Total Synthesis and Absolute Configuration of Riccardiphenols A and B, Isolated from the Liverwort *Riccardia crassa*

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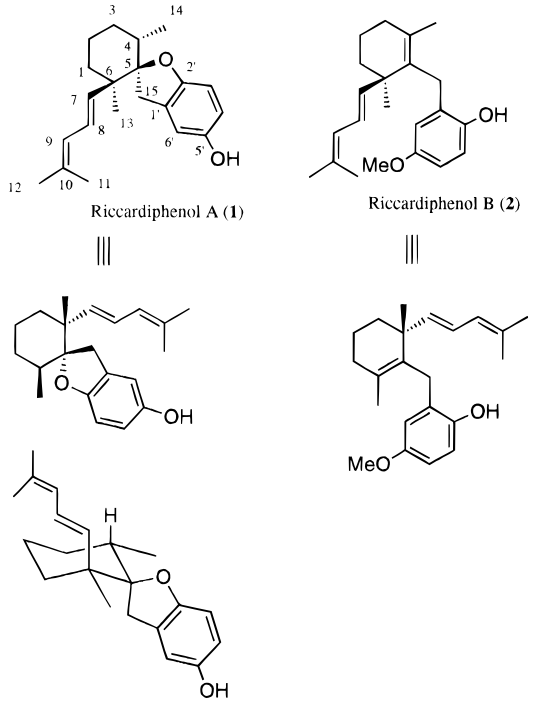
The title compounds were synthesized as optically active forms using chiral Michael addition of the imine, prepared from 2-methylcyclohexanone and (S)-(−)-phenylethylamine, to methyl propiolate. The etherification of the intermediate triol was accomplished by TsOH-catalyzed cyclization. The absolute configurations of the natural products, riccardiphenols A and B, were established as **1** and **2**, respectively.

Introduction

Riccardiphenols A (**1**) and B (**2**) were isolated from the liverwort *Riccardia crassa* by Toyota and Asakawa[1] and have a seco-eudesmane skeleton connected to a phenol, which is rare in nature.[2] Similar examples have recently been isolated from another liverwort.[3] Wu and coworkers reported the isolation of tridensone (**3**)[4] and tridensenal (**4**),[5] which were thought to have seco-eremophilane and seco-eudesmane skeletons, respectively (Scheme 1). On the other hand, terpenoids having a benzylic substituent are well precedented.[6] We are interested in the absolute configuration of terpenoids isolated from liverworts[2] and have reported several synthetic studies concerning the absolute configuration.[7] Now we report the details of a total synthesis of riccardiphenols A (**1**) and B (**2**) and their absolute configuration.

Results and Discussion

Synthesis of Aromatic Part. When gentisic acid (**5**) was treated with diazomethane, a mixture of the monomethyl ether methyl ester (two positional isomers) and a permethylated compound were produced. The reaction of **5** with methyl iodide in the presence of potassium carbonate afforded the permethylated compound. Thus methyl gentisate (**6**) was treated with dihydropyran to give a mono-protected ester **7** in excellent yield (Scheme 2). The *ortho* phenolic hydroxyl group was protected with a MOM group, followed by deprotection of the THP group and treatment with MeI and K_2CO_3 to afford the desired ester **9**. Reduction of **9** with $LiAlH_4$ and chlorination with PPh_3 and CCl_4 gave chloride **10**. If the corresponding alcohol was treated with PPh_3 and CBr_4, the reaction was messy, presumably due to the instability of the bromide. In order to synthesize riccardiphenol A (**1**), a bis-MOM-protected chloride **12**, prepared by a route analogous to that of **10**, was used for the sake of convenience of deprotection.



Preparation of the Optically Active Ketones 20 and 21. Pfau *et al.* reported a highly practical method for constructing the quaternary center using a chiral phenylethylamine.[8] For example, the imine of 2-methylcyclohexanone of (*S*)-(−)-phenylethylamine **13** was reacted with methyl acrylate without any solvent at rt for 5 days. A slow Michael reaction proceeded to yield a keto ester **14**, after acid hydrolysis of the imine (Scheme 3). The chemical yield and %ee were generally good. We explored this type of reaction using methyl propiolate as

[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1996.

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(2) (a) Asakawa, Y. *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., and Kirby, G. W., Ed.; Springer-Verlag: Wien, 1982; Vol. 42, pp 1−285. (b) Asakawa, Y. *Bryophytes: Their Chemistry and Chemical Taxonomy*; Zinsmeister, H. D., Mues, R., Ed.; Oxford University Press: Oxford, 1990; pp 369−410. (c) Asakawa, Y. *Bioactive Natural Products: Detection, Isolation and Structural Determination*; Colegate, S. M., Molyneux, R. J., Ed.; CRC Press: Boca Raton, Florida, 1993; pp 319−347.

(3) Perry, N. B.; Foster, L. M. *J. Nat. Prod.* **1995**, *58*, 1131−1135.

(4) Wu, C.-L.; Chen, C.-L. *Phytochemistry* **1992**, *31*, 4213−4217.

(5) (a) Wu, C.-L. *Bryophytes: Their Chemistry and Chemical Taxonomy*; Zinsmeister, H. D., Mues, R., Ed.; Oxford University Press: Oxford, 1990; pp 71−82. (b) Wu, C.-L.; Chang, S.-J.; Tori, M.; Furuta, H.; Sumida, A.; Asakawa, Y. *J. Chin. Chem. Soc.* **1990**, *37*, 387−391.

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(7) (a) Tori, M.; Kosaka, K.; Asakawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2039−2041. (b) Tori, M.; Uchida, N.; Sumida, A.; Furuta, H.; Asakawa, Y. *J. Chem. Soc., Perkin Trans 1* **1995**, 1513−1517.

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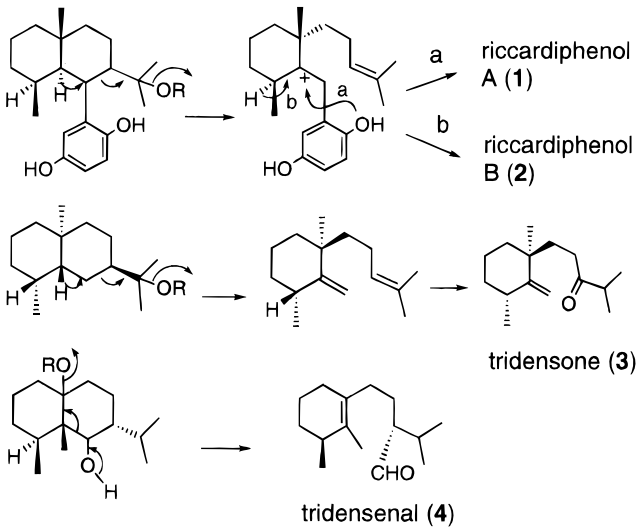
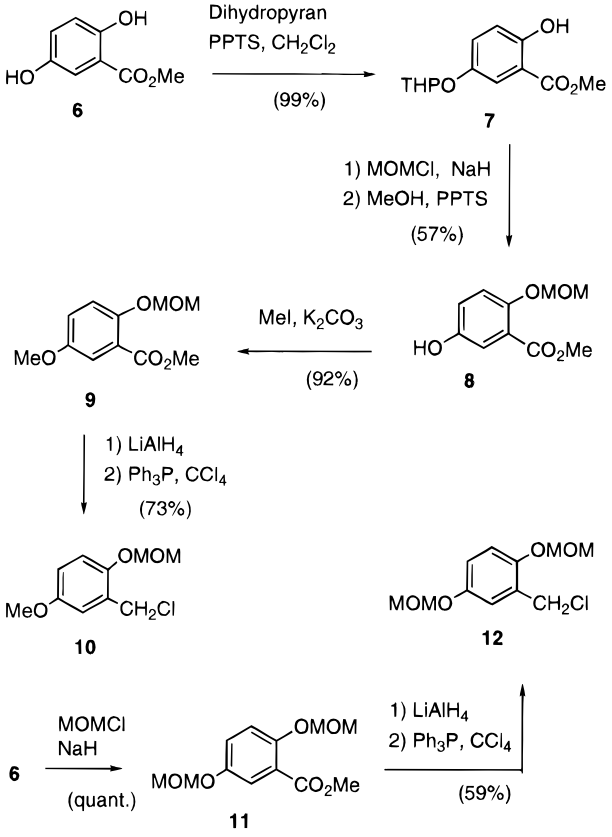
S0022-3263(95)02253-5 CCC: $12.00

Scheme 1



Scheme 2



a Michael acceptor because our synthetic targets have diene units in their side chains. Thus the reaction of the imine **13** with methyl propiolate proceeded smoothly to give an α,β-unsaturated ester **15**[9] in 79% yield and with 80% ee after hydrolysis. The absolute configuration of the product **15** was established by hydrogenation of the double bond into the known ester **14**.[8] Keto ester **14** could also be converted into an α,β-unsaturated ester **16**.[9]

Ketalization of **15** to **16** was followed by $LiAlH_4$ reduction, Swern oxidation, and the Wittig olefination ($Ph_3P^+CH(CH_3)_2I^-$, nBuLi) to afford diene **18**. The ketal group was removed (TsOH, aqueous acetone) to yield a ketone **19**. The methylation was accomplished using LDA/MeI to yield the *cis*-**20** and *trans*-ketone **21**. The ratio of these ketones was almost 1:1, but separation was easily carried out by HPLC. The assignment of the stereochemistry was realized using the NOESY spectra. Because the two substituents at the 2 and 6 positions of these ketones adopt equatorial positions due to 1,3-diaxial repulsion, the two methyl groups of ketone **20** are in equatorial positions, and the diene chain is in an axial position. Thus, in the case of ketone **20**, the NOE between the olefinic proton at C-1′ and the α axial proton at C-4 and between the methine proton at C-6 and the α axial proton at C-4 was observed. For ketone **21**, the NOE between the tertiary methyl group and the methine proton at C-6 was observed. These conformations of ketones **20** and **21** also influence the stereochemistry of the subsequent Grignard reactions.

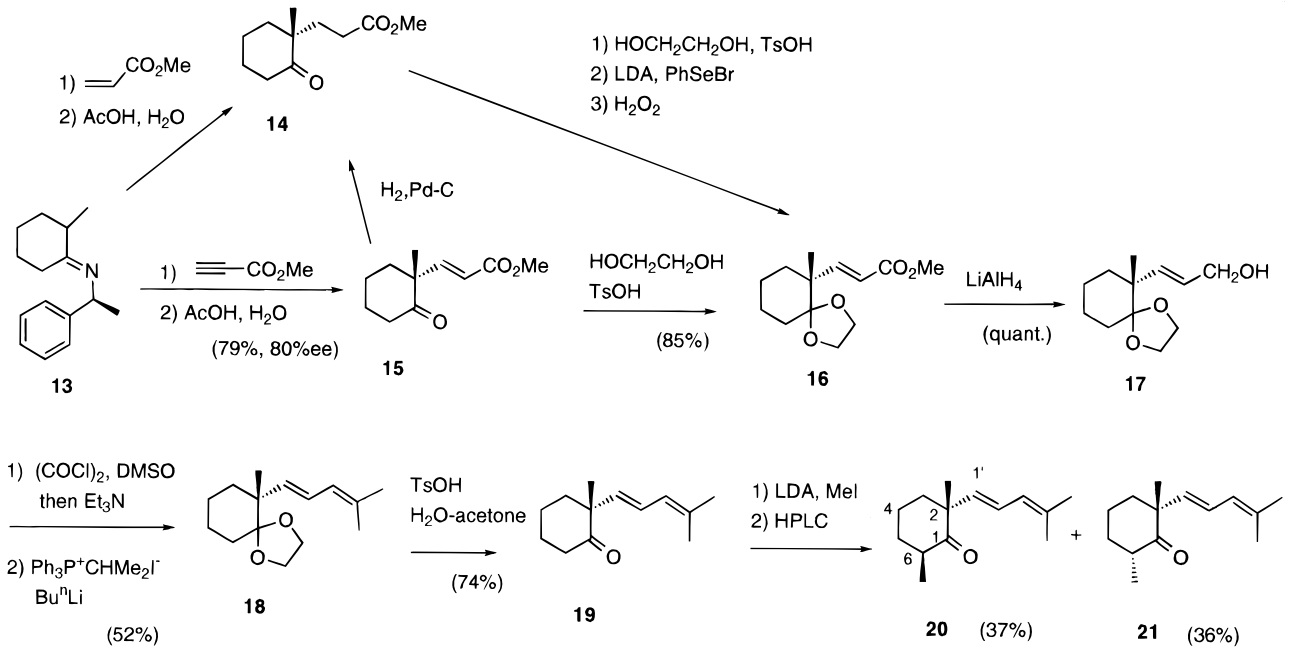
Total Synthesis. The Grignard reagent derived from chloride **10** attacked the ketone **20** to give the equatorial alcohol **22** predominantly (Scheme 4). It was deduced from the NOESY spectrum of adduct **22** that both the benzyl group and the side chain adopted axial positions. NOEs between the olefinic proton at C-7 and the methine proton at C-4, between the benzylic proton and the secondary methyl group, and between the tertiary methyl group and the benzylic proton were observed. The ratio of **22** and **23** was 4:1 according to GC. However, the minor axial alcohol **23** was not isolated pure by chromatographic separation. In the case of the trans methylated ketone **21**, the equatorial alcohol **26** was the major and **27** was the minor product; the ratio of **26**:**27** was 96:4. The structure of **26** was established by NOESY as well. However, the minor alcohol **27** could not be isolated pure by chromatographic separation.

We next used bis-MOM chloride **12** for the Grignard reaction with ketones **20** and **21**. The major product of these reactions were the adducts **24** and **28**, both being the equatorial alcohols (Scheme 4). The minor compounds were isolated pure after hydrolysis of the MOM groups in each case. The protecting groups of **24**, **25**, **28**, and **29** were cleaved by treatment with hydrochloric acid in THF to give triols **30**, **31**, **32**, and **33**, respectively.

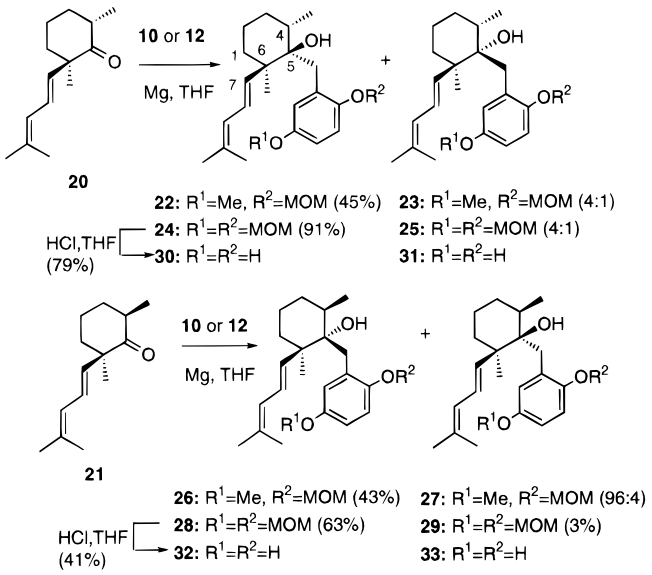
The triol **31** was treated with TsOH[10] in PhH at 65 °C for 5 h to afford riccardiphenol A (**1**), as well as the diastereoisomers **34** and **35** (Scheme 5); unfortunately, the yield of **1** was very poor. The spectral data (^1H and ^{13}C NMR, IR, and MS) of **1** were identical with those of the natural product.[1] The specific rotation of the synthetic product was $[\alpha]^{21}_D + 107.6°$ (*c* 0.7, $CHCl_3$), while the literature value was $[\alpha]_D + 143°$ (*c* 0.51, $CHCl_3$). The difference is attributable to the 80% ee obtained in the chiral Michael addition reaction. Thus the absolute configuration of riccardiphenol A was established as depicted in formula **1**. The structure of the major compound was assigned as **34** by careful analysis of the NOESY spectrum. The benzylic protons at C-15 had NOEs relative to the proton at C-4 and the olefinic proton at C-7, which indicated that the benzylic protons were in the equatorial and hence β-position. The fact that the major compound was the diastereoisomer of riccardiphenol A (**1**) is attributed to the same reason why the major one for the Grignard reaction was produced by an attack from the opposite side of the axially oriented substituent. The cationic center at C-6 produced by abstraction of the hydroxyl group was attacked by a phenolic hydroxyl group at C-2′ from the opposite side of the axially oriented side chain. The third product was isolated from the

(9) Takemoto, T.; Fukaya, C.; Yokoyama, K. *Tetrahedron Lett.* **1989**, *30*, 723−724.

Scheme 3



Scheme 4



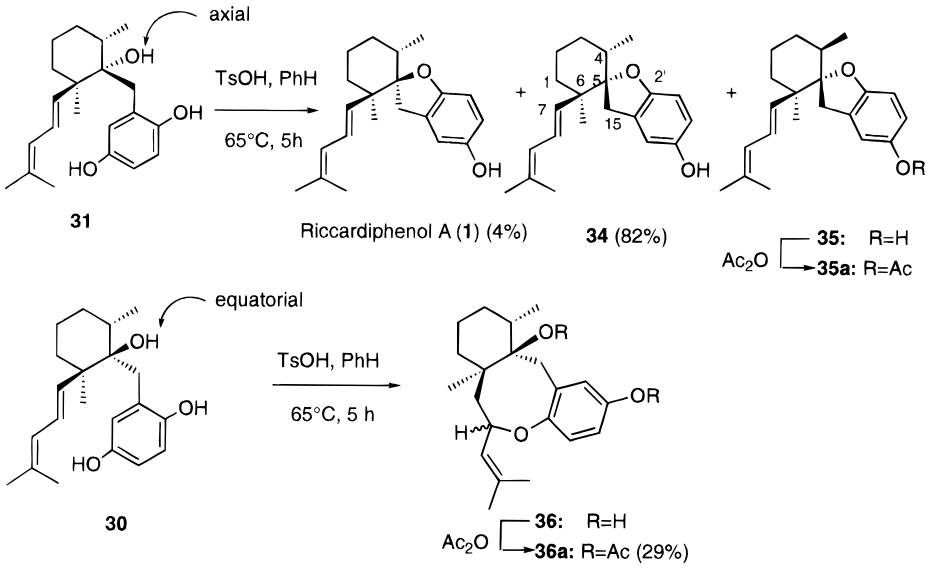
mixture by acetylation with Ac_2O in Py. The structure of **35a** was assigned by careful examination of the NOESY spectrum. Even if the lifetime of the cation was long enough to rearrange, the hydrogen could not be in the α position at C-4. The reason why compound **35** was produced is not yet clear.

When triol **30**, which was derived from the major adduct **24**, was subjected to similar cyclization conditions, the product was not a spiro compound nor a benzopyran derivative (Scheme 5). The product was a mixture of two inseparable compounds in the ratio of 1:1. They could not be separated after acetylation. The ^{1}H NMR spectrum of **36a** showed the presence of two sets of olefinic methyl groups (δ 1.58, 1.58, 1.68, 1.69) for each isomer. The structure having an eight-membered ring was revealed after the analogous compound **37a** was isolated from the reaction of **32** with TsOH and was fully analyzed by the 2D NMR method (*vide infra*).

In the case of the major adduct **28**, the corresponding triol **32** afforded a mixture of inseparable compounds **37** by treatment with TsOH in PhH (Scheme 6). This mixture could not be separated by acetylation to **37a**. The structure **37a** was established by examination of the 2D NMR spectra including HMQC, HMBC, COSY, and NOESY spectra. Namely, it had eight sets of sp^2 carbons (6 aromatic and one double bond) and four oxygen-bearing carbons (two sp^3 and two sp^2). Moreover, there were two sets of olefinic methyl groups (δ 1.58, 1.58, 1.64, 1.64). These data indicate that the tertiary hydroxyl group at C-5 was not abstracted, but that one double bond reacted under the acidic conditions. The methine proton at C-8 attached to the oxygen atom had the ^2J and ^3J correlations to the olefinic carbons and also to the quaternary center at C-6 in the HMBC spectrum. This means that the cyclization occurred not at C-5 but at C-8 to form an eight-membered ring. Because the hydroxyl group at C-5 was equatorial, the abstraction by protonation was rather hindered or very slow, but instead protonation at C-7 occurred followed by an attack of the C-2′ phenolic hydroxyl group. The C-5′ hydroxyl group did not react because of the steric nature. However, the minor product **33**, derived from **29**, afforded a single product **38**. The structure was easily deduced from the NMR spectrum. The presence of the secondary methyl group as well as the tertiary methyl group and the diene system was easily detected in the NMR spectrum. The benzylic protons appeared as an AB pattern. The stereochemistry was established from the NOESY spectrum. The phenolic hydroxyl group at C-2′ attacked the cationic center at C-5 from the side opposite to the axially oriented tertiary methyl group.

Riccardiphenol B (**2**) could be derived from either **22**, **23**, **26**, or **27** by dehydration of the tertiary hydroxyl group. The major product **26** was treated with thionyl chloride in pyridine to yield **39** (Scheme 7). Deprotection of the MOM group afforded riccardiphenol B (**2**), whose ^{1}H and ^{13}C NMR spectra as well as the IR and MS spectra were identical with those of the natural product.[1] The specific rotation of the synthetic material was $[\alpha]^{21}_D$ −59.4° (*c* 1.1, $CHCl_3$) [lit.[1] −72° (*c* 0.73 ($CHCl_3$)]. The discrepancy can again be ascribed to the % ee obtained in the initial Michael addition of the chiral imine. The

Scheme 5



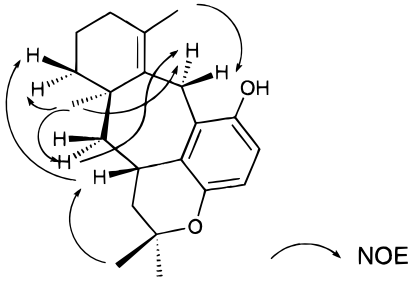
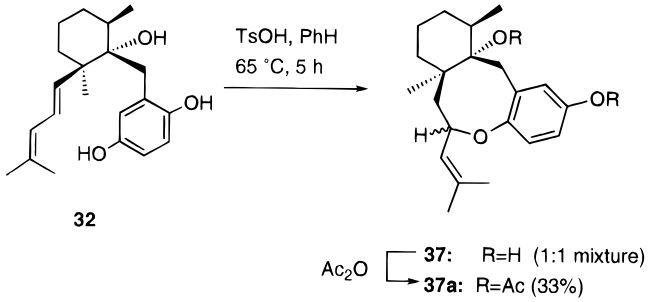
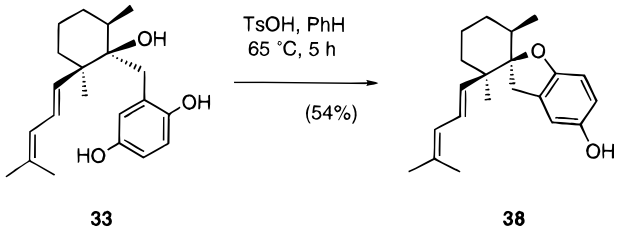


Figure 1. The NOEs detected for compound **41**.

Scheme 6





bis-MOM ether **28** was also dehydrated followed by deprotection to yield the diol **40**. Acid-catalyzed cyclization of this compound **40** unexpectedly afforded the tetracyclic compound **41** as a single product.[10] The structure was deduced by 2D NMR. There were no olefins except for the one at C-4 and C-5. The *gem*-dimethyl groups were deshielded (1.20 and 1.35 ppm) due to the attachment of the electron-withdrawing substituent. The methine proton at 2.90 ppm had ^2J and ^3J correlation peaks to quaternary carbon centers at C-6 and C-10 as well as one of the aromatic carbon at C-6′. Furthermore the NOEs as shown in Figure 1 were detected. Therefore, the structure of **41** was established as formulated. This presumably arose by protonation at C-7 followed by an attack of the hydroxyl group at C-5′ on the resulting cationic center at C-10 by rearrangement of the double bond. Finally, the Friedel−Crafts type cyclization occurred to form the C−C bond between C-6′ and C-8. Because there is a double bond between C-4 and C-5, the hydroxyl group at C-2′ cannot attack the cationic center at C-10 due to steric hindrance.

In conclusion, we have completed the total synthesis of riccardiphenols A (**1**) and B (**2**) from the chiral Michael addition product **15** by combination of a Grignard reaction and an acid-catalyzed cyclization reaction of the corresponding triol. The absolute configurations of these natural products were established as formulated by **1** and **2**. The reactivity for the four kinds of the Grignard adducts, **30**, **31**, **32**, and **33**, were very different due to the steric nature of the tertiary hydroxyl groups present. The diol **40** reacted much differently to give the tetracyclic phenol **41**.

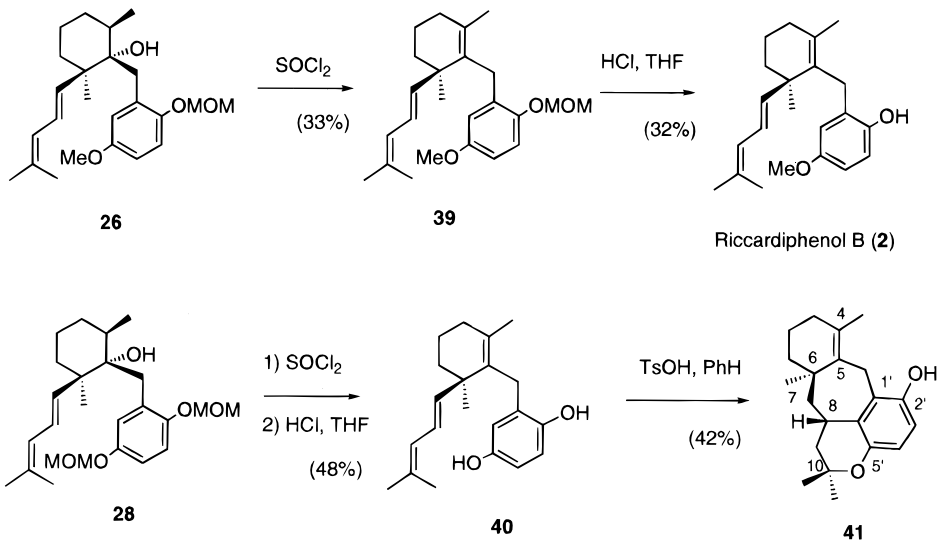
(10) (a) Fish, P. V.; Pattenden, G. *Tetrahedron Lett.* **1988**, *31*, 3857−3860. (b) Begley, M. J.; Fish, P. V.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2263−2271.

Experimental Section

General. For the measurement of %ee a DAICEL CHIRALCEL OB-H (4.6 × 20 cm) column was used in the HPLC system. Silica gel 60 (70−230 mesh, Merck) was used for column chromatography and silica gel 60F_{254} plates (0.25, 0.5, 1.0 mm, Merck) were used for TLC.

Methyl 2-Hydroxy-5-(tetrahydropyranyloxy)benzoate (7). A solution of methyl gentisate (**6**) (26.7 g, 0.16 mol) in CH_2Cl_2 (400 mL) was treated with dihydropyran (24.0 mL, 0.26 mol) and PPTS (2.7 g) at rt overnight. Water was added, and the mixture was extracted with CH_2Cl_2. The organic phase was washed with water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated to give pale yellow crystalline ether **7** (39.9 g, 99%): FTIR 3220, 1700, 1630, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.5−2.1 (6 H, m), 3.5−3.9 (2 H, m), 3.94 (3 H, s), 5.3−5.4 (1 H, m), 6.91 (1 H, d, J = 9.0 Hz), 7.20 (1 H, dd, J = 9.0, 3.0 Hz), 7.52 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.7 (t), 25.2 (t), 30.3 (t), 52.3 (q), 61.9 (t), 97.2 (d), 112.0 (s), 116.3 (d), 118.2 (d), 125.9 (d), 149.2 (s), 156.6 (s), 170.3 (s); MS (EI) m/z 252 (M^+), 221, 194, 169, 168, 137 (base), 136, 108, 85; EI-HRMS m/z calcd for $C_{13}H_{16}O_5$: 252.0998. Found: 252.1005.

Scheme 7



Methyl 5-Hydroxy-2-(methoxymethyloxy)benzoate (8). A suspension of THP ether **7** (49.9 g, 0.20 mol) and NaH (15.8 g, 0.40 mol) in dry THF (600 mL) was stirred for 1 h. Chloromethyl methyl ether (30 mL, 0.40 mol) was added to the mixture, and the reaction was stirred for 6 h at rt. Water and saturated NH_4Cl were added to adjust the pH to 7.0, and the solvent was evaporated. The residue was extracted with ether, and the organic phase was washed with water and brine. The ether layer was dried ($MgSO_4$) and evaporated to afford the MOM ether (57.4 g, 98%) as a brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.4−2.1 (6 H, m), 3.52 (3 H, s), 3.89 (3 H, s), 5.15 (2 H, s), 6.94 (1 H, dd, J = 9.0, 3.0 Hz), 7.07 (1 H, d, J = 9.0 Hz), 7.30 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.2 (t), 25.1 (t), 31.9 (t), 52.3 (q), 56.3 (q), 63.9 (t), 94.5 (d), 96.3 (t), 117.6 (d), 119.3 (d), 120.6 (d), 122.0 (s), 150.5 (s), 150.7 (s), 166.7 (s).

A solution of the MOM ether (57.4 g, 0.19 mol) in MeOH (400 mL) was treated with PPTS (5.9 g) overnight at rt. Water was added, and the solvent was evaporated to afford a residue, which was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give alcohol **8** (24.1 g, 57% from **7**) as an oil: FTIR 3400, 1710, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.50 (3 H, s), 3.89 (3 H, s), 5.15 (2 H, s), 6.40 (1 H, br s), 6.95 (1 H, dd, J = 9.0, 3.0 Hz), 7.07 (1 H, d, J = 9.0 Hz), 7.30 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 52.3 (q), 56.3 (q), 96.3 (t), 117.6 (d), 119.2 (d), 120.7 (d), 122.0 (s), 150.6 (s), 150.8 (s), 166.8 (s); MS (EI) m/z 212 (M^+), 182, 165, 151, 136, 121, 108, 93, 83, 75, 45 (base); EI-HRMS m/z calcd for $C_{10}H_{12}O_5$: 212.0684. Found: 212.0705.

Methyl 5-Methoxy-2-(methoxymethyloxy)benzoate (9). A suspension of alcohol **8** (21.7 g, 0.10 mol), MeI (68 mL, 1.1 mol), and K_2CO_3 (42 g, 0.30 mol) in acetone (350 mL) was heated under reflux overnight. The precipitates were filtered off, and the solvent was evaporated. The residue was extracted with ether, and the organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give methyl ether **9** (21.5 g, 92%) as an oil: FTIR 1750, 1620, 1600, 1510 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.53 (3 H, s), 3.80 (3 H, s), 3.90 (3 H, s), 5.17 (2 H, s), 6.99 (1 H, dd, J = 9.0, 3.0 Hz), 7.13 (1 H, d, J = 9.0 Hz), 7.30 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 52.1 (q), 55.7 (q), 56.2 (q), 96.4 (t), 115.4 (d), 119.2 (d), 119.4 (d), 122.4 (s), 150.8 (s), 154.2 (s), 166.4 (s); MS (EI) m/z 226 (M^+), 196, 181, 165, 150, 135, 122, 107, 92, 79, 75, 45 (base); EI-HRMS m/z calcd for $C_{11}H_{14}O_5$: 226.0841. Found: 226.0847.

5-Methoxy-2-(methoxymethyloxy)benzyl Chloride (10). A solution of the ether **9** (10.0 g, 44.3 mmol) in dry ether (50 mL) was slowly added into a suspension of $LiAlH_4$ (3.56 g, 93.8 mmol) in dry ether (25 mL), and the mixture was further stirred for 3 h. EtOAc (30 mL) was slowly added followed successively by water (3.5 mL), 15% aqueous NaOH solution (3.5 mL), and water (10.0 mL). The mixture was filtered, and the solvent was evaporated to give the alcohol (9.0 g, quant): FTIR: 3440, 1600, 1510 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.48 (3 H, s), 3.78 (3 H, s), 4.70 (2 H, br d, J = 4.5 Hz), 5.14 (2 H, s), 6.76 (1 H, dd, J = 9.0, 3.0 Hz), 6.91 (1 H, d, J = 3.0 Hz), 7.02 (1 H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.6 (q), 56.2 (q), 61.6 (t), 95.6 (t), 113.5 (d), 114.3 (d), 116.0 (d), 131.5 (s), 149.0 (s), 154.7 (s); MS (EI) m/z 198 (M^+), 166, 152, 136 (base), 125, 108, 93, 85, 77; EI-HRMS m/z calcd for $C_{10}H_{14}O_4$: 198.0892. Found: 198.0895.

A mixture of the alcohol (10.6 g, 53.6 mmol), CCl_4 (64.0 mL, 0.66 mol), Ph_3P (27.0 g, 0.10 mol), and CH_3CN (56 mL) was stirred at rt under Ar in the dark. The solvent was evaporated, and the residue was separated by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give chloride **10** (8.42 g, 73%); FTIR 1600, 1510 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.50 (3 H, s), 3.77 (3 H, s), 4.64 (2 H, s), 5.18 (2 H, s), 6.81 (1 H, dd, J = 9.0, 3.0 Hz), 6.93 (1 H, d, J = 3.0 Hz), 7.05 (1 H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 41.5 (t), 55.7 (q), 56.1 (q), 95.2 (t), 115.0 (d), 115.8 (d), 116.1 (d), 127.7 (s), 149.0 (s), 154.4 (s); MS (EI) m/z 218, 216 (M^+), 187, 171, 151, 136 (base), 121, 108, 91, 83; EI-HRMS m/z calcd for $C_{10}H_{13}O_3Cl$: 216.0553. Found: 216.0554.

Methyl 2,5-Bis(methoxymethyloxy)benzoate (11). A solution of methyl gentisate (**6**) (27.3 g, 0.16 mol) in dry THF (50 mL) was added into a suspension of NaH (19.5 g, 0.81 mol) in dry THF (500 mL) and was stirred for 1 h. Chloromethyl methyl ether (38.5 mL, 0.51 mol) was added, and the mixture was stirred for 5 h at rt under Ar. Water and saturated NH_4-Cl was added to adjust the pH to ∼7. The solvent was evaporated, and the residue was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give bis-MOM ether **11** (55.8 g, quant): FTIR 1740, 1500, 1410 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.47 (3 H, s), 3.52 (3 H, s), 3.89 (3 H, s), 5.14 (2 H, s), 5.18 (2 H, s), 7.13 (2 H, d, J = 2.0 Hz), 7.46 (1 H, t, J = 2.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 52.1 (q), 55.9 (q), 56.2 (q), 94.9 (t), 96.1 (t), 118.7 (d), 118.7 (d), 121.5 (d), 122.4 (s), 151.6 (s), 151.7 (s), 166.1 (s); MS (EI) m/z 256 (M^+), 225, 196, 181, 180, 165, 150, 45 (base); EI-HRMS m/z calcd for $C_{12}H_{16}O_6$: 256.0946. Found: 256.0948.

2,5-Bis(methoxymethyloxy)benzyl Chloride (12). A solution of ester **11** (13.5 g, 44.3 mmol) in dry ether (100 mL) was slowly added into a suspension of $LiAlH_4$ (4.0 g, 0.11 mol) in dry ether (300 mL) and was stirred for 4 h. EtOAc was added followed in order by water (4 mL), 15% aqueous NaOH (4 mL), and water (12.0 mL). Evaporation after filtration gave the alcohol (10.2 g, quant): FTIR 3450, 1600, 1500, 1460 cm^{-1};

^{1}H NMR (200 MHz, $CDCl_3$) δ 2.28 (1 H, br s), 3.46 (3 H, s), 3.48 (3 H, s), 4.66 (2 H, s), 5.11 (2 H, s), 5.16 (2 H, s), 6.91 (1 H, dd, J = 9.0, 3.0 Hz), 7.02 (1 H, d, J = 9.0 Hz), 7.04 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.8 (q), 56.1 (q), 61.4 (t), 95.0 (t), 95.3 (t), 115.7 (d), 116.3 (d), 117.0 (d), 131.5 (s), 150.0 (s), 152.1 (s); MS (EI) m/z 228 (M^+), 196, 166, 151, 136, 122, 85, 83, 45 (base); EI-HRMS m/z calcd for $C_{11}H_{16}O_5$: 228.0998. Found: 228.0991.

The alcohol (8.4 g, 36.8 mmol) was similarly chlorinated by using Ph_3P (19.4 g, 74.0 mmol), CCl_4 (44.0 mL, 0.46 mol), and CH_3CN (40 mL). Similar workup and chromatography afforded chloride **12** (5.3 g, 59%) as a colorless oil: FTIR 1600, 1510 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.48 (3 H, s), 3.50 (3 H, s), 4.63 (2 H, s), 5.12 (2 H, s), 5.19 (2 H, s), 6.96 (1 H, dd, J = 9.0, 3.0 Hz), 7.05 (1 H, d, J = 9.0 Hz), 7.08 (1 H, d, J = 3.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 41.5 (t), 55.9 (q), 56.1 (q), 95.0 (t), 95.1 (t), 115.7 (d), 117.7 (d), 118.6 (d), 127.6 (s), 150.0 (s), 152.0 (s); MS (EI) m/z 248, 246 (M^+), 215, 166, 136, 78, 45 (base); EI-HRMS m/z calcd for $C_{11}H_{15}O_4Cl$: 246.0553. Found: 246.0663.

Methyl (1′*R*)-3-(1′-Methyl-2′-oxocyclohexyl)prop-2-enoate (15). A solution of 2-methylcyclohexanone (95.1 g, 0.85 mol), (*S*)-(−)-phenylethylamine (106 mL, 0.82 mol), and TsOH (9.1 g) in PhH (600 mL) was heated under reflux with the aid of the Dean−Stark water separator overnight. The mixture was washed with water, 5% aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated to afford a residue (115.4 g). The residue was distilled under reduced pressure. The imine **13** was immediately reacted with methyl propiolate (50 mL, 0.562 mol) without the solvent at rt for 4 days. A mixture of AcOH: H_2O = 9:1 (750 mL) was added into the mixture, and the solution was heated at 60 °C for 1 h. The mixture was extracted with ether, and the organic phase was washed with water, saturated $NaHCO_3$, 1 M HCl, and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give keto-ester **15** (131.3 g, two steps 79%; 80% ee) as an oil: $[\alpha]^{21}_D$ +63.4° (c 1.2, $CHCl_3$); CD $[\theta]_{305\ nm}$ + 7700 ($CHCl_3$) $\Delta\epsilon$ = +2.3; FTIR 1730, 1710, 1660, 1450, 1190 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (3 H, s), 1.7−1.8 (4 H, m), 1.9−2.1 (2 H, m), 2.4−2.5 (2 H, m), 3.75 (3 H, s), 5.78 (1 H, d, J = 16.2 Hz), 7.15 (1 H, d, J = 16.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.6 (t), 23.2 (q), 27.4 (t), 39.4 (t), 39.6 (t), 51.7 (q, s), 120.8 (d), 151.7 (d), 166.7 (s), 211.4 (s); MS (EI) m/z 196 (M^+), 181, 168, 165, 152, 137, 125, 114, 108, 93 (base), 82; EI-HRMS m/z calcd for $C_{11}H_{16}O_3$: 196.1099. Found: 196.1105.

Methyl (1′*R*)-3-[2′-(Ethylenedioxy)-1′-methylcyclohexyl]-prop-2-enoate (16). A solution of keto-ester **15** (5.0 g, 25.5 mmol), ethylene glycol (14.0 mL, 0.251 mol), and TsOH (1.1 g) in PhH (200 mL) was heated under reflux with the Dean−Stark water separator overnight. The mixture was washed wth water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give ketal **16** (5.19 g, 85%) as a greenish yellow oil: $[\alpha]^{21}_D$ +50.0° (c 1.1, $CHCl_3$); FTIR 1730, 1660, 1450, 1190 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (3 H, s), 1.5−1.9 (8 H, m), 3.73 (3 H, s), 3.94 (4 H, m), 5.78 (1 H, d, J = 16.2 Hz), 7.23 (1 H, d, J = 16.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.7 (q), 20.8 (t), 23.5 (t), 31.7 (t), 35.0 (t), 45.3 (s), 51.4 (q), 65.1 (t), 65.2 (t), 111.4 (s), 119.4 (d), 154.6 (d), 167.5 (s); MS (EI) m/z 240 (M^+), 225, 209, 183, 167, 158, 139, 125, 113, 99 (base), 86, 79; EI-HRMS m/z calcd for $C_{13}H_{20}O_4$: 240.1362. Found: 240.1366.

(1′*R*)-3-[2′-(Ethylenedioxy)-1′-methylcyclohexyl]prop-2-en-1-ol (17). A solution of ketal **16** (9.0 g, 37.5 mmol) in dry ether (100 mL) was slowly added into a suspension of $LiAlH_4$ (4.08 g, 0.107 mol) in dry ether (300 mL), and the mixture was stirred for 3 h. Ethyl acetate (40 mL) was slowly added into the mixture, and then water (4 mL), 15% aqueous NaOH solution (4 mL), and water (12.0 mL) were added successively. The precipitates were filtered off, and the solvent was evaporated to give alcohol **17** (8.1 g, quant): $[\alpha]^{21}_D$ +17.2° (c 1.1, $CHCl_3$); FTIR (KBr) 3400, 1660, 1620, 1450 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.06 (3 H, s), 1.4−1.8 (8 H, m), 1.96 (1 H, br s), 3.92 (4 H, m), 4.13 (2 H, dd, J = 5.8, 1.2 Hz), 5.67 (1 H, dt, J = 16.0, 5.8 Hz), 5.95 (1 H, dt, J = 16.0, 1.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.9 (t), 21.4 (q), 23.6 (t), 31.5 (t), 35.7 (t), 44.1 (s), 64.3 (q), 65.0 (t), 65.0 (t), 112.0 (s), 127.4 (d), 137.8 (d); MS (EI) m/z 212 (M^+), 195, 181, 167, 155, 139, 130, 125, 112, 99 (base), 93, 86, 78; EI-HRMS m/z calcd for $C_{12}H_{20}O_3$: 212.1413. Found: 212.1424.

(1*E*)-(1′*R*)-4-Methyl-1-[2′-(ethylenedioxy)-1′-methylcyclohexyl]penta-1,3-diene (18). The alcohol **17** (8.1 g, 38.0 mmol) was treated with oxalyl chloride (7.0 mL, 80.2 mmol) and DMSO (46 mL, 0.648 mol) in CH_2Cl_2 (150 mL) at −78 °C. In 15 min Et_3N (53 mL, 0.38 mol) was added, and the mixture was stirred at 0 °C for 10 min. Water was added, and the mixture was extracted with CH_2Cl_2. The organic phase was washed with 1 M HCl and brine, dried over $MgSO_4$, and evaporated to afford the aldehyde (10.9 g) as an oil: FTIR 1700, 1650 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.14 (3 H, s), 1.4−1.8 (8 H, m), 3.94 (4 H, m), 3.75 (3 H, s), 6.16 (1 H, dd, J = 16.2, 7.8 Hz), 7.10 (1 H, d, J = 16.2 Hz), 9.54 (1 H, d, J = 7.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.7 (q), 20.8 (t), 23.4 (t), 31.7 (t), 34.8 (t), 46.0 (s), 65.1 (t), 65.2 (t), 111.3 (s), 131.3 (d), 164.4 (d), 194.7 (d); MS (EI) m/z 210 (M^+), 195, 182, 167, 148, 125, 112, 99 (base), 86, 73.

Isopropyltriphenylphosphonium iodide (23.7 g, 54.8 mmol) was treated with nBuLi (1.69 mol/L: 46 mL, 77.7 mmol) in dry ether (200 mL), and the mixture was stirred at rt for 1 h. A solution of the aldehyde (10.9 g) in dry ether (10 mL) was added into the mixture, and the solution was stirred for 50 min. Water was added, and the mixture was extracted with ether. The organic phase was washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give the diene **18** (5.2 g, two steps 52%) as a pale yellow oil: $[\alpha]^{21}_D$ +18.2° (c 1.1, $CHCl_3$); FTIR 1660, 1620, 1450, 970 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08 (3 H, s), 1.4−1.6 (8 H, m), 1.75 (3 H, s), 1.76 (3 H, s), 3.91 (4 H, m), 5.80 (1 H, d, J = 15.6 Hz), 5.83 (1 H, br dt, J = 11.0, 1.0 Hz), 6.28 (1 H, dd, J = 15.6, 11.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.4 (q), 21.0 (t), 21.6 (q), 23.8 (t), 26.0 (q), 31.8 (t), 35.9 (t), 44.6 (s), 65.1 (t), 65.2 (t), 112.2 (s), 124.7 (d), 125.9 (d), 133.1 (s), 137.1 (d); MS (EI) m/z 236 (M^+), 221, 193, 179, 165, 149, 140, 125 (base) 107, 99, 86, 79; EI-HRMS m/z calcd for $C_{15}H_{24}O_2$: 236.1776. Found: 236.1807.

(1′*E*)-(2*R*)-2-Methyl-2-(4′-methylpenta-1′,3′-dienyl)cyclohexanone (19). A solution of the diene **18** (1.26 g, 5.36 mmol) and TsOH (55 mg) in acetone:H_2O = 1:2 (20 mL) was stirred at 50 °C overnight. Acetone was evaporated, and the residue was extracted with ether. The organic phase was washed with water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give ketone **19** (761.4 mg, 74%) as a pale yellow oil: $[\alpha]^{21}_D$ + 119.6° (c 1.1, $CHCl_3$); CD $[\theta]_{297\ nm}$ +12000 ($CHCl_3$) $\Delta\epsilon$ = +3.6; FTIR 1710, 1660, 1610, 1460, 970 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (3 H, s), 1.6−1.9 (4 H, m), 1.9−2.1 (2 H, m), 2.2−2.4 (1 H, m), 2.5−2.7 (1 H, m), 1.72 (3 H, s), 1.77 (3 H, s), 5.70 (1 H, d, J = 15.6 Hz), 5.80 (1 H, br d, J = 10.7 Hz) 6.16 (1 H, dd, J = 15.6, 10.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.4 (q), 21.8 (t), 24.6 (q), 26.0 (q), 27.7 (t), 39.3 (t), 40.5 (t), 51.5 (s), 124.8 (d), 126.8 (d), 134.9 (d), 135.3 (s), 213.5 (s); MS (EI) m/z 192 (M^+, base), 177, 164, 149, 135, 121, 112, 107, 97, 93, 79; EI-HRMS m/z calcd for $C_{13}H_{20}O$: 192.1515. Found: 192.1514.

(1′*E*)-(2*R*,6*S*)-2,6-Dimethyl-2-(4′-methylpenta-1′,3′-dienyl)cyclohexanone (20) and (1′*E*)-(2*R*,6*R*)-2,6-Dimethyl-2-(4′-methylpenta-1′,3′-dienyl)cyclohexanone (21). A solution of the ketone **19** (652.1 mg, 3.40 mmol) in dry THF (5 mL) was added into a solution of LDA, prepared from diisopropylamine (1.0 mL, 7.63 mmol), nBuLi (1.69 M: 4.5 mL, 7.61 mmol), in dry THF (10 mL) at −78 °C. In 1 h, MeI (1.2 mL, 19.3 mmol) was added into the mixture, and the solution was stirred for 9 h. Water was added and the solvent was evaporated to afford a residue, which was extracted with ether. The organic phase was washed with 1 M HCl and brine, dried ($MgSO_4$), and evaporated to afford a residue (570.6 mg). The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) followed by HPLC (Develosil 60-10, 20 × 250 mm; hexane−EtOAc = 95:5) to give

ketone **20** (255.7 mg, 37%), ketone **21** (252.1 mg, 36%), and unreacted ketone **19** (20.5 mg).

Compound **20**: $[\alpha]^{21}_D$ + 134.3° (*c* 1.1, $CHCl_3$); CD $[\theta]_{297\ nm}$ +17500 ($CHCl_3$) $\Delta\epsilon$ = +5.3; FTIR 1720, 1660, 1620, 1460, 960 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (3 H, d, *J* = 6.6 Hz), 1.15 (3 H, s), 1.2−2.1 (6 H, m), 1.72 (3 H, s), 1.77 (3 H, s), 2.6−2.8 (1 H, m), 5.69 (1 H, d, *J* = 15.6 Hz), 5.79 (1 H, br dt, *J* = 11.0, 1.0 Hz), 6.14 (1 H, dd, *J* = 15.6, 11.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.9 (q), 18.4 (q), 22.0 (t), 24.9 (q), 26.0 (q), 37.0 (t), 41.3 (t), 42.0 (d), 51.6 (s), 124.8 (d), 127.0 (d), 135.2 (d), 135.4 (d), 214.7 (s); MS (EI) *m*/*z* 206 (M^+), 163, 149, 135, 126, 107, 96, 78 (base), 69, 52, 39; EI-HRMS *m*/*z* calcd for $C_{14}H_{22}O$: 206.1670. Found: 206.1664.

Compound **21**: $[\alpha]^{21}_D$ −37.1° (*c* 0.98, $CHCl_3$); CD $[\theta]_{293\ nm}$ −4500 ($CHCl_3$) $\Delta\epsilon$ = −1.4; FTIR 1710, 1460, 1390 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.01 (3 H, d, *J* = 6.6 Hz), 1.32 (3 H, s), 1.74 (3 H, s), 1.76 (3 H, s), 1.6−2.1 (6 H, m), 2.6−2.8 (1 H, m), 5.87 (1 H, br dt, *J* = 11.0, 1.0 Hz), 5.92 (1 H, d, *J* = 15.6 Hz), 6.21 (1 H, dd, *J* = 15.6, 11.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.4 (q), 18.3 (q), 20.9 (t), 23.6 (q), 26.0 (q), 35.7 (t), 39.2 (t), 41.2 (d), 50.4 (s), 124.1 (d), 125.2 (d), 134.0 (s), 136.1 (d), 215.5 (s); MS (EI) *m*/*z* 206 (M^+, base), 191, 178, 163, 149, 135, 121, 107, 96, 81, 67, 55, 41; EI-HRMS *m*/*z* calcd for $C_{14}H_{22}O$: 206.1670. Found: 206.1664.

(1″*E*)-(1*R*,2*R*,6*S*)-1-[5′-Methoxy-2′-(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (22). Chloride **10** (4.5 g, 20.8 mmol) was converted to its Grignard reagent by treatment with Mg (506.5 mg, 20.83 mmol) in dry THF (8 mL) containing catalytic amount of I_2. The mixture was stirred at rt for 1 h, and a solution of ketone **20** (448.5 mg, 2.18 mmol) in dry THF (0.5 mL) was added slowly. The mixture was stirred for 40 min, and saturated NH_4Cl was added. The mixture was extracted with ether, and the ethereal solution was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give a mixture of **22** and **23** (4:1 by GC) (381.0 mg, 45%) as a yellow oil: $[\alpha]^{21}_D$ +20.1° (*c* 1.1, $CHCl_3$); FTIR 3550, 1620, 1600, 1500 cm^{-1}; (for the major isomer) ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (3 H, s), 0.96 (3 H, d, *J* = 6.6 Hz), 1.1−2.0 (7 H, m), 1.76 (3 H, s), 1.80 (3 H, s), 2.77 (1 H, d, *J* = 14.6 Hz), 2.99 (1 H, d, *J* = 14.6 Hz), 3.51 (3 H, s), 3.71 (3 H, s), 5.15 (2 H, s), 5.89 (1 H, br d, *J* = 9.0 Hz), 6.18 (1 H, d, *J* = 2.6 Hz), 6.19 (1 H, d, *J* = 9.0 Hz), 6.65 (1 H, d, *J* = 3.2 Hz), 6.67 (1 H, dd, *J* = 7.4, 3.2 Hz), 7.00 (1 H, d, *J* = 7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.7 (q), 18.3 (q), 21.6 (t), 22.2 (q), 26.0 (q), 31.6 (t), 37.9 (d, t), 39.5 (t), 45.5 (s), 55.4 (q), 56.4 (q), 77.7 (s), 95.7 (t), 112.3 (d), 115.4 (d), 119.0 (d), 124.9 (d), 126.0 (d), 130.8 (s), 133.2 (s), 137.2 (d), 149.4 (s), 154.4 (s); MS (CI) *m*/*z* 388 (M^+, base), 371, 357, 343, 339, 325, 301, 289, 251, 229, 215, 181, 149, 137, 109, 95; CI-HRMS *m*/*z* calcd for $C_{24}H_{36}O_4$: 388.2614. Found: 388.2617.

(1″*E*)-(1*R*,2*R*,6*S*)-1-[2′,5′-Bis(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (24) and (1″*E*)-(1*S*,2*R*,6*S*)-1-[2′,5′-Bis(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (25). Chloride **12** (1.46 g, 5.93 mmol) was converted to its Grignard reagent by treatment with Mg (140.2 mg, 5.77 mmol) in dry THF (3.5 mL) containing the catalytic amount of I_2. The mixture was stirred for 30 min at rt. A solution of ketone **20** (146.0 mg, 7.09 mmol) in dry THF (0.5 mL) was added, and the mixture was stirred for 20 min. Saturated NH_4Cl was added, and the mixture was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc, in gradient) to give **24** (165.5 mg) and a mixture of **24** and **25** (105.0 mg) (combined yield: 91%, **24**:**25** = 80:20 from GC-MS).

Compound **24**: $[\alpha]^{21}_D$ +49.4° (*c* 0.9, $CHCl_3$); FTIR: 3550, 1670, 1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.93 (3 H, s), 0.94 (3 H, d, *J* = 6.0 Hz), 1.1−2.0 (7 H, m), 1.76 (3 H, s), 1.80 (3 H, s), 2.81 (1 H, d, *J* = 14.6 Hz), 2.96 (1 H, d, *J* = 14.6 Hz), 3.44 (3 H, s), 3.51 (3 H, s), 3.53 (1 H, br s), 5.07 (2 H, s), 5.15 (2 H, s), 5.89 (1 H, dt, *J* = 9.6, 1.2 Hz), 6.10 (1 H, d, *J* = 15.2 Hz), 6.24 (1 H, dd, *J* = 15.2, 9.6 Hz), 6.80 (1 H, d, *J* = 3.0 Hz), 6.82 (1 H, dd, *J* = 8.4, 3.0 Hz), 7.00 (1 H, d, *J* = 8.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.7 (q), 18.3 (q), 21.5 (t), 22.3 (q), 26.0 (q), 31.6 (t), 37.8 (d, t), 39.2 (t), 45.6 (s), 55.8 (q), 56.4 (q), 77.7 (s), 94.9 (t), 95.5 (t), 115.1 (d), 115.2 (d), 121.7 (d), 124.8 (d), 126.0 (d), 130.8 (s), 133.1 (s), 137.2 (d), 150.4 (s), 151.9 (s); MS (EI) *m*/*z* 418 (M^+), 386, 374, 373, 355, 323, 299, 255, 245, 224, 212, 207, 205, 189, 180, 167, 161, 149, 135, 123, 109, 93, 45 (base); EI-HRMS *m*/*z* calcd for $C_{25}H_{38}O_5$: 418.2720. Found: 418.2718.

(1″*E*)-(1*R*,2*R*,6*S*)-1-(2′,5′-Dihydroxybenzyl)-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (30) and (1″*E*)-(1*S*,2*R*,6*S*)-1-(2′,5′-Dihydroxybenzyl)-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (31). A mixture of **24** and **25** (289.9 mg, 0.69 mmol) was treated with THF:3 M HCl = 1:1 (15 mL) at 50 °C for 4.5 h. The solvent was evaporated, and the residue was extracted with ether. The organic phase was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) and HPLC (Develosil 60-10, 20 × 250 mm, hexane−EtOAc = 1:1) to give **30** (102.3 mg) and **31** (78.4 mg) (combined yield; 79%).

Compound **30**: $[\alpha]^{21}_D$ +74.6° (*c* 1.0, $CHCl_3$); FTIR: 3250, 1640, 1610, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (3 H, s), 0.98 (3 H, d, *J* = 6.6 Hz), 1.2−1.7 (6 H, m), 1.78 (3 H, s), 1.81 (3 H, s), 1.9−2.1 (1 H, m), 2.49 (1 H, br s), 2.71 (1 H, d, *J* = 15.0 Hz), 2.99 (1 H, d, *J* = 15.0 Hz), 4.65 (1 H, br s), 5.89 (1 H, dt, *J* = 10.6, 1.2 Hz), 6.02 (1 H, d, *J* = 15.4 Hz), 6.26 (1 H, dd, *J* = 15.4, 10.6 Hz), 6.49 (1 H, d, *J* = 3.0 Hz), 6.58 (1 H, dd, *J* = 8.6, 3.0 Hz), 6.72 (1 H, d, *J* = 8.6 Hz), 8.52 (1 H, br s); ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.4 (q), 18.4 (q), 20.7 (t), 22.4 (q), 26.1 (q), 31.2 (t), 36.9 (d), 37.4 (t), 40.1 (t), 44.8 (s), 80.7 (s), 114.6 (d), 117.4 (d), 119.3 (d), 125.5 (d), 125.9 (d), 127.6 (s), 134.5 (s), 134.9 (d), 148.5 (s), 149.8 (s); MS (EI) *m*/*z* 330 (M^+), 312, 277, 269, 255, 243, 232, 219, 215, 207, 189, 180, 161, 150, 139, 123, 109 (base), 95; EI-HRMS *m*/*z* calcd for $C_{21}H_{30}O_3$: 330.2195. Found: 330.2188.

Compound **31**: $[\alpha]^{21}_D$ +10.1° (*c* 1.0, $CHCl_3$); FTIR 3300, 1640, 1610, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.71 (3 H, d, *J* = 7.0 Hz), 1.15 (3 H, s), 1.4−1.9 (7 H, m), 1.78 (6 H, s), 2.53 (1 H, br s), 2.91 (1 H, d, *J* = 15.0 Hz), 3.02 (1 H, d, *J* = 15.0 Hz), 5.51 (1 H, br s), 5.83 (1 H, d, *J* = 10.6 Hz), 6.00 (1 H, d, *J* = 15.4 Hz), 6.37 (1 H, dd, *J* = 15.4, 10.6 Hz), 6.58 (1 H, dd, *J* = 8.2, 2.8 Hz), 6.62 (1 H, d, *J* = 2.8 Hz), 6.72 (1 H, d, *J* = 8.2 Hz), 8.82 (1 H, br s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.0 (q), 18.5 (q), 20.5 (t), 22.8 (q), 26.0 (q), 31.6 (t), 34.8 (t), 36.5 (t), 40.0 (d), 45.6 (s), 80.9 (s), 114.2 (d), 117.6 (d), 119.2 (d), 125.1 (d), 127.0 (s), 128.3 (d), 134.7 (d), 135.7 (s), 148.5 (s), 150.1 (s); MS (EI) *m*/*z* 330 (M^+), 312, 277, 269, 255, 243, 232, 219, 215, 207, 189, 180, 161, 150, 139, 123, 109 (base), 95; EI-HRMS *m*/*z* calcd for $C_{21}H_{30}O_3$: 330.2195. Found: 330.2203.

Riccardiphenol A (1). A solution of **31** (78.4 mg, 0.24 mmol) and TsOH (16 mg) in PhH (50 mL) was heated at 65 °C for 4.5 h. The mixture was washed with water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was purified by HPLC (Develosil 60-10, 20 × 250 mm, hexane−EtOAc = 4:1) to give riccardiphenol A (**1**) (3.0 mg, 4%), **34** (61.7 mg, 83%), and the mixture of the third compound (10.0 mg). The mixture was treated with acetic anhydride (1 mL) in pyridine (1 mL) at rt overnight. The mixture was worked up as usual, and the residue was purified by HPLC (Develosil 50-5, 10 × 250 mm, hexane−EtOAc = 9:1) to give acetate **35a** (8.4 mg) as a yellow oil.

Riccardiphenol A (**1**): $[\alpha]^{21}_D$ +107.6° (*c* 0.7, $CHCl_3$); FTIR: 3400, 1670, 1620, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.76 (3 H, d, *J* = 6.6 Hz), 0.91 (3 H, s), 1.1−1.7 (6 H, m), 2.1−2.2 (1 H, m), 1.79 (3 H, s), 1.80 (3 H, s), 2.85 (1 H, d, *J* = 16.8 Hz), 3.15 (1 H, d, *J* = 16.8 Hz), 3.74 (3 H, s), 5.86 (1 H, d, *J* = 10.4 Hz), 5.87 (1 H, d, *J* = 15.6 Hz), 6.33 (1 H, dd, *J* = 15.6, 10.4 Hz), 6.55 (1 H, dd, *J* = 8.2 Hz), 6.58 (1 H, d, *J* = 8.2 Hz), 6.64 (1 H, d, *J* = 1.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.8 (q), 18.3 (q), 21.0 (t), 24.1 (q), 26.0 (q), 31.0 (t), 31.8 (t), 34.0 (t), 37.4 (d), 45.3 (s), 95.6 (s), 108.1 (d), 111.7 (d), 114.1 (d), 125.3 (d), 126.1 (d), 128.4 (s), 132.8 (s), 136.2 (d), 148.8 (s), 154.9 (s); MS (EI) *m*/*z* 312 (M^+, base), 297, 277, 269, 255, 243, 241, 227, 215, 201, 189, 174, 162, 161, 147, 133, 123, 109, 91; EI-HRMS *m*/*z* calcd for $C_{21}H_{28}O_2$: 312.2089. Found: 312.2096.

5-*epi*-Riccardiphenol A (**34**): $[\alpha]^{21}_D$ +81.9° (*c* 1.1, $CHCl_3$); FTIR: 3600, 3400, 1670, 1620, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.77 (3 H, d, J = 6.2 Hz), 0.97 (3 H, s), 1.4−1.9 (7 H, m), 1.78 (6 H, s), 2.81 (1 H, d, J = 16.8 Hz), 3.12 (1 H, d, J = 16.8 Hz), 4.44 (1 H, br s), 5.84 (1 H, d, J = 10.4 Hz), 5.85 (1 H, d, J = 15.8 Hz), 6.32 (1 H, dd, J = 15.8, 10.4 Hz), 6.45−6.60 (3 H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.1 (q), 18.4 (q), 21.4 (t), 22.0 (q), 26.0 (q), 30.7 (t), 35.8 (t), 35.9 (t), 38.0 (d), 44.8 (s), 93.3 (s), 108.1 (d), 111.6 (d), 114.1 (d), 125.6 (d), 126.1 (d), 128.6 (s), 134.1 (s), 135.2 (d), 148.7 (s), 155.3 (s); MS (EI) *m*/*z* 312 (M^+, base), 297, 277, 269, 255, 243, 241, 227, 215, 201, 189, 174, 162, 161, 147, 133, 123, 109, 91; EI-HRMS *m*/*z* calcd for $C_{21}H_{28}O_2$: 312.2089. Found: 312.2075.

4,5-*Diepi*-Riccardiphenol A 5′-*O*-acetate (**35a**): $[\alpha]^{21}_D$ −57.6° (*c* 0.9, $CHCl_3$); FTIR 1760, 1500, 1380, 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (3 H, d, J = 6.8 Hz), 1.40 (3 H, s), 1.50 (3 H, s), 1.69 (3 H, s), 1.3−1.8 (6 H, m), 1.8−2.0 (1 H, m), 2.26 (3 H, s), 2.52 (1 H, d, J = 17.2 Hz), 3.02 (1 H, d, J = 17.2 Hz), 5.47 (1 H, d, J = 15.6 Hz), 5.74 (1 H, dt, J = 10.6, 1.2 Hz), 6.01 (1 H, dd, J = 15.6, 10.6 Hz), 6.72 (1 H, d, J = 8.4 Hz), 6.76 (1 H, dd, J = 8.4, 2.7 Hz), 6.84 (1 H, d, J = 2.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.4 (q), 18.1 (q), 21.1 (q), 22.3 (q), 22.5 (t), 25.9 (q), 26.4 (t), 29.2 (t), 33.6 (t), 36.3 (d), 42.9 (s), 80.3 (s), 117.1 (d), 119.9 (d), 121.4 (s), 121.5 (d), 125.4 (d), 127.0 (d), 133.8 (s), 134.9 (d), 143.5 (s), 150.5 (s), 169.9 (s); MS (EI) *m*/*z* 354 (M^+, base), 339, 312, 297, 269, 257, 244, 243, 230, 215, 201, 189, 174, 162, 147, 133, 123, 119, 109, 91; EI-HRMS *m*/*z* calcd for $C_{23}H_{30}O_3$: 354.2195. Found: 354.2196.

Cyclization of Triol 30. A solution of triol **30** (49.1 mg, 0.15 mmol) and TsOH (14 mg) in PhH (50 mL) was heated at 65 °C for 4.5 h. The mixture was washed with water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. As the products could not be separated by HPLC, the residue (12.6 mg) was acetylated with Ac_2O (1 mL) in pyridine (1 mL) overnight. Workup as usual afforded a residue, which was purified by HPLC (Develosil 60-3, 4.6 × 20 cm, hexane−EtOAc = 9:1) to give the inseparable mixture **36a** (15.3 mg, 29%) as a yellow oil: FTIR 1760, 1500, 1370, 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.79 (3 H, d, J = 7.2 Hz), 0.86 (3 H, d, J = 7.2 Hz), 1.06 (3 H, s), 1.10 (3 H, s), 1.2−2.2 (14 H, m), 1.58 (6 H, s), 1.68 (3 H, s), 1.69 (3 H, s), 2.25 (6 H, s), 2.31 (3 H, s), 2.32 (3 H, s), 2.57 (1 H, d, J = 15.6 Hz), 2.65 (1 H, d, J = 15.6 Hz), 2.79 (1 H, d, J = 15.6 Hz), 2.86 (1 H, d, J = 15.6 Hz), 4.7−5.0 (2 H, m), 5.34 (2 H, tt, J = 9.6, 1.4 Hz), 6.9−7.0 (4 H, m), 7.64 (1 H, d, J = 2.4 Hz), 7.83 (1 H, d, J = 2.6 Hz); MS (EI) *m*/*z* 414 (M^+), 372, 354, 330, 315, 273, 231, 207 (base), 189, 179, 165, 149, 139, 123, 109, 95, 81; HRMS *m*/*z* calcd for $C_{24}H_{34}O_5$: 414.2406. Found: 414.2397.

(1″*E*)-(1*S*,2*R*,6*R*)-1-[5′-Methoxy-2′-(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (26). Grignard reaction was carried out similarly as described above using chloride **10** (3.92 g, 18.2 mmol), Mg (424.3 mg, 17.5 mmol), and **21** (392.7 mg, 1.91 mmol) in dry THF (5 mL). Saturated NH_4Cl was added, and the solvent was evaporated. The residue was extracted with ether, and the organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel chromatography (elution with hexane−EtOAc in gradient) to give a mixture of **26** and **27** (96:4 by GC) (315.8 mg, 43%) as an oil: $[\alpha]^{21}_D$ −2.2° (*c* 0.99, $CHCl_3$); FTIR: 3550, 1620, 1600, 1500 cm^{-1}; (for the major isomer) ^1H NMR (200 MHz, $CDCl_3$) δ 0.93 (3 H, d, J = 6.6 Hz), 1.23 (3 H, s), 1.3−2.0 (7 H, m), 1.67 (3 H, s), 1.70 (3 H, s), 2.82 (1 H, d, J = 14.6 Hz), 2.95 (1 H, d, J = 14.6 Hz), 3.49 (3 H, s), 3.73 (3 H, s), 5.11 (2 H, s), 5.51 (1 H, br d, J = 11.0 Hz), 5.57 (1 H, d, J = 15.6 Hz), 6.06 (1 H, dd, J = 15.6, 11.0 Hz), 6.63 (1 H, dd, J = 9.0, 3.0 Hz), 6.76 (1 H, d, J = 3.0 Hz), 6.97 (1 H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.7 (q), 18.2 (q), 20.4 (q), 21.4 (t), 25.9 (q), 31.5 (t), 35.5 (t), 37.4 (d), 39.2 (t), 44.9 (s), 55.5 (q), 56.2 (q), 77.7 (s), 95.6 (t), 111.7 (d), 115.3 (d), 119.1 (d), 123.9 (d), 126.2 (d), 130.6 (s), 132.0 (s), 139.9 (d), 149.7 (s), 154.3 (s); MS (CI) *m*/*z* 388 (M^+, base), 371, 357, 343, 339, 325, 301, 289, 251, 229, 215, 181, 149, 137, 109, 95; CI-HRMS *m*/*z* calcd for $C_{24}H_{36}O_4$: 388.2614. Found: 388.2617.

(1″*E*)-(1*S*,2*R*,6*R*)-1-[2′,5′-Bis(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (28) and (1″*E*)-(1*R*,2*R*,6*R*)-1-[2′,5′-Bis(methoxymethyloxy)benzyl]-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (29). Grignard reaction was similarly carried out as described above using **12** (5.3 g, 21.7 mmol), Mg (516.0 mg, 21.2 mmol), and ketone **21** (362.0 mg, 1.76 mmol) in dry THF (10 mL). The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) and HPLC (Develosil 60−10, 20 × 250 mm, hexane−EtOAc = 85:15) to give **28** (465.1 mg, 63%) and **29** (19.0 mg, 3%).

Compound **28**: $[\alpha]^{24}_D$ −3.2° (*c* 1.0, $CHCl_3$); FTIR 3550, 2950, 2850, 1620, 1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (3 H, d, J = 6.6 Hz), 1.22 (3 H, s), 1.3−1.6 (6 H, m), 1.66 (3 H, s), 1.69 (3 H, s), 1.8−2.0 (1 H, m), 2.82 (1 H, d, J = 14.4 Hz), 2.94 (1 H, d, J = 14.4 Hz), 3.45 (3 H, s), 3.48 (3H, s), 5.07 (2 H, s), 5.11 (2 H, s), 5.51 (1 H, d, J = 10.6 Hz), 5.57 (1 H, d, J = 15.6 Hz), 6.05 (1 H, dd, J = 15.6, 10.6 Hz), 6.77 (1 H, dd, J = 8.8, 3.0 Hz), 6.89 (1 H, d, J = 3.0 Hz), 6.95 (1 H, d, J = 8.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.7 (q), 18.2 (q), 20.4 (q), 21.4 (t), 25.8 (q), 31.5 (t), 35.6 (t), 37.4 (d), 39.2 (t), 44.9 (s), 55.7 (q), 56.2 (q), 77.8 (s), 95.1 (t), 95.5 (t), 114.8 (d), 115.1 (d), 121.5 (d), 123.9 (d), 126.2 (d), 130.6 (s), 132.0 (s), 139.9 (d), 150.6 (s), 151.9 (s); MS (EI) *m*/*z* 418 (M^+), 386, 373, 355, 341, 323, 267, 245, 224, 205, 167, 161, 149, 133, 123, 107, 93, 45 (base); EI-HRMS *m*/*z* calcd for $C_{25}H_{38}O_5$: 418.2719. Found: 418.2710.

Compound **29**: $[\alpha]^{24}_D$ + 75.5° (*c* 0.95, $CHCl_3$); FTIR: 3550, 1620, 1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (3 H, d, J = 7.0 Hz), 1.13 (3 H, s), 1.2−1.8 (6 H, m), 1.74 (6 H, s), 1.9−2.1 (1 H, m), 2.95 (2 H, s), 3.45 (3 H, s), 3.49 (3 H, s), 5.05 (1 H, d, J = 6.6 Hz), 5.10 (1 H, d, J = 6.6 Hz), 5.12 (1 H, d, J = 6.6 Hz), 5.16 (1 H, d, J = 6.6 Hz), 5.69 (1 H, d, J = 10.6 Hz), 5.83 (1 H, d, J = 15.6 Hz), 6.16 (1 H, dd, J = 15.6, 10.6 Hz), 6.81 (1 H, dd, J = 8.8, 3.0 Hz), 6.89 (1 H, d, J = 3.0 Hz), 6.98 (1 H, d, J = 8.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.2 (q), 18.3 (q), 25.9 (q x 2), 33.3 (t x 2), 33.7 (t x 2), 37.5 (d), 45.3 (s), 55.8 (q), 56.3 (q), 78.3 (s), 94.9 (t), 95.4 (t), 115.0 (d), 115.1 (d), 121.9 (d), 122.8 (d), 126.1 (d x 2), 129.9 (s), 132.4 (s), 150.7 (s), 151.8 (s); MS (EI) *m*/*z* 418 (M^+), 386, 373, 355, 341, 323, 267, 245, 224, 205, 167, 161, 149, 133, 123, 107, 93, 45 (base).

(1″*E*)-(1*S*,2*R*,6*R*)-1-(2′,5′-Dihydroxybenzyl)-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (32). A solution of **28** (200 mg, 0.48 mmol) in THF:3 M HCl = 10:1 (15 mL) was heated at 50 °C for 4.5 h. The solvent was evaporated, and the residue was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give **32** (64.8 mg, 41%) as a brown oil: FTIR 3400, 1620, 1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (3 H, d, J = 6.8 Hz), 1.24 (3 H, s), 1.3−1.6 (6 H, m), 1.68 (6 H, s), 1.8−2.0 (1 H, m), 2.66 (1 H, br s), 2.78 (1 H, d, J = 14.8 Hz), 2.95 (1 H, d, J = 14.8 Hz), 5.40 (1 H, br s), 5.54 (1 H, d, J = 10.6 Hz), 5.63 (1 H, d, J = 15.6 Hz), 6.11 (1 H, dd, J = 15.6, 10.6 Hz), 6.54 (1 H, dd, J = 8.2, 2.8 Hz), 6.57 (1 H, d, J = 2.8 Hz), 6.68 (1 H, d, J = 8.2 Hz), 8.50 (1 H, br s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.4 (q), 18.3 (q), 19.8 (t), 21.4 (q), 25.9 (q), 30.9 (t), 35.6 (t), 36.2 (d), 39.6 (t), 44.4 (s), 80.2 (s), 114.5 (d), 117.4 (d), 119.0 (d), 125.4 (d), 125.5 (d), 127.0 (s), 133.7 (s), 137.1 (d), 148.8 (s), 149.5 (s); MS (EI) *m*/*z* 330 (M^+), 312, 297, 269, 255, 241, 207, 193, 189, 180, 161, 149, 139, 133, 123, 109 (base), 95; EI-HRMS *m*/*z* calcd for $C_{21}H_{30}O_3$: 330.2195. Found: 330.2205.

Cyclization of 32 to 37. A solution of triol **32** (64.8 mg, 0.196 mmol) and TsOH (16 mg) in PhH (40 mL) was heated at 60 °C for 4.5 h. Workup as usual afforded a residue, which was purified by HPLC (Develosil 60-10, 20 × 250 mm, hexane−EtOAc = 4:1) to give a mixture of products **37**. The mixture was acetylated with Ac_2O (1 mL) in pyridine (1 mL) overnight. Workup as usual afforded a residue, which was purified by HPLC (Develosil 60-3, 4.6 × 20 cm, hexane−EtOAc = 9:1) to give a mixture of products **37a** (26.7 mg, two steps: 33%) as an oil: FTIR 1760, 1500, 1370, 1210 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (3 H, d, J = 7.2 Hz), 0.72 (3 H, d, J = 6.6 Hz), 1.07 (3 H, s), 1.12 (3 H, s), 1.2−2.2 (14 H, m), 1.58 (6 H, s), 1.64 (3 H, s), 1.64 (3 H, s), 2.25 (3 H, s), 2.26 (3 H, s),

2.32 (6 H, s), 2.60 (1 H, d, J = 15.6 Hz), 2.65 (1 H, d, J = 15.0 Hz), 2.73 (1 H, d, J = 15.0 Hz), 2.74 (1 H, d, J = 15.6 Hz), 4.6−4.7 (1 H, m), 4.88 (1 H, q, J = 8.8 Hz), 5.24 (1 H, dt, J = 8.5, 1.5 Hz), 5.42 (1 H, dt, J = 8.3, 1.5 Hz), 6.93 (2 H, dd, J = 8.8, 2.9 Hz), 6.99 (1 H, d, J = 8.8 Hz), 6.99 (1 H, d, J = 8.8 Hz), 7.45 (1 H, d, J = 2.9 Hz), 7.56 (1 H, d, J = 2.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.3, 169.2, 148.0, 147.7, 146.5, 146.3, 135.1, 134.24, 134.18, 134.1, 128.4, 128.1, 125.0, 124.6, 122.5, 122.5, 119.67, 119.58, 87.7, 87.2, 73.1, 71.3, 47.8, 47.2, 45.6, 45.5, 38.7, 37.8, 37.8, 37.0, 36.4, 35.3, 32.3, 32.3, 32.1, 32.0, 25.9, 25.8, 22.1, 21.8, 21.4, 21.2, 21.1, 20.9, 18.7, 18.5, 18.2, 18.1; MS (EI) m/z 414 (M^+), 372, 354, 330, 315, 273, 231, 207 (base), 189, 179, 165, 149, 139, 123, 109, 95, 81; EI-HRMS m/z calcd for $C_{25}H_{34}O_5$: 414.2406. Found: 414.2379.

(1″*E*)-(1*R*,2*R*,6*R*)-1-(2′,5′-Dihydroxybenzyl)-2,6-dimethyl-2-(4″-methylpenta-1″,3″-dienyl)cyclohexan-1-ol (33). Compound **29** (19.0 mg, 0.046 mmol) was similarly treated with THF:3 M HCl = 10:1 (6 mL) to afford **33** (8 mg, 53%): FTIR 3340, 1620, 1600, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.82 (3 H, d, J = 7.2 Hz), 1.13 (3 H, s), 1.0−2.1 (7 H, m), 1.75 (6 H, s), 2.81 (1 H, d, J = 15.0 Hz), 3.04 (3 H, d, J = 15.0 Hz), 5.75 (1 H, br d, J = 10.6 Hz), 5.85 (1 H, d, J = 15.4 Hz), 6.19 (1 H, dd, J = 15.4, 10.6 Hz), 6.5−6.8 (3 H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.1 (q), 18.3 (q), 25.9 (q), 26.0 (q), 33.9 (t × 2), 35.5 (t × 2), 37.8 (d), 44.9 (s), 81.7 (s), 114.5 (d), 117.4 (d), 119.6 (d), 123.8 (d), 125.6 (d), 126.7 (s), 133.6 (s), 137.8 (s), 148.6 (s), 149.8 (s); MS (EI) m/z 330 (M^+), 312, 297, 269, 255, 241, 207, 193, 189, 180, 161, 149, 139, 133, 123, 109 (base), 95; EI-HRMS m/z calcd for $C_{21}H_{30}O_3$: 330.2195. Found: 330.2193.

4-*epi*-Riccardiphenol A (38). A solution of **33** (36.8 mg, 0.11 mmol) and TsOH (14 mg) in PhH (30 mL) was heated at 65 °C for 4 h. The mixture was worked up as usual and the residue was purified by HPLC (Develosil 60-3, 4.6 × 20 cm, hexane−EtOAc = 9:1) to give **38** (7.7 mg, 54%) as a pale yellow oil: $[\alpha]^{21}_D$ −72.7° (c 0.77, $CHCl_3$); FTIR: 3400, 1670, 1620, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.68 (3 H, d, J = 6.8 Hz), 1.06 (3 H, s), 1.2−1.9 (7 H, m), 1.81 (6 H, s), 2.69 (1 H, d, J = 16.6 Hz), 2.93 (1 H, d, J = 16.6 Hz), 4.40 (1 H, br s), 5.86 (1 H, d, J = 15.8 Hz), 5.90 (1 H, br d, J = 10.2 Hz), 6.27 (1 H, dd, J = 15.8, 10.2 Hz), 6.5−6.67 (3 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.4 (q), 18.5 (q), 21.1 (t), 23.1 (q), 26.0 (q), 29.3 (t), 30.0 (t), 32.2 (d), 34.7 (t), 42.7 (s), 78.5 (s), 114.5 (d), 115.6 (d), 117.1 (d), 121.1 (s), 125.6 (d), 127.5 (s), 131.4 (s), 134.1 (d), 146.5 (s), 148.5 (s); MS (EI) m/z 312 (M^+, base), 297, 277, 269, 255, 243, 241, 227, 215, 201, 189, 174, 162, 161, 147, 133, 123, 109, 91; EI-HRMS m/z calcd for $C_{21}H_{28}O_2$: 312.2089. Found: 312.2096.

Riccardiphenol B (2). A solution of **26** (101.3 mg, 0.26 mmol) in pyridine (1 mL) was treated with $SOCl_2$ (0.2 mL, 2.74 mmol) at 0 °C for 1 h. Water was added, and the mixture was extracted with ether. The organic phase was washed with 1 M HCl and brine, dried ($MgSO_4$), and evaporated. The residue was purified by preparative TLC to give **39** (31.5 mg, 33%) as a pale yellow oil and **26** (12.1 mg): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.98 (3 H, s), 1.3−2.2 (6 H, m), 1.56 (3 H, s), 1.75 (6 H, s), 3.57 (3 H, s), 3.74 (3 H, s), 5.13 (2 H, s), 5.46 (1 H, d, J = 15.4 Hz), 5.77 (1 H, br d, J = 10.6 Hz), 6.11 (1 H, dd, J = 15.4, 10.6 Hz), 6.65−7.00 (3 H, m).

A solution of **39** (31.5 mg, 0.085 mmol) in THF:3 M HCl = 1:1 (2 mL) was heated at 50 °C for 14 h. The solvent was evaporated, and the residue was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), and evaporated. The residue was purified by preparative TLC and HPLC (Develosil 60-3, 4.6 × 20 cm, hexane−EtOAc = 9:1) to give riccardiphenol B (**2**) (8.8 mg, 32%): $[\alpha]^{21}_D$ −59.4° (c 1.1, $CHCl_3$); FTIR: 3400, 1670, 1620, 1510 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3 H, s), 1.4−2.2 (6 H, m), 1.60 (3 H, s), 1.74 (3 H, s), 1.75 (3 H, s), 3.20 (1 H, d, J = 17.0 Hz), 3.37 (1 H, d, J = 17.0 Hz), 3.73 (3 H, s), 4.71 (1 H, br s), 5.47 (1 H, d, J = 15.4 Hz), 5.77 (1 H, br d, J = 10.7 Hz), 6.11 (1 H, dd, J = 15.4, 10.7 Hz), 6.59 (1 H, dd, J = 8.6, 3.0 Hz), 6.63 (1 H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4 (q), 18.9 (t), 20.7 (q), 25.5 (q), 25.9 (q), 29.6 (t), 32.5 (t), 38.4 (t), 41.8 (s), 55.7 (q), 110.8 (d), 115.4 (d), 115.5 (d), 124.6 (d), 125.3 (d), 128.0 (s), 131.3 (s), 133.0 (s), 133.2 (s), 140.5 (d), 147.8 (s), 153.6 (s); MS (EI) m/z 326 (M^+), 311, 283, 257, 244, 229 (base), 215, 201, 189, 175, 161, 149, 137, 133, 109, 107, 93.

Demethyl Riccardiphenol B (40). A solution of **28** (147.0 mg, 0.35 mmol) in pyridine (2 mL) was treated with $SOCl_2$ (0.2 mL, 2.74 mmol) at 0 °C for 30 min. Workup as usual afforded a residue, which was purified by silica gel column chromatography (elution with hexane−EtOAc in gradient) to give the olefin (77.9 mg, 55%). A solution of the olefin (93.4 mg, 0.23 mmol) in THF:3 M HCl = 10:1 (6 mL) was heated at 50 °C for 3.5 h. Workup as usual and purification by short silica gel afforded the diol **40** (63.8 mg, two steps 48%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.00 (3 H, s), 1.1−2.1 (6 H, m), 1.57 (3 H, s), 1.72 (3 H, s), 1.74 (3 H, s), 3.17 (1 H, d, J = 17.2 Hz), 3.33 (1 H, d, J = 17.2 Hz), 5.01 (1 H, br s), 5.45 (1 H, d, J = 15.4 Hz), 5.76 (1 H, d, J = 10.6 Hz), 6.11 (1 H, dd, J = 15.4, 10.6 Hz), 6.50 (1 H, dd, J = 8.2, 3.0 Hz), 6.56 (1 H, d, J = 3.0 Hz), 6.61 (1 H, d, J = 8.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.3 (q), 18.9 (t), 20.6 (q), 25.4 (q), 25.9 (q), 29.4 (t), 32.4 (t), 38.3 (t), 41.8 (s), 112.9 (d), 115.8 (d), 115.9 (d), 116.0 (s), 124.5 (d), 125.3 (d), 131.2 (s), 132.9 (s), 133.2 (s), 140.5 (d), 147.5 (s), 149.2 (s); MS (EI) m/z 312 (M^+), 297, 269, 255, 243, 230, 215 (base), 201, 189, 175, 147, 133, 123, 107, 91; EI-HRMS m/z calcd for $C_{21}H_{28}O_2$: 312.2089. Found: 312.2112.

Cyclization of 40. A solution of **40** (63.8 mg, 0.20 mmol) and TsOH (16 mg) in PhH ((50 mL) was heated at 65 °C for 6.5 h. Workup as usual afforded a residue, which was purified by HPLC (Develosil 60-3, 4.6 × 20 cm, hexane−EtOAc = 9:1) to give **41** (26.7 mg, 42%); $[\alpha]^{21}_D$ +10.7° (c 1.05, $CHCl_3$); FTIR: 3400, 1590, 1450, 1370, 1250 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.12 (3 H, s), 1.21 (3 H, s), 1.35 (3 H, s), 1.53 (3 H, s), 1.2−2.1 (10 H, m), 2.90 (1 H, m), 3.03 (1 H, d, J = 16.2 Hz), 3.94 (1 H, d, J = 16.2 Hz), 4.50 (1 H, br s), 6.53 (1 H, d, J = 8.6 Hz), 6.47 (1 H, d, J = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2 (q), 19.4 (t), 24.5 (q), 26.0 (t), 26.1 (q), 28.0 (d), 30.1 (t), 32.1 (t), 35.1 (t), 38.0 (s), 42.9 (t), 46.2 (t), 73.3 (s), 113.9 (d), 114.6 (d), 126.2 (s), 126.3 (d), 129.6 (s), 133.2 (s), 145.8 (s), 147.6 (s); MS (EI) m/z 312 (M^+, base), 297, 269, 255, 241, 229, 215, 175, 161, 147, 109, 95; EI-HRMS m/z calcd for $C_{21}H_{28}O_2$: 312.2089. Found: 312.2104.

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Supporting Information Available: Copies of ^{1}H NMR spectra (35 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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