Stereospecific Synthesis of the 2,3-*trans*-3,4-*cis* Trisubstituted Tetrahydrofuran Lignan (±)-Dihydrosesamin

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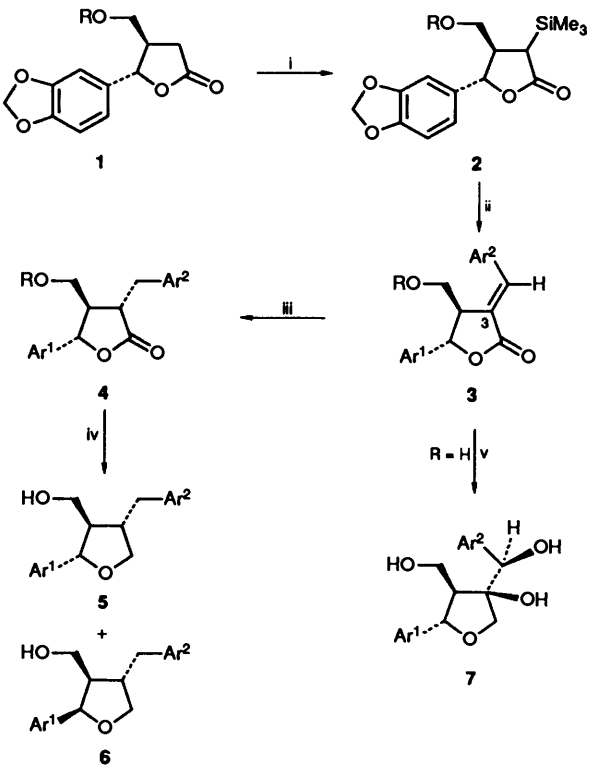
It is shown that the stereochemistry of additions to the 3-arylidene lactones **3** and **9** is controlled by the 5- rather than the 4-substituent; synthesis of the 2,3-*trans*-3,4-*cis* lignan dihydrosesamin **11b** (R = H) thus requires use of the 4,5-*cis*- lactone **8**, in the sequence **8** (R^1 = TBDMS, R^2 = TMS) → **9b** → **10b** → **11b** (R = H), with epimerisation at C-2 following establishment of *cis,cis* geometry.

The natural lignans display a wide variety of constitution based on phenolic and *O*-heterocyclic substructures, and an equally wide range of biological activities are shown by a number of members.[1] A major sub-group is comprised of tri- and tetra-substituted tetrahydrofurans, and the synthesis of this type of compound poses interesting and often unsolved problems of stereocontrol. Following our recent work on the synthesis of 3,7-dioxabicyclo lignans,[2] we turned our attention to (−)-dihydrosesamin **11**. This lignan was isolated from *Daphne tangutica* Maxim., the Chinese drug 'Ai tuotuo' used in the treatment of rheumatism, *etc.*[3] Dihydrosesamin has been obtained only by hydrogenation of natural sesamin.[4] Related natural products are lariciresinol from a variety of conifers, and sanshodiol, from *Xanthoxylum piperitum* DC.[5]

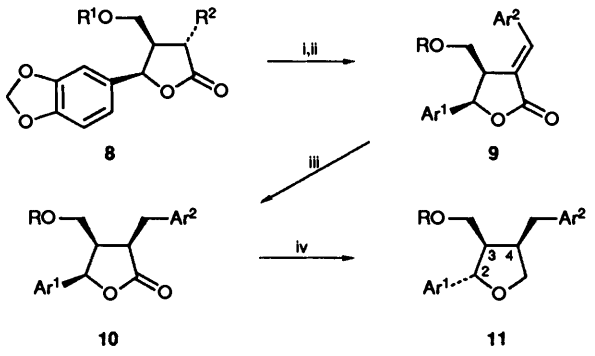
In this paper, we report a total synthesis of racemic dihydrosesamin, employing the lactone alcohols **1** and **8**,[2] available through borane reduction of the corresponding paraconic acids,[6] based on elaboration through α-arylidene lactones. Thus, the (±)-*trans* lactone **1** (R = TBDMS) was treated with trimethylsilyl triflate[7] to yield the *C*-trimethylsilyl lactone **2** (R = TBDMS) (38% when purified chromatographically) which was converted by lithium diisopropylamide and benzaldehyde into the unsaturated lactone **3a** (R = TBDMS) (57%) with the spectroscopic characteristics of an *E*-cinnamate. The arylidene lactones **3a** (R = H) and **3b** (R = H) could also be prepared by reaction of **1** (R = H) with piperonal and benzaldehyde respectively, and sodium methoxide in benzene,[8] in moderate yield. The stereochemistry of **3a** (R = H) was checked by X-ray crystallography[9] and was confirmed as 4,5-*trans* 3-*E*. Hydrogenation of **3b** (R = H) then afforded a single saturated lactone **4b** (R = H). It was expected that this product would have the 3,4-*cis*, -4,5-*trans* stereochemistry with the direction of hydrogenation controlled by the adjacent 4-substituent. However, subsequent chemistry demonstrated the 3,4-trans-4,5-trans geometry. Thus, reduction of the lactone **4b** (R = H) followed by cyclisation in the acidic work-up gave two 2,3,4-trisubstituted tetrahydrofuran alcohols (1:1), neither of which had spectroscopic data matching those of dihydrosesamin, and which were assigned structures **5b** and **6b** on the basis of their mode of preparation (Scheme 1). It was not possible to deduce with complete confidence which isomer had which stereochemistry from the data available from the very small samples. However it was clear that initial addition of hydrogen to the double bond had occurred from the β-face exclusively. Parallel results were obtained with the benzylidene lactone **3a** (R = H). That this was not a hydrogen bonding effect was shown by hydrogenation of the unsaturated lactone as its trisisopropylsilyl derivative **3a** (R = TIPS) which gave the same stereochemical result, despite the bulkier silyl group.

A number of attempts were made to effect other additions to the cinnamyl double bond in **3a** (R = H). However, this function proved surprisingly unreactive; the unsaturated lactone was recovered unchanged from treatment with *m*-chloroperbenzoic acid (reflux chloroform, 7 days); benzeneselenenyl chloride (room temp., 7 days); mercuric trifluoroacetate (tetrahydrofuran, reflux, 7 days); 3,5-dinitroperbenzoic acid; hydrogen peroxide–sodium hydrogencarbonate; and sodium hypochlorite–pyridine. Finally, treatment of **3a** (R = H) or **3b** (R = H) with *N*-methylmorpholine *N*-oxide and catalytic osmium tetraoxide gave the single crystalline triols **7a** and **7b** which were stable under acidic conditions expected to induce ring closure in a 3,4-*cis* compound. Thus, the stereochemistry shown is implied, with addition again occurring at the β-face.



Throughout **a**; Ar^1 = 3,4-methylenedioxyphenyl, Ar^2 = phenyl and r.o.
b; Ar^1 = Ar^2 = 3,4-methylenedioxyphenyl

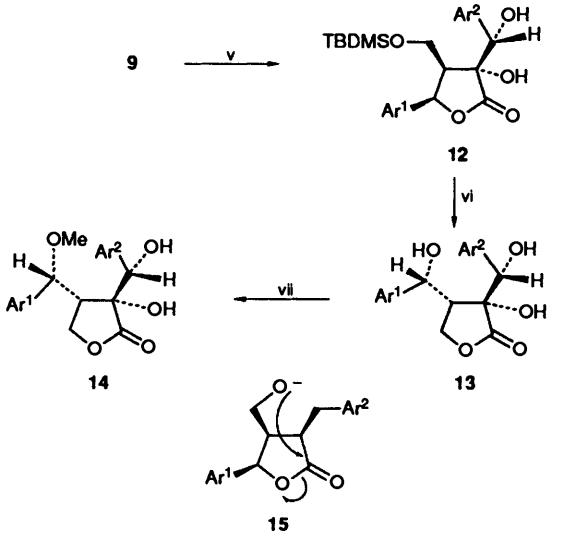
Scheme 1 *Reagents and conditions for all Schemes:* i, TMSOTf, Et_3N, THF, 0 °C, 2 h; ii, LDA, THF, −78 °C; ArCHO, 2 h, −78 °C, 1 h room temp.; iii, H_2, EtOAc, 10% Pd–C; iv, $LiAlH_4$, THF, reflux, 1 h; 2 mol dm^{-3} HCl; v, OsO_4, NMMNO, Bu^{t}OH–THF–H_2O; vi, TBAF, THF, room temp.; vii, MeOH–0.5% HCl, reflux, 1 h



Scheme 2 *Reagents and conditions:* see Scheme 1

However the C-1 epimerisation observed in the conversion of **4b** → **6b** suggested that a successful sequence could be initiated from the *cis*-lactone **8**. The α-arylidene lactone **9b** (R = TBDMS) was formed by the Peterson procedure as above, *via* **8** (R^1 = TBDMS, R^2 = H) and **8** (R^1 = TBDMS, R^2 = TMS) and hydrogenation proceeded smoothly to give the 3,4-*cis*-4,5-*cis* tetrahydrofuranone **10b** (Scheme 2). Lithium aluminium hydride reduction of this lactone gave a diol which cyclised and was deprotected in isolation with aqueous acid and ethyl acetate, to afford (±)-dihydrosesamin **11b** (R = H) and its acetate **11b** (R = Ac) (34%). The ^{1}H NMR data of the alcohol and of its acetate agreed well with those reported in the literature. No 2,3-*cis* products were isolated.

In an effort to exploit this chemistry to form 3,7-dioxabicyclo[3.3.0]octane lignans, requiring *cis* tetrahydrofuran fusion, we effected hydroxylation of the arylidene lactone **9b** (R = TBDMS) to the diol **12b**. However, desilylation using tetrabutylammonium fluoride gave a triol which was clearly, from NMR spectroscopy, a 3,4-disubstituted tetrahydrofuranone rather than a 3,4,5-trisubstituted one. Rearrangement as in **15** is envisaged to lead to the 3,4-*trans*-triol **13b** (Scheme 3).



Scheme 3 *Reagents and conditions:* see Scheme 1

In accord with this geometry, treatment of **13b** with acidic methanol did not induce ring closure but gave only the monomethyl ether **14b**.* The structure and stereochemistry deduced on mechanistic grounds were confirmed by X-ray crystallography.[9] Anchimeric assistance to methanolysis by the 3-hydroxy group at the further benzylic site, with retention of configuration, is proposed.

* The configurations of **13b** and **14b** were incorrectly shown in a preliminary publication.[10]

Experimental

All solvents were dried before use by standard methods. Petroleum means light petroleum, b.p. 40–60 °C. For other experimental generalisations see *J. Chem. Soc. Perkin Trans. 1*, 1991, 1901.

trans-4-(tert-*Butyldimethylsilyloxymethyl*)-5-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The *trans*-lactone alcohol **1** (R = H)[2] (3.24 g), imidazole (2.33 g) and *tert*-butyldimethylsilyl chloride (2.5 g) were dissolved in dry dimethylformamide (50 ml) and the solution was stirred overnight. The mixture was diluted with aq. sodium hydrogencarbonate and extracted with petroleum (4 × 60 cm^3). Drying, evaporation, and chromatography of the residue (ether–petroleum gradient) afforded the *title compound* **1** (R = TBDMS) (3.50 g, 73%), m.p. 57 °C from hexane (Found: C, 61.7; H, 7.8%; $M^+ - Bu^t$ 293.087. $C_{18}H_{26}O_5Si$ requires C, 61.7; H, 7.5%; *M* − Bu^t 293.085); ν_{max}/cm^{-1} 1770, 1500, 1005, 950, 840 and 785; δ_H(250 MHz, $CDCl_3$) 0.07 and 0.08 (each 3 H, s, SiMe), 0.91 (9 H, s, $SiMe_3$), 2.56 (1 H, m, 4-H), 2.62–2.67 (2 H, m, 3-H_2), 3.66 (2 H, d, *J* 4, CH_2O), 5.27 (1 H, d, *J* 6.6, 5-H), 5.97 (2 H, s, OCH_2O) and 6.78–6.82 (3 H, m, ArH).

trans-4-(tert-*Butyldimethylsilyloxymethyl*)-5-(3,4-*methylenedioxyphenyl*)-3E-*benzylidenedihydrofuran*-2(3H)-*one*.—The lactone **1** (R = TBDMS) (1.06 g) in tetrahydrofuran (THF) (25 cm^3) under nitrogen at 0 °C was treated with triethylamine (1.26 cm^3) and then trimethylsilyl trifluoromethanesulphonate (1.46 cm^3). The mixture was stirred for 2 h. Ether (50 cm^3) was added and the solution was washed with dil. hydrochloric acid, dried, and evaporated. Chromatography of the residue (ether–petroleum gradient) gave the title *silyl lactone* **2** (R = TBDMS) (0.47 g, 38%) as an oil (Found: M^+, 422.195. $C_{21}H_{34}O_5Si$ requires *M*, 422.195). Lithium diisopropylamide was prepared from diisopropylamine (0.18 cm^3) and butyl-lithium (1.4 mol dm^{-3} in hexane; 0.90 cm^3) in THF (25 cm^3) at 0 °C. This solution was cooled to −78 °C and the lactone **2** (R = TBDMS) (0.47 g) in THF (2 cm^3) was added. The mixture was stirred for 15 min, when benzaldehyde (0.21 g) in THF (1 cm^3) was added. Stirring was continued for 2 h, when the mixture was allowed to warm to room temperature. The mixture was quenched with water and extracted with ether. The washed, dried, extracts were evaporated and the residue was chromatographed (ether–petroleum gradient) to yield the *title compound* **3a** (R = TBDMS) (0.27 g, 59%), m.p. 97–98 °C from hexane (Found: C, 68.85; H, 7.25%; M^+, 438.185. $C_{25}H_{30}O_5Si$ requires C, 68.5; H, 6.9%; *M*, 438.186); ν_{max}/cm^{-1} 1740, 1645, 1495, 1035, 850, 785 and 695; δ_H(400 MHz, $CDCl_3$) 0.03 and 0.05 (each 3 H, s, $SiMe_2$), 0.91 (9 H, s, Bu^t), 3.78 (2 H, m, CH_2O), 3.92 (1 H, m, 4-H), 5.59 (1 H, s, 5-H), 4.94 (2 H, s, OCH_2O), 6.78–6.79 (3 H, m, ArH) and 7.39–7.53 (5 H, PhH).

trans-4-*Hydroxymethyl*-5-(3,4-*methylenedioxyphenyl*)-3E-(3,4-*methylenedioxybenzylidene*)*dihydrofuran*-2(3H)-*one*.—The hydroxymethyl lactone **1** (R = H) (4.0 g), piperonal (3.80 g) and sodium methoxide (2.01 g) were stirred together in dry benzene (80 cm^3) overnight. Dilute sulfuric acid was added, and the mixture was stirred for a further 4 h. The organic layer was separated, dried, and evaporated; the residue was chromatographed (ethyl acetate–hexane gradient) to yield the *title compound* **3b** (R = H) (2.1 g, 34%), m.p. 150 °C from ethyl acetate–hexane (Found: C, 64.9; H, 4.4%; M^+, 368.088.

$C_{20}H_{16}O_7$ requires C, 65.2; H, 4.4%; *M*, 368.090); ν_{max}(KBr)/cm^{-1} 3420, 1715, 1640, 1610, 1500, 1455, 1045, 935 and 825; δ_H(400 MHz, [$^2H_6$]acetone) 3.72 (2 H, m, 4-H, C*H*HOH), 3.99 (1 H, m, CH*H*OH), 5.64 (1 H, d, *J* 0.9, 5-H), 5.99 (1 H, ABq, *J* 0.9, OCH_2O), 6.08 (1 H, ABq, *J* 0.9, OCH_2O), 6.81–7.24 (6 H, m, ArH) and 7.49 (1 H, d, *J* 1.2, C=CH).

The corresonding lactone **3a** (R = H) was made by a parallel method, and afforded the triisopropylsilyl derivative **3a** (R = TIPS) using the method above for TBDMS derivatives; the compound was an oil (Found: M$^+$, 480.233. $C_{28}H_{36}O_5Si$ requires *M*, 480.233); δ_H(250 MHz, $CDCl_3$) 0.96 (21 H, s, Pr$^i_3$), 3.60 (1 H, m, 4-H), 3.64 (1 H, dd, *J* 1.8, 9.2, C*H*HOSi), 3.91 (1 H, dd, *J* 3.5, 9.2, CH*H*OSi), 5.57 (1 H, s, 5-H), 5.83 (2 H, s, OCH_2O), 6.65–6.73 (ArH), 7.27–7.30 (2 H, PhH), 7.41–7.44 (2 H, m, PhH) and 7.56 (1 H, d, *J* 1.7, C=CH).

4β-*Hydroxymethyl*-3α-(3,4-*methylenedioxybenzyl*)-5α-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The lactone **3b** (R = H) (103.1 mg) in ethyl acetate (5 cm^3) was hydrogenated over palladium on carbon catalyst until all the starting material had reacted (TLC). Filtration, evaporation, and PLC (ethyl acetate–hexane, 1:1) gave the *title compound* **4b** (R = H) (68.0 mg, 66%), as a gum (Found: M$^+$, 370.105. $C_{20}H_{18}O_7$ requires *M*, 370.105); ν_{max}(KBr)/cm^{-1} 1765, 1490, 1445, 1040, 935, 815 and 735; δ_H(400 MHz, $CDCl_3$) 2.17 (1 H, br s, OH), 2.23 (1 H, m, 4-H), 2.95 (1 H, dd, *J* 15.4, 8.4, CH*H*Ar), 3.06–3.12 (1 H, m, 3-H, C*H*HAr), 3.42 (1 H, dd, *J* 11.4, 4.1, C*H*HOH), 3.53 (1 H, dd, *J* 11.2, 3.4, CH*H*OH), 5.14 (1 H, d, *J* 9.0, 5-H), 5.92 and 5.93 (each 2 H, s, OCH_2O), and 6.56–6.73 (6 H, m, ArH).

3α-*Benzyl*-4β-*hydroxymethyl*-5α-(3,4-*methylenedioxyphenyl*)-*dihydrofuran*-2(3H)-*one*.—The benzylidene lactone **3a** (R = H) (72.9 mg) was hydrogenated over palladium on carbon catalyst until all the starting material had reacted (TLC). Filtration, evaporation, and PLC (ethyl acetate–hexane, 1:1) gave the *title compound* **4a** (R = H) (71.8 mg, 98%), as a gum (Found: M$^+$, 326.116. $C_{19}H_{18}O_5$ requires *M*, 326.115); ν_{max}(KBr)/cm^{-1} 3460, 1760, 1490, 1450, 1040, 995, 810 and 705; δ_H(400 MHz, $CDCl_3$) 2.10 (1 H, br s, OH), 2.21 (1 H, m, 4-H), 3.02 (1 H, m, C*H*HPh), 3.12–3.22 (2 H, m, 3-H, CH*H*Ph), 3.32 (1 H, dd, *J* 11.3, 4.0, C*H*HOH), 3.46 (1 H, dd, *J* 11.3, 3.3, CH*H*OH), 5.13 (1 H, d, *J* 9.2, 5-H), 5.91 (2 H, s, OCH_2O), 6.53–6.77 (3 H, m, ArH) and 7.17–7.36 (5 H, m, PhH).

3β-*Hydroxy*-4α,(3,4-*methylenedioxybenzyl*)-2α-(3,4-*methylenedioxyphenyl*)*tetrahydrofuran* *and* 3β-*Hydroxy*-4α-(3,4-*methylenedioxybenzyl*)-2β-(3,4-*methylenedioxyphenyl*)*tetrahydrofuran*.—The lactone **4** (R = H) (38.6 mg) was refluxed in THF (5 cm^3) with lithium aluminium hydride (20 mg) for 2 h. The mixture was poured into ethyl acetate and washed with dil. hydrochloric acid. The organic layer was collected, dried, and evaporated. PLC (ethyl acetate–hexane) gave two products, the tetrahydrofurans **5b** and **6b**. The higher R_F isomer (3.0 mg) had δ_H(400 MHz, $CDCl_3$) 1.59 (1 H, OH), 1.95 (1 H, m, 4-H), 2.45 (1 H, m, 3-H), 2.66 (1 H, dd, *J* 13.7, 8.4, C*H*HAr), 2.76 (1 H, dd, *J* 13.7, 6.9, CH*H*Ar), 3.62 (2 H, d, *J* 5.5, 5-H_2), 3.82 (1 H, dd, *J* 8.8, 6.0, C*H*HOH), 3.94 (1 H, dd, *J* 8.8, 7.3, CH*H*OH), 4.59 (1 H, d, *J* 8.0, 2-H), 5.93 and 5.96 (each 2 H, s, OCH_2O) and 6.61–6.91 (6 H, m, ArH).

The lower R_F isomer (2.9 mg) (Found: M$^+$, 356.123. $C_{20}H_{20}O_6$ requires *M*, 356.126) had δ_H(400 MHz, $CDCl_3$) 1.59 (1 H, OH), 2.08 (1 H, m, 4-H), 2.41 (1 H, m, 3-H), 2.63 (1 H, dd, *J* 13.8, 8.7, C*H*HAr), 2.79 (1 H, dd, *J* 13.8, 6.4, CH*H*Ar), 3.83 (1 H, dd, *J* 8.9, 6.0, C*H*HOH), 3.93 (1 H, dd, *J* 8.9, 7.3, CH*H*OH), 4.07 (2 H, d, *J* 5.5, 5-H_2), 4.52 (1 H, d, *J* 8.1, 2-H), 5.93 and 5.96 (each 2 H, s, OCH_2O) and 6.58–6.87 (6 H, m, Ar-H).

3β-*Hydroxy*-4β-*hydroxymethyl*-3α-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-5α-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The arylidene lactone **3b** (R = H) (200.1 mg) was dissolved in *tert*-butyl alcohol–THF–water (10:3:1; 10 cm^3) and osmium tetroxide (6.9 mg in *tert*-butyl alcohol, 0.69 cm^3) and *N*-methylmorpholine *N*-oxide (127 mg) were added. The solution was stirred for 10 days, when sodium metabisulfite (1 g) and water (2 cm^3) were added. After being stirred for a further 1 h, the mixture was added to ethyl acetate (20 cm^3), which was then washed with brine. The aqueous layers were extracted again, and the combined organic layers were dried and evaporated. Purification of the product by PLC gave the *title compound* **7b** (60.3 mg, 28%; 47% based on recovered starting material), m.p. 185 °C from chloroform (Found: C, 59.9; H, 4.4%; M$^+$, 402.093. $C_{20}H_{18}O_9$ requires C, 59.7; H, 4.5%; *M*, 402.095); ν_{max}(KBr)/cm^{-1} 3510–3340, 1735, 1490, 1035, 930 and 820; δ_H(250 MHz, [$^2H_6$]acetone) 2.76 (1 H, m, 4-H), 4.06–4.08 (2 H, m, CH_2OH), 4.17 (1 H, s, OH), 4.53 (1 H, m, OH), 5.12 (1 H, s, C*H*OHAr), 5.37 (1 H, d, *J* 4.0, CHO*H*Ar), 5.41 (1 H, d, *J* 10.4, 5-H), 5.97 and 6.03 (each 2 H, s, OCH_2O) and 6.73–6.96 (6 H, m, ArH).

3β-*Hydroxy*-4β-*hydroxymethyl*-3α-(α-*hydroxybenzyl*)-5α-(3,-4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The benzylidene lactone **3a** (R = H) (87 mg) was treated with *N*-methylmorpholine *N*-oxide and osmium tetroxide as in the previous experiment. Product isolation in a parallel fashion afforded the *title compound* **7a** (39.0 mg, 41%), m.p. 151–154 °C from chloroform (Found: C, 63.4; H, 5.1%; M$^+$, 358.107. $C_{19}H_{18}O_7$ requires C, 63.7; H, 5.1%; *M*, 358.105); ν_{max}(KBr)/cm^{-1} 3520–3340, 1740, 1490, 1040, 980, and 825; δ_H(250 MHz, [$^2H_6$]acetone) 2.78 (1 H, m, 4-H), 4.08–4.11 (2 H, m, CH_2OH), 4.21 (1 H, br s, OH), 4.56 (1 H, br s, OH), 5.19 (1 H, s, C*H*OHPh), 5.39 (1 H, br s, OH), 5.42 (1 H, d, *J* 10.3, 5-H), 6.03 (2 H, s, OCH_2O), 6.85–6.97 (3 H, m, ArH) and 7.23–7.45 (5 H, m, PhH).

cis-4-*Hydroxymethyl*-5-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The *cis*-paraconic acid[6] (4.00 g) was dissolved in dry THF (50 cm^3) under nitrogen, and cooled to 0 °C. Borane–methyl sulfide (2 mol dm^{-3} solution in THF; 12.0 cm^3) was added over 10 min. The reaction mixture was stirred overnight and then was allowed to warm to room temperature. Methanol was added dropwise and the solution was then evaporated. The residue was partitioned between ethyl acetate and aq. sodium hydrogen bicarbonate. The organic layers were dried and evaporated to give a residue which was chromatographed (ethyl acetate–petroleum gradient) to yield the *title compound* **8** (R^1 = R^2 = H) (3.06 g, 81%) as a viscous oil (Found: M$^+$, 236.067. $C_{12}H_{12}O_5$ requires *M*, 236.069); ν_{max}/cm^{-1} 3460, 1790, 1511, 1050, 945, and 815; δ_H(400 MHz, $CDCl_3$) 1.86 (1 H, br s, OH), 2.63 (1 H, dd, *J* 17.5, 4.9, 3-Ha), 2.76 (1 H, dd, *J* 17.5, 8.3, 3-Hb), 2.86–2.93 (1 H, m, 4-H), 3.31–3.36 (2 H, m, CH_2OH), 5.60 (1 H, d, *J* 6.8, 5-H), 5.98 (2 H, s, OCH_2O) and 6.74–6.82 (3 H, m, ArH).

This product formed a tert-*butyldimethylsilyl derivative* **8** (R^1 = TBDMS, R^2 = H) using the method above, m.p. 69 °C from hexane (Found: C, 61.75; H, 7.7%; M$^+$, 350.154. $C_{18}H_{26}O_5Si$ requires C, 61.7; H, 7.5%; *M*, 350.155); ν_{max}(KBr)/cm^{-1} 1755; δ_H(250 MHz, $CDCl_3$) −0.09 and −0.07 (each 3 H, s, SiMe), 0.85 (9 H, s, Bu^{t}Si), 2.54–2.82 (3 H, m, 3-H_2, 4-H), 3.28–3.30 (2 H, m, CH_2OSi), 5.56 (1 H, d, *J* 6.3, 5-H), 5.97 (2 H, ABq, *J* 1.3, OCH_2O) and 6.72–6.84 (3 H, m, ArH).

4β-(tert-*Butyldimethylsilyloxymethyl*)-5β-(3,4-*methylenedioxyphenyl*)-3α-*trimethylsilyldihydrofuran*-2(3H)-*one*.—The *cis*-lactone **8** (R = TBDMS) (1.79 g) in ether (25 cm^3) under nitrogen at 0 °C was treated with triethylamine (1.64 cm^3) and

trimethylsilyl trifluoromethanesulfinate (2.07 cm^3). After 1 h, ether (50 cm^3) and dil. hydrochloric acid were added. The organic fraction was washed with aq. sodium hydrogen carbonate, dried, and evaporated. The residue was chromatographed (ether–petroleum, 1:2) to provide the *title compound* **8** (R^1 = TBDMS, R^2 = TMS) (0.59 g, 27%) as a solid (M^+, 365.121. $C_{21}H_{34}O_5Si_2$–C_4H_9 requires *M*, 365.124); δ_H(90 MHz, $CDCl_3$) −0.09 (6 H, s, $SiMe_2$), 0.26 (9 H, s, $SiMe_3$), 0.83 (9 H, s, SiBu^t), 2.36 (1 H, d, *J* 2.2, 3-H), 2.71 (1 H, m, 4-H), 3.15–3.24 (2 H, m, CH_2OSi), 5.42 (1 H, d, *J* 7.0, 5-H), 5.97 (2 H, s, OCH_2O) and 6.77–6.83 (3 H, m, ArH).

4β-tert-*Butyldimethylsilyloxymethyl*-5β-(3,4-*methylenedioxyphenyl*)-3E-(3,4-*methylenedioxybenzylidene*)*dihydrofuran*-2(3H)-*one*.—LDA [from diisopropylamine (0.22 cm^3), 1.54 mmol) and butyl-lithium (1.54 mmol) in hexane] in THF (20 cm^3) at −78 °C was treated with the silyl lactone **8** (0.59 g) in THF (2 cm^3). After 15 min piperonal (0.23 g) in THF (2 cm^3) was added, and the mixture was stirred at −78 °C for 1 h and then was allowed to warm to 0 °C over 1 h. Water was added followed by ether and brine; the organic layer was separated, washed, and dried. Evaporation and chromatography (ether–petroleum, 1:3) of the residue afforded the *title compound* **9b** (R = TBDMS) (0.477 g, 60%), m.p. 167–168 °C from hexane (Found: C, 64.6; H, 6.4%; M^+, 482.177. $C_{26}H_{30}O_7Si$ requires C, 64.7; H, 6.3%; *M*, 482.176); ν_{max}(KBr)/cm^{-1} 1745, 1650, 1490, 1040, 940, 815 and 780; δ_H(400 MHz, $CDCl_3$) −0.24 (6 H, s, $SiMe_2$), 0.73 (9 H, s, SiBu^t), 3.41 (1 H, dd, *J* 10.3, 4.0, C*H*HOSi), 3.60 (1 H, dd, *J* 10.3, 5.2, CH*H*OSi), 3.74–3.79 (1 H, m, 4-H), 5.53 (1 H, d, *J* 6.4, 5-H), 5.96–5.97 (2 H, ABq, *J* 1.4, OCH_2O), 6.01–6.02 (2 H, ABq, *J* 1.3, OCH_2O), 6.77–7.15 (6 H, m, ArH) and 7.54 (1 H, d, *J* 1.5, C=CH).

4β-tert-*Butyldimethylsilyloxymethyl*-3β-(3,4-*methylenedioxybenzyl*)-5β-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The arylidene lactone **9b** (R = TBDMS) (151.4 mg) was hydrogenated in ethyl acetate over 10% palladium on carbon using TLC monitoring. Filtration, evaporation and chromatography (ether–petroleum, 1:4 → 1:3) gave the *title compound* **10b** (R = TBDMS) (112.8 mg, 74%), m.p. 107 °C from hexane (Found: C, 64.4; H, 6.9%; M^+, 484.190. $C_{26}H_{32}O_7Si$ requires C, 64.4; H, 6.7%; *M*, 484.192); ν_{max}(KBr)/cm^{-1} 1760, 1500, 1450, 1045, 925, 840 and 785; δ_H(400 MHz, $CDCl_3$) −0.18 and −0.01 (each 3 H, s, SiMe), 0.92 (9 H, s, Bu^{t}Si), 2.52 (1 H, m, 3-H), 2.84 (1 H, dd, *J* 15.0, 10.5, C*H*HAr), 3.10 (1 H, m, 4-H), 3.28 (1 H, d, *J* 10.8, C*H*HOSi), 3.35 (1 H, dd, *J* 15.0, 3.4, CH*H*Ar), 3.57 (1 H, dd, *J* 10.8, 2.6, CH*H*OSi), 5.43 (1 H, d, *J* 5.4, 5-H), 5.94 (4 H, s, 2 × OCH_2O), 6.71–6.79 (5 H, m, ArH) and 6.93 (1 H, s, ArH).

Dihydrosesamin and Dihydrosesamin Acetate.—The lactone **10b** (R = TBDMS) (91 mg), lithium aluminium hydride (60 mg), and THF (5 cm^3) were refluxed together for 1 h. Ethyl acetate was added followed by dil. hydrochloric acid. The organic extracts were dried and evaporated and the residue was chromatographed (ether–petroleum gradient) to yield *dihydrosesamin* **11b** (R = H) (17.2 mg, 26%) and its *acetate* **11b** (R = Ac) (6.2 mg, 8%), as colourless oils. The former (Found: M^+, 356.127. $C_{20}H_{20}O_6$ requires *M*, 356.126) showed ν_{max}/cm^{-1} 3380, 1610, 1500, 1440, 1110, 1030 and 950; δ_H(400 MHz, $CDCl_3$) 1.67 (1 H, br s, OH), 2.35 (1 H, m, 3-H), 2.52 (1 H, dd, *J* 13.5, 10.4, C*H*HAr), 2.69 (1 H, m, 4-H), 2.87 (1 H, dd, *J* 13.5, 5.2, CH*H*Ar), 3.71 (1 H, dd, *J* 8.6, 6.5, 5-H), 3.74 (1 H, dd, *J* 12.6, 6.5, C*H*HOH), 3.88 (1 H, dd, *J* 10.8, 6.9, CH*H*OH), 4.04 (1 H, dd, *J* 8.5, 6.6, 5-H), 4.79 (1 H, d, *J* 6.2, 2-H), 5.93 and 5.94 (each 2 H, s, OCH_2O) and 6.62–6.83 (6 H, m, ArH); δ_C(400 MHz, $CDCl_3$) 33.3, 42.3, 52.6, 60.9, 72.9, 82.9, 100.9, 101.0, 106.3, 108.1, 108.3, 108.9, 119.1, 121.4, 134.2, 137.1, 146.0, 147.7, 147.8 and 147.9.

The latter (Found: M^+, 398.134. $C_{22}H_{22}O_7$ requires *M*, 398.134) showed ν_{max}/cm^{-1} 1725, 1480, 1430, 1120 and 930; δ_H(400 MHz, $CDCl_3$) 2.04 (3 H, s, COMe), 2.47–2.54 (2 H, m, C*H*HAr, 4-H), 2.69 (1 H, m, 3-H), 2.80 (1 H, dd, *J* 13.4, 5.0, CH*H*Ar), 3.71 (1 H, dd, *J* 8.6, 6.9, 5-Ha), 4.05 (1 H, dd, *J* 8.6, 6.6, 5-Hb), 4.15 (1 H, dd, *J* 11.2, 7.5, C*H*HOAc), 4.31 (1 H, dd, *J* 11.2, 4.3, CH*H*OAc), 4.76 (1 H, d, *J* 6.1, 2-H), 5.93 and 5.94 (each 2 H, s, OCH_2O), 6.60–6.81 (6 H, m, ArH); δ_C(400 MHz, $CDCl_3$) 21.0, 33.3, 42.4, 49.2, 62.7, 72.8, 83.1, 101.0, 101.1, 106.3, 108.1, 108.4, 108.9, 119.2, 121.5, 133.8, 136.6, 146.1, 147.1, 147.9 and 171.0.

4β-tert-*Butyldimethylsilyloxymethyl*-3α-*hydroxy*-3β-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-5β-(3,4-*methylenedioxyphenyl*)*dihydrofuran*-2(3H)-*one*.—The arylidene lactone **9b** (R = TBDMS) (106.9 mg) was dissolved in *tert*-butyl alcohol–THF–water (10:3:1; 10 cm^3) and osmium tetroxide (2.8 mg in *tert*-butyl alcohol, 0.28 cm^3) and *N*-methylmorpholine *N*-oxide (52 mg) were added. The solution was stirred for 17 days at room temperature, and the product was isolated as in the preceding experiment, using chromatography (ether–petroleum, 1:3 → 1:1) to provide the *title diol* **12b** (70.8 mg, 62%), m.p. 188–190 °C from hexane containing a little chloroform (Found: C, 60.5; H, 6.4 $C_{26}H_{32}O_9Si$ requires C, 60.45; H, 6.2%); ν_{max}(KBr)/cm^{-1} 3500, 3445, 1770, 1490, 1040, 940, 815, 775 and 705; δ_H(400 MHz, $CDCl_3$) −0.25 and −0.05 (each 3 H, s, SiMe), 0.95 (9 H, s, Bu^{t}Si), 2.39 (1 H, m, 4-H), 3.16 (1 H, d, *J* 10.9, C*H*HOSi), 3.33 (1 H, dd, *J* 10.9, 2.4, CH*H*OSi), 4.14 (1 H, d, *J* 2.7, CHO*H*Ar), 4.25 (1 H, s, 3-OH), 5.23 (1 H, d, *J* 2.3, C*H*OHAr), 5.96–5.99 (4 H, m, 2 × OCH_2O), 6.03 (1 H, d, *J* 5.2, 5-H) and 6.75–7.06 (6 H, m, ArH).

3α-*Hydroxy*-3β,4α-*bis*(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-*dihydrofuran*-2(3H)-*one*.—The diol **12b** (58.0 mg) in THF (10 cm^3) was treated with tetrabutyl ammonium fluoride (1.0 mol dm^3 in THF; 0.34 cm^3). The solution was stirred overnight. The solution was evaporated to dryness and the residue was dissolved in methanol (10 cm^3) containing conc. hydrochloric acid (2 drops). After 1 h at room temperature the solution was evaporated and the residue was chromatographed (ether–petroleum gradient) to yield the *title triol* **13b** (25.6 mg, 59%) as an amorphous solid (Found: C, 60.0; H, 4.9. $C_{20}H_{18}O_9$ requires C, 59.7; H, 4.5%); δ_H(400 MHz, $CDCl_3$) 2.26 (1 H, br s, OH), 2.66 (1 H, m, 4-H), 3.33 (1 H, dd, *J* 8.2, 9.4, 5-Ha), 3.70 (1 H, br s, OH), 4.24 (1 H, br s, OH), 4.26 (1 H, dd, *J* 9.4, 5.1, 5-Hb), 4.91 (1 H, s, C*H*OHAr), 4.93 (1 H, s, C*H*OHAr′), 5.03 (1 H, br s, OH), 5.92 and 5.93 (each 2 H, s, OCH_2O) and 6.65–6.97 (6 H, m, ArH).

3α-*Hydroxy*-3β-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-4α(α-*methoxy*-3,4-*methylenedioxybenzyl*)*dihydrofuran*-2(3H)-*one*.—The previous experiment was repeated using the diol prepared as above from the lactone **9** (165.4 mg); the methanolic hydrochloric acid solution was this time refluxed for 1 h. Product isolation in the same way yielded the *title methoxy diol* **14b** (55.5 mg, 39%), m.p. 172–173 °C) (Found: C, 60.0; H, 4.9%; M^+, 384.083. $C_{21}H_{20}O_9$ requires C, 60.6; H, 4.8%; *M*, 384.085); ν_{max}(KBr)/cm^{-1} 3470, 3000, 1750, 1490, 1040, 930 and 815; δ_H(400 MHz, $CDCl_3$) 1.68 (1 H, br s, OH), 2.58 (1 H, m, 4-H), 3.25 (3 H, s, OMe), 3.36 (1 H, dd, *J* 9.4, 7.9, 5-Ha), 4.30 (1 H, dd, *J* 9.4, 5.1, 5-Hb), 4.33 (1 H, br s, OH), 4.52 (1 H, d, *J* 2.8, C*H*OMeAr), 4.90 (1 H, s, C*H*OHAr), 5.95 (2 H, ABq, *J* 1.4, OCH_2O), 5.97 (2 H, ABq, *J* 1.4, OCH_2O) and 6.65–6.98 (6 H, m, ArH).

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