in 72% yield from **5a**. Reduction of the carbonyl group of **8a** with L-Selectride® proceeded stereoselectively to give the alcohol **9a** as the sole product (87%).[9b] In order to examine the effect of the protecting group on the oxygen atom of the α′-hydroxy group, the hydroxy group of **9a** thus obtained was protected by trimethylsilyl (TMS), methoxymethyl (MOM), acetyl (Ac) and methyl (Me) groups to afford the desired substrate $\mathbf{4a}_1$, $\mathbf{4a}_2$, $\mathbf{4a}_3$ and $\mathbf{4a}_4$ in 80, 73, 63 and 70% yields, respectively.

With the four types of requisite substrate **4** in hand, we examined hydroxylation of the metal enolates of γ-butyrolactones **4** using oxodiperoxymolybdenum(pyridine)hexamethylphosphoric triamide (MoOPH) as an oxidising reagent (Scheme 3).



Scheme 2 *Reagents:* i, LDA, but-2-enolide, substituted benzyl bromide **6**; ii, Bu_4NF–AcOH; iii, L-Selectride; iv, TMSCl, imidazole; v, MOMCl, Pr^i_2NEt; vi, Ac_2O, Et_3N; vii, MeI, NaH



Scheme 3 *Reagents:* i, $KN(SiMe_3)_2$, MoOPH; ii, Bu_4NF; iii, TFA–CH_2Cl_2; iv, $LiAlH_4$–THF; v, H_2, Pd–C

We had previously observed that the electrophilic addition proceeded more efficiently with the potassium enolate of α,β-dibenzyl-γ-butyrolactone than with the corresponding lithium and sodium enolates.[9] Thus, the potassium enolate of $\mathbf{4a}_1$ was prepared by treatment of $\mathbf{4a}_1$ with potassium bis(trimethylsilyl)-amide [$KN(SiMe_3)_2$] in THF at −78 °C. Addition of MoOPH powder in one portion to this reaction mixture resulted in smooth hydroxylation to afford α-hydroxylated compounds. Without isolation of these products, the residue was treated with Bu_4NF–AcOH in CH_2Cl_2 to furnish $\mathbf{3a}_1$ (R = H) in 86% yield as a single isomer; the structure of $\mathbf{3a}_1$ (R = H) was determined by 200 MHz ^1H NMR spectroscopy (4.2% of NOE was observed between H_a and H_b, $H_{b'}$, the results of which are

Table 1 Reaction of the metal enolate of **4** with MoOPH[a]

Entry	Substrate	Yield (%)[b] (3 + 3′)	Selectivity (3:3′)
1	$\mathbf{4a_1}$	86	>99:1
2	$\mathbf{4a_2}$	50	>99:1
3	$\mathbf{4a_3}$	29	>99:1
4	$\mathbf{4a_4}$	42	>99:1
5	$\mathbf{4b_1}$	86	>99:1
6	$\mathbf{4c_1}$	89	>99:1
7	$\mathbf{4d_1}$	95	>99:1

[a] The reaction was carried out in THF at −78 °C. [b] Isolated yield.

shown in Scheme 3). Careful examination revealed that the relative stereochemistry between C-2 and C-3 (cycloolivil's numbering) was completely controlled by this electrophilic addition, none of the diastereoisomer $\mathbf{3'a_1}$ (R = H) being isolated. In contrast, although $\mathbf{4a_2}$, $\mathbf{4a_3}$ and $\mathbf{4a_4}$ also underwent highly stereoselective hydroxylation the chemical yields of the desired product [$\mathbf{3a_2}$ (R = MOM), $\mathbf{3a_3}$ (R = Ac) and $\mathbf{3a_4}$ (R = Me)] were very low (50, 29 and 42%) (entries 1–4 in Table 1).

Since a TMS group is a suitable protecting group for the α′-hydroxyl group, we next examined the hydroxylation of compounds $\mathbf{4b_1}$–$\mathbf{d_1}$, analogous to $\mathbf{4a_1}$ in order to clarify the generality of this reaction. Compounds $\mathbf{4b_1}$–$\mathbf{d_1}$ were prepared starting from the *O*-silylated cyanohydrin **5b–d** (see Scheme 2). The hydroxylation of $\mathbf{4b_1}$–$\mathbf{d_1}$ proceeded smoothly, with similar high diastereoselectivities and chemical yields (Scheme 3, entries 5–7 in Table 1).

We next examined the conversion of the dibenzyl type compound **3** into the desired 1-aryltetralin lignans **1** and **2**. Treatment of $\mathbf{3a_1}$ with trifluoroacetic acid (TFA) in CH_2Cl_2 at 0 °C gave the 1-aryltetralin lactone **2a** (84%), the structure of which was determined by 200 MHz ^{1}H NMR analysis.† Reduction of **2a** with $LiAlH_4$ in THF afforded 1-aryltetralin triol **1a** (91%) and, in a similar manner, **2b–d** and **1b–d** were obtained from $\mathbf{3b_1}$–$\mathbf{d_1}$ in good yields (Scheme 3).

Synthesis of (±)-cycloolivil 1e

(±)-Cycloolivil **1e** was synthesised by a similar procedure from $\mathbf{4d_1}$; $\mathbf{4d_1}$ itself was prepared from **5d** in 4 steps (65% overall yield; Scheme 2). The hydroxylation of $\mathbf{4d_1}$ proceeded in a highly stereoselective manner as expected to afford $\mathbf{3d_1}$ (95%); the relative stereochemistry between C-2 and C-3 was determined by 400 MHz ^{1}H NMR spectroscopy (5.7% of NOE was observed between H_a and H_b, $H_{b'}$, the diastereoisomer $\mathbf{3'd_1}$ not being isolated). The resulting α-hydroxylated product $\mathbf{3d_1}$ underwent the Friedel–Crafts type intramolecular cyclisation by treatment with TFA to afford the 3-hydroxy-1-aryltetralin lignan lactone **2d** as a single isomer. Reduction of the lactone ring of **2d** followed by deprotection of the hydroxy groups on the benzene ring gave (±)-cycloolivil **1e**‡ in 86% yield (reduction: 90%, deprotection: 96%; Scheme 3); the structure of **1e** was unambiguously determined by X-ray crystallographic analysis (Fig. 2).

Conclusion

We have described the first stereoselective synthesis of 3-hydroxy-1-aryltetralin lignans **1** and **2** by using highly stereoselective electrophilic addition to the metal enolate of **4** followed by Friedel–Crafts type intramolecular cyclisation. The stereoselectivity observed in this reaction originates from the conformational rigidity of the metal enolate of **4** induced by 1,3-allylic strain. This method is applicable to the stereoselective synthesis of a variety of 3-substituted 1-aryltetralin lignans and related compounds having potential biological activity.

Experimental

Mps were determined in open capillary tubes on a Yamato MP-21 melting point apparatus and are uncorrected. IR spectra were obtained using a Perkin-Elmer 1640 IR spectrometer. ^{1}H NMR (200 MHz) spectra were recorded on a Bruker AC-200 instrument and ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a JEOL GSX-400 instrument using Me_4Si as the internal standard. *J* Values are given in Hz. Mass spectra were obtained on a Hitachi M-2000A spectrometers. Column chromatography was performed with silica gel (Merck 7734 and 9385, Kiesel gel 60, 230–400 mesh). THF was dried over 4 Å molecular sieves and used without further purification. All other solvents were used as received.

Preparation of *trans*-3-(3,4-methylenedioxybenzyl)-4-(3,4-dimethoxybenzoyl)-γ-butyrolactone 8a

LDA (0.35 mol) was prepared by addition of butyllithium (1.6 M in hexane; 220 cm^3, 0.35 mol) to a solution of diisopropylamine (49.0 cm^3, 0.35 mol) in THF (200 cm^3) at −78 °C under a nitrogen atmosphere and the mixture was stirred for 20 min at 0 °C. To the mixture, re-cooled to −78 °C, was successively added dropwise **5a**[5b] (90.0 g, 0.29 mol) in THF (100 cm^3), but-2-enolide (9.20 cm^3, 0.29 mol) in THF (100 cm^3) and 3,4-methylenedioxybenzyl bromide (63.0 g, 0.29 mol) in THF (50 cm^3) at the same temperature for 7 h. The mixture was quenched by addition to it of saturated aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was extracted with AcOEt. The combined organic layers were washed with water and brine, dried ($MgSO_4$) and evaporated to provide the crude product **7a** as an oil. To a solution of the oil in CH_2Cl_2 (700 cm^3) was added 1 M Bu_4NF in THF (130 cm^3, 0.29 mol) at 0 °C. After 30 min, the solution was washed with water, 10% citric acid and brine, dried ($MgSO_4$) and evaporated to afford a crude product, which was crystallised from MeOH to give **8a** (80.2 g; 72% yield from **5a**) as the sole product; mp 140–141 °C (AcOEt–acetone) (Found: C, 65.69; H, 5.12. Calc. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24%); ν_{max}(KBr)/cm^{-1} 1772 and 1665; δ_H($CDCl_3$) 2.93 (dd, 1 H, *J* 7.2, 14.2), 3.06 (dd, 1 H, *J* 5.5, 14.2), 3.42–3.63 (m, 1 H), 3.92 (s, 3 H), 3.96 (s, 3 H), 4.01–4.23 (m, 2 H), 4.32–4.51 (m, 1 H), 5.85 (d, 1 H, *J* 1.3), 5.88 (d, 1 H, *J* 1.4), 6.53 (dd, 1 H, *J* 1.8, 7.8), 6.59 (d, 1 H, *J* 1.6), 6.62 (d, 1 H, *J* 8.0), 6.84 (d, 1 H, *J* 8.4), 7.30 (dd, 1 H, *J* 2.0, 8.4) and 7.36 (d, 1 H, *J* 2.0); *m/z* 384 (M^+, 37%), 192 (100), 165 (61) and 135 (35).

Preparation of (3*R**,4*R**)-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-trimethylsilyloxy-3,4-dimethoxybenzyl]-γ-butyrolactone 4a$_1$

To a solution of the ketone **8a** (10.0 g, 26.1 mmol) in THF (150 cm^3) was added dropwise L-Selectride® (1.0 M in THF; 28.6 cm^3, 28.6 mmol) at −78 °C, and stirring was continued for 5 h at −20 °C. The mixture was quenched by the addition to it of AcOH (1.73 cm^3, 28.7 mmol) and concentrated. The residue was diluted with AcOEt (100 cm^3) and washed with water and brine, dried ($MgSO_4$) and evaporated to provide a crude product, which was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (1 : 1 : 1) as eluent to afford **9a** (8.76 g, 87%). The alcohol **9a** (2.20 g, 5.70 mmol) and imidazole (466 mg, 6.84 mmol) were dissolved in DMF (10 cm^3) and to the ice-cooled mixture was added trimethylsilyl chloride (0.868 cm^3, 6.84 mmol); the resulting mixture was stirred at room temperature for 12 h and then poured into water and extracted with AcOEt. The combined extracts were washed with water, 10% aqueous citric acid, saturated aqueous $NaHCO_3$ and brine,

† A large coupling constant (J_{ab} 12.1) observed between H-1 and H-2 in **2a** strongly supported that the stereochemistry at C-1 and C-2 of **2a** was *trans*.

‡ The ^{1}H and ^{13}C NMR spectra of the synthetic product **1e** obtained here were consistent with those of (±)-cycloolivil reported in refs. 2 and 3.

dried ($MgSO_4$) and evaporated. The resulting crude oil was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:1) as eluent to afford **4a**$_1$ (2.12 g, 80%) as a colourless syrup; ν_{max}(KBr)/cm^{-1} 2958 and 1761; δ_H($CDCl_3$) 0.05 (s, 9 H), 2.43–2.59 (m, 1 H), 2.70–2.95 (m, 3 H), 3.83 (s, 3 H), 3.88 (s, 3 H), 3.92–4.12 (m, 2 H), 4.62 (d, 1 H, *J* 5.1), 5.90 (d, 1 H, *J* 1.5), 5.93 (d, 1 H, *J* 2.7), 6.43 (s, 3 H), 6.45 (dd, 1 H, *J* 1.7, 8.7), 6.61 (s, 3 H), 6.63 (d, 1 H, *J* 8.5), 6.72 (dd, 1 H, *J* 1.6, 8.3) and 6.79 (d, 1 H, *J* 8.2); *m/z* 458 (M$^+$, 53%), 368 (23), 240 (96) and 135 (100).

Preparation of (3*R,4*R**)-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-methoxymethoxy-3,4-dimethoxybenzyl]-γ-butyrolactone 4a$_2$**

The alcohol **9a** (1.70 g, 4.40 mmol) and diisopropylethylamine (1.38 cm^3, 7.92 mmol) were dissolved in DMF (10 cm^3) and to the ice-cooled mixture was added chloromethyl methyl ether (0.50 cm^3, 6.60 mmol). The resulting mixture was stirred at room temperature for 12 h after which it was poured into water and extracted with AcOEt. The combined extracts were washed with water, 10% aqueous citric acid, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated to provide a crude oil. This was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:1) as eluent to afford **4a**$_2$ (1.38 g, 73%) as a white solid; mp 137–138 °C (AcOEt–hexane) (Found: C, 64.42; H, 6.18. Calc. for $C_{23}H_{26}O_8$: C, 64.18; H, 6.09%); ν_{max}(KBr)/cm^{-1} 1760; δ_H($CDCl_3$) 2.51–2.71 (m, 1 H), 2.82–3.08 (m, 3 H), 3.41 (s, 3 H), 3.83 (s, 3 H), 3.88 (s, 3 H), 4.53 (s, 2 H), 4.97 (d, 2 H, *J* 7.3), 4.57 (d, 1 H, *J* 6.5), 5.88–5.99 (m, 2 H) and 6.50–6.87 (m, 6 H); *m/z* 430 (M$^+$, 25%), 368 (6), 151 (93) and 135 (100).

Preparation of (3*R,4*R**)-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-acetyloxy-3,4-dimethoxybenzyl]-γ-butyrolactone 4a$_3$**

The alcohol **9a** (1.90 g, 4.92 mmol), acetic anhydride (0.835 cm^3, 8.86 mmol) and triethylamine (1.37 cm^3, 9.84 mmol) were dissolved in DMF (10 cm^3) and to the ice-cooled mixture was added dimethylaminopyridine (60.1 mg, 0.492 mmol). The resulting mixture was stirred at room temperature for 12 h after which it was poured into water and extracted with AcOEt. The combined extracts were washed with water, 10% aqueous citric acid, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated to provide a crude solid product. This was purified by recrystallisation from AcOEt–hexane to afford **4a**$_3$ (1.32 g, 63%) as a white solid; mp 158–159 °C (AcOEt–hexane) (Found: C, 64.45; H, 5.76. Calc. for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65); ν_{max}(KBr)/cm^{-1} 1755 and 1740; δ_H($CDCl_3$) 2.13 (s, 3 H), 2.65–3.04 (m, 4 H), 3.82 (s, 3H), 3.87 (s, 3 H), 3.88–4.11 (m, 2 H), 5.77 (d, 1 H, *J* 6.2), 5.93 (d, 1 H, *J* 1.4), 5.95 (d, 1 H, *J* 1.4), 6.48–6.61 (m, 3 H), 6.69 (d, 1 H, *J* 7.9), 6.74 (dd, 1 H, *J* 1.8, 8.4) and 6.81 (d, 1 H, *J* 8.3); *m/z* 428 (M$^+$, 38%), 368 (16), 167 (100) and 135 (66).

Preparation of (3*R,4*R**)-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-methoxy-3,4-dimethoxybenzyl]-γ-butyrolactone 4a$_4$**

The alcohol **9a** (1.89 g, 4.92 mmol) and methyl iodide (0.915 cm^3, 14.7 mmol) were dissolved in DMF (10 cm^3) and to the ice-cooled mixture was added sodium hydride (235 mg, 5.88 mmol). The resulting mixture was stirred at room temperature for 1 h after which it was poured into water and extracted with AcOEt. The combined extracts were washed with water, 10% aqueous citric acid, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated to provide a crude oil. This was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:1) as eluent to afford **4a**$_4$ (1.37 g, 70%) as a colourless syrup (Found: C, 65.88; H, 6.01. Calc. for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04%); ν_{max}(KBr)/cm^{-1} 1769; δ_H($CDCl_3$) 2.47–2.72 (m, 1 H), 2.83–3.19 (m, 3 H), 3.23 (s, 3 H), 3.73–3.96 (m, 2 H), 3.86 (s, 3 H), 3.89 (s, 3 H), 4.03 (d, 1 H, *J* 6.9), 5.91 (d, 1 H, *J* 1.5), 5.93 (d, 1 H, *J* 1.4) and 6.52–6.92 (m, 6 H); *m/z* 400 (M$^+$, 25%), 181 (100) and 135 (13).

Hydroxylation of the metal enolate of 4 with MoOPH: preparation of (3*S,4*R**)-3-hydroxy-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-hydroxy-3,4-dimethoxybenzyl]-γ-butyrolactone 3a$_1$**

A solution of **4a**$_1$ (2.80 g, 6.11 mmol) in THF (20 cm^3) was added to the solution of $KN(SiMe_3)_2$ (Aldrich, 2.57 g, 12.2 mmol) in THF (50 cm^3) at −78 °C and the mixture was stirred for 30 min at the same temperature. To the mixture was added MoOPH (3.25 g, 9.17 mmol) in one portion. After being stirred for 30 min, the mixture was quenched by addition to it of saturated aqueous sodium sulfate (15 cm^3). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer and extracts were washed with 2 M HCl, water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 (30 cm^3) and to the ice cooled solution was added Bu_4NF (6.72 cm^3, 6.72 mmol). After being stirred for 6 h, the reaction mixture was poured into water and the organic layer was separated and washed with 10% aqueous citric acid, water and brine, dried ($MgSO_4$) and evaporated to afford **3a**$_1$. This was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:3) as eluent to give **3a**$_1$ (86%) as a colourless crystalline solid; mp 171–172 °C (CH_2Cl_2) (Found: C, 62.77; H, 5.53. Calc. for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51%); ν_{max}(KBr)/cm^{-1} 3506 and 1774; δ_H($CDCl_3$) 2.73 (ddd, 1 H, *J* 5.2, 7.2, 9.8), 3.11 (d, 1 H, *J* 13.5), 3.19 (d, 1 H, *J* 13.5), 3.21 (d, 1 H, *J* 2.4), 3.25 (s, 1 H), 3.68 (dd, 1 H, *J* 7.3, 9.7), 3.82 (dd, 1 H, *J* 5.1, 9.7), 3.88 (s, 3 H), 3.90 (s, 3 H), 4.84 (dd, 1 H, *J* 2.3, 9.8), 5.96 (s, 2 H) and 6.71–6.91 (m, 6 H); *m/z* 402 (M$^+$, 21%), 386 (9) and 135 (100).

Preparation of (3*S,4*R**)-3-hydroxy-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-methoxymethoxymethyl-3,4-dimethoxybenzyl]-γ-butyrolactone 3a$_2$**

A solution of **4a**$_2$ (350 mg, 0.814 mmol) in THF (5 cm^3) was added to a solution of $KN(SiMe_3)_2$ (342 mg, 1.63 mmol) in THF (10 cm^3) at −78 °C and the mixture was stirred for 30 min at the same temperature before MoOPH (431 mg, 1.22 mmol) was added to it in one portion. After being stirred for 30 min, the mixture was quenched by the addition to it of saturated aqueous sodium sulfate (5 cm^3). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer and extracts were washed with 2 M HCl, water and brine, dried ($MgSO_4$) and evaporated to afford **3a**$_2$. This was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:1) as an eluent to give **3a**$_2$ (178 mg, 50%) as a colourless crystalline solid; mp 167–168 °C (AcOEt–hexane) (Found: C, 61.77; H, 5.63. Calc. for $C_{23}H_{26}O_9$: C, 61.88; H, 5.87%); ν_{max}(KBr)/cm^{-1} 3469 and 1779; δ_H($CDCl_3$) 2.81 (ddd, 1 H, *J* 8.1, 9.5, 9.7), 3.16 (s, 1 H), 3.27 (d, 1 H, *J* 12.9), 3.35 (d, 1 H, *J* 12.9), 3.44 (s, 3 H), 3.53 (dd, 1 H, *J* 8.1, 9.5), 3.81 (dd, 1 H, *J* 9.5, 9.5), 3.87 (s, 3 H), 3.88 (s, 3 H), 4.53 (d, 1 H, *J* 6.3), 4.62 (d, 1 H, *J* 6.2), 4.88 (d, 1 H, *J* 9.9), 5.95 (s, 2 H), 6.70–6.89 (m, 4 H), 6.87 (dd, 1 H, *J* 1.6, 7.9) and 6.95 (d, 1 H, *J* 1.5); *m/z* 446 (M$^+$, 76%), 211 (60) and 135 (100).

Preparation of (3*S,4*R**)-3-hydroxy-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-acetyloxy-3,4-dimethoxybenzyl]-γ-butyrolactone 3a$_3$**

A solution of **4a**$_3$ (347 mg, 0.810 mmol) in THF (5 cm^3) was added to a solution of $KN(SiMe_3)_2$ (342 mg, 1.63 mmol) in THF (10 cm^3) at −78 °C and the mixture stirred for 30 min at the same temperature. To the mixture was added MoOPH (431 mg, 1.22 mmol) in one portion. After being stirred for 30 min, the mixture was quenched by the addition to it of saturated aqueous sodium sulfate (5 cm^3). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer and extracts were washed with 2 M HCl, water and brine, dried ($MgSO_4$) and evaporated to afford **3a**$_3$ (104 mg, 29% yield) as a colourless crystalline solid; mp 183–184 °C (AcOEt–hexane) (Found: C, 62.09; H, 5.38. Calc. for $C_{23}H_{24}O_9$: C, 62.16; H, 5.44%); ν_{max}(KBr)/cm^{-1} 3456, 1750;

$\delta_H(CDCl_3)$ 1.76 (s, 3 H), 2.57 (d, 1 H, *J* 13.4), 2.95 (br s, 1 H), 2.97–3.25 (m, 1 H), 3.49 (d, 1 H, *J* 13.3), 3.91 (s, 3 H), 3.93 (s, 3 H), 4.01 (dd, 1 H, *J* 9.1, 9.1), 4.26 (dd, 1 H, *J* 5.9, 9.0), 5.17 (d, 1 H, *J* 5.1), 5.90 (s, 2 H), 6.46 (dd, 1 H, *J* 1.7, 7.9), 6.56 (d, 1 H, *J* 1.6), 6.65 (d, 1 H, *J* 7.9), 6.86 (d, 1 H, *J* 1.3) and 6.89 (s, 2 H); *m/z* 444 (M^+, 1.6%) and 428 (100).

Preparation of (3*S,4*S**)-3-hydroxy-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-methoxy-3,4-dimethoxybenzyl]-γ-butyrolactone $3a_4$**

A solution of $4a_4$ (324 mg, 0.810 mmol) in THF (5 cm^3) was added to a solution of $KN(SiMe_3)_2$ (342 mg, 1.63 mmol) in THF (10 cm^3) at −78 °C and the mixture stirred for 30 min at the same temperature. To the mixture was added MoOPH (431 mg, 1.22 mmol) in one portion. After being stirred for 30 min, the mixture was quenched by the addition to it of saturated aqueous sodium sulfate (5 cm^3). The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layers and extracts were washed with 2 M HCl, water and brine, dried ($MgSO_4$) and evaporated to afford $3a_4$. This was purified by silica gel column chromatography using hexane–$CHCl_3$–AcOEt (5:5:1) as eluent to give $3a_4$ (141 mg, 42%) as a syrup (Found: C, 63.30; H, 5.78. Calc. for $C_{22}H_{24}O_8$: C, 63.45; H, 5.81); ν_{max}(KBr)/cm^{-1} 3458 and 1776; $\delta_H(CDCl_3)$ 2.60–2.78 (m, 1 H), 3.08–3.31 (m, 3 H), 3.21 (s, 3 H), 3.56 (dd, 1 H, *J* 7.8, 9.2), 3.77 (dd, 1 H, *J* 9.2, 11.0), 3.88 (s, 3 H), 3.89 (s, 3 H), 4.40 (d, 1 H, *J* 9.7), 5.95 (s, 2 H), 6.66–6.90 (m, 5 H), 6.91 (d, 1 H, *J* 1.4); *m/z* 416 (M^+, 41%), 181 (100) and 135 (66).

Compounds 8b–d

Compounds **8b–d** were prepared in a manner similar to that used for the synthesis of **8a**.

***trans*-3-(3,4,5-Trimethoxybenzyl)-4-(3,4-methylenedioxybenzoyl)-γ-butyrolactone 8b.** Obtained in 71% yield; mp 117–118 °C (AcOEt) (Found: C, 63.69; H, 5.33. Calc. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35%); ν_{max}(KBr)/cm^{-1} 1781 and 1665; $\delta_H(CDCl_3)$ 2.96 (dd, 1 H, *J* 7.2, 14.2), 3.08 (dd, 1 H, *J* 5.5, 14.2), 3.48–3.68 (m, 1 H), 3.71 (s, 6 H), 3.77 (s, 3 H), 3.95–4.18 (m, 2 H), 4.36–4.51 (m, 1 H), 6.06 (s, 2 H), 6.29 (s, 2 H), 6.80 (d, 1 H, *J* 8.1), 7.23 (d, 1 H, *J* 1.7) and 7.28 (dd, 1 H, *J* 1.8, 8.1); *m/z* 414 (M^+, 63%), 208 (100) and 151 (61).

***trans*-3-(3,4-Methylenedioxybenzyl)-4-(3-furoyl)-γ-butyrolactone 8c.** Obtained in 72% yield; mp 96–97 °C (AcOEt–acetone) (Found: C, 64.84; H, 4.50. Calc. for $C_{17}H_{14}O_6$: C, 64.97; H, 4.49%); ν_{max}(KBr)/cm^{-1} 1759 and 1667; $\delta_H(CDCl_3)$ 2.93 (dd, 1 H, *J* 7.5, 14.2), 3.07 (dd, 1 H, *J* 5.4, 14.3), 3.42 (ddd, 1 H, *J* 5.4, 7.5, 8.9), 3.67 (dd, 1 H, *J* 8.6, 17.3), 4.19 (dd, 1 H, *J* 8.4, 8.4), 4.37 (dd, 1 H, *J* 8.7, 8.7), 5.91 (s, 2 H), 6.55 (dd, 1 H, *J* 1.6, 7.8), 6.60–6.71 (m, 3 H), 7.40–7.42 (m, 1 H) and 7.73 (s, 1 H); *m/z* 314 (M^+, 45%), 219 (8), 192 (90) and 135 (100).

***trans*-3-(3-Methoxy-4-benzyloxybenzyl)-4-(3-methoxy-4-benzyloxybenzyl)-γ-butyrolactone 8d.** Obtained in 75% yield; mp 164–165 °C (AcOEt) (Found: C, 73.76; H, 5.67. Calc. for $C_{34}H_{32}O_7$: C, 73.90; H, 5.84%); ν_{max}(KBr)/cm^{-1} 1774, 1662 and 1585; $\delta_H(CDCl_3)$ 3.00 (br d, 2 H, *J* 6.2), 3.42–3.61 (m, 1 H), 3.71 (s, 3 H), 3.90 (s, 3 H), 3.97–4.17 (m, 2 H), 4.25–4.42 (m, 1 H), 5.04 (s, 2 H), 5.22 (s, 2 H), 6.53 (dd, 1 H, *J* 1.9, 8.1), 6.63 (d, 1 H, *J* 2.7), 6.66 (d, 1 H, *J* 8.3), 6.81 (d, 1 H, *J* 8.4), 7.14 (dd, 1 H, *J* 2.0, 8.4), 7.21–7.49 (m, 11 H); *m/z* 552 (M^+, 100%) and 461 (13).

Compounds $4b_1$–d_1

Compound $4b_1$–d_1 were prepared in a manner similar to that used for the synthesis of $4a_1$.

(3*R,4*R**)-3-(3,4,5-Trimethoxybenzyl)-4-[α(*S**)-α-trimethylsilyloxy-3,4-methylenedioxybenzyl]-γ-butyrolactone $4b_1$.** Obtained in 85% yield as a syrup; ν_{max}(KBr)/cm^{-1} 1740; $\delta_H(CDCl_3)$ 0.05 (s, 9 H), 2.45–2.64 (m, 1 H), 2.78 (dd, 1 H, *J* 4.7, 12.1), 2.79–2.94 (m, 1 H), 3.00 (dd, 1 H, *J* 4.7, 11.9), 3.81 (s, 3 H), 3.82 (s, 6 H), 3.86–4.05 (m, 2 H), 4.58 (d, 1 H, *J* 5.6), 5.96 (d, 1 H, *J* 1.3), 5.98 (d, 1 H, *J* 1.3), 6.30 (s, 2 H), 6.62 (s, 3 H), 6.64 (dd, 1 H, *J* 1.5, 6.3), 6.72 (d, 1 H, *J* 8.4); *m/z* 386 (M^+, 40%) and 151 (100).

(3*R,4*R**)-3-(3,4-Methylenedioxybenzyl)-4-[α(*S**)-α-trimethylsilyloxy-3-furyl]-γ-butyrolactone $4c_1$.** Obtained in 73% yield as a syrup; ν_{max}(KBr)/cm^{-1} 1771; $\delta_H(CDCl_3)$ 0.05 (s, 9 H), 2.42–2.62 (m, 1 H), 2.72–2.84 (m, 1 H), 2.85–3.01 (m, 2 H), 3.96 (dd, 1 H, *J* 9.4, 17.5), 3.99 (dd, 1 H, *J* 9.4, 19.4), 4.60 (d, 1 H, *J* 5.6), 5.92 (d, 1 H, *J* 1.2), 5.94 (d, 1 H, *J* 1.3), 6.17 (d, 1 H, *J* 1.0), 6.59 (dd, 1 H, *J* 1.5, 7.8), 6.63 (s, 1 H), 6.72 (d, 1 H, *J* 7.8), 7.23 (d, 1 H, *J* 0.6) and 7.39–7.49 (m, 1 H); *m/z* 388 (M^+, 16%), 135 (79) and 73 (100).

(3*R,4*R**)-3-(3-Methoxy-4-benzyloxybenzyl)-4-[α(*S**)-α-trimethylsilyloxy-3-methoxy-4-benzyloxybenzyl]-γ-butyrolactone $4d_1$.** Obtained in 87% yield as a syrup; ν_{max}(KBr)/cm^{-1}1771; $\delta_H(CDCl_3)$ 0.04 (s, 9 H), 2.41–2.60 (m, 1 H), 2.71 (dd, 1 H, *J* 4.8, 12.8), 2.81–2.96 (m, 1 H), 2.97 (dd, 1 H, *J* 5.5, 12.8), 3.79 (s, 3 H), 3.83 (s, 3 H), 3.92 (d, 2 H, *J* 7.4), 4.58 (d, 1 H, *J* 5.4), 5.10 (s, 2 H), 5.13 (s, 2 H), 6.42 (dd, 1 H, *J* 1.9, 8.1), 6.58 (dd, 1 H, *J* 1.8, 7.6), 6.69 (d, 1 H, *J* 6.3), 6.72 (s, 1 H), 6.77 (d, 1 H, *J* 8.1) and 7.23–7.50 (m, 10 H); *m/z* 626 (M^+, 37%), 413 (25) and 91 (100).

Compounds $3b_1$–d_1

Hydroxylation of compounds $4b_1$–$4d_1$ was carried out under reaction conditions similar to those used in the synthesis of $4a_1$ to afford the α-hydroxylated products $3b_1$–d_1, respectively.

(3*S,4*R**)-3-Hydroxy-3-(3,4,5-trimethoxybenzyl)-4-[α(*S**)-α-hydroxy-3,4-methylenedioxybenzyl]-γ-butyrolactone $3b_1$.** Obtained in 86% yield; mp 119–120 °C (AcOEt–hexane) (Found: C, 61.22; H, 5.53. Calc. for $C_{22}H_{24}O_9$: C, 61.11; H, 5.59%); ν_{max}(KBr)/cm^{-1} 3434 and 1773; $\delta_H(CDCl_3)$ 2.64–2.81 (m, 1 H), 3.10 (d, 1 H, *J* 2.6), 3.16 (d, 1 H, *J* 13.2), 3.25 (d, 1 H, *J* 13.2), 3.26 (s, 1 H), 3.64 (dd, 1 H, *J* 7.6, 9.5), 3.81 (dd, 1 H, *J* 4.7, 11.0), 3.85 (s, 3 H), 3.86 (s, 6 H), 4.88 (dd, 1 H, *J* 2.5, 9.7), 5.96 (s, 2 H), 6.55 (s, 2 H), 6.76 (s, 2 H) and 6.82 (s, 1 H); *m/z* 432 (M^+,24%), 414 (12) and 181 (100).

(3*S,4*R**)-3-Hydroxy-3-(3,4-methylenedioxybenzyl)-4-[α(*S**)-α-hydroxy-3-furyl]-γ-butyrolactone $3c_1$.** Obtained in 89% yield; mp 121–122 °C (AcOEt–hexane) (Found: C, 61.19; H, 4.76. Calc. for $C_{17}H_{16}O_7$: C, 61.44; H, 4.87%); ν_{max}(KBr)/cm^{-1} 3418 and 1736; $\delta_H(CDCl_3)$ 2.74 (ddd, 1 H, *J* 4.8, 7.1, 9.3), 3.12 (s, 2 H), 3.16 (d, 1 H, *J* 2.8), 3.19 (s, 1 H), 3.81 (dd, 1 H, *J* 7.1, 9.9), 3.89 (dd, 1 H, *J* 4.8, 9.8), 4.96 (dd, 1 H, *J* 2.7, 9.4), 5.96 (s, 2 H), 6.40 (s, 1 H), 6.69–6.86 (m, 3 H) and 7.42 (s, 2 H); *m/z* 332 (M^+, 3.4%) and 135 (100).

(3*S,4*R**)-3-Hydroxy-3-(3-methoxy-4-benzyloxybenzyl)-4-[α(*S**)-α-hydroxy-3-methoxy-4-benzyloxybenzyl]-γ-butyrolactone $3d_1$.** Obtained in 95% yield; mp 118–119 °C (AcOEt–hexane) (Found: C, 71.78; H, 5.92. Calc. for $C_{34}H_{34}O_8$: C, 71.56; H, 6.01%); ν_{max}(KBr)/cm^{-1} 3423 and 1755; δ_H(400 MHz, $CDCl_3$) 2.70 (ddd, 1 H, *J* 2.6, 3.7, 4.9), 3.13 (d, 1 H, *J* 13.4), 3.20 (d, 1 H, *J* 13.4), 3.24 (d, 1 H, *J* 2.4), 3.39 (s, 1 H), 3.58 (dd, 1 H, *J* 7.4, 9.7), 3.76 (dd, 1 H, *J* 5.2, 9.7), 3.87 (s, 6 H), 4.83 (dd, 1 H, *J* 2.4, 9.8), 5.13 (s, 2 H), 5.14 (s, 2 H), 6.74 (dd, 1 H, *J* 2.0, 5.4), 6.76 (dd, 1 H, *J* 1.9, 5.2), 6.82 (d, 1 H, *J* 2.3), 6.84 (d, 1 H, *J* 2.3), 6.86 (dd, 1 H, *J* 1.9, 4.0) and 7.26–7.45 (m, 10 H); *m/z* 570 (M^+, 3.0%), 300 (4), 270 (8) and 91 (100).

Intramolecular Friedel–Crafts type cyclisation of 3: preparation of (1*S,2*S**,3*S**)-1-(3,4-dimethoxyphenyl)-2-hydroxymethyl-3-hydroxy-6,7-methylenedioxytetralin-3-carboxylic acid lactone 2a**

The lactone $3a_1$ (1.60 g, 3.98 mmol) was dissolved in CH_2Cl_2 (24 cm^3) and the solution cooled in an ice bath. TFA (2.4 cm^3) was added to the stirred solution and stirring was continued for 12 h. The reaction mixture was then poured into water, and the organic layer was separated, washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated *in vacuo* to afford **2a** (1.34 g) as a white solid (84%). Recrystallisation of this from AcOEt–hexane furnished pure **2a**; mp 247–248 °C (THF–AcOEt) (Found: C, 65.80; H, 5.25. Calc. for $C_{21}H_{20}O_7$: 65.62; H, 5.24%); ν_{max}(KBr)/cm^{-1} 3387 and 1771; $\delta_H(CDCl_3)$

2.39 (s, 1 H), 2.44–2.62 (m, 1 H), 3.08 (d, 1 H, *J* 17.0), 3.22 (d, 1 H, *J* 17.1), 3.83 (s, 3 H), 3.89 (s, 3 H), 4.10 (dd, 1 H, *J* 7.0, 8.3), 4.18 (d, 1 H, *J* 12.1), 4.35 (dd, 1 H, *J* 8.5, 10.7), 5.88 (d, 1 H, *J* 1.3), 5.90 (d, 1 H, *J* 1.3), 6.33 (s, 1 H), 6.61 (br s, 1 H), 6.66 (s, 1 H), 6.75 (dd, 1 H, *J* 1.8, 8.2) and 6.85 (d, 1 H, *J* 8.2); *m/z* 384 (M^+, 100%), 368 (36), 335 (29) and 291 (23).

Cyclisation of the other compounds **3b$_1$–d$_1$** was carried out under similar reaction conditions to afford the 1-aryltetralin lactones **2b–d**.

(1*S,2*S**,3*S**)-1-(3,4-Methylenedioxyphenyl)-2-hydroxymethyl-3-hydroxy-6,7,8-trimethoxytetralin-3-carboxylic acid lactone 2b.** Obtained in 90% yield; mp 204–205 °C (AcOEt) (Found: C, 63.92; H, 5.38. Calc. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35%); ν_{max}(KBr)/cm^{-1} 3384 and 1756; δ_H($CDCl_3$) 2.06 (s, 1 H), 2.26–2.46 (m, 1 H), 3.05 (d, 1 H, *J* 16.8), 3.22 (d, 1 H, *J* 16.8), 3.22 (s, 3 H), 3.75 (s, 3 H), 3.87 (s, 3 H), 4.12–4.25 (m, 2 H), 4.40 (dd, 1 H, *J* 8.3, 10.7), 5.93 (s, 2 H), 6.49–6.65 (m, 3 H) and 6.74 (d, 1 H, *J* 7.9); *m/z* 414 (M^+, 100%) and 135 (30).

(1*R,2*S**,3*S**)-1-(3-Furyl)-2-hydroxymethyl-3-hydroxy-6,7-methylenedioxytetralin-3-carboxylic acid lactone 2c.** Obtained in 91% yield; mp 201–202 °C (AcOEt–hexane) (Found: C, 65.03; H, 4.62. Calc. for $C_{17}H_{14}O_6$: C, 64.97; H, 4.49%); ν_{max}(KBr)/cm^{-1} 3492 and 1760; δ_H($CDCl_3$) 2.27 (s, 1 H), 2.39–2.60 (m, 1 H), 3.06 (d, 1 H, *J* 17.0), 3.19 (d, 1 H, *J* 17.1), 4.13–4.41 (m, 3 H), 5.91 (s, 2 H), 6.15 (s, 1 H), 6.51 (s, 1 H), 6.66 (s, 1 H) and 7.45 (m, 2 H); *m/z* 314 (M^+, 100%), 296 (14) and 252 (22).

(1*S,2*S**,3*S**)-1-(3-Methoxy-4-benzyloxybenzyl)-2-hydroxymethyl-3-hydroxy-6-methoxy-7-benzyloxytetralin-3-carboxylic acid lactone 2d.** Obtained in 93% yield; mp 128–129 °C (THF–AcOEt) (Found: C, 73.85; H, 5.64. Calc. for $C_{34}H_{32}O_7$: C, 73.90; H, 5.84%); ν_{max}(KBr)/cm^{-1} 3484 and 1760; δ_H($CDCl_3$) 2.29 (s, 1 H), 2.36–2.57 (m, 1 H), 3.07 (d, 1 H, *J* 17.0), 3.21 (d, 1 H, *J* 16.9), 3.72 (s, 3 H), 3.88 (s, 3 H), 4.01–4.19 (m, 2 H), 4.32 (dd, 1 H, *J* 8.5, 10.7), 4.83 (d, 1 H, *J* 12.6), 4.93 (d, 1 H, *J* 12.6), 5.18 (s, 2 H), 6.34 (s, 1 H), 6.48 (br s, 1 H), 6.60 (dd, 1 H, *J* 1.7, 9.9), 6.68 (s, 1 H), 6.82 (d, 1 H, *J* 8.2) and 7.08–7.54 (m, 10 H); *m/z* 552 (M^+, 13%), 181 (4) and 91 (100).

Reduction of the lactone ring of 2: preparation of (1*S**,2*S**,3*S**)-1-(3,4-dimethoxyphenyl)-2,3-bis(hydroxymethyl)-3-hydroxy-6,7-methylenedioxytetralin 1a

To an ice-cooled suspension of $LiAlH_4$ (1.00 g, 26.32 mmol) in THF (50 cm^3) was added a solution of **2a** (2.50 g, 6.51 mmol) in THF (50 cm^3), and the resultant mixture was stirred at room temperature for 12 h. The reaction mixture was ice cooled and quenched by successive addition of water (1 cm^3), 15% aqueous NaOH (1 cm^3) and water (3 cm^3). The mixture was stirred for 6 h after which the insoluble material was filtered off, and the filtrate was concentrated *in vacuo* to afford **1a** (2.30 g, 91%) as a white solid. Recrystallisation of this from EtOH–hexane furnished pure **1a**; mp 184–185 °C (EtOH–hexane) (Found: C, 65.23; H, 6.11. Calc. for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23%); ν_{max}(KBr)/cm^{-1} 3330; δ_H($CDCl_3$) 1.99 (ddd, 1 H, *J* 2.5, 5.2, 11.5), 2.47 (br s, 1 H), 2.72 (d, 1 H, *J* 16.7), 2.92 (br t, 1 H, *J* 6.2), 3.07 (d, 1 H, *J* 14.6), 3.11 (s, 1 H), 3.55–3.88 (m, 4 H), 3.82 (s, 3 H), 3.88 (s, 3 H), 4.01 (d, 1 H, *J* 11.4), 5.78–5.90 (m, 2 H), 6.21 (s, 1 H), 6.57 (s, 1 H), 6.62 (d, 1 H, *J* 1.8), 6.75 (dd, 1 H, *J* 1.9, 8.2) and 6.83 (d, 1 H, *J* 8.2); *m/z* 388 (M^+, 33%), 339 (57) and 309 (100).

Reduction of the other compounds **2b–d** was carried out under reaction conditions similar to those described above to afford the 1-aryltetralin triol **1b–d**.

(1*S,2*S**,3*S**)-1-(3,4-Methylenedioxyphenyl)-2,3-bis(hydroxymethyl)-3-hydroxy-6,7,8-trimethoxytetralin-3-carboxylic acid lactone 1b.** Obtained in 81% yield; mp 116–117 °C (AcOEt–hexane) (Found: C, 63.07; H, 6.29. Calc. for $C_{22}H_{26}O_8$: C, 63.15; H, 6.26%); ν_{max}(KBr)/cm^{-1} 3330; δ_H($CDCl_3$) 1.83–1.95 (m, 1 H), 2.73 (s, 1 H), 2.73 (d, 1 H, *J* 16.1), 2.88–3.00 (m, 2 H), 3.04 (d, 1 H, *J* 16.1), 3.20 (s, 3 H), 3.62 (dd, 1 H, *J* 6.7, 11.1), 3.70–3.97 (m, 3 H), 3.74 (s, 3 H), 3.84 (s, 3 H), 4.00 (d, 1 H, *J* 9.4), 5.89 (m, 2 H), 6.45 (s, 1 H), 6.58 (d, 1 H, *J* 1.5), 6.63 (dd, 1 H, *J* 1.6, 8.0) and 6.71 (d, 1 H, *J* 7.9); *m/z* 418 (M^+, 93%), 369 (78) and 339 (100).

(1*R,2*S**,3*S**)-1-(3-Furyl)-2,3-bis(hydroxymethyl)-3-hydroxy-6,7-methylenedioxytetralin-3-carboxylic acid lactone 1c.** Obtained in 71% yield; mp 98–99 °C (AcOEt–hexane) (Found: C, 64.32; H, 5.99. Calc. for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70%); ν_{max}(KBr)/cm^{-1} 3388; δ_H($CDCl_3$) 1.90 (ddd, 1 H, *J* 2.7, 5.2, 11.2), 2.49 (br s, 1 H), 2.71 (d, 1 H, *J* 16.6), 2.83 (br s, 1 H), 3.02 (d, 1 H, *J* 16.6), 3.11 (s, 1 H), 3.60–3.97 (m, 4 H), 4.05 (d, 1 H, *J* 11.2), 5.86 (s, 2 H), 6.10 (s, 1 H), 6.43 (s, 1 H), 6.57 (s, 1 H) and 7.35–7.50 (m, 2 H); *m/z* 388 (M^+, 35%), 300 (31), 296 (68) and 239 (100).

(1*S,2*S**,3*S**)-1-(3-Methoxy-4-benzyloxybenzyl)-2,3-bis(hydroxymethyl)-3-hydroxy-6-methoxy-7-benzyloxytetralin 1d.** Obtained in 90% yield; mp 181–182 °C (AcOEt–hexane) (Found: C, 73.25; H, 6.64. Calc. for $C_{34}H_{36}O_7$: C, 73.36; H, 6.52%); ν_{max}(KBr)/cm^{-1} 3386; δ_H($CDCl_3$) 1.94 (dm, 1 H, *J* 8.9), 2.49 (br s, 1 H), 2.71 (d, 1 H, *J* 16.7), 2.97 (br s, 1 H), 3.05 (d, 1 H, *J* 16.6), 3.10 (s, 1 H), 3.42–3.93 (m, 4 H), 3.73 (s, 3 H), 3.84 (s, 3 H), 3.94 (d, 1 H, *J* 11.5), 4.84 (s, 2 H), 5.17 (s, 2 H), 6.21 (s, 1 H), 6.50 (d, 1 H, *J* 1.8), 6.58 (s, 1 H), 6.60 (dd, 1 H, *J* 1.8, 8.1), 6.80 (d, 1 H, *J* 8.1) and 7.10–7.52 (m, 10 H); *m/z* 556 (M^+, 100%), 507 (33) and 137 (100).

Preparation of (±)-cycloolivil 1e

A mixture of **1d** (750 mg, 1.35 mmol) and Pd–C (200 mg) in MeOH (10 cm^3) and THF (10 cm^3) was shaken for 3 h under a hydrogen atmosphere (1 atm). The insoluble materials were filtered off and the filtrate was evaporated *in vacuo* to give **1e** as a white solid (486 mg, 96%); mp 173–174 °C (EtOH–AcOEt) [lit.,[2] 168–170 °C (EtOH), lit.,[3] 170–171 °C (acetone–hexane)] (Found: C, 63.98; H, 6.17. Calc. for $C_{20}H_{24}O_7$: C, 63.82; H, 6.43%); ν_{max}(KBr)/cm^{-1} 3426; δ_H(400 MHz, CD_3OD) 2.03 (ddd, 1 H, *J* 1.3, 2.0, 5.8), 2.61 (d, 1 H, *J* 16.7), 3.21 (d, 1 H, *J* 16.7), 3.56 (dd, 1 H, *J* 4.4, 11.0), 3.58 (d, 1 H, *J* 11.0), 3.74–3.84 (m, 2 H), 3.77 (s, 3 H), 3.79 (s, 3 H), 3.80 (dd, 1 H, *J* 2.6, 11.0), 4.01 (d, 1 H, *J* 11.7), 6.18 (s, 1 H), 6.63 (s, 1 H), 6.67 (dd, 1 H, *J* 1.9, 8.0), 6.70 (d, 1 H, *J* 1.9) and 6.75 (d, 1 H, *J* 8.0); δ_C(100 MHz, CD_3OD) 39.93, 44.89, 47.56, 56.41, 60.86, 69.42, 74.97, 112.96, 113.94, 116.03, 117.35, 123.57, 126.42, 133.55, 138.47, 145.29, 146.10, 147.49 and 149.11; *m/z* 376 (M^+, 29%), 327 (64), 297 (100) and 137 (567).

X-Ray analysis of 1e

Crystal data. $C_{20}H_{24}O_7$, *M*, 376.40, a = 8.401(3), b = 13.576(4), c = 15.755(2) Å, α = 90.00(0)°, β = 91.46(2)°, γ = 90.00(0)°, V = 1796.3(9) Å^3, monoclinic, $P2_1/a$, Z = 4, D_x = 1.39 g cm^{-3}, $F(000)$ = 800, μ = 0.878 cm^{-1}. The diffraction experiment was carried out using a colourless transparent, columnar crystal, recrystallized from a solution of aqueous acetonitrile, with dimensions of 0.4 × 0.2 × 0.2 mm. The diffractometer AFC 5R (RIGAKU) was used with graphite-monochromated Cu-Kα (λ = 1.5418 Å) radiation. The unit-cell dimensions were determined from angular setting of 25 reflections (2θ values in the range of 70–90°). 2733 Unique reflections (2θ = <130) were measured, of which 2703 with $|F_o| > = 2.0\sigma(F_o)$ were considered reliable. No absorption correction was applied. The structure was solved by a direct method using SHELXS-86[12] and subsequent difference Fourier method. The refinement of atomic parameters was carried out using SHELXL-93[13] with anisotropic thermal parameters for non-H atoms. All hydrogen atoms were located geometrically and fixed. The final R_1 and wR_2 were 0.0536 and 0.1475, respectively. Detailed crystallographic results (atomic coordinates, bond lengths and bond angles and thermal parameters) have been deposited with the Cambridge Crystallographic Data Centre.§ Any request for

§ For details of the scheme, see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1.

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