Enantioselective total synthesis of the di-*O*-methyl ethers of (−)-agatharesinol, (+)-hinokiresinol and (−)-sugiresinol, characteristic norlignans of *Coniferae* [1]

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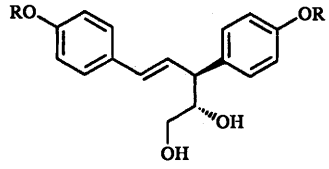
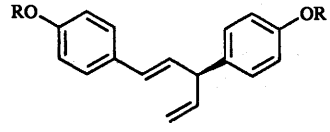
Facile enantioselective syntheses of the di-*O*-methyl ethers of the norlignans, (−)-agatharesinol (−)-1a, (+)-hinokiresinol (+)-2a and (−)-sugiresinol (−)-3a are described. Grignard addition of vinylmagnesium bromide to an aldimine (−)-13, prepared from the *tert*-butyl ester 11 and 4-methoxycinnamaldehyde 12, afforded a homochiral vinyl aldehyde, (−)-3-(4-methoxyphenyl)pent-4-enal (−)-14 in >95% ee, which was converted into a diastereoisomeric mixture of 1,3-bis(4-methoxyphenyl)pent-4-en-1-ols (3*R*)-6 by a second Grignard reaction with 4-methoxyphenylmagnesium bromide. Sharpless' asymmetric dihydroxylation of the vinyl alcohols (3*R*)-6 proceeded diastereoselectively to give the triol of desired relative stereochemistry (2*S*,3*S*)-7. This, upon dehydration, afforded (−)-di-*O*-methylsugiresinol (−)-3b, the subsequent acid-catalysed cyclization of which gave (−)-di-*O*-methyl agatharesinol (−)-1b. (+)-Di-*O*-methylhinokiresinol (+)-2b was readily obtained by the dehydration of the vinyl alcohols (3*R*)-6.

Introduction

The heartwood constituents of some members of the *Coniferae* include a small group of phenols apparently related biogenetically to lignans but with a C_{17} skeleton, *i.e.*, norlignans. Among them, agatharesinol **1a** (*Agathis* spp.[2] and other spp.[3]), hinokiresinol **2a** (*Chamaecyparis obtusa*[4] and other spp.[3f,3g,3i–3k,3o,5]) and sugiresinol **3a** (*Cryptomeria japonica*[3d,3g–3m,6] and other spp.[3p,6a,7]) form a group likely to be related in a biosynthetic sequence: a hypothetical biogenesis sharing the common origin from coumaric acid and coumaryl alcohol has been reported.[8] The norlignans **1a**, **2a**, **3a** and related compounds have been reported to exhibit both biological activity and industrial utility: *e.g.* inhibitory activity against *C. shiitake* hyphae growth and fruiting body formation,[3m] antifungal activity,[5a] inhibitory effect on cyclic AMP phosphodiesterase,[5d,5e] improvement of the quality of an epoxy resin[3f] and vinyl polymerization–inhibitory activity.[6b] Several synthetic approaches[1,8,9] to the dimethyl ethers of compounds **1a**, **2a** and **3a** have also been described. Although the absolute configuration of **3a** was determined on the basis of degradation studies,[10] no asymmetric synthesis has been established: we describe here full details of the enantioselective total synthesis of (−)-di-*O*-methylsugiresinol (−)-**3b**, together with those of (−)-di-*O*-methylagatharesinol (−)-**1b** and (+)-di-*O*-methylhinokiresinol (+)-**3b**, by employing newly developed asymmetric induction methods.



1a: R=H
1b: R=Me



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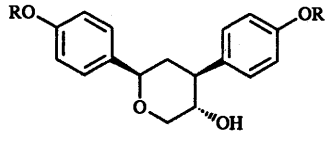


3a: R=H
3b: R=Me

Scheme 1

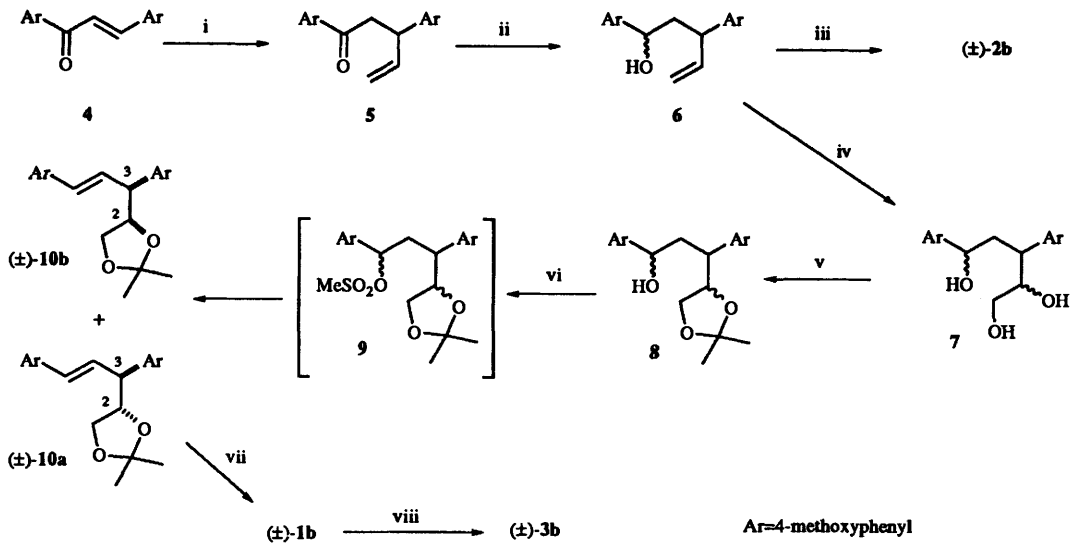
Synthesis of the (±)-di-*O*-methyl ethers of agatharesinol 1a, hinokiresinol 2a and sugiresinol 3a

As a preliminary study, we developed a common synthetic route to the racemates of di-*O*-methyl ethers (±)-**1b**, (±)-**2b** and (±)-**3b**, and the sequence was then applied to their asymmetric syntheses.

The key synthetic intermediate was the chalcone, 1,3-bis(4-methoxyphenyl)prop-2-en-1-one 4, which was prepared according to the reported method.[11] Treatment of the chalcone **4** with vinylmagnesium bromide in the presence of cuprous iodide gave the 1,4-adduct, 1,3-bis(4-methoxyphenyl)pent-4-en-1-one **5**, in 91% yield which, when treated with sodium boranuide, yielded a diastereoisomeric mixture of the vinyl alcohol, 1,3-bis(4-methoxyphenyl)pent-4-en-1-ol **6**, in 95% yield. The ^{1}H NMR spectrum of the crude mixture showed signals arising from two carbinol protons at δ_H 4.46 and 4.57 and the stereoselectivity of the reduction was determined to be 2:3 on the basis of their integration ratio. The acid-catalysed dehydration of the mixture of the stereoisomers **6** gave (±)-di-*O*-methylhinokiresinol (±)-**2b** in 65% yield.

The vinyl alcohol **6** when treated with osmium tetroxide, however, gave the corresponding triol, 3,5-bis(4-methoxyphenyl)pentane-1,2,5-triol **7**, in 73% yield. Although four separate signals appeared in the range δ_H 4.30–4.53, arising from the carbinol proton at C-5, in the ^{1}H NMR spectrum, the stereoselectivity of the reaction was left undetermined at this stage.

The triol **7** readily afforded its acetonide **8** upon treatment



Scheme 2 *Reagents and conditions:* i, CH_2=CHMgBr, CuI; ii, $NaBH_4$; iii, H^+, MeOH, reflux; iv, OsO_4, *N*-methylmorpholine *N*-oxide; v, CH_2=C(OMe)Me, PPTS; vi, $MeSO_2Cl$, pyridine and then reflux; vii, H^+, MeOH, RT; viii, H^+, MeOH, 70 °C

with isopropenyl methyl ether in the presence of pyridinium toluene-*p*-sulfonate, and subsequent dehydration *via* the corresponding mesylate **9**, gave the (2*S**,3*S**)- and (2*R**,3*S**)-olefins (±)-**10a** and (±)-**10b**, in 49% combined yield. The ^{1}H NMR spectrum of the crude mixture showed two doublets, at δ_H 6.30 and 6.40, arising from the olefinic proton at C-5, in a ratio of *ca.* 1:3. The diastereoisomers (±)-**10a** and (±)-**10b** were separated successfully by silica gel column chromatography and the major one, (±)-**10a**, was deprotected to give quantitatively (±)-di-*O*-methylagatharesinol (±)-**1b**. Cyclization of compound (±)-**1b** to the desired ring-closed compound (±)-**3b** was effected by heating it in methanol containing hydrochloric acid. The physical and spectral properties of compound (±)-**3b** were in accord with those of the authentic sample obtained by an independent route.[9a]

Synthesis of (−)-di-*O*-methylagatharesinol (−)-1b, (+)-di-*O*-methylhinokiresinol (+)-2b and (−)-di-*O*-methylsugiresinol (−)-3b

Enantiomerically pure samples of compounds (−)-**1b**, (+)-**2b** and (−)-**3b** were obtained by employing two asymmetric induction processes: asymmetric β-alkylation of α,β-unsaturated imines and enantioselective dihydroxylation of olefins, developed by Koga[12] and Sharpless,[13] respectively. Treatment of the *tert*-butyl ester **11** with 4-methoxycinnamaldehyde **12**[14] gave an aldimine (−)-**13** quantitatively which upon Grignard addition of vinylmagnesium bromide followed by careful hydrolysis with dilute hydrochloric acid afforded the β-vinyl aldehyde, (−)-3-(4-methoxyphenyl)pent-4-enal (−)-**14**, in 82% yield. The IR spectrum of this showed carbonyl absorption at 1724 cm^{-1}, supporting the occurrence of 1,4-addition. The enantiomeric excess (ee) of the product was determined to be > 95% on examination of the 500 MHz ^{1}H NMR spectrum of the corresponding Mosher's ester (+)-**15**, which was derived by treatment of alcohol (−)-**16** with Mosher's acid chloride (MTPA-Cl).[15]

A further Grignard addition of 4-methoxyphenylmagnesium bromide to the aldehyde (−)-**14** yielded a 1:1 diastereoisomeric mixture of two γ-vinyl alcohols, (1*R*,3*R*)- and (1*S*,3*R*)-1,3-bis(4-methoxyphenyl)pent-4-en-1-ol (3*R*)-**6**, in 86% yield. Thus, the key intermediate with the desired absolute stereochemistry at C-3, (3*R*)-**6**, has been synthesized. The mixture of compounds (3*R*)-**6** was converted into (+)-di-*O*-methylhinokiresinol (+)-**2b** in the same manner as was described for the synthesis of its racemate (±)-**2b**, and its ee was determined to be > 95% on the basis of its HPLC characteristics.

The diastereoselective dihydroxylation of compounds (3*R*)-**6** was carried out according to the Sharpless' modified method.[13a] Slow addition of compounds (3*R*)-**6** to a mixture of osmium tetroxide, dihydroquinidine 4-chlorobenzoate (DHQCB) and *N*-methylmorpholine *N*-oxide gave a triol, (2*S*,3*S*)-3,5-bis(4-methoxyphenyl)pentane-1,2,5-triol (2*S*,3*S*)-**7**, in 76% yield. The diastereoisomeric excess (de) of the product was estimated to be > 95% by comparison of the 500 MHz ^{1}H NMR spectrum of the crude product with that of the diastereoisomeric mixture obtained in the run lacking DHQCB: the latter displayed four separate multiplets at δ_H 4.35, 4.41, 4.45 and 4.51, arising from 5-H of each of the four possible diastereoisomers (Fig. 1).

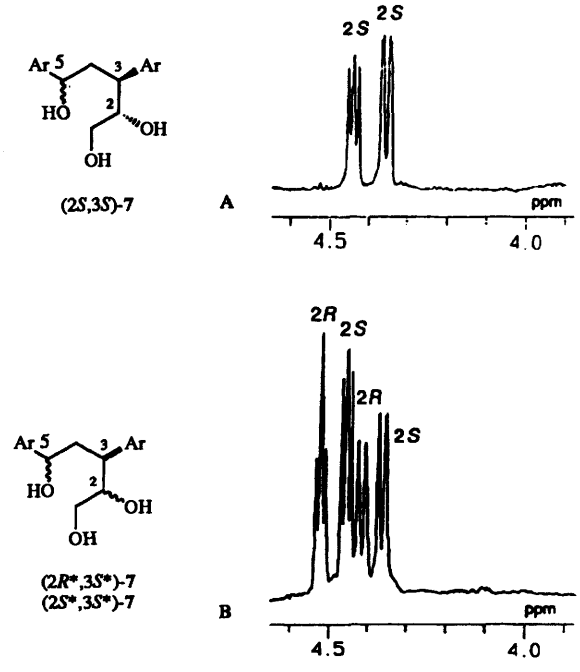
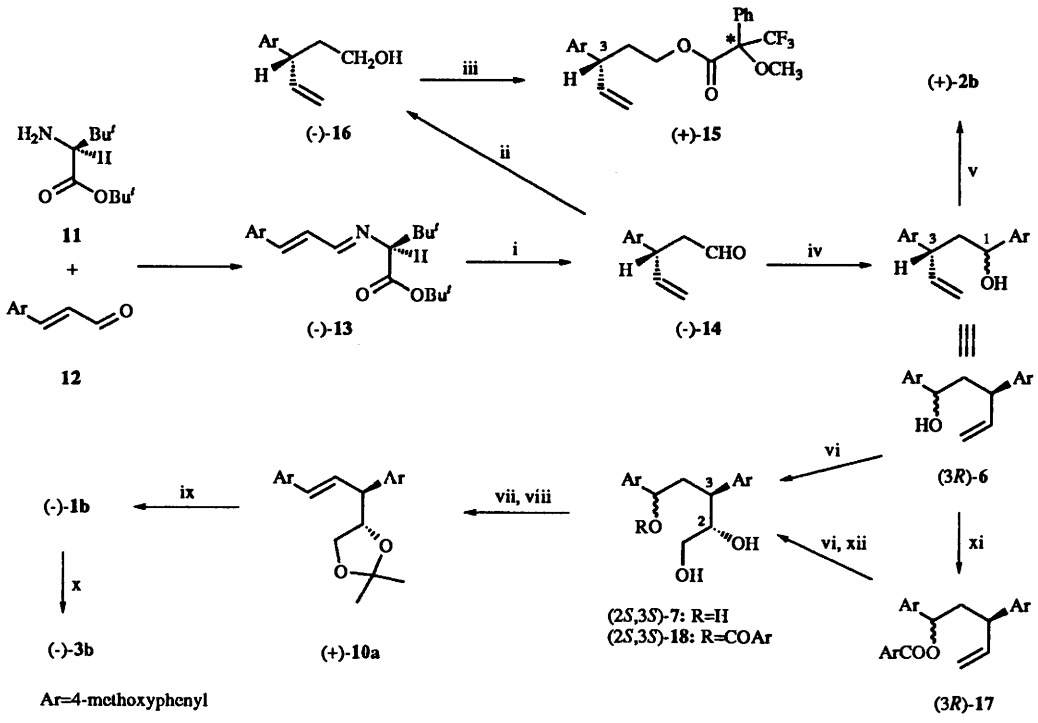


Fig. 1 ^{1}H NMR spectra of dihydroxylation products A: spectrum from the run with DHQCB; B: spectrum from the run lacking DHQCB

The attempted asymmetric dihydroxylation of (3*R*)-**6** by the commercially available AD-mix-α[16] proved impractical, starting material being recovered. Although additional ligand †

† Inefficiency of the asymmetric dihydroxylation of the double bond in allylic alcohols, and a modified method for the reaction have been reported (ref. 16*c*).



Scheme 3 *Reagents and conditions:* i, CH_2=CHMgBr; ii, $NaBH_4$; iii, MTPA-Cl, pyridine; iv, 4-methoxyphenylmagnesium bromide; v, H^+, MeOH, reflux; vi, OsO_4, *N*-methylmorpholine *N*-oxide, dihydroquinine 4-chlorobenzoate or AD-mix-α, $(DHQ)_2PHAL$, Bu'OH, H_2O; vii, CH_2=C(OMe)Me, PPTS; viii, $MeSO_2Cl$, pyridine and then reflux; ix, H^+, MeOH, RT; x, H^+, MeOH, 70 °C; xi, 4-methoxybenzoyl chloride, pyridine; xii, 10% NaOH, MeOH

(*ca.* 3 mol%) enhanced the reaction velocity to give the triol (2*S*,3*S*)-**7** in 81% yield, the reaction was still very slow even at room temperature. The de of the dihydroxylation was almost identical with that obtained in the run using DHQCB.

A superior de for the dihydroxylation was obtained when 4-methoxybenzoate (3*R*)-**17** was employed as a reactant,‡ where efficiency of the reaction was increased to give readily the corresponding diol (2*S*,3*S*)-**18**. Thus, treatment of the vinyl alcohols (3*R*)-**6** with 4-methoxybenzoyl chloride gave the 4-methoxybenzoate (3*R*)-**17** in 95% yield. This when oxidized with AD-mix-α gave the corresponding diol (2*S*,3*S*)-**18**, which was hydrolysed with sodium hydroxide to give the triol (2*S*,3*S*)-**7** in 88% overall yield from the vinyl alcohols (3*R*)-**6**. No evidence for the formation of undesired diastereoisomeric isomers (2*R*,3*S*)-**7** was detected in the ^1H NMR spectrum of the crude products.

Conversion of the triol (2*S*,3*S*)-**7** into compounds (−)-**1b** and (−)-**3b** was achieved in a similar way to that described above. As for di-*O*-methylsugiresinol, a single recrystallization of the crude product gave an optically pure specimen of (−)-**3b**, the physical and spectral properties of which, including the optical rotation, were in accord with those reported.[10]

Experimental

Mps (Yanagimoto MP-3S micromelting point apparatus) and bps are uncorrected. Optical rotations were measured in $CHCl_3$ solutions using a JASCO DIP-370 digital polarimeter. $[\alpha]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were measured on a Shimadzu IR-435 grating infrared spectrophotometer. NMR spectra were recorded on either a JEOL JNM-GSX 270 (270 MHz ^1H, 67.5 MHz ^{13}C) or a JEOL JNM-GSX 500 (500 MHz ^1H, 125 MHz ^{13}C) spectrometer. Chemical shifts and coupling constants (*J*) are given as δ values (ppm) and in Hz, respectively. All the NMR spectra were taken for $CDCl_3$ solutions with tetramethylsilane as internal standard. Low-resolution mass and high-resolution mass spectra (electron impact) were recorded on either a Shimadzu QP 1000EX spectrometer or a JEOL JMS-HX 100 spectrometer. Column chromatography was effected over either Merck Kieselgel 60 (230–400 mesh) with a pump (FMI model RP) or Merck Kieselgel 60 (70–230 mesh). All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation. Light petroleum refers to the fraction distilling in the range 30–70 °C.

‡ Improvement of the enantioselectivity *via* the corresponding 4-methoxybenzoates of allylic alcohols has been reported (ref. 16*b*).

1,3-Bis(4-methoxyphenyl)pent-4-en-1-one 5

Under argon, a 1.09 mol dm^{-3} solution of vinylmagnesium bromide in tetrahydrofuran (THF; 50 cm^3, 54.5 mmol) was added to a suspension of cuprous iodide (519 mg, 2.7 mmol) in THF (50 cm^3) at 0 °C, and the mixture was stirred at 0 °C for 15 min. To the mixture was added a solution of the chalcone 4[11] (6.9 g, 25.7 mmol) in THF (20 cm^3) at 0 °C, and the resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched by addition of 10% hydrochloric acid to the mixture which was then extracted with diethyl ether. The extract was washed successively with aq. sodium hydrogen carbonate and brine and then evaporated to give an orange solid (7.27 g). This, on recrystallization from ethanol, gave *vinyl ketone* **5** (6.93 g, 91%) as needles, mp 44–46 °C (Found: M^+, 296.1410. $C_{19}H_{20}O_3$ requires *M*, 296.1413); $\nu_{max}(CHCl_3)$/cm^{-1} 1670, 1600, 1509 and 1253; δ_H 3.27 (1 H, dd, *J* 16.5 and 7.0), 3.34 (1 H, dd, *J* 16.5 and 7.5), 3.77 (3 H, s), 3.86 (3 H, s), 4.07 (1 H, br q-like, *J* 7.5), 5.00 (1 H, ddd, *J* 17.0, 1.5 and 1.5), 5.04 (1 H, ddd, *J* 10.0, 1.5 and 1.5), 6.02 (1 H, ddd, *J* 17.0, 10.0 and 7.0), 6.83 (2 H, dm, *J* 9.0), 6.91 (2 H, dm, *J* 9.0), 7.17 (2 H, dm, *J* 9.0) and 7.91 (2 H, dm, *J* 9.0); δ_C 43.8 (t), 43.9 (d), 55.2 (q), 55.4 (q), 113.7 (d), 113.9 (d), 114.2 (t), 128.6 (d), 130.27 (s), 130.33 (d), 135.3 (s), 141.1 (d), 158.1 (s), 163.4 (s) and 196.9 (s); *m*/*z* 296 (M^+, 7%), 147 (14) and 135 (100).

1,3-Bis(4-methoxyphenyl)pent-4-en-1-ol 6

A mixture of the vinyl ketone **5** (5.37 g, 18.1 mmol), sodium boranuide (1.31 g, 34.6 mmol) and ethanol (70 cm^3) was stirred

at room temperature for 12 h, and then concentrated under reduced pressure. The residue was diluted with brine (50 cm^3), and the resulting mixture was acidified with 10% hydrochloric acid and extracted with benzene. The extract was washed successively with aq. sodium hydrogen carbonate and brine and then evaporated to give a brown oil. This, on distillation at reduced pressure, gave a 3:2 diastereoisomeric mixture of the *vinyl alcohol* **6** (5.12 g, 95%) as a pale yellow oil, bp 150–152 °C/0.01 mmHg (Found: M^+, 298.1558. $C_{19}H_{22}O_3$ requires *M*, 298.1569); $\nu_{max}(CHCl_3)/cm^{-1}$ 3582, 3450, 1610, 1510 and 1250; δ_H 1.74 (0.6 H, br s, exchangeable with D_2O), 1.79 (0.4 H, br s, exchangeable with D_2O), 1.98 (0.4 H, ddd, *J* 14.0, 9.0 and 5.0), 2.04 (0.6 H, ddd, *J* 14.0, 8.0 and 6.0), 2.19 (0.6 H, ddd, *J* 14.0, 8.0 and 8.0), 2.20 (0.4 H, ddd, *J* 14.0, 9.0 and 7.0), 3.33 (0.6 H, br q-like, *J* 8.0), 3.45 (0.4 H, br q-like, *J* 7.5), 3.79 (1.8 H, s), 3.80 (2.4 H, s), 3.81 (1.8 H, s), 4.46 (0.4 H, dd, *J* 9.0 and 5.0), 4.57 (0.6 H, dd, *J* 8.0 and 6.0), 5.01 (0.4 H, ddd, *J* 17.0, 1.5 and 1.5), 5.02 (0.4 H, ddd, *J* 11.0, 1.5 and 1.5), 5.03 (0.6 H, ddd, *J* 10.0, 1.5 and 1.5), 5.04 (0.6 H, ddd, *J* 17.0, 1.5 and 1.5), 5.91 (0.6 H, ddd, *J* 17.0, 10.0 and 7.5), 5.99 (0.4 H, ddd, *J* 17.0, 11.0 and 7.5), 6.83–6.90 (4 H, m), 7.08–7.15 (2 H, m) and 7.19–7.26 (2 H, m); δ_C 44.3/44.4 (t), 45.5 (d), 55.21/55.23 (q), 71.7/72.0 (d), 113.8/113.9 (d), 114.0 (d), 114.2 (t), 127.1/127.3 (d), 128.5/128.7 (d), 135.5/135.8 (s), 136.6/136.9 (s), 142.0/142.5 (d), 158.1 (s) and 159.1/159.2 (s); *m/z* 298 (M^+, 5%), 280 (35), 172 (23), 147 (40) and 137 (100).

(±)-Di-*O*-methylhinokiresinol (±)-2b

A mixture of the vinyl alcohol **6** (100 mg, 0.34 mmol), 7% hydrochloric acid (1.5 cm^3) and methanol (2.5 cm^3) was heated under reflux for 6 h. After being cooled, the reaction mixture was poured into aq. sodium hydrogen carbonate and extracted with chloroform. The extracted was washed with brine and evaporated to give an oil (80 mg). This, on column chromatography ($CHCl_3$), gave title compound (±)-**2b** (61 mg, 65%) as an oil, bp 201–203 °C/0.1 mmHg (lit.,[8] gum) (Found: M^+, 280.1458. $C_{19}H_{20}O_2$ requires *M*, 280.1463); $\nu_{max}(CHCl_3)/cm^{-1}$ 1606, 1505 and 1245; δ_H 3.80 (6 H, s), 4.15§ (1 H, br t-like, *J* 7.0), 5.10 (1 H, ddd, *J* 17.0, 1.5 and 1.5), 5.15 (1 H, ddd, *J* 10.0, 1.5 and 1.5), 6.08 (1 H, ddd, *J* 17.0, 10.0 and 7.0), 6.24 (1 H, dd, *J* 16.0 and 7.0), 6.35 (1 H, d, *J* 16.0), 6.81–6.88 (4 H, m), 7.15–7.19 (2 H, m) and 7.27–7.32 (2 H, m); δ_C 51.5 (d), 55.3 (q), 113.9 (d), 115.1 (t), 127.3 (d), 129.0 (d), 129.7 (d), 129.9 (d), 130.2 (s), 134.9 (s), 140.5 (d), 158.2 (s) and 158.9 (s); *m/z* 280 (M^+, 100%), 279 (15), 265 (19), 249 (16) and 172 (31).

3,5-Bis(4-methoxyphenyl)pentane-1,2,5-triol 7

A mixture of the vinyl alcohol **6** (1.44 g, 4.8 mmol), acetone (1.8 cm^3) and water (0.2 cm^3) was added dropwise to a well-stirred mixture of 4-methylmorpholine *N*-oxide (780 mg, 6.7 mmol) and a 0.5 mol dm^{-3} solution of osmium tetroxide in toluene (38 ml, 19 mmol), acetone (6.8 cm^3) and water (0.7 cm^3) at 0 °C. The mixture was stirred at room temperature for 12 h after which it was treated with sodium metabisulfite (1.5 g, 7.9 mmol) at 0 °C, and extracted with dichloromethane. Evaporation of the extract left a brown oil (1.6 g), which, on column chromatography ($CHCl_3$–EtOH, 20:1), gave a *ca.* 1.2:1.2:1:1 diasteroisomeric mixture of the triols **7** (1.17 g, 73%) as an oil, bp 155–157 °C/0.004 mmHg (Found: M^+, 332.1646. $C_{19}H_{24}O_5$ requires *M*, 332.1624); $\nu_{max}(CHCl_3)/cm^{-1}$ 3574, 3410, 1611, 1510 and 1240; δ_H 1.86 (0.23 H, ddd, *J* 14.5, 9.0 and 2.0), 1.93 (0.27 H, ddd, *J* 14.0, 10.5 and 2.5), 2.09 (0.27 H, ddd, *J* 14.0, 10.5 and 5.0), 1.85–2.14 (1 H, br s, exchangeable with D_2O), 2.12 (0.27 H, ddd, *J* 13.5, 8.0 and 5.5), 2.16–2.24 (0.23 H, m), 2.25 (0.27 H, ddd, *J* 13.5, 10.0 and 6.0), 2.31–2.45 (0.69 H, m), 2.28–2.48 (1 H, br s, exchangeable with D_2O), 2.49 (0.27 H, ddd, *J* 10.0, 5.5 and 5.5), 2.51–2.80 (1 H, br s, exchangeable with D_2O), 2.80 (0.23 H, ddd, *J* 9.0, 9.0 and 5.0), 3.08 (0.27 H, ddd, *J* 10.5, 6.0 and 5.0), 3.15 (0.23 H, dd, *J* 11.5 and 7.5), 3.23 (0.23 H, dd, *J* 11.5 and 7.0), 3.28 (0.23 H, dd, *J* 11.5 and 3.0), 3.31 (0.27 H, dd, *J* 11.5 and 7.5), 3.35 (0.23 H, *J* 11.5 and 3.0), 3.48 (0.27 H, dd, *J* 11.5 and 7.0), 3.56 (0.27 H, dd, *J* 11.5 and 3.0), 3.64 (0.27 H, dd, *J* 11.5 and 3.0), 3.72–3.87 (1 H, m), 3.76 (0.68 H, s), 3.77 (0.82 H, s), 3.785 (2.04 H, s), 3.79 (1.64 H, s), 3.80 (0.82 H, s), 4.35 (0.27 H, dd, *J* 10.5 and 2.5), 4.41 (0.23 H, dd, *J* 10.5 and 2.0), 4.45 (0.27 H, dd, *J* 8.0 and 6.0), 4.51 (0.23 H, t-like, *J* 6.5), 6.78–6.90 (4 H, m) and 7.06–7.20 (4 H, m); δ_C 40.8/41.3/41.6/43.0 (t), 43.9/44.5/44.7/45.4 (d), 55.10/55.13 (q), 64.3/64.84/64.87/64.9 (t), 71.4/71.7/71.8/72.0 (d), 74.7/75.2/75.7/75.9 (d), 113.58/113.64/113.67/113.73 (d), 113.78/113.91/113.98/114.04 (d), 126.67/126.74/127.49/127.55 (d), 128.9/129.0/129.7/129.8 (d), 132.3/132.7/133.6/134.1 (s), 135.7/135.8/137.3/137.4 (s), 158.2/158.2/158.3/158.3 (s) and 158.6/158.7/158.9/159.0 (s).

(2′*E*)-4-[1,3-Bis(4-methoxyphenyl)prop-2-enyl]-2,2-dimethyl-1,3-dioxolane[(4*E*)-3,5-bis(4-methoxyphenyl)pent-4-ene-1,2-diol acetonide] 10

A mixture of the triol **7** (800 mg, 2.41 mmol), isopropenyl methyl ether (0.5 cm^3, 5.34 mmol), pyridinium toluene-*p*-sulfonate (40 mg, 0.16 mmol) and chloroform (40 cm^3) was stirred at room temperature for 15 h after which it was washed successively with aq. sodium hydrogen carbonate and brine, and evaporated to give the corresponding acetonide **8** (920 mg) as a brown oil. This was treated with methanesulfonyl chloride (1.4 cm^3, 18.1 mmol) in pyridine (14 cm^3) at 60 °C for 3.5 h, and then under reflux for a further 3.5 h. After being cooled, the reaction mixture was poured into ice–water (10 cm^3) and extracted with chloroform. The extract was washed successively with 5% hydrochloric acid, aq. sodium hydrogen carbonate and brine and then evaporated to give a brown oil (719 mg). This, on column chromatography (benzene), gave compound (±)-**10a** (318 mg, 37%) and its diastereoisomer (±)-**10b** (102 mg, 12%).

Major isomer (±)-**10a**: needles (from methanol), mp 75.5–76 °C (lit.,[8] mp 78–79 °C). The physical and spectral properties of compound (±)-**10a** were in accord with those reported.[8]

Minor isomer (±)-**10b**: oil, bp 185–188 °C/0.01 mmHg (Found: M^+, 354.1855. $C_{22}H_{26}O_4$ requires *M*, 354.1831); $\nu_{max}(CHCl_3)/cm^{-1}$ 1608, 1508 and 1249; δ_H 1.38 (3 H, s), 1.45 (3 H, s), 3.45 (1 H, t-like, *J* 7.5), 3.60 (1 H, dd, *J* 8.5 and 7.0), 3.79 (3 H, s), 3.80 (3 H, s), 3.81 (1 H, dd, *J* 8.5 and 6.0), 4.42 (1 H, q-like, *J* 7.0), 6.30 (1 H, d, *J* 16.0), 6.38 (1 H, dd, *J* 16.0 and 7.0), 6.81 (2 H, dm, *J* 9.0), 6.87 (2 H, dm, *J* 9.0), 7.18 (2 H, dm, *J* 9.0) and 7.29 (2 H, dm, *J* 9.0); δ_C 25.7 (q), 26.9 (q), 51.9 (d), 55.2 (q), 55.3 (q), 68.2 (t), 78.9 (d), 109.6 (s), 113.8 (d), 114.1 (d), 127.4 (d), 128.3 (d), 129.3 (d), 130.2 (s), 130.7 (d), 133.0 (s), 158.5 (s) and 158.9 (s); *m/z* 354 (M^+, 2%), 253 (100), 145 (23), 121 (14) and 101 (19).

(±)-Di-*O*-methylagatharesinol (±)-1b

A mixture of the acetonide (±)-**10a** (70 mg, 0.20 mmol), concentrated hydrochloric acid (1 cm^3) and methanol (5 cm^3) was stirred at room temperature for 12 h after which it was neutralized with aq. sodium hydrogen carbonate and extracted with chloroform. The extract was washed with brine and evaporated to give compound (±)-**1b** (62 mg) as a pale yellow solid, mp 122–124 °C (lit.,[8] 124–126 °C). This was used in the next step without purification. Spectral properties of compound (±)-**1b** were in accord with those reported.[8]

(±)-Di-*O*-methylsugiresinol (±)-3b

A mixture of compound (±)-**1b** (50 mg, 0.16 mmol), concentrated hydrochloric acid (1 cm^3) and methanol (5 cm^3) was heated at 70 °C for 10 h. Work-up in a manner similar to that for the preparation of compound (±)-**1b** gave a pale

§ A discrepancy between our results and the literature has been found; δ_H 4.6 (dd, *J* 6 and 10).[8]

yellow solid (47 mg). This, on recrystallization from hexane, gave compound (±)-**3b** [40 mg, 81% from compound (±)-**10a**] as needles, mp 122–123 °C [lit.,[8] 108–110 °C (MeOH), lit.,[9a] 121–122 °C]. The spectral properties of compound (±)-**3b** were in accord with those reported.[8]

***tert*-Butyl (−)-2-[3-(4-methoxyphenyl)prop-2-enylideneamino]-3,3-dimethylbutanoate (−)-13**

A mixture of 3-(4-methoxyphenyl)propenal[14] **12** (790 mg, 4.88 mmol), *tert*-butyl 2-amino-3,3-dimethylbutanoate **11** (935 mg, 5.00 mmol) and diethyl ether (10 cm^3) was stirred at room temperature for 16 h after which it was concentrated under reduced pressure. The residue was dissolved in benzene (10 cm^3) and evaporated to dryness: this process was repeated three times until all the water had been removed. The resulting pale yellow solid (1.85 g) was recrystallized from light petroleum to give the aldimine (−)-**13** (1.57 g, 97%) as needles, mp 78–80 °C (Found: M^+, 331.2126. $C_{20}H_{29}NO_3$ requires *M*, 331.2148); $[\alpha]_D^{17}$ −76.1 (*c* 1.34, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1728, 1634, 1601 and 1144; δ_H 1.01 (9 H, s), 1.48 (9 H, s), 3.41 (1 H, s), 3.82 (3 H, s), 6.87–6.96 [4 H, m, including two aromatic protons at 6.89 as doublet of multiplet (*J* 8.5) and two olefinic protons], 7.42 (2 H, dm, *J* 8.5) and 7.92 (1 H, dd, *J* 6.0 and 2.5); δ_C 26.8 (q), 28.1 (q), 35.1 (s), 55.3 (q), 80.9 (s), 83.9 (d), 114.3 (d), 126.1 (d), 128.6 (s), 128.7 (d), 142.0 (d), 160.5 (s), 164.3 (d) and 170.7 (s); *m/z* 331 (M^+, 2%), 230 (99), 218 (61), 174 (33), 145 (49) and 57 (100).

(−)-3-(4-Methoxyphenyl)pent-4-enal (−)-14

A solution of the aldimine (−)-**13** (500 mg, 1.51 mmol) in diethyl ether (3 cm^3) was added dropwise to a stirred mixture of 1.09 mol dm^{-3} vinylmagnesium bromide in THF (5.9 cm^3, 6.41 mmol) and diethyl ether (30 cm^3) at 0 °C. After being stirred at 0 °C for 1.5 h, the reaction mixture was quenched with 1 mol dm^{-3} hydrochloric acid (18 cm^3), and extracted with diethyl ether. The extract was washed successively with aq. sodium hydrogen carbonate and brine and then evaporated to give an oil (360 mg). This, on distillation *in vacuo*, gave the enal (−)-**14** (235 mg, 82%) as a pale yellow oil, bp 95–97 °C/0.01 mmHg (Found: M^+, 190.0970. $C_{12}H_{14}O_2$ requires *M*, 190.0994); $[\alpha]_D^{25}$ −18.0 (*c* 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1724, 1609, 1509 and 1252; δ_H 2.77 (1 H, ddd, *J* 16.5, 7.5 and 2.0), 2.83 (1 H, ddd, *J* 16.5, 7.5 and 2.0), 3.78 (3 H, s), 3.90 (1 H, br q-like, *J* 7.0), 5.04 (1 H, ddd, *J* 17.0, 1.0 and 1.0), 5.09 (1 H, ddd, *J* 10.0, 1.0 and 1.0), 5.97 (1 H, ddd, *J* 17.0, 10.0 and 6.8), 6.85 (2 H, dm, *J* 8.5), 7.12 (2 H, dm, *J* 8.5) and 9.71 (1 H, t, *J* 2.0); δ_C 42.6 (d), 48.6 (t), 55.2 (q), 114.1 (d), 114.7 (t), 128.5 (d), 134.1 (s), 140.4 (d), 158.4 (s) and 201.4 (d); *m/z* 190 (M^+, 62%), 162 (12), 147 (100), 132 (11) and 115 (21).

(−)-3-(4-Methoxyphenyl)pent-4-en-1-ol (−)-16

According to the method similar to that used for the reduction of the vinyl ketone **5**, the enal (−)-**14** (270 mg, 1.4 mmol) was treated with sodium boranuide (107 mg, 2.8 mmol) to give the enol (−)-**16** (253 mg, 93%) as an oil, bp 130–132 °C/0.01 mmHg (Found: M^+, 192.1121. $C_{12}H_{16}O_2$ requires *M*, 192.1150); $[\alpha]_D^{17}$ −32.0 (*c* 1.2, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3590, 3450, 1610 and 1240; δ_H 1.60 (1 H, br s, exchangeable with D_2O), 1.92 (1 H, ddt, *J* 14.0, 8.0 and 6.5), 1.99 (1 H, ddt, *J* 14.0, 7.0 and 7.0), 3.42 (1 H, br q-like, *J* 7.0), 3.60 (1 H, dt, *J* 10.5 and 6.5), 3.64 (1 H, dt, *J* 10.5 and 6.5), 3.79 (3 H, s), 5.03 (1 H, ddd, *J* 10.0, 1.5 and 1.5), 5.05 (1 H, ddd, *J* 17.0, 1.5 and 1.5), 5.95 (1 H, ddd, *J* 17.0, 10.0 and 7.5), 6.85 (2 H, dm, *J* 8.5) and 7.13 (2 H, dm, *J* 8.5); δ_C 38.0 (t), 45.4 (d), 55.2 (q), 61.0 (t), 113.98 (d), 114.04, (t), 128.5 (d), 135.7 (s), 142.2 (d) and 158.1 (s); *m/z* 192 (M^+, 24%), 147 (100), 132 (10), 115 (25) and 91 (57).

Mosher's ester of (−)-3-(4-methoxyphenyl)pent-4-en-1-ol (+)-(3*R*)-15

The enol (−)-**16** (10 mg, 0.05 mmol) was treated with (*R*)-(+)-methoxy(trifluoromethyl)phenylacetyl chloride[15] (MTPA-Cl, 15 mg, 0.06 mmol) in pyridine (0.6 cm^3) for 30 min to give the corresponding *Mosher's ester* (+)-**15** (20 mg, 94%) as an oil, bp 111–113 °C/0.004 mmHg (Found: M^+, 408.1556. $C_{22}H_{23}F_3O_4$ requires M, 408.1548); $[\alpha]_D^{23}$ +39.6 (*c* 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1746, 1509 and 1270; δ_H 1.98–2.13 (2 H, m), 3.29 (1 H, q-like, *J* 7.0), 3.56 (3 H, s), 3.78 (3 H, s), 4.22 (1 H, dt, *J* 11.0 and 6.5), 4.27 (1 H, dt, *J* 11.0 and 6.5), 5.00 (1 H, dt, *J* 17.0 and 1.0), 5.04 (1 H, dt, *J* 10.5 and 1.0), 5.89 (1 H, ddd, *J* 17.0, 10.5 and 7.5), 6.83 (2 H, dm, *J* 9.0), 7.03 (2 H, dm, *J* 9.0) and 7.37–7.54 (5 H, m); δ_C 33.8 (t), 45.0 (d), 55.2 (q), 55.4 (q), 64.5 (t), 84.6 (q), 114.1 (d), 114.7 (t), 121.3 (q), 127.3 (d), 128.4 (d), 128.7 (d), 129.6 (d), 132.3 (s), 134.6 (s), 141.0 (d), 158.3 (s) and 166.5 (s); *m/z* 408 (M^+, 10%), 174 (69), 159 (29), 147 (100) and 91 (33). No signal ascribable to the diastereoisomeric isomer (3*S*)-**15** was detected in the ^1H NMR spectrum.

The racemic enol (±)-**16** derived from compound **12** was converted into the corresponding diastereoisomeric mixture of Mosher's ester **15** in the same manner as described above. Compound **15**: δ_H 1.98–2.13 (2 H, m), 3.28 (0.5 H, q-like, *J* 7.0), 3.29 (0.5 H, q-like, *J* 7.0), 3.56 (3 H, s), 3.78 (3 H, s), 4.18 (0.5 H, dt, *J* 11.0 and 6.5), 4.22 (0.5 H, dt, *J* 11.0 and 6.5), 4.27 (0.5 H, dt, *J* 11.0 and 6.5), 4.33 (0.5 H, dt, *J* 11.0 and 6.5), 4.98 (0.5 H, dt, *J* 17.0 and 1.0), 5.00 (0.5 H, dt, *J* 17.0 and 1.0), 5.03 (0.5 H, dt, *J* 10.5 and 1.0), 5.04 (0.5 H, dt, *J* 10.5 and 1.0), 5.88 (0.5 H, ddd, *J* 17.0, 10.5 and 7.5), 5.89 (0.5 H, ddd, *J* 17.0, 10.5 and 7.5), 6.83 (1 H, dm, *J* 9.0), 6.84 (1 H, dm, *J* 9.0), 7.03 (1 H, dm, *J* 9.0), 7.04 (1 H, dm, *J* 9.0) and 7.37–7.63 (5 H, m).

(3*R*)-1,3-Bis(4-methoxyphenyl)pent-4-en-1-ol (3*R*)-6

A solution of the enal (−)-**14** (590 mg, 3.1 mmol) in THF (4 cm^3) was added to a solution of *p*-methoxyphenylmagnesium bromide [prepared from *p*-bromoanisole (2.80 g, 15.0 mmol) and magnesium (350 mg, 14.4 mmol)] in THF (25 cm^3) at 0 °C, after which the mixture was stirred at 0 °C for 2 h. The reaction was quenched by the addition of 1 mol dm^{-3} hydrochloric acid (20 cm^3) to the mixture which was then extracted with diethyl ether. The extract was washed successively with aq. sodium hydrogen carbonate and brine and then evaporated to give a pale yellow oil (1.34 g). This, on distillation *in vacuo*, gave a 1:1 diasteroisomeric mixture of the *enol* (3*R*)-**6** (795 mg, 86%) as a pale yellow oil, bp 150–152 °C/0.01 mmHg. Spectral properties of the enol (3*R*)-**6** were completely in accord with those of the specimen prepared from the vinyl ketone 4.

(+)-Di-*O*-methylhinokiresinol (+)-2b

By a method similar to that used for the preparation of (±)-**2b**, the enol (3*R*)-**6** (200 mg, 0.67 mmol) was converted into the title compound (+)-**2b** (126 mg, 67%); it formed needles, mp 60–62 °C (MeOH) (lit.,[4b] mp 64 °C); $[\alpha]_D^{17}$ +4.8 (*c* 2.5, $CHCl_3$) (lit.,[4b] 8.4).¶ Spectral properties of compound (+)-**2b** were in accord with those of the specimen of the racemate (±)-**2b** prepared as described above, and the ee was determined as >95% by HPLC on a chiral column AS (Daicel Chemical Industries, Ltd.) using a mixture of propan-2-ol–hexane (0.5:95.5) as eluent.

Asymmetric dihydroxylation of the pentenol (3*R*)-6

Method A. By a method similar to that used for the dihydroxylation of compound **6**, compound (3*R*)-**6** (118 mg, 0.39 mmol) was treated with osmium tetroxide in the presence of dihydroquinine 4-chlorobenzoate (93 mg, 0.2 mmol) for 1 h to give (2*S*,3*S*)-3,5-bis(4-methoxyphenyl)pentane-1,2,5-triol (2*S*,3*S*)-**7** (98 mg, 76%) as an oil. A trace amount of its diastereoisomer (2*R*,3*S*)-**7** was detected in the ^1H NMR spectrum of the crude product.

¶ $[\alpha]_D$ Value has been reported, but without description of the solvent.

Isomer (2*S*,3*S*)-**7**: oil, bp 163–165 °C/0.004 mmHg (Found: M^+, 332.1619. $C_{19}H_{24}O_5$ requires *M*, 332.1624); ν_{max}($CHCl_3$)/cm^{-1} 3574, 3425, 1611, 1510 and 1240; δ_H 1.90–2.50 (3 H, br s, exchangeable with D_2O), 1.96 (0.5 H, ddd, *J* 14.0, 10.5 and 2.5), 2.10 (0.5 H, ddd, *J* 14.0, 10.5 and 5.0), 2.13 (0.5 H, ddd, *J* 13.5, 8.0 and 5.5), 2.26 (0.5 H, ddd, *J* 13.5, 10.0 and 6.0), 2.50 (0.5 H, ddd, *J* 10.0, 5.5 and 5.5), 3.10 (0.5 H, ddd, *J* 10.0, 6.0 and 5.0), 3.35 (0.5 H, dd, *J* 11.5 and 7.5), 3.50 (0.5 H, dd, *J* 11.5 and 7.0), 3.60 (0.5 H, dd, *J* 11.5 and 3.0), 3.67 (0.5 H, dd, *J* 11.5 and 3.0), 3.778 (1.5 H, s), 3.802 (1.5 H, s), 3.805 (3 H, s), 3.74–3.87 (1 H, m), 4.35 (0.5 H, dd, *J* 10.5 and 2.5), 4.44 (0.5 H, dd, *J* 8.0 and 6.0), 6.824 (1 H, dm, *J* 8.5), 6.862 (1 H, dm, *J* 8.5), 6.865 (1 H, dm, *J* 8.5), 6.883 (1 H, dm, *J* 8.5), 7.10 (1 H, dm, *J* 8.5), 7.15 (1 H, dm, *J* 8.5), 7.17 (1 H, dm, *J* 8.5) and 7.20 (1 H, dm, *J* 8.5); δ_C 40.8/41.6 (t), 43.9/44.7 (d), 55.10/55.13 (q), 64.3/64.9 (t), 71.4/71.8 (d), 74.7/75.2 (d), 113.64/113.73 (d), 113.78/113.91 (d), 126.67/127.49 (d), 129.7/129.8 (d), 132.3/132.7 (s), 135.8/137.3 (s), 158.3/158.3 (s) and 158.7/158.9 (s); *m*/*z* 332 (M^+, 1%), 254 (40), 137 (100) and 121 (35).

Method B. Compound (3*R*)-**6** (450 mg, 1.51 mmol) was added to a well stirred mixture of AD-mix-α [4.2 g, contains $K_3Fe(CN)_6$ (2.9 g, 8.8 mmol), K_2CO_3 (1.2 g, 8.7 mmol), $(DHQ)_2PHAL$ (23 mg, 0.03 mmol) and $K_2OsO_2(OH)_4$ (2.2 mg, 0.006 mmol)], $(DHQ)_2PHAL$ (70 mg, 0.09 mmol), *tert*-butyl alcohol (16 cm^3) and water (16 cm^3) at 0 °C. The mixture was stirred at room temperature for 24 h after which it was treated with sodium sulfite (4.2 g, 33 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 30 min after which it was extracted with ethyl acetate. The extract was washed with brine and evaporated to leave a pale yellow oil (598 mg). This, on column chromatography (acetone–benzene, 1 : 2), gave the triol (2*S*,3*S*)-**7** (406 mg, 81%). Spectral properties of the product were in accord with those of the specimen prepared in method A.

(3*R*)-1,3-Bis(4-methoxyphenyl)pent-4-enyl 4-methoxybenzoate (3*R*)-17

A solution of 4-methoxybenzoyl chloride (194 mg, 1.14 mmol) in chloroform (2 cm^3) was added to a mixture of compound (3*R*)-**6** (226 mg, 0.76 mmol), pyridine (240 mg, 3.03 mmol) and chloroform (6 cm^3) at 0 °C which was then stirred at room temperature for 3 h. After the mixture had been diluted with chloroform (20 cm^3) it was washed successively with 5% hydrochloric acid, aq. sodium hydrogen carbonate and brine and then evaporated to leave a pale yellow oil (410 mg). This, on column chromatography (acetone–benzene, 1 : 5), gave a 1 : 1 diastereoisomeric mixture of the 4-methoxybenzoates (3*R*)-**17** (311 mg, 95%) as an oil, bp 132–134 °C/0.004 mmHg [Found: M^+, 432.1953.|| $C_{27}H_{28}O_5$ requires *M*, 432.1937]; ν_{max}($CHCl_3$)/cm^{-1} 1706, 1607, 1509 and 1250; δ_H 2.18 (0.5 H, ddd, *J* 14.0, 8.0 and 6.0), 2.22 (0.5 H, ddd, *J* 14.0, 7.5 and 6.0), 2.51 (1 H, ddd, *J* 14.0, 8.0 and 8.0), 3.27 (0.5 H, br q-like, *J* 7.5), 3.31 (0.5 H, br q-like, *J* 7.5), 3.77 (1.5 H, s), 3.775 (1.5 H, s), 3.78 (1.5 H, s), 3.79 (1.5 H, s), 3.84 (1.5 H, s), 3.85 (1.5 H, s), 4.97 (0.5 H, ddd, *J* 17.5, 1.0 and 1.0), 5.02 (0.5 H, dd, *J* 10.5 and 1.0), 5.05 (0.5 H, ddd, *J* 16.5, 1.0 and 1.0), 5.07 (0.5 H, dd, *J* 10.0 and 1.0), 5.75 (0.5 H, dd, *J* 8.0 and 6.0), 5.82 (0.5 H, dd, *J* 8.0 and 6.0), 5.91 (0.5 H, ddd, *J* 17.5, 10.0 and 7.0), 6.01 (0.5 H, ddd, *J* 16.5, 10.5 and 7.0), 6.78–6.94 (6 H, m), 7.05 (1 H, dm, *J* 8.5), 7.11 (1 H, dm, *J* 8.5), 7.26–7.34 (2 H, m) and 7.92–8.02 (2 H, m); δ_C 41.6/42.0 (t), 45.2/45.5 (d), 55.1/55.3 (q), 74.3/74.4 (d), 113.4/113.5 (d), 113.8/114.0 (d), 114.2/114.4 (t), 122.8/122.9 (s), 127.9/128.1 (d), 128.4/128.5 (d), 131.51/131.54 (d), 132.7/132.8 (s), 135.1/135.2 (s), 141.5 (d), 158.1 (s), 159.2/159.3 (s), 163.2/163.3 (s) and 165.3/165.4 (s); *m*/*z* 280 ($M^+ - ArCO_2H$, 50%), 172 (41), 152 (37), 135 (100) and 91 (37).

|| Molecular ion peak M^+ instead of quasimolecular ion peak $[M + H]^+$ was detected by the positive ion mode in FAB-MS analysis.

(2*S*,3*S*)-5-(4-Methoxybenzoyloxy)-3,5-bis(4-methoxyphenyl)-pentane-1,2-diol (2*S*,3*S*)-18

By a method similar to that used for the asymmetric dihydroxylation of compound (3*R*)-**6**, the benzoate (3*R*)-**17** (124 mg, 0.29 mmol) was treated with AD-mix-α (243 mg) and $(DHQ)_2PHAL$ (4 mg, 0.005 mmol) for 16 h to give an oil (145 mg). This, on column chromatography (benzene–acetone, 5 : 1), gave a 1 : 1 diastereoisomeric mixture of *title compound* (2*S*,3*S*)-**18** (126 mg, 94%) as an oil, bp 114 °C/0.003 mmHg (decomp.) (Found: $[M + H]^+$, 467.2080. $C_{27}H_{31}O_7$ requires $[M + H]^+$, 467.2070); ν_{max}($CHCl_3$)/cm^{-1} 3554, 1708, 1608, 1510 and 1250; δ_H 1.93 (1 H, br s, exchangeable with D_2O), 2.08 (1 H, br s, exchangeable with D_2O), 2.16 (0.5 H, ddd, *J* 14.0, 10.0 and 4.0), 2.30 (0.5 H, ddd, *J* 14.0, 9.0 and 4.0), 2.38–2.64 (1.5 H, m), 2.90 (0.5 H, ddd, *J* 11.5, 7.0 and 4.0), 3.35 (0.5 H, dd, *J* 11.5 and 7.0), 3.45 (0.5 H, dd, *J* 11.5 and 7.0), 3.60 (0.5 H, dd, *J* 11.5 and 3.0), 3.69 (0.5 H, dd, *J* 11.5 and 3.0), 3.76 (1.5 H, s), 3.777 (1.5 H, s), 3.78 (1.5 H, s), 3.79 (1.5 H, s), 3.83 (1.5 H, s), 3.85 (1.5 H, s), 3.80–3.90 (1 H, m), 5.59 (0.5 H, dd, *J* 10.0 and 4.0), 5.66 (0.5 H, dd, *J* 9.0 and 6.0), 6.80–6.88 (5 H, m), 6.91 (1 H, dm, *J* 9.0), 7.07–7.13 (2 H, m), 7.22 (2 H, dm, *J* 8.5), 7.87 (1 H, dm, *J* 9.0) and 7.97 (1 H, dm, *J* 9.0); δ_C 37.8/39.6 (t), 44.3/44.5 (d), 55.1/55.2 (q), 55.3/55.4 (q), 64.8/64.9 (t), 73.9 (d), 74.8/74.9 (d), 113.4/113.6 (d), 113.8 (d), 114.1/114.2 (d), 122.7/122.8 (s), 128.3/128.4 (d), 129.7/129.8 (d), 131.2/131.8 (s), 131.5/131.6 (d), 133.1 (s), 158.7 (s), 159.1/159.4 (s), 163.2/163.4 (s) and 165.4/165.5 (s); *m*/*z* 314 ($M^+ - ArCO_2H$, 2%), 254 (38), 152 (38), 135 (100) and 121 (42).

Hydrolysis of the dihydroxypentyl benzoate (2*S*,3*S*)-18

A mixture of compound (2*S*,3*S*)-**18** (33 mg, 0.07 mmol), 10% sodium hydroxide (0.5 cm^3) and methanol (3 cm^3) was stirred at room temperature for 15 h after which it was poured into brine and extracted with ethyl acetate. The extract was washed with brine and evaporated to give an oil (28 mg). This, on column chromatography (acetone–benzene, 1:2), gave the *triol* (2*S*,3*S*)-**7** (23 mg, 98%). The spectral properties of compound (2*S*,3*S*)-**7** were identical with those of the specimen obtained by the direct asymmetric dihydroxylation of compound (3*R*)-**6**.

(2*E*)-(+)-4-[1,3-Bis(4-methoxyphenyl)prop-2-enyl]-2,2-dimethyl-1,3-dioxolane [(4*E*)-(+)-3,5-Bis(4-methoxyphenyl)pent-4-ene-1,2-diol acetonide] (+)-10a

By a method similar to that used for the preparation of the diastereoisomeric mixture of the acetonides (±)-**10a** and (±)-**10b**, the triol (2*S*,3*S*)-**7** (26 mg, 0.08 mmol) was converted into title compound (+)-**10a** (25 mg, 90%) as an oil, $[\alpha]_D^{17}$ +38.2 (*c* 0.7, $CHCl_3$). The spectral properties of compound (+)-**10a** were in accord with those of the specimen (±)-**10a** prepared from the diastereoisomeric mixture of the triols **7**.

(−)-Di-*O*-methylagatharesinol (−)-1b

By a method similar to that used for the preparation of compound (±)-**1b**, the acetonide (+)-**10a** (14 mg, 0.04 mmol) was converted into title compound (−)-**1b** (12 mg, 97%) as an oil, bp 151–153 °C/0.004 mmHg, $[\alpha]_D^{17}$ −35.0 (*c* 0.4, $CHCl_3$). The spectral properties of compound (−)-**1b** were in accord with those of the specimen (±)-**1b** prepared from compound (±)-**10a**.

(−)-Di-*O*-methylsugiresinol (−)-3b

By a method similar to that used for the cyclisation of compound (±)-**1b**, compound (−)-**1b** (13 mg, 0.04 mmol) was converted into title compound (−)-**3b** (11 mg, 87%) as colourless needles, mp 104–105 °C (lit.,[10] 104–105 °C); $[\alpha]_D^{17}$ −4.0 (*c* 1.0, $CHCl_3$) (lit.,[10] $[\alpha]_D$ −4). The spectral properties of compound (−)-**3b** were in accord with those of the specimen (±)-**3b** prepared from compound (±)-**1b**.

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References

1 A part of the work has been published as a communication, O. Muraoka, N. Fujiwara, G. Tanabe and T. Momose, *Tetrahedron: Assymmetry*, 1991, **2**, 357.

2 R. C. Cambie, J. M. Coddington, M. J. Stone, N. Tanaka, Y.-H. Li and S. Arigayo, *Phytochemistry*, 1989, **28**, 1675; C. R. Enzell and B. R. Thomas, *Tetrahedron Lett.*, 1966, 2395; C. R. Enzell and B. R. Thomas, *Acta Chem. Scand.*, 1965, **19**, 913.

3 (*a*) S. Yasuda, Y. Iwase, Y. Seguchi, T. Takemura and Y. Matsushita, *Mokuzai Gakkaishi*, 1992, **38**, 52 (*Chem. Abstr.*, 1992, **117**, 51045k); (*b*) H. Ohashi, N. Kato, T. Imai and S. Kawai, *Holzforschung*, 1991, **45**, 245; (*c*) H. Ohashi and T. Imai, *Holzforschung*, 1990, **44**, 317; (*d*) H. Ohashi, T. Imai, K. Yoshida and M. Yasue, *Holzforschung*, 1990, **44**, 79; (*e*) S. Hasegawa, H. Koyanagi and Y. Hirose, *Phytochemistry*, 1990, **29**, 261; (*f*) N. Fujita (Matsushita Electric Works, Ltd.) Jpn. Kokai Tokkyo Koho, JP 62 96520/1987 (*Chem. Abstr.*, 1988, **108**, 76456x); (*g*) H. Ohashi, T. Goto, T. Imai and M. Yasue, *Res. Bull. Fac. Agr. Gifu Univ.*, 1988, **53**, 301 (*Chem. Abstr.*, 1990, **112**, 52163f); (*h*) T. Nobuchi, K. Takai and H. Harada, *Mokuzai Gakkaishi*, 1987, **33**, 88 (*Chem. Abstr.*, 1987, **106**, 192808w); (*i*) K. Takahashi and K. Ogiyama, *Mokuzai Gakkaishi*, 1986, **32**, 457 (*Chem. Abstr.*, 1986, **105**, 174611b); (*j*) K. Takahashi and K. Ogiyama, *Mokuzai Gakkaishi*, 1985, **31**, 677 (*Chem. Abstr.*, 1986, **104**, 52232n); (*k*) K. Takahashi and K. Ogiyama, *Mokuzai Gakkaishi*, 1985, **31**, 28 (*Chem. Abstr.*, 1985, **102**, 133777e); (*l*) K. Takahashi, M. Yasue and K. Ogiyama, *Mokuzai Gakkaishi*, 1983, **29**, 806 (*Chem. Abstr.*, 1984, **100**, 123006x); (*m*) T. Sato and T. Sato, *Gyomu Hokoku-Akita-ken Ringyo Senta*, 1979, 185 (*Chem. Abstr.*, 1981, **95**, 93999g); (*n*) K. Takahashi, *Mokuzai Gakkaishi*, 1981, **27**, 654 (*Chem. Abstr.*, 1981, **95**, 205649b); (*o*) H. Erdtman and J. Harmatha, *Phytochemistry*, 1979, **18**, 1495; (*p*) P. Henley-Smith and D. A. Whiting, *Phytochemistry*, 1976, **15**, 1285.

4 (*a*) H. Ohashi, H. Hayashi, M. Yamada and M. Yasue, *Res. Bull. Fac. Agr. Gifu Univ.*, 1987, **52**, 131 (*Chem. Abstr.*, 1989, **110**, 92049p); (*b*) Y. Hirose, N. Oishi, H. Nagaki and T. Nakatsuka, *Tetrahedron Lett.*, 1965, 3665.

5 (*a*) K. Ootsuka, K. Sakurada and H. Nakamura (Kishimoto Sangyo Co.) Jpn. Kokai Tokkyo Koho, JP 07 25719/1995 (*Chem. Abstr.*, 1995, **122**, 233344t); (*b*) H. Ohashi, S. Kawai, Y. Sakurai and M. Yasue, *Phytochemistry*, 1992, **31**, 1371; (*c*) N. Fujita, T. Yoshimoto and M. Samejima, *Mokuzai Gakkaishi*, 1984, **30**, 264 (*Chem. Abstr.*, 1984, **100**, 206513m); (*d*) T. Nikaido, T. Ohmoto, H. Noguchi, T. Kinoshita, H. Saitoh and U. Sankawa, *Planta Med.*, 1981, **43**, 18; (*e*) U. Sankawa, *Saengyak Hakhoe Chi*, 1980, **11**, 125 (*Chem. Abstr.*, 1981, **95**, 125747s); (*f*) R. J. Anderegg and J. W. Rowe, *Holzforschung*, 1974, **28**, 171; (*g*) V. G. Weißmann, *Holzforschung*, 1973, **27**, 193.

6 (*a*) S. Mibayashi, K. Satoh and T. Yokota, *Mem. Coll. Agric., Kyoto Univ.*, 1985, **127**, 49 (*Chem. Abstr.*, 1986, **105**, 116823m); (*b*) H. Funakoshi, K. Nobashi and T. Yokota, *Mokuzai Gakkaishi*, 1978, **24**, 141 (*Chem. Abstr.*, 1978, **88**, 170579e); (*c*) Y. Kai, *Mokuzai Gakkaishi*, 1965, **11**, 23 (*Chem. Abstr.*, 1965, **62**, 16553g); (*d*) K. Funaoka, Y. Kuroda, Y. Kai and T. Kondo, *Mokuzai Gakkaishi*, 1963, **9**, 139 (*Chem. Abstr.*, 1964, **60**, 1626c).

7 R. Riffer and A. B. Anderson, *Phytochemistry*, 1967, **6**, 1557; B. Balogh and A. B. Anderson, *Phytochemistry*, 1965, **4**, 569; H. Erdtman and H. Vorbrüggen, *Acta Chem. Scand.*, 1960, **14**, 2161.

8 A. P. Beracierta and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1257.

9 (*a*) Z. Horii, C. Iwata, T. Tanaka and T. Momose, *Heterocycles*, 1977, **6**, 697; (*b*) A. P. Beracierta and D. A. Whiting, *Tetrahedron Lett.*, 1976, 2367.

10 C. R. Enzell, Y. Hirose and B. R. Thomas, *Tetrahedron Lett.*, 1967, 793.

11 S. Wattanasin and W. S. Murphy, *Synthesis*, 1980, 647.

12 S. Hashimoto, S. Yamada and K. Koga, *Chem. Pharm. Bull.*, 1979, **27**, 771; S. Hashimoto, S. Yamada and K. Koga, *J. Am. Chem. Soc.*, 1976, **98**, 7450.

13 (*a*) J. S. M. Wai, I. Markó, J. S. Svendsen, M. G. Finn, E. N. Jacobsen and K. B. Sharpless, *J. Am. Chem. Soc.*, 1989, **111**, 1123; (*b*) B. B. Lohray, T. H. Kalantar, B. M. Kim, C. Y. Park, T. Shibata, J. S. M. Wai and K. B. Sharpless, *Tetrahedron Lett.*, 1989, **30**, 2041; (*c*) E. N. Jacobsen, I. Markó, W. S. Mungall, G. Schröder and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 1968.

14 H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 1963, 1171.

15 J. A. Dale, D. L. Dull and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.

16 (*a*) H. Becker, M. A. Soler and K. B. Sharpless, *Tetrahedron*, 1995, **51**, 1345; (*b*) E. J. Corey, G.-P. Angel and M. C. Noe, *J. Am. Chem. Soc.*, 1994, **116**, 12109; (*c*) Z.-M. Wang and K. B. Sharpless, *Tetrahedron Lett.*, 1993, **34**, 8225; (*d*) K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu and X.-L. Zhang, *J. Org. Chem.*, 1992, **57**, 2768

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