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CONJUGATE ADDITION OF ARYLMETAL REAGENTS TO AN α,β-UNSATURATED KETONE. SHORT SYNTHESES OF (-)-AGATHARESINOL DIMETHYL ETHER AND (-)-SUGIRESINOL DIMETHYL ETHER

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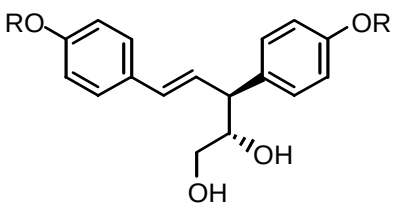
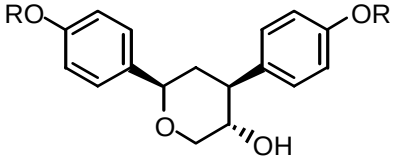
Abstract – (-)-Agatharesinol dimethyl ether and (-)-sugiresinol dimethyl ether, derivatives of (-)-agatharesinol and (-)-sugiresinol isolated from *Agathis australis* and *Cryptomeria Japonica*, respectively were synthesized starting from a protected D-glyceraldehyde in five steps through 1,4-conjugate addition of arylmetal reagents to an α,β-unsaturated ketone.

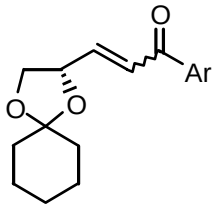
(-)-Agatharesinol (**1a**) and (-)-sugiresinol (**2a**) are norlignans isolated from heartwood of *Agathis australis* by Enzell and Thomas[1] in 1965 and *Cryptomeria Japonica* by Funaoka *et al.*[2] in 1963, respectively, and their chemical structures including absolute stereochemistry were determined by Enzell *et al.*[3] in 1966. The norlignans (**1a** and **2a**) have been reported to show biological activities such as antifungal activity,[4] inhibitory effect on cyclic AMP phosphodiesterase,[5] inhibitory activity against *C. shiitake* hyphae growth and fruiting body formation, [6] and vinyl polymerization-inhibitory activity.[7]
Syntheses of agatharesinol dimethyl ether (**1b**) and sugiresinol dimethyl ether (**2b**) have been reported by Horii *et al.*[8] and Beracierta and Whiting[8] as racemic form and by Muraoka *et al.*[9] and Dujardin *et al.*[10] as optically active form, respectively. Recently, we also reported the synthesis of (-)-**2b** utilizing (-)-quinic acid as the chiral source.[11]



(-)-1a: R=H (Agatharesinol)
(-)-1b: R= Me (Agatharesinol dimethyl ether)



(-)-2a: R=H (Sugiresinol)
(-)-2b: R= Me (Sugiresinol dimethyl ether)



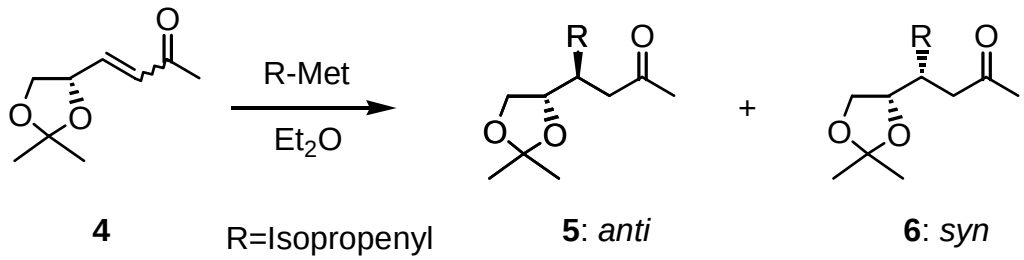
3: Ar=4-Methoxyphenyl

Scheme 1

As a part of our synthetic studies on biologically active natural products, we would like to report here the

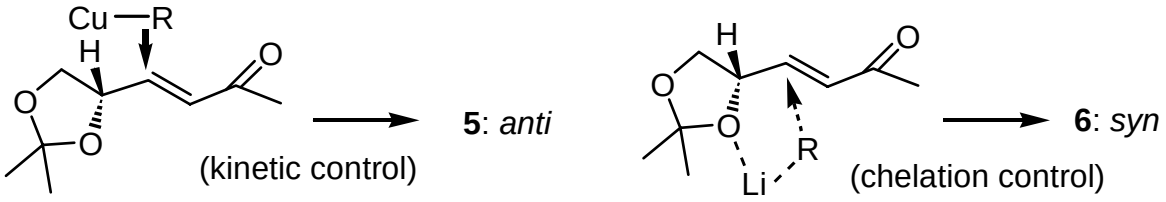
short syntheses (five steps) of (-)-**1b** and (-)-**2b** starting from a protected D-glyceraldehyde[12] through 1,4-conjugate addition of arylmetal reagents to the α,β-unsaturated chiral ketone (**3**).[13]

Leonard and Ryan[14] have reported that isopropenylcopper reacted with α,β-unsaturated ketone (**4**) (*E*:*Z*=6:1) which has an oygen function at γ-position to give a mixture of *anti*- and *syn*-adducts (**5**:**6**=7:1) in 79% yield, on the other hand, in the reaction of isopropenyllithium with **4** (*E*:*Z*=7:2), a mixture of *anti*- and *syn*-adducts (**5**:**6**=1:36) in 60% yield (Scheme 2). These results indicated that the copper reagent added to **4** from the less hindered side to afford the *anti*-isomer (**5**) predominantly (kinetic control), but the lithium reagent chelated first to the oxygen atom at γ-position and then the alkyl group attacked the β-position of the α,β-unsaturated ketone from the same face to give the *syn*-isomer (**6**) predominantly (chelation control) (Scheme 3).



4 **5**: *anti* **6**: *syn*

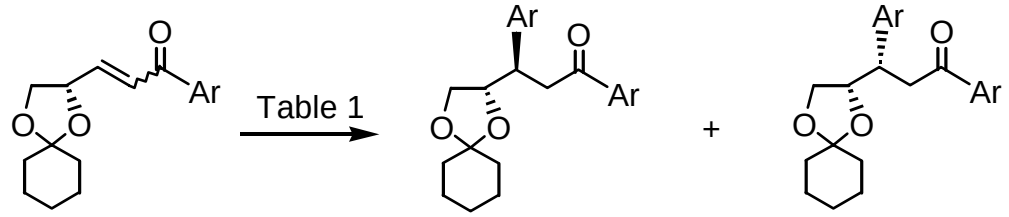
Scheme 2



5: *anti* **6**: *syn*

Scheme 3

According to the results of above Leonard and Ryan's experiment, if the 4-methoxyphenyl-metal reagents react with **3** under chelation control, the *syn*-adduct (**8**) would be obtained predominantly (Scheme 4). Two stereogenic centers of **8** suit for the stereochemistry of 2 and 3 positions of (-)-**1b** and 4 and 5 positions of (-)-**2b**.



3: *E*:*Z*=3:1 **7** **8**

Scheme 4

In our synthetic work on (-)-**1b** and (-)-**2b**, the α,β-unsaturated chiral ketone (**3**) was synthesized first to investigate the 1,4-conjugate addition of arylmetal reagents. Thus, the protected D-gryceraldehyde,[12]

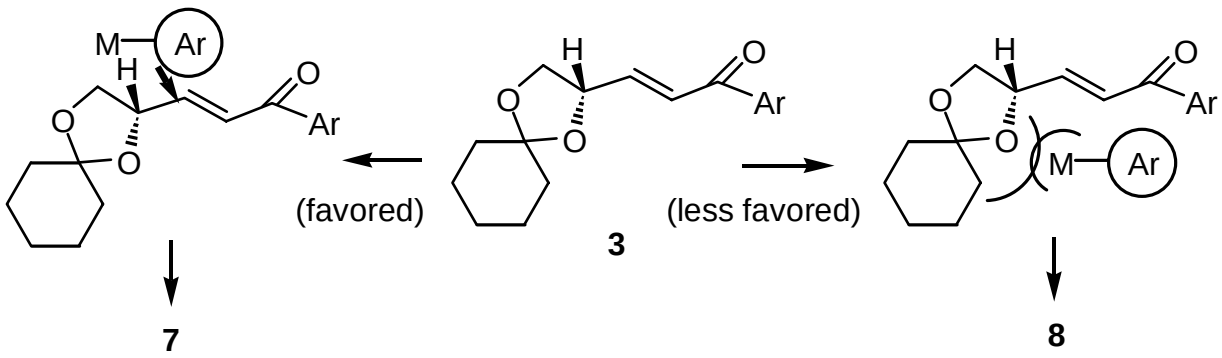
which was derived from D-mannitol, was treated with 4-methoxybenzoylmethylenetriphenylphosphorane[15] to give a mixture (3:1) of (*E*)- and (*Z*)-α,β-unsaturated ketones (**3**) in quantitative yield, which possessed chiral oxygen functions at γ-position. Then the conjugate addition reaction of the various 4-methoxyphenyl-metal reagents to **3** was investigated. The results are summarized in Table 1.

Table 1. Conjugate Addition of Arylmetal Reagents to **3**

Entry	Reagents[a)]	Temp. (°C)	Yield (%)	**7** : **8**
1	ArMgBr (3.3 eq.) CuBr-Me_2S (1.6 eq.), THF	-15	46	3 : 1[b)]
2	Ar-Li (1.2 eq.), THF	-78	45	4 : 1[c)]
3	Ar-Li (1.8 eq.), Et_2O	-78	38	nd[d)]
4	Ar-I (1.2 eq.), $(Ph_3P)_4Pd$, Et_3N	reflux	28	3 : 1[c)]

a) Ar=4-Methoxyphenyl.
b) Each compound was isolated by preparative SiO_2 TLC.
c) The ratio was determined with ^{1}H-NMR.
d) Not determined.

When a mixture of 4-methoxyphenylmagnesium bromide (3.3 eq.) and CuBr-Me_2S complex (1.6 eq.)[16] was treated with **3** (a mixture of *E*:*Z*=3:1) in THF at –15 °C, a mixture (3:1) of **7** and **8** was obtained in 46% yield (Entry 1). The reaction of 4-methoxyphenyllithium (prepared from 4-iodoanisole and *n*-butyllithium)[17] with **3** in THF at –78 °C resulted in formation of a mixture (4:1) of **7** and **8** in 45 % yield (Entry 2). In this reaction, change of the solvent from THF to Et_2O caused to lower the yield (Entry 3). When a mixture of 4-iodoanisole and $(Ph_3P)_4Pd$ [18] was treated with **3** in the presence of Et_3N at refluxing temperature, a mixture (3:1) of **7** and **8** was also produced in 28% yield (Entry 4). These results suggested that the reaction of the arylmetal reagents used above took place to give the kinetically controlled product (**7**) predominantly, even when the lithium reagent was employed (Entry 2). These evidences are probably attributable to the steric hindrance of both the arylmetal reagents and the

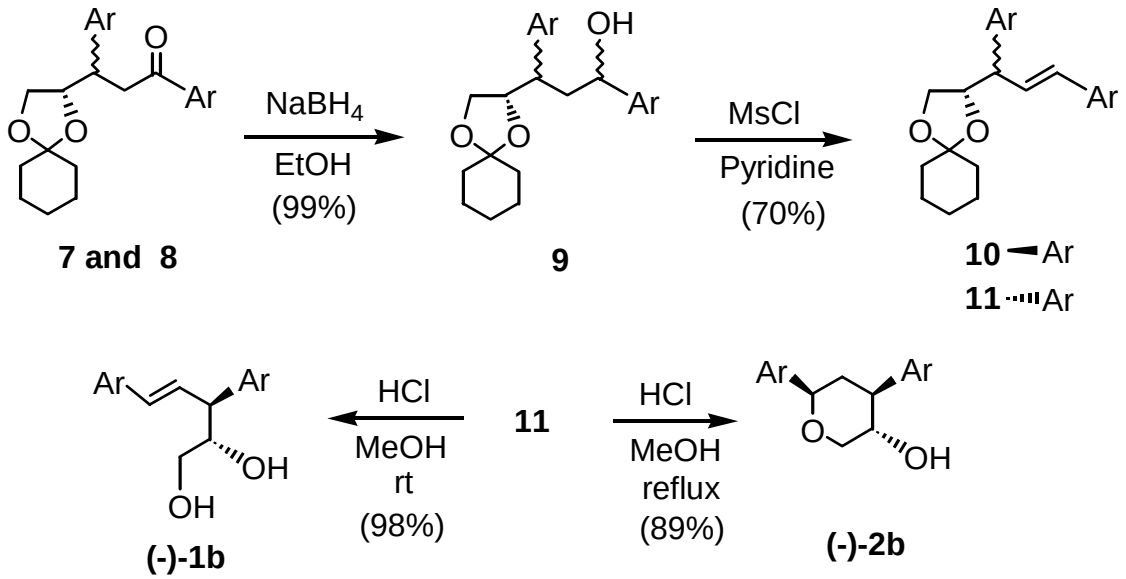


Scheme 5

cyclohexylidene protective group (Scheme 5). Although the starting compound (**3**) was almost

consumed throughout the above reactions, the chemical yields of the mixture of **7** and **8** were moderate to relatively low. We thought that this result might be attributable to the formation of 1,2-addition products, but it was failed to isolate those compounds.

The compound (**8**) is suitable for the synthesis of (-)-**1b** and (-)-**2b**. Therefore, transformations of **8** into (-)-**1b** and (-)-**2b** were examined. As the isolation of **8** from the mixture in this stage and in practical scale was difficult, the mixture was used as such in the next reaction. Thus, $NaBH_4$ reduction of the mixture (3:1) of **7** and **8** in EtOH gave the alcohol (**9**) in 99% yield. The alcohol (**9**) was treated with methanesulfonyl chloride in pyridine at refluxing temperature to afford a mixture (3:1) of olefins (**10**) and (**11**) in 70% yield, which were separated easily into each compound by silica gel column chromatography (benzene:ethyl acetate=10:1). The structures of **10** and **11** were determined by comparing the spectral data with those of the related compounds appeared in the literatures.[4, 8, 11, 19] In the ^{1}H-NMR spectrum, the methine proton attached to the aryl group appeared at δ 3.45 (t, *J*=7.0 Hz) in **10** and 3.55 (t, *J*=8.0 Hz) in



Scheme 6

11, respectively. Treatment of the olefin (**11**) with hydrochloric acid in methanol at room temperature furnished (-)-agatharesinol dimethyl ether (**1b**) ($[\alpha]_D^{20}$ –24.8° (*c*=1.24, $CHCl_3$)) in 98% yield. When **11** was treated with hydrochloric acid in methanol at refluxing temperature, (-)- sugiresinol dimethyl ether (**2b**) (mp 103.5-104.5 °C, $[\alpha]_D^{21}$ –4.0° (*c*=1.01, $CHCl_3$); lit.[3, 8, 11]: $[\alpha]_D$ –4.0° ($CHCl_3$), mp 104-105 °C) was obtained in 89% yield. IR and ^{1}H-NMR spectral data of both synthesized **1b** and **2b** were identical with those of the authentic samples.[4, 8, 11, 19] Thus, (-)-agatharesinol dimethyl ether (**1b**) and (-)-sugiresinol dimethyl ether (**2b**) were synthesized starting from the known protected D-glyceraldehyde in 5 steps through conjugate addition of arylmetal reagent to the chiral α,β-unsaturated ketone (**3**) (Scheme 6) .

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro-melting point apparatus, model MP-S3, and are uncorrected. IR spectra were measured with a Hitachi 260-30 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GSX270 (270 MHz) spectrometer using tetramethylsilane as the

internal standard. High-resolution MS spectra (HRMS) were measured with a JEOL JMS-HX100 instrument at 70 eV.

(4*S*)-4,5-Cyclohexylidenedioxy-1-(4-methoxyphenyl)pent-2-en-1-one (3)

4-Methoxybenzoylmethylenetriphenylphosphorane[15] (6.20 g, 15.1 mmol) was added to a solution of (2*R*)-2,3-cyclohexylidenedioxypropanal[12] (2.57 g, 15.1 mmol) in MeCN (100 mL), and the whole was stirred at room rt for 1 h and refluxed for 30 min. The reaction mixture was concentrated under reduced pressure and ether (100 mL) was added to the residue. The mixture was stirred vigorously to form precipitates, which were removed by filtration. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane:AcOEt=4:1) to give a mixture of (*E*)- and (*Z*)-**3** (4.56 g, quantitative yield). ^{1}H-NMR spectrum of the mixture showed *E*:*Z*=3:1. Repeated silica gel column chromatography (*n*-hexane:AcOEt=6:1) of the mixture afforded (*E*)- and (*Z*)-**3** as oils. (*E*)-**3**: IR (neat): 1665 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38-1.74 (10H, m, cyclohexylidene), 3.73 (1H, dd, *J*= 8.5, 7.0Hz, OCH_2), 3.88 (3H, s, OCH_3), 4.23 (1H, dd, *J*= 8.0, 7.0 Hz, OCH_2), 4.79 (1H, m, OCH), 6.94 (1H, dd, *J* = 15.5, 5.5 Hz, OCHC<u>H</u>=CH), 6.96 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.20 (1H, dd, *J*=15.5, 1.5 Hz, CH=C<u>H</u>CO), 7.97 (2H, dt, *J*=9.0, 2.5 Hz, ArH). HRMS (*m/z*): Calcd for $C_{18}H_{22}O_4$ (M^+): 302.1518. Found:302.1523. (*Z*)-**3**: IR (neat): 1665 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38-1.74 (10H, m, cyclohexylidene), 3.69 (1H, dd, *J*=8.5, 7.0 Hz, OCH_2), 3.88 (3H, s, OCH_3), 4.50 (1H, dd, *J*=8.0, 7.0 Hz, OCH_2), 5.35 (1H, m, OCH), 6.43 (1H, dd, *J*=12.0, 7.0 Hz, OCHC<u>H</u>=CH), 6.92 (1H, dd, *J*=12.0, 2.0 Hz, CH=C<u>H</u>CO), 6.96 (1H, dt, *J*=9.0, 2.5 Hz, ArH), 7.97 (1H, dt, *J*=9.0, 2.5 Hz, ArH).

(4*S*)-4,5-Cyclohexylidenedioxy-1,3-bis(4-methoxyphenyl)pentan-1-ones (7 and 8)

Entry 1. A THF solution of 4-methoxyphenylmagnesium bromide was prepared from magnesium turnings (80 mg, 3.3 mmol), 4-bromoanosole (0.42 mL, 3.4 mmol) and THF (1.5 mL) by usual method. A cold solution of CuBr-Me_2S complex (0.322 g, 1.6 mmol) and Me_2S (1.8 mL) in THF (3.5mL) was added through cannula to the above Grignard reagent at –40 ^{o}C. A solution of **3** (*E*:*Z*=3:1)(0.294 g, 1.0 mmol) in THF (2.0 mL) was added dropwise to the above reaction mixture at –15 ^{o}C and the whole was stirred at that temperature for 15 min. After the reaction mixture was warmed to rt, saturated aqueous solution of NH_4Cl was added and then the solution was concentrated to remove THF under reduced pressure. Water (10 mL) was added to the concentrated solution and the mixture was extracted with AcOEt. The extract was washed with 10% ammonia solution, H_2O and brine, successively. After drying over anhydrous Na_2SO_4, the organic layer was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (benzene:AcOEt=30:1) to give a mixture of **7** and **8** (0.399 g, 46%) as a pale yellow oil. The compounds (**7**) and (**8**) were isolated from the mixture by repeated silica gel preparative TLC (*n*-hexane: AcOEt=10:1) and the ratio of **7** and **8** was 3:1. **7**: oil. IR (neat): 1675 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32 –1.68 (10H, m, cyclohexylidene), 3.28 (1H, dd, *J*= 15.5, 9.5 Hz, ArCHC<u>H</u>$_2$CO), 3.39 (1H, td, *J*=9.5, 3.0 Hz, OCHC<u>H</u>Ar), 3.58 (1H, dd, *J*=9.0, 6.0 Hz, OC<u>H</u>$_2$CHO), 3.62 (1H, dd, *J*=15.5, 3.0 Hz, ArCHC<u>H</u>$_2$CO), 3.71-3.78 (1H, m, OC<u>H</u>$_2$CHO), 3.75 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 4.26 (1H, td, *J*=9.5, 6.0 Hz, OCH_2C<u>H</u>O), 6.79 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 6.89 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.16 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.90 (2H, dt, *J*=9.0, 2.5 Hz, ArH). **8**: oil. IR (neat): 1675 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.32-1.68 (10H, m, cyclohexylidene), 3.34 (1H, dd, *J*=16.5, 8.0 Hz, ArCHC<u>H</u>$_2$CO), 3.47 (1H,

dd, *J*=16.5, 8.0 Hz, ArCHC$\underline{H}_2$CO), 3.52 (1H, t, *J*=8.0 Hz, ArC$\underline{H}$CH$_2$), 3.56-3.63 (1H, m, OC$\underline{H}_2$CH), 3.75 (3H, s, OCH$_3$), 3.85 (3H, s, OCH$_3$), 3.92 (1H, dd, *J*=8.0, 6.0 Hz, OC$\underline{H}_2$CH), 4.36 (1H, ddd, *J* =8.0, 6.0, 5.0 Hz, OCH$_2$C$\underline{H}$O), 6.79 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 6.89 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.16 (2H, dt, *J* =9.0, 2.5 Hz, ArH), 7.90 (2H, dt, *J*=9.0, 2.5 Hz, ArH). HRMS (*m/z*): Calcd for $C_{25}H_{30}O_5$ (M^+): 410.2093. Found: 410.2101.

Entry 2. *n*-BuLi (1.58 M *n*-hexane solution, 1.27 mL, 2.01 mmol) was added to a stirred solution of 4-iodoanisole (0.46 g, 1.98 mmol) in THF (2.5 mL) at –78 ^{o}C. A solution of **3** (*E*:*Z*=3:1)(0.50 g, 1.65 mmol) in THF (1.0 mL) was added to the above reaction mixture at –78 ^{o}C and the whole was stirred at that temperature for 20 min. After addition of H_2O, the mixture was extracted with AcOEt (x 3) and the combined extract was washed with H_2O and brine, successively. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography (benzene:AcOEt=30:1) as above. A mixture of **7** and **8** (0.39 g, 45%) was obtained as a pale yellow oil and the ratio of each determined as 4:1 by ^{1}H-NMR spectral data.

Entry 3. *n*-BuLi (1.58 M *n*-hexane solution, 0.78 mL, 1.23 mmol) was added to a stirred solution of 4-iodoanisole (0.28 g, 0.79 mmol) in Et_2O (5.0 mL) at –78 ^{o}C. A solution of **3** (*E*:*Z*=3:1)(0.20 g, 0.66 mmol) in Et_2O (1.5 mL) was added to the above reaction mixture at –78 ^{o}C and the whole was stirred at that temperature for 25 min. After addition of H_2O, the mixture was extracted with AcOEt and the combined extract was washed with H_2O and brine, successively. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography (benzene:AcOEt=30:1) as above. A mixture of **7** and **8** (0.10 g, 38%) was obtained as a pale yellow oil.

Entry 4. A mixture of **3** (*E*:*Z*=3:1)(0.20 g, 0.66 mmol), 4-iodoanisole (0.19 g, 0.80 mmol), $(Ph_3P)_4Pd$ (7 mg, 6 x 10^{-3} mmol) and Et_3N (0.30 mL, 2.15 mmol) was refluxed for 7 h. After addition of 10% HCl and H_2O, the mixture was extracted with AcOEt (x 2) and the combined extract was washed with H_2O and brine, respectively. The organic layer was dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography (*n*-hexane:AcOEt=19:1) as above. A mixture of **7** and **8** (76 mg, 28%) was obtained as pale yellow oil and the ratio of each determined as 3:1 by ^{1}H-NMR spectral data.

(2*S*)-1,2-Cyclohexylidenedioxy-3,5-bis(4-methoxyphenyl)pentan-5-ol (9)

$NaBH_4$ (93.5 mg, 2.5 mmol) was added to a solution of **7** and **8** (3:1 mixture, 0.496 g, 1.2 mmol) in EtOH (6.0 mL) under ice-cooling and the whole was stirred at rt for 7 h. After addition of H_2O and sodium chloride, the mixture was extracted with $CHCl_3$ (x 3) and the combined organic layer was washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to give **9** (0.491 g, 99%) as a pale yellow oil. Since this compound was relatively unstable, it was submitted for the next reaction immediately after taking the IR spectrum. IR (neat): 3450 cm^{-1}.

(2*S*,3*R*)-(4*E*)- and (2*S*,3*S*)-(4*E*)-1,2-Cyclohexylidenedioxy-3,5-bis(4-methoxyphenyl)pent-4-enes (10 and 11)

Methanesulfonyl chloride (0.375 mL, 4.8 mmol) was added to a solution of **9** (0.483 g, 1.2 mmol) in dry pyridine (12.0 mL) and the reaction mixture was stirred at rt for 14 h and then refluxed for 5 h. The reaction was quenched by addition of cold water and the mixture was extracted with $CHCl_3$ (x 5). The

combined extract was washed with 5% HCl, saturated $NaHCO_3$ aqueous solution and brine, successively and dried over anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure to give a brown oil which was purified by silica gel column chromatography (*n*-hexane:AcOEt=10:1) to furnish a mixture of **10** and **11** (0.322 g, 70%) as a pale yellow oil. The oil was separated into each **10** and **11** (3:1) by careful silica gel column chromatography (benzene). **10**: oil. IR (neat): 965 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.75 (10H, m, cyclohexylidene), 3.45 (1H, t, *J*=7.0 Hz, ArCH), 3.60 (1H, dd, *J*=8.0, 7.0 Hz, OCH_2), 3.79 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.82 (1H, dd, *J*=8.0, 6.0 Hz, OCH_2), 4.40 (1H, ddd, *J*=8.0, 7.0, 6.0 Hz, OCH), 6.28 (1H, d, *J*=16.0 Hz, CH=C<u>H</u>Ar), 6.40 (1H, dd, *J*=16.0, 6.5 Hz, CHC<u>H</u>=CH), 6.81 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 6.86 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.18 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.28 (2H,dt, *J*=9.0, 2.5 Hz, ArH). $[\alpha]_D^{22}$: -10.8^o (*c*=1.00, $CHCl_3$). **11**: oil. IR (neat): 960 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.29-1.68 (10H, m, cyclohexylidene), 3.55 (1H, t, *J*=8.0 Hz, ArCH), 3.79 (6H, s, 2 x OCH_3), 3.80 (1H,dd, *J*=8.0, 7.0 Hz, OCH_2), 4.03 (1H, dd, *J*=8.0, 6.0 Hz, OCH_2), 4.41 (1H, ddd, *J*=8.0, 7.0, 6.0 Hz,OCH) ,6.16 (1H, dd, *J*=15.5, 8.0 Hz, CHC<u>H</u>=CH), 6.41 (1H, d, *J*=15.5 Hz, CH=C<u>H</u>Ar), 6.82 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 6.86 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.23 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.27 (2H, dt, *J*=9.0, 2.5 Hz, ArH). HRMS (*m/z*): Calcd for $C_{25}H_{30}O_4$ (M^+): 394.2144. Found:394.2150. $[\alpha]_D^{22}$: -12.0^o (*c*=1.06, $CHCl_3$).

(-)-Agatharesinol dimethyl ether (1b)

Concentrated HCl (0.52 mL) was added to a solution of **11** (20 mg, 0.051 mmol) in MeOH (3.5 mL) under ice-cooling and the whole was stirred at rt for 2 h. After addition of saturated $NaHCO_3$ aqueous solution, the mixture was extracted with $CHCl_3$ (x 5) and the combined extract was washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue, which was purified by silica gel PTLC (*n*-hexane:AcOEt=1:1) to give (-)-**1b** (16 mg, 98%) as a colorless oil. IR (neat): 3400, 1610, 1510, 1250 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.95 (2H, br s, 2 x OH), 3.52 (1H, t, *J*=9.0 Hz, OCHC<u>H</u>Ar), 3.62 (1H, dd, *J*=11.5, 6.5 Hz, C<u>H</u>$_2$OH), 3.79 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.82 (1H, dd, *J*=11.5, 3.0 Hz, C<u>H</u>$_2$OH), 3.99 (1H, ddd, *J*=9.0, 6.5, 3.0 Hz, C<u>H</u>OH), 6.16 (1H, dd, *J*=16.0, 9.0 Hz, C<u>H</u>=CHAr), 6.42 (1H, d, *J*=16.0 Hz, CH=C<u>H</u>Ar), 6.82 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 6.90 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.24 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.26 (2H, dt, *J*=9.0, 2.5 Hz, ArH). $[\alpha]_D^{20}$: -24.8^o (*c*=1.24, $CHCl_3$). HRMS (*m/z*): Calcd for $C_{19}H_{22}O_4$ (M^+): 314.1518. Found: 314.1513.

(-)-Sugiresinol dimethyl ether (2b)

Concentrated HCl (0.52 mL) was added to a solution of **11** (20 mg, 0.05 mmol) in MeOH (3.5 mL) and the whole was refluxed for 20 h. After cooling and neutralization by addition of saturated $NaHCO_3$ aqueous solution, the mixture was extracted with $CHCl_3$ (x 5). The combined extract was washed with brine and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave asolid, which was purified by silica gel PTLC (*n*-hexane:AcOEt=1:1) to give **(-)-1b** (14 mg, 89%) as colorless crystalline powder. Sample for spectra was obtained by recrystallization from *n*-hexane. mp 103.5-104.5 ^{o}C (lit.,[3] 104-105 ^{o}C). IR (Nujol): 3400, 1610, 1585, 1510 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.62 (1H, br s, OH), 1.91 (1H, ddd, *J*=14.0, 12.5, 11.0 Hz, ArCHC<u>H</u>$_2$CHAr), 2.07 (1H, ddd, *J*=14.0, 4.0, 2.0 Hz, ArCHC<u>H</u>$_2$CHAr), 2.78 (1H, ddd, *J*=12.5, 10.0, 4.0 Hz, CH$_2$C<u>H</u>ArCH), 3.48 (1H, dd, *J*=11.0, 10.0 Hz, OC<u>H</u>$_2$CH), 3.79 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.86 (1H, dt *J*=10.0, 5.0Hz, C<u>H</u>OH), 4.29 (1H, dd, *J*=11.0, 5.0 Hz, OC<u>H</u>$_2$CH), 4.47 (1H, dd, *J*=11.0, 2.0 Hz, OC<u>H</u>ArCH$_2$), 6.86 (2H, dt, *J*=9.0, 2.5 Hz, ArH),

6.89 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.22 (2H, dt, *J*=9.0, 2.5 Hz, ArH), 7.30 (2H, dt, *J*=9.0, 2.5 Hz, ArH). HRMS (*m/z*): Calcd for $C_{19}H_{22}O_4$: 314.1518. Found: 314.1499. $[\alpha]_D^{21}$: -4.0° (*c*=1.01, $CHCl_3$)(lit.,[3,19] $[\alpha]_D$: -4.0° ($CHCl_3$)).

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