Effect of Benzylic Oxygen on the Antioxidant Activity of Phenolic Lignans

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It has been clarified in the present investigation that a high degree of oxidation at the benzylic position of phenolic lignans bearing a 4-hydroxy-3-methoxybenzyl group reduces their antioxidant activity and that the antioxidant activity of the bis(4-hydroxy-3-methoxybenzyl)tetrahydrofuran lignan **2** is higher than that of the corresponding γ-butyrolactone lignan **1**. This was demonstrated by comparing the antioxidant activities of compounds **1** and **2** with those of the (benzyl)(hydroxybenzyl)tetrahydrofurans **3** and **4**, the bis(hydroxybenzyl)tetrahydrofurans **7** and **8**, the (benzoyl)(benzyl)tetrahydrofuran **6**, and the dibenzoyltetrahydrofuran **9**. The activity level of compound **2** was approximately the same potency as that of the tetrahydronaphthalene-tetrahydrofuran **5**. These compounds possess either a 4-hydroxy-3-methoxybenzyl group or a 4-hydroxy-3-methoxybenzoyl group as the benzyl or benzoyl group. An examination of radical scavenging activity showed differences of activity between diastereomers. To make this comparison possible, compounds **1**−**9** were synthesized using new synthetic routes for several of these lignans. In this investigation, stereoisomers of the (benzyl)(hydroxybenzyl)tetrahydrofurans **3** and **4** and liovils **7** and **8** were synthesized for the first time.

Phenolic lignans are found in a wide variety of dietary and other plants. The relationship between antioxidant activity and protection against the effects of various diseases in adults has recently become a topic of considerable interest.[1] Mechanistic studies of the antioxidant activity of phenolic lignans are therefore an important subject for research into the effects of dietary plants on health. Although the catechol structure is known to be important in terms of high antioxidant activity, there have been no reports concerning the relationship between plant lignan structures and their antioxidant activity. It has been reported recently that the presence of a tertiary hydroxy group on the main lignan structure decreases antioxidant activity.[2,3] Eklund and co-workers have shown that the treatment of dibenzylbutyrolactone lignans with a radical initiator yielded compounds that were oxidized at the benzylic position.[4]

The aim of the present investigation is to clarify the effect of the degree of benzylic oxidation on the resultant antioxidant activity using plant lignans. To achieve this, it was considered necessary to synthesize lignans **1**−**9** (Figure 1) and to evaluate their antioxidant activity. As a phenyl moiety, the 4-hydroxy-3-methoxyphenyl group was selected, since this is one of the most common groups among lignans. The assay systems used were not enzymatic in character, so the use of racemic **1**−**9** would be sufficient for this project. However, we assumed that optically active compounds could be obtained from less expensive starting materials, and, for this reason, optically active compounds of **1**−**9** were synthesized in the present work. To achieve effective syntheses, synthetic routes that yielded several of lignans **1**−**9** were selected. During this synthetic process, two stereoisomers of a (benzyl)(hydroxybenzyl)tetrahydrofuran lignan[5] (**3** and **4**) and of liovil[6] (**7** and **8**) were synthesized for the first time.

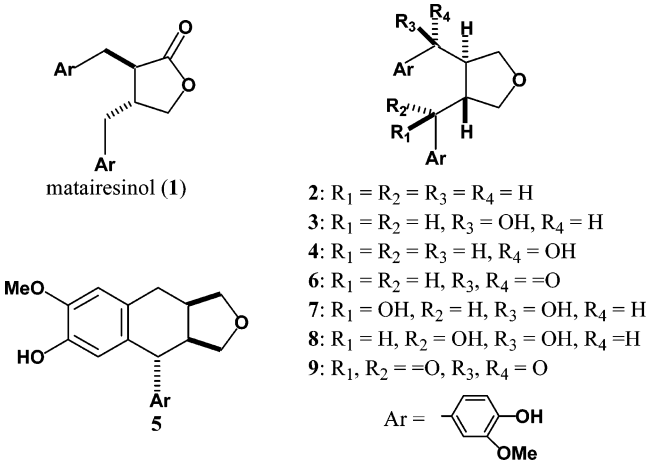

Figure 1. Structures of compounds **1**−**9**.

Results and Discussion

The syntheses of **1**−**4** and **6**−**9** began with γ-butyrolactone **10**[7] (Schemes 1 and 2). Benzylation on the α-position of γ-butyrolactone **10** using LDA yielded **11**. On the other hand, the aldol condensation of **10** with 4-benzyloxy-3-methoxybenzaldehyde using LDA yielded aldol products **12** and **13**, which could then be separated (1:1). The hydroxy groups of these aldol products were protected as triisopropylsilyl (TIPS) ethers. After the $LiAlH_4$ reductions of **11**, **14**, and **15**, the corresponding diols were subjected to cleavage of the trityl ether under acidic conditions to give triols **16**−**18**, respectively. In this detritylation, partial epimerization was observed at the benzylic position of **17**, giving a 4:1 mixture of **17**/**18** from **14**. Oxidative cleavage of the glycol portions on the triols **16**−**18**, followed by PCC oxidation, gave lactones **19**−**21**, respectively. The *erythro* selective aldol condensation of lactones **19**−**21** with 4-benzyloxy-3-methoxybenzadehyde was observed by employing potassium hexamethyldisilazane (KHMDS).[8] The aldol products **22** and **23**, which were separated (9:1), were obtained from **19**. In the case of the aldol condensations of

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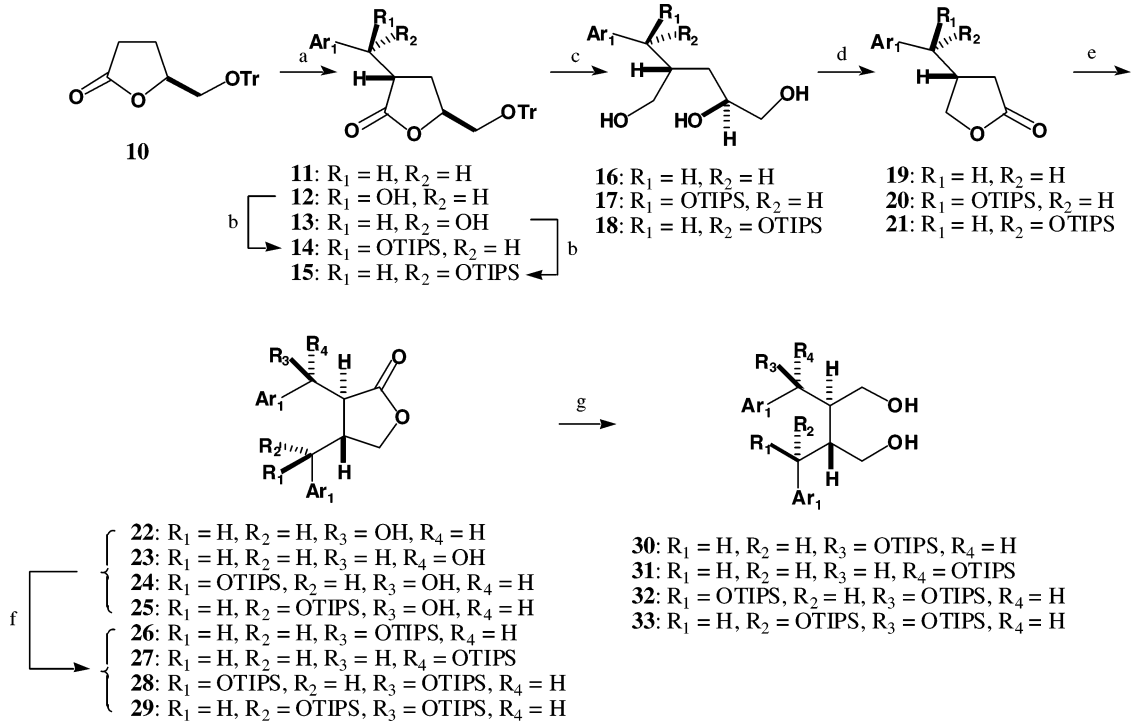
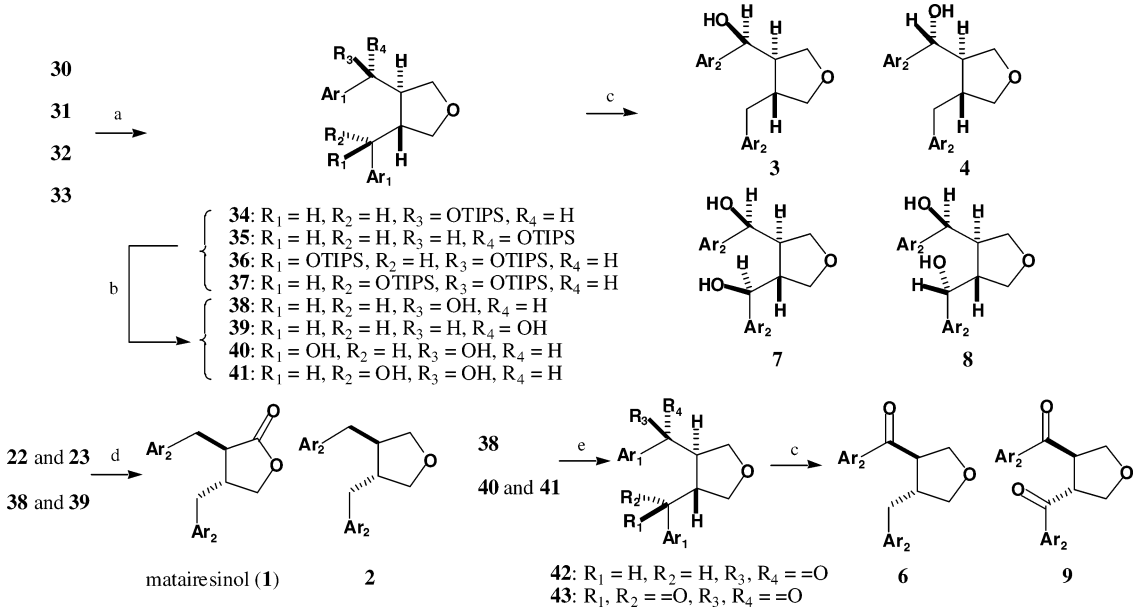
Scheme 1. Syntheses of **1**−**4** and **6**−**9**[a]



[a] Ar_1 = 4-benzyloxy-3-methoxyphenyl. (a) **11**: LDA, 4-benzyloxy-3-methoxybenzyl bromide, THF, −70 °C, 1 h (41%); **12**, **13**: ArCHO, LDA, THF, −70 °C, 30 min, silica gel column (**12**: 46%, **13**: 47%); (b) TIPSOTf, 2,6-lutidine, CH_2Cl_2, rt, 30 min (**14**: 85%, **15**: 83%); (c) **16**: (i) $LiAlH_4$, THF, rt, 30 min; (ii) concentrated HCl, EtOH, rt, 1.5 h (77%, 2 steps); **17**, **18**: (i) $LiAlH_4$, THF, rt, 30 min; (ii) HCO_2H, ether, −10 °C, 10 min (**17**: 44% as a 4:1 mixture with **18**, **18**: 46%, 2 steps); (d) (i) $NaIO_4$, MeOH, rt, 3 h; (ii) PCC, CH_2Cl_2, rt, 16 h (**19**: 90%, **20**: 77% as a 4:1 mixture with **21**, **21**:82%, 2 steps); (e) **22**, **24**, **25**: KHMDS, 4-benzyloxy-3-methoxybenzaldehyde, THF, −70 °C, 1 h (41%); (f) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 1.5 h (**26**: 87%, **27**: 65%, **28**: 84%, **29**: 100%); (g) **30**, **31**: $LiAlH_4$, THF, rt, 30 min (**30**: 72%, **31**: 84%); **32**: (i) DIBAL-H, CH_2Cl_2, −70 °C, 30 min; (ii) $LiBH_4$, THF, rt, 20 h (58%, 2 steps); **33**: $LiBH_4$, THF, rt, 48 h (65%).

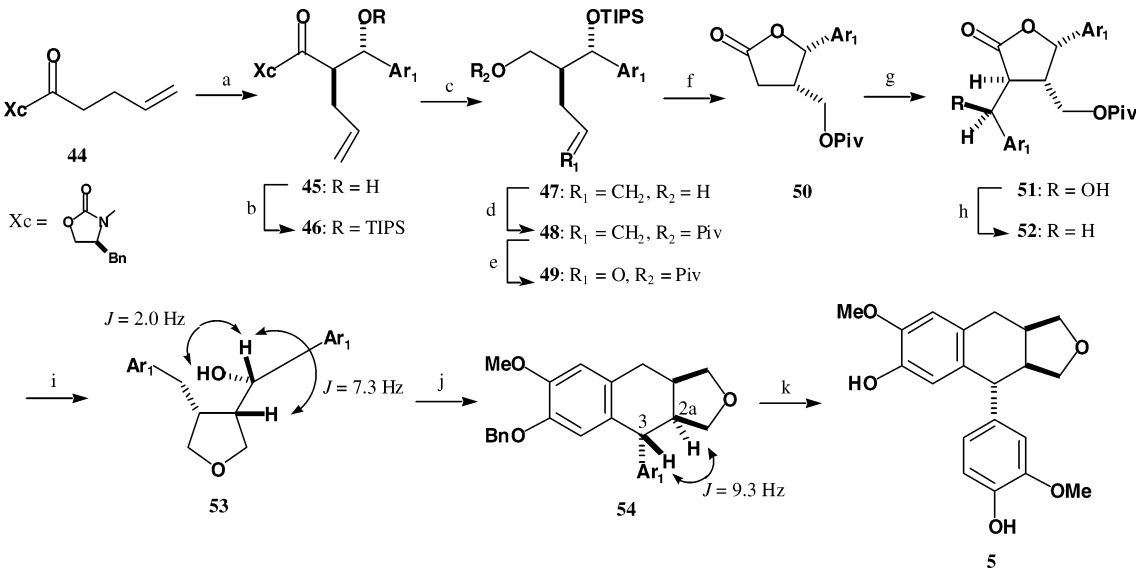
Scheme 2. Syntheses of **1**−**4** and **6**−**9**[a]



[a] Ar_1 = 4-benzyloxy-3-methoxyphenyl, Ar_2 = 4-hydroxy-3-methoxyphenyl. (a) *p*-TsCl, pyridine, CH_2Cl_2, rt, 21 h (**34**: 77%, **35**: 62%, **36**: 50%, **37**: 52%); (b) $(n\text{-Bu})_4NF$, THF, rt, 1 h (**38**: 76%, **39**: 87%, **40**: 100%, **41**: 70%); (c) H_2, 5% Pd/C, EtOAc, rt, 2 h (**3**: 67%, **4**: 92%, **7**: 84%, **8**: 80%, **6**: 66%, **9**: 100%); (d) H_2, $Pd(OH)_2$, EtOAc, rt, 22 h (**1**: 63%, **2**: 78%); (e) PCC, MS 4A, CH_2Cl_2, rt, 16 h (**42**: 94%, **43**: 78%).

20 and **21**, the production of *threo* isomers was not observed, yielding **24** and **25** as single isomers, respectively. Although lactone **20** contained **21** as an impurity, the pure aldol product **24** was obtained by purification. In the aldol condensation of **19** using LDA, the ratio of the production of *threo* isomer **23** was increased (**22**/**23** = 1:1). The benzylic hydroxy groups were protected as TIPS ethers, and the resulting silyloxy lactones **26**−**29** were reduced to diols **30**−**33** using $LiAlH_4$. The intramolecular etherification of diols **30**−**33** was accomplished by treatment with *p*-TsCl, leading to the tetrahydrofuran derivatives **34**−**37**, respectively. Cleavage of the silyl ether using $(n\text{-Bu})_4NF$, followed by hydrogenolysis in the presence of Pd/C, yielded **3**, **4**, **7**, and **8**, respectively. Matairesinol (**1**) and the dibenzyltetrahydrofuran lignan **2** were obtained from mixtures of **22**/**23** and **38**/**39**, respectively, by reduction of a hydroxy

Scheme 3. Synthesis of **5**[a]



[a] Ar_1 = 4-benzyloxy-3-methoxyphenyl. (a) (i) 4-benzyloxy-3-methoxybenzaldehyde, $MgCl_2$, Et_3N, Me_3SiCl, EtOAc, rt, 1 h; (ii) CF_3CO_2H, MeOH, rt, 1 h (99%, 2 steps); (b) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 1.5 h (78%); (c) $LiBH_4$, MeOH, THF, rt, 16 h, (61%); (d) PivCl, pyridine, CH_2Cl_2, rt, 2 h (100%); (e) (i) OsO_4, NMO, aqueous acetone, *t*-BuOH, rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 1 h (86%); (f) (i) (*n*-Bu)$_4$NF, THF, 0 °C, 1 h; (ii) PCC, MS 4A, CH_2Cl_2, rt, 16 h (77%, 2 steps); (g) KHMDS, 4-benzyloxy-3-methoxybenzaldehyde, THF, −75 °C, 1 h (86%); (h) Et_3SiH, BF_3·OEt_2, CH_2Cl_2, 3 °C, 2 h (57%); (i) (i) $LiAlH_4$, THF, rt, 30 min; (ii) *N*-TsIm, HaH, −20 °C, 24 h (31%, 2 steps); (j) rt, 48 h (100%); (k) H_2, 5% Pd/C, rt, 16 h (100%).

group at the benzyl position and cleavage of the benzyl protecting group by hydrogenolysis using $Pd(OH)_2$. Ketones **6** and **9** were prepared from **38** and a mixture of **40/41**, respectively, by PCC oxidation followed by cleavage of benzyl ether by hydrogenolysis using Pd/C. The spectroscopic data of **1** and **2** agreed with literature values.[9−11] However, the NMR data of both **3** and **4** did not agree with the published data for the natural compound,[5] while the published NMR data of (+)-liovil[12] did not agree with that measured for compounds **7** and **8**. These observations were used to infer that these natural products are the other stereoisomers.

To synthesize **5**, the *cis*-(4-hydroxy-3-methoxybenzyl))-[(hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofuran **53** was selected as a key intermediate (Scheme 3). The *anti*-aldol adduct **45** was obtained by Evans' *anti*-aldol condensation.[13] After protection as a TIPS ether, auxiliary material was removed by reduction with $LiBH_4$ to yield primary alcohol **47**, which was transformed into the aldehyde **49** by protection as a pivaloyl ester and subsequent oxidative cleavage of the olefin. After desilylation, the resulting hemiacetal was subjected to PCC oxidation to give lactone **50**. The 2-benzyllactone **52** was obtained through aldol condensation with 4-benzyloxy-3-methoxyaldehyde and silane reduction.[14] The direct benzylation to lactone **50** resulted in a poor yield. After the $LiAlH_4$ reduction of lactone **52** to the corresponding triol, the tetrahydrofuran derivative **53** was obtained by etherification between two primary hydroxy groups by treatment of the resulting triol with *N*-TsIm.[15] The presence of the secondary benzylic hydroxy group was confirmed by coupling of the benzylic proton (dd, J = 7.3, 2.0 Hz). The tetrahydrofuran derivative **53** was unstable and gradually cyclized to **54** at room temperature by the Friedel−Crafts-type cyclization.[16] The coupling constant between the 3-position and the 2a-position (J = 9.3 Hz) confirmed this steric configuration.[17] Hydrogenolysis of **54** yielded **5**. Two stereoisomers each of (4-hydroxy-3-methoxybenzyl)[(hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofuran (**3** and **4**) and liovil (**7** and **8**) were synthesized for the first time. The Friedel−Crafts-type cyclization of *cis*-(4-hydroxy-3-methoxybenzyl)-[(hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofuran **53** was demonstrated.

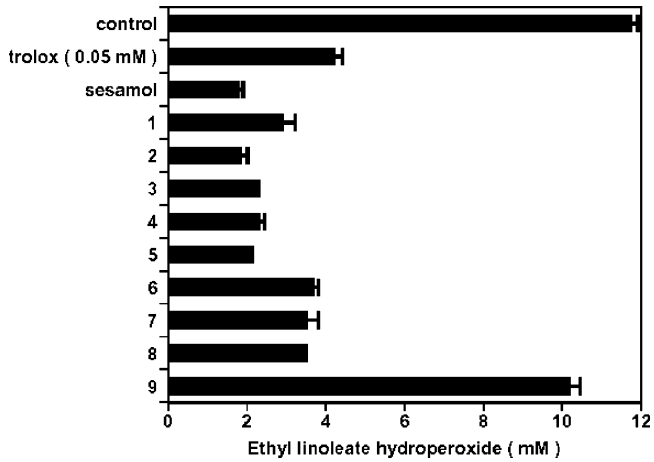


Figure 2. Antioxidant activity of compounds **1**−**9** in a Tween 20 micelle system [0.3 M Tween 20/0.05 M phosphate buffer (pH 7.4)]. Conditions: final concentration of a test sample and sesamol, 0.10 mM (0.05 mM for trolox); AAPH, 10 mM; ethyl linoleate, 50 mM (AAPH: 2,2′-azobis(2-aminopropane)dihydrochloride).

After ethyl linoleate was treated with 2,2′-azobis(2-aminopropane)dihydrochloride (AAPH) and **1**−**9**, the concentration of the resultant ethyl linoleate hydroperoxide was calculated in order to evaluate antioxidant activity (Figure 2). It was shown that the antioxidant activity of bis(4-hydroxy-3-methoxybenzyl)lactone **1** was less potent than that of the corresponding bis(4-hydroxy-3-methoxybenzyl)tetrahydrofuran **2**. This confirmed that the degree of oxidation, except for the benzylic position, has an effect on antioxidant activity for plant lignans. The activity level of dibenzyltetrahydrofuran **2** was approximately the same potency as that of the tetrahydronaphthalene-tetrahydrofuran **5** and sesamol. The degree of oxidation on the benzylic positions of **5** is the same as that for **1**. The activities of the (4-hydroxy-3-methoxybenzyl)[(hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofurans **3** and **4** were a little weaker than that of **2**. The presence of the hydroxy group on the benzylic position reduced the activity. This

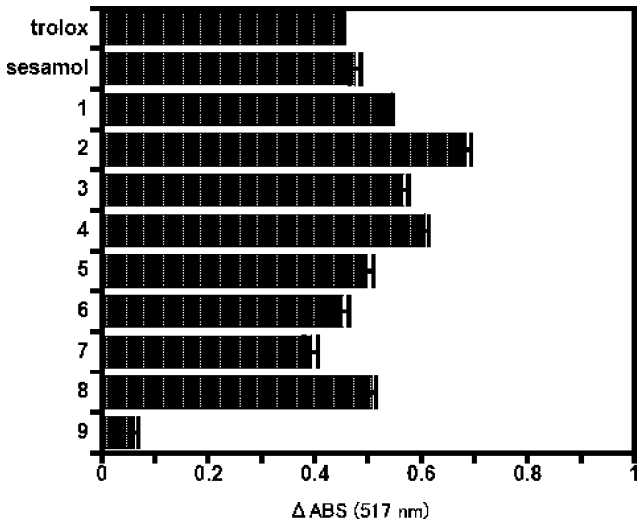


Figure 3. Radical scavenging activity of compounds **1**−**9**. Conditions: final concentration of a test sample, 20 μM; DPPH, 0.1 mM (DPPH: 1,1-diphenyl-2-picrylhydrazyl).

tendency was more clearly apparent between bis(4-hydroxy-3-methoxybenzyl)tetrahydrofuran **2** and the less active bis[(hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]-tetrahydrofurans **7** and **8**. The presence of a carbonyl group on the benzylic position also reduced the activity, since the activity of (4-hydroxy-3-methoxybenzoyl)(4-hydroxy-3-methoxybenzyl)tetrahydrofuran **6** was less than that of **2**. The potency level of **6** was the same as that of the bis[(hydroxy)-(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofurans **7** and **8**. It is interesting to note that bis(4-hydroxy-3-methoxybenzoyl)tetrahydrofuran **9**, which is fully oxidized on the benzylic position, showed the weakest activity in this assay. The differences in activity between diastereomers **3** and **4** was not as marked as those between **7** and **8**.

Radical scavenging activity of **1**−**9** was also examined (Figure 3). In this assay system, a profile of activity almost identical to that of Figure 2 was observed except for differences between diastereomers. The activity of **3** was weaker than that of **4**. This phenomenon was more clearly apparent between **7** and **8**, with obviously higher activity of **8** than that of **7** being shown.

This investigation confirmed that a higher degree of oxidation on the benzylic position of phenolic lignans bearing a 4-hydroxy-3-methoxyphenyl group decreased antioxidant activity. Accordingly, the relationship between the functionality at the benzylic position and the antioxidant activity of phenolic lignans bearing a 4-hydroxy-3-methoxyphenyl group has been clarified for the first time. This is also the first report showing differences of radical scavenging activity between diastereomers. The radical scavenging activity is affected by the stereochemistry of the lignans.

Experimental Section

General Experimental Procedures. Melting points are uncorrected. Optical rotation values were measured on a Horiba SEPA-200 instrument. NMR data were obtained using a JNM-EX400 spectrometer. FABMS data were measured with a JMS-MS700V spectrometer. The silica gel used was Wakogel C-300 (Wako, 200−300 mesh). The numbering of compounds follows IUPAC nomenclatural rules.

(2*R*,4*S*)-2-(4-Benzyloxy-3-methoxybenzyl)-5-trityloxy-4-pentanolide (11). To a solution of LDA (0.013 mol) in THF (150 mL) was added a solution of the butyrolactone **10** (9.50 g, 0.027 mol) in THF (50 mL). After stirring at −70 °C for 30 min, a solution of 4-benzyloxy-3-methoxybenzyl bromide (8.10 g, 0.026 mol) in THF (50 mL) was added, and then the resulting reaction solution was stirred at −70 °C for 1 h before addition of a saturated aqueous NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc/hexane, 1:5) to give the benzyl butyrolactone **11** (6.43 g, 0.011 mol, 41%) as a colorless oil: $[\alpha]^{20}_D$ +5.6° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94−2.07 (2H, m, H-3), 2.70 (1H, dd, J = 14.7, 10.3 Hz, C*H*HAr-2), 3.07 (1H, dd, J = 10.7, 3.9 Hz, *H*H-5), 3.10−3.15 (2H, m, H-2, CH*H*Ar-2), 3.40 (1H, dd, J = 10.7, 3.4 Hz, H*H*-5), 3.82 (3H, s, OCH_3), 4.44 (1H, m, H-4), 5.12 (2H, s, OCH_2-Ph), 6.63 (1H, dd, J = 7.8, 2.0 Hz, ArH), 6.72 (1H, d, J = 2.0 Hz, ArH), 6.80 (1H, d, J = 7.8 Hz, ArH), 7.20−7.29 (12H, m, ArH), 7.33−7.44 (8H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.6, 36.4, 41.3, 56.0, 65.2, 71.2, 87.1, 112.6, 114.3, 120.9, 127.2, 127.3, 127.8, 127.9, 128.5, 128.6, 131.6, 137.2, 143.4, 147.0, 149.8, 179.0; *anal*. C 79.85%, H 6.46%, calcd for $C_{39}H_{36}O_5$, C 80.11%, H 6.21%.

(2*S*,4*S*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(hydroxy)-methyl]-5-trityloxy-4- pentanolide (12) (*erythro* isomer) and (2*S*,4*S*)-2-[(*R*)-(4-Benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-5-trityloxy-4-pentanolide 13 (*threo* isomer). To a solution of LDA (33.5 mmol) in THF (200 mL) was added a solution of the lactone **10** (10 g, 27.9 mmol) in THF (80 mL). After the solution was stirred at −70 °C for 15 min, a solution of 4-benzyloxy-3-methoxybenzaldehyde (3.41 g, 27.9 mmol) in THF (20 mL) was added. The resulting reaction solution was stirred at −70 °C for 30 min, and then saturated aqueous NH_4Cl solution was added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc/toluene) gave the *erythro* aldol product **12** (7.71 g, 12.8 mmol, 46%) as a colorless oil ($[\alpha]^{20}_D$ +2.1° (*c* 1.4, $CHCl_3$)) and the *threo* aldol product **13** (7.87 g, 13.1 mmol, 47%) as colorless crystals (mp 159−160 °C; $[\alpha]^{20}_D$ +45° (*c* 1.2, $CHCl_3$)). *erythro* isomer **12**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.74 (1H, ddd, J = 12.8, 9.8, 3.4 Hz, *H*H-3), 2.39 (1H, ddd, J = 12.8, 8.8, 8.8 Hz, H*H*-3), 2.80 (1H, d, J = 4.9 Hz, OH), 3.04 (1H, dd, J = 10.8, 3.7 Hz, *H*H-5), 3.18 (1H, m, H-2), 3.42 (1H, dd, J = 10.8, 2.9 Hz, H*H*-5), 3.82 (3H, s, OCH_3), 4.59 (1H, m, H-4), 5.12 (2H, s, OCH_2Ph), 5.31 (1H, dd, J = 4.9, 2.9 Hz, ArC*H*OH), 6.79 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.84 (1H, d, J = 8.3 Hz, ArH), 6.88 (1H, d, J = 2.0 Hz, ArH), 7.18−7.29 (12H, m, ArH), 7.32−7.37 (6H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.7, 48.2, 55.9, 65.3, 70.97, 71.0, 77.9, 87.0, 109.1, 113.9, 117.3, 127.1, 127.2, 127.8, 127.9, 128.48, 128.52, 134.9, 137.0, 143.3, 147.4, 149.7, 178.2; *anal*. C 77.72%, H 6.12%, calcd for $C_{39}H_{36}O_6$, C 77.98%, H 6.04%. *threo* isomer **13**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.73 (1H, ddd, J = 13.2, 10.0, 2.4 Hz, *H*H-3), 1.90 (1H, ddd, J = 13.2, 9.3, 9.3 Hz, H*H*-3), 3.02 (1H, dd, J = 10.7, 3.4 Hz, *H*H-5), 3.25 (1H, m, H-2), 3.46 (1H, dd, J = 10.7, 2.9 Hz, H*H*-5), 3.79 (3H, s, OCH_3), 4.32 (1H, s, OH), 4.46 (1H, m, H-4), 4.68 (1H, d, J = 8.8 Hz, ArC*H*OH), 5.14 (2H, s, OCH_2Ph), 6.76 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.83 (1H, d, J = 8.3 Hz, ArH), 6.91 (1H, d, J = 2.0 Hz, ArH), 7.20−7.30 (12H, m, ArH), 7.33−7.38 (6H, m, ArH),7.41−7.46 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.6, 46.4, 55.9, 65.1, 71.0, 74.7, 77.5, 87.2, 109.8, 113.7, 119.0, 127.22, 127.24, 127.8, 127.9, 128.5, 128.6, 133.5, 137.0, 143.2, 148.1, 149.9, 179.4; *anal*. C 77.58%, H 6.04%, calcd for $C_{39}H_{36}O_6$, C 77.98%, H 6.04%.

(2*S*,4*S*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-5-trityloxy-4-pentanolide (14). To an ice-cooled solution of the *erythro* aldol product **12** (8.62 g, 14.3 mmol) and 2,6-lutidine (3.66 mL, 31.4 mmol) in CH_2Cl_2 (80 mL) was added TIPSOTf (4.23 mL, 15.7 mmol). The resulting reaction solution was stirred at room temperature for 30 min before addition of saturated aqueous $NaHCO_3$ solution. The organic solution was separated, washed with saturated aqueous $CuSO_4$ solution, saturated aqueous $NaHCO_3$ solution, and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane, 1:9) gave the silyl ether **14** (9.25 g, 12.2 mmol, 85%) as a colorless oil: $[\alpha]^{20}_D$ −12° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99−1.09 (21H, m, *i*-Pr), 1.74 (1H, ddd, J = 12.2,

9.8, 3.4 Hz, *H*H-3), 2.65 (1H, ddd, *J* = 12.2, 8.3, 8.3 Hz, H*H*-3), 2.94 (1H, dd, *J* = 9.8, 8.3 Hz, H-2), 3.05 (1H, dd, *J* = 10.3, 3.9 Hz, *H*H-5), 3.40 (1H, dd, *J* = 10.3, 2.9 Hz, H*H*-5), 3.84 (3H, s, OCH_3), 4.65 (1H, m, H-4), 5.14 (2H, s, OCH_2Ph), 5.47 (1H, s, ArCHOSi), 6.79 (1H, d, *J* = 8.3 Hz, ArH), 6.84 (1H, d, *J* = 6.8 Hz, ArH), 6.89 (1H, s, ArH), 7.17−7.26 (12H, m, ArH), 7.29−7.37 (7H, m, ArH), 7.43−7.45 (1H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6, 17.9, 18.0, 23.0, 50.0, 55.9, 65.5, 71.1, 72.7, 77.7, 86.9, 109.3, 113.8, 117.6, 127.1, 127.3, 127.8, 128.5, 128.6, 136.8, 137.1, 143.4, 147.3, 149.5, 177.8; *anal*. C 76.02%, H 7.49%, calcd for $C_{48}H_{56}O_6Si$, C 76.15%, H 7.46%.

(2*S*,4*S*)-2-[(*R*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-5-trityloxy-4-pentanolide (15): colorless oil; 83% yield; $[\alpha]^{20}_D$ +26° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99−1.03 (18H, m, *i*-Pr), 1.04−1.17 (3H, m, *i*-Pr), 2.05 (1H, m, *H*H-3), 2.20 (1H, m, H*H*-3), 2.91 (1H, dd, *J* = 10.5, 3.7 Hz, *H*H-5), 3.32 (1H, dd, *J* = 10.5, 3.2 Hz, H*H*-5), 3.43 (1H, m, H-2), 3.85 (3H, s, OCH_3), 3.80−3.88 (1H, m, H-4), 5.11 (2H, s, OCH_2Ph), 5.44 (1H, d, *J* = 4.4 Hz, ArCHOSi), 6.83 (1H, d, *J* = 8.3 Hz, ArH), 6.87 (1H, d, *J* = 8.3 Hz, ArH), 6.99 (1H, s, ArH), 7.20−7.34 (12H, m, ArH), 7.38−7.42 (8H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1, 17.9, 18.0, 24.4, 49.6, 55.8, 65.1, 71.0, 72.8, 77.8, 86.9, 110.3, 113.6, 118.7, 127.1, 127.4, 127.8, 127.9, 128.4, 128.6, 133.4, 137.0, 143.4, 147.5, 149.2, 176.9; *anal*. C 76.05%, H 7.63%, calcd for $C_{48}H_{56}O_6Si$, C 76.15%, H 7.46%.

(2*S*,4*R*)-4-(4-Benzyloxy-3-methoxybenzyl)-1,2,5-pentanetriol (16). To an ice-cooled suspension of $LiAlH_4$ (0.20 g, 5.27 mmol) in THF (20 mL) was added a solution of the benzylbutyrolactone **11** (3.10 g, 5.30 mmol) in THF (40 mL). After the reaction mixture was stirred at room temperature for 1 h, saturated aqueous $MgSO_4$ solution and K_2CO_3 were added. The resulting mixture was stirred at room temperature for 30 min and then filtered. After the filtrate was concentrated, the residue was dissolved in EtOH (150 mL). To this solution was added concentrated HCl (1.5 mL), and then the reaction solution was stirred at room temperature for 1.5 h before addition of saturated aqueous $NaHCO_3$ solution. After concentration, the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was subjected to silica gel column chromatography (hexane/EtOAc, 1:1) to give the triol **16** (1.41 g, 4.08 mmol, 77%) as a colorless oil: $[\alpha]^{20}_D$ −17° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42−1.57 (2H, m, H-3), 2.05 (1H, brs, OH), 2.48 (1H, dd, *J* = 13.7, 7.3 Hz, ArC*H*H-4), 2.60 (1H, dd, *J* = 13.7, 7.8 Hz, ArCH*H*-4), 2.70−3.45 (2H, br, OH), 3.40 (1H, dd, *J* = 10.7, 7.8 Hz, C*H*HOH), 3.48−3.52 (2H, m, C*H*$_2$OH), 3.62 (1H, dd, *J* = 10.7, 3.4 Hz, CH*H*OH), 3.80−3.86 (1H, m, H-2), 3.84 (3H, s, OCH_3), 5.09 (2H, s, OCH_2Ph), 6.62 (1H, d, *J* = 8.4 Hz, ArH), 6.71 (1H, s, ArH), 6.78 (1H, d, *J* = 8.4 Hz, ArH), 7.26−7.36 (3H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 35.2, 37.4, 38.9, 56.1, 65.1, 66.9, 69.3, 71.2, 113.0, 114.3, 121.1, 127.3, 127.8, 128.5, 133.4, 137.3, 146.6, 149.6; HREIMS *m/z* 346.1778 (calcd for $C_{20}H_{26}O_5$, 346.1767).

(2*S*,4*R*)-4-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-1,2,5-pentanetriol (17). To an ice-cooled suspension of $LiAlH_4$ (0.46 g, 12.2 mmol) in THF (20 mL) was added a solution of the lactone **14** (9.25 g, 12.2 mmol). The resulting reaction mixture was stirred at room temperature for 30 min before additions of saturated aqueous $MgSO_4$ and K_2CO_3. After the mixture was filtered, the filtrate was concentrated to give a crude diol. To a solution of this crude diol in ether (500 mL) was added HCO_2H (500 mL) at −10 °C. After the mixture was stirred at −10 °C for 10 min, EtOAc and H_2O were added. The organic solution was separated, washed with saturated aqueous $NaHCO_3$ solution and brine, and dried (Na_2SO_4). Concentration, followed by silica gel column chromatography (EtOAc/hexane, 1:6 and 1:1), gave the triol **17** (2.79 g, 5.38 mmol, 44%) as a 4:1 mixture with the benzylic epimer **18**. The production of some unknown products was observed. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95−1.05 (21H, m, *i*-Pr), 1.15 (1H, m, *H*H-3), 1.51 (1H, m, H*H*-3), 2.27 (1H, m, H-4), 3.03 (1H, br s, OH), 3.09 (1H, br s, OH), 3.40−3.50 (3H, m, C*H*$_2$O*H*), 3.67−3.78 (3H, m, C*H*$_2$OH, H-2), 3.86 (3H, s, OCH_3), 4.85 (1H, d, *J* = 4.9 Hz, ArCHOSi), 5.11 (2H, s, OCH_2Ph), 6.73 (1H, d, *J* = 8.3 Hz, ArH), 6.81 (1H, d, *J* = 8.3 Hz, ArH), 6.95 (1H, s, ArH), 7.27−7.37 (3H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 12.2, 17.9, 18.0, 31.7, 44.2, 55.9, 63.2, 66.9, 69.9, 71.1, 77.9, 110.7, 113.4, 119.4, 127.3, 127.8, 128.4, 135.0, 137.0, 147.36, 147.41, 149.3; *anal*. C 67.45%, H 8.93%, calcd for $C_{29}H_{46}O_6Si$, C 67.14%, H 8.94.

(2*S*,4*R*)-4-[(*R*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-1,2,5-pentanetriol (18): colorless oil; 46% yield; $[\alpha]^{20}_D$ +36° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94−1.04 (21H, m, *i*-Pr), 1.35 (1H, ddd, *J* = 14.7, 7.8, 2.9 Hz, *H*H-3), 1.47 (1H, ddd, *J* = 14.7, 9.3, 4.9 Hz, H*H*-3), 2.10 (1H, m, H-4), 2.18 (1H, brs, OH), 2.87 (1H, brs, OH), 3.21 (1H, brs, OH), 3.38 (1H, dd, *J* = 10.7, 7.8 Hz, C*H*HOH), 3.48 (1H, dd, *J* = 10.7, 4.3 Hz, CH*H*OH), 3.61 (1H, dd, *J* = 9.5, 4.9 Hz, C*H*HOH), 3.65 (1H, dd, *J* = 9.5, 4.9 Hz, CH*H*OH), 3.75 (1H, m, H-2), 3.86 (3H, s, OCH_3), 4.88 (1H, d, *J* = 5.4 Hz, ArCHOSi), 5.11 (2H, s, OCH_2O), 6.74 (1H, dd, *J* = 8.3, 2.0 Hz, ArH), 6.81 (1H, d, *J* = 8.3 Hz, ArH), 6.94 (1H, d, *J* = 2.0 Hz, ArH), 7.26−7.37 (3H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 17.9, 18.0, 31.3, 45.3, 55.9, 63.1, 66.9, 70.2, 71.1, 77.4, 110.8, 113.4, 119.3, 127.3, 127.8, 128.4, 135.6, 137.0, 147.4, 149.3; *anal*. C, 66.73%, H 9.07%, calcd for $C_{29}H_{46}O_6Si$, C 67.14%, H 8.94%.

(3*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-butanolide (19). A reaction mixture of the triol **16** (1.10 g, 3.18 mmol) and $NaIO_4$ (0.76 g, 3.55 mmol) in MeOH (40 mL) was stirred at room temperature for 3 h. After concentration, the residue was dissolved in H_2O and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration gave a crude hemiacetal. A reaction mixture of this hemiacetal and PCC (0.75 g, 3.50 mmol) in CH_2Cl_2 (80 mL) was stirred at room temperature for 16 h before filtration. The filtrate was concentrated, and then the residue was subjected to silica gel column chromatography (hexane/EtOAc, 1:1) to give the butanolide **19** (0.89 g, 2.85 mmol, 90%) as colorless crystals: mp 73 °C (EtOH); $[\alpha]^{20}_D$ −16° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.27 (1H, dd, *J* = 17.6, 6.8 Hz, H-2), 2.59 (1H, dd, *J* = 17.6, 7.8 Hz, H-2), 2.67 (1H, dd, *J* = 13.7, 8.3 Hz, C*H*HAr-3), 2.72 (1H, dd, *J* = 13.7, 7.1 Hz, CH*H*Ar-3), 2.80 (1H, m, H-3), 3.87 (3H, s, OCH_3), 4.02 (1H, dd, *J* = 9.0, 6.1 Hz, H-4), 4.32 (1H, dd, *J* = 9.0, 7.1 Hz, H-4), 5.12 (2H, s, OCH_2Ph), 6.62 (1H, dd, *J* = 8.3, 2.0 Hz, ArH), 6.67 (1H, d, *J* = 2.0 Hz, ArH), 6.82 (1H, d, *J* = 8.3 Hz, ArH), 7.25−7.38 (3H, m, ArH), 7.42−7.44 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 34.2, 37.2, 38.6, 56.0, 71.1, 72.6, 112.4, 114.4, 120.6, 127.2, 127.8, 128.5, 131.4, 137.1, 147.1, 149.8, 176.8; *anal*. C 73.20%, H 6.56%, calcd for $C_{19}H_{20}O_4$, C 73.06%, H 6.45%.

(3*R*)-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4- butanolide (20): colorless oil; 77% yield (4:1 mixture with benzylic epimer **21**); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94−1.02 (21H, m, *i*-Pr), 2.53 (1H, dd, *J* = 17.6, 8.8 Hz, *H*H-2), 2.65 (1H, dd, *J* = 17.6, 8.8 Hz, H*H*-2), 2.85 (1H, m, H-3), 3.87 (3H, s, OCH_3), 4.08 (1H, dd, *J* = 9.3, 7.1 Hz, *H*H-4), 4.14 (1H, dd, *J* = 9.3, 7.3 Hz, H*H*-4), 4.70 (1H, d, *J* = 6.4 Hz, ArCHOSi), 5.13 (2H, s, OCH_2Ar), 6.71 (1H, dd, *J* = 7.8, 2.0 Hz, ArH), 6.83 (1H, d, *J* = 7.8 Hz, ArH), 6.89 (1H, d, *J* = 2.0 Hz, ArH), 7.29−7.37 (3H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 17.86, 17.93, 30.9, 44.5, 55.9, 69.6, 71.0, 75.4, 109.8, 113.7, 118.7, 127.3, 127.8, 128.4, 135.1, 136.9, 147.9, 149.8, 176.8; *anal*. C 69.55%, H 8.29%, calcd for $C_{28}H_{40}O_5Si$, C 69.38%, H 8.32%.

(3*R*)-[(*R*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4- butanolide (21): colorless oil; 82% yield; $[\alpha]^{20}_D$ +44° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94−0.99 (21H, m, *i*-Pr), 2.31 (2H, d, *J* = 8.3 Hz, H_2-2), 2.84 (1H, m, H-3), 3.87 (3H, s, OCH_3), 4.33 (1H, dd, *J* = 9.3, 7.2 Hz, *H*H-4), 4.39 (1H, dd, *J* = 9.3, 6.8 Hz, H*H*-4), 4.65 (1H, d, *J* = 7.3 Hz, ArCHOSi), 5.13 (2H, s, OCH_2Ph), 6.71 (1H, dd, *J* = 8.3, 2.0 Hz, ArH), 6.82 (1H, d, *J* = 8.3 Hz, ArH), 6.87 (1H, d, *J* = 2.0 Hz, ArH), 7.26−7.37 (3H, m, ArH), 7.41−7.43 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 17.9, 18.0, 31.2, 44.6, 55.9, 70.2, 71.0, 75.8, 109.8, 113.7, 118.8, 127.3, 127.8,

128.4, 135.4, 136.9, 147.9, 149.8, 176.6; *anal*. C 69.23%, H 8.45%, calcd for $C_{28}H_{40}O_5Si$, C 69.38%, H 8.32%.

(2*S*,3*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-2-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-4-butanolide (22). To a solution of KHMDS (3.07 mL, 0.5 M in toluene, 1.54 mmol) in THF (10 mL) was added a solution of the butanolide **19** (0.40 g, 1.28 mmol) in THF (10 mL) at −70 °C. After stirring at −70 °C for 15 min, a solution of 4-benzyloxy-3-methoxybenzaldehyde (0.31 g, 1.28 mmol) in THF (5 mL) was added. The reaction solution was stirred at −70 °C for 2 h before addition of saturated aqueous NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was purified by silica gel column chromatography (hexane/EtOAc, 1:1) to give the *erythro*-aldol product **22** (0.62 g, 1.12 mmol, 88%) as a colorless oil: $[\alpha]^{20}_D$ −34° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.24 (1H, dd, *J* = 13.7, 6.8 Hz, ArC*H*H), 2.39 (1H, dd, *J* = 13.7, 8.3 Hz, ArCH*H*), 2.63 (1H, dd, *J* = 6.6, 3.2 Hz, H-2), 2.77 (1H, m, H-3), 2.85 (1H, d, *J* = 4.9 Hz, OH), 3.76 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.92 (1H, dd, *J* = 8.8, 5.9 Hz, H-4), 4.28 (1H, dd, *J* = 8.8, 8.8 Hz, H-4), 5.05−5.15 (4H, m, OCH_2Ar), 5.25 (1H, dd, *J* = 4.9, 3.4 Hz, ArC*H*OH), 6.30 (1H, dd, *J* = 7.8, 2.0 Hz, ArH), 6.35 (1H, d, *J* = 2.0 Hz, ArH), 6.66 (1H, d, *J* = 7.8 Hz, ArH), 6.71 (1H, dd, *J* = 8.3, 1.5 Hz, ArH), 6.79 (1H, d, *J* = 8.3 Hz, ArH), 6.81 (1H, d, *J* = 1.5 Hz, ArH), 7.24−7.35 (6H, m, ArH), 7.39−7.41 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 36.4, 39.1, 52.7, 55.8, 55.9, 70.9, 71.6, 72.6, 108.9, 112.3, 113.8, 113.9, 117.3, 120.4, 127.2, 127.8, 128.5, 130.9, 134.0, 136.9, 137.1, 146.8, 147.5, 149.5, 149.7, 178.3; *anal*. C 73.45%, H 6.33%, calcd for $C_{34}H_{34}O_7$, C 73.63%, H 6.18%.

(2*S*,3*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-2-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-4-butanolide (23). To a solution of LDA (13.2 mmol) in THF (60 mL) was added a solution of the butanolide **19** (3.43 g, 11.0 mmol) in THF (20 mL) at −70 °C. After the mixture was stirred at −70 °C for 30 min, a solution of 4-benzyloxy-3-methoxybenzaldehyde (2.93 g, 12.1 mmol) in THF (40 mL) was added. The reaction solution was stirred at −70 °C for 1 h before addition of saturated aqueous NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration and silica gel column chromatography (hexane/EtOAc, 2:1) gave the *erythro*-aldol product **22** (2.55 g, 4.60 mmol, 42%) and the *threo*-aldol product **23** (2.50 g, 4.51 mmol, 41%) as colorless crystals: mp 128 °C (EtOH); $[\alpha]^{20}_D$ −47° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.06 (1H, dd, *J* = 13.9, 4.9 Hz, C*H*HAr-3), 2.15 (1H, dd, *J* = 13.9, 9.5 Hz, CH*H*Ar-3), 2.45 (1H, m, H-3), 2.58 (1H, dd, *J* = 9.3, 8.3 Hz, H-2), 3.79 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.09 (1H, d, *J* = 8.3 Hz, H-4), 4.11 (1H, d, *J* = 8.3 Hz, H-4), 4.79 (1H, d, *J* = 8.3 Hz, ArC*H*OH), 5.10−5.15 (4H, m, OCH_2Ph), 6.32 (1H, dd, *J* = 7.8, 2.0 Hz, ArH), 6.35 (1H, d, *J* = 2.0 Hz, ArH), 6.70 (1H, d, *J* = 7.8 Hz, ArH), 6.86 (2H, s, ArH), 6.99 (1H, s, ArH), 7.22−7.31 (6H, m, ArH), 7.33−7.42 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.0, 39.8, 51.5, 55.9, 56.1, 71.0, 72.0, 74.4, 82.1, 110.0, 112.3, 113.9, 114.2, 119.0, 120.3, 127.2, 127.8, 128.5, 130.9, 133.2, 136.8, 137.1, 146.9, 148.3, 149.6, 150.2, 179.0; HREIMS *m/z* 554.2300 (calcd for $C_{34}H_{34}O_7$, 554.2304).

(2*S*,3*R*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-3-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-butanolide (24): colorless oil: 79% yield; $[\alpha]^{20}_D$ +19° (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.86−0.98 (21H, m, *i*-Pr), 2.79 (1H, m, H-2), 2.90 (2H, m, H-3, OH), 3.76 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 4.31−4.33 (2H, m, H_2-4), 4.59 (1H, d, *J* = 4.4 Hz, ArCHOSi), 5.05−5.14 (4H, m, OCH_2Ph), 5.17 (1H, dd, *J* = 3.7, 3.7 Hz, ArC*H*OH), 6.35 (1H, dd, *J* = 8.3, 2.0 Hz, ArH), 6.61 (1H, d, *J* = 2.0 Hz, ArH), 6.65−6.67 (2H, m, ArH), 6.74−6.77 (2H, m, ArH), 7.25−7.37 (6H, m, ArH), 7.39−7.40 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 17.85, 17.9, 43.1, 49.0, 55.79, 55.8, 69.5, 70.9, 71.0, 72.5, 75.2, 109.2, 110.0, 113.2, 113.7, 117.6, 118.8, 127.17, 127.21, 127.3, 127.4, 127.78, 127.84, 128.4, 128.47, 128.51, 133.8, 134.2, 136.98, 137.05, 147.61, 147.65, 149.3, 149.6, 178.6; *anal*. C 70.75%, H 7.56%, calcd for $C_{43}H_{54}O_8Si$, C 71.04%, H 7.49%.

(2*S*,3*R*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-3-[(*R*)-(4-benzyloxy-3-methoxyphenyl)-(triisopropylsilyloxy)methyl]-4-butanolide (25): colorless oil; 81% yield; $[\alpha]^{20}_D$ +11° (*c* 1.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.86−0.91 (21H, m, *i*-Pr), 2.65 (1H, m, H-2), 2.71 (1H, m, H-3), 2.92 (1H, d, *J* = 4.4 Hz, OH), 3.71 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 4.23 (1H, d, *J* = 6.4 Hz, ArCHOSi), 4.28 (1H, dd, *J* = 8.8, 8.3 Hz, *H*H-4), 4.59 (1H, dd, *J* = 8.8, 4.4 Hz, H*H*-4), 5.05−5.15 (5H, m, OCH_2Ph, ArC*H*OH), 6.36 (1H, d, *J* = 8.3 Hz, ArH), 6.47 (1H, s, ArH), 6.59 (1H, d, *J* = 8.3 Hz, ArH), 6.64 (1H, d, *J* = 8.3 Hz, ArH), 6.70 (1H, s, ArH), 6.73 (1H, d, *J* = 7.8 Hz, ArH), 7.27−7.33 (6H, m, ArH), 7.40−7.42 (4H, m, ArH). By hydrogenolysis to the corresponding diphenol lactone, the *J* value of ArC*H*OH appeared as 3.6, 3.6 Hz. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 17.8, 17.9, 43.9, 50.5, 55.5, 55.7, 69.2, 70.77, 70.81, 72.3, 75.5, 108.8, 109.5, 113.1, 113.3, 117.3, 118.6, 127.2, 127.4, 127.8, 128.41, 128.44, 133.8, 134.9, 136.9, 137.0, 147.4, 147.6, 149.3, 149.5, 178.7; *anal*. C 71.02%, H 7.52%, calcd for $C_{43}H_{54}O_8Si$, C 71.04%, H 7.49%.

(2*S*,3*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-2-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-butanolide (26). To an ice-cooled solution of the *erythro*-aldol product **22** (0.26 g, 0.47 mmol) and 2,6-lutidine (0.11 mL, 0.94 mmol) in CH_2Cl_2 (40 mL) was added TIPSOTf (0.19 mL, 0.71 mmol). The resulting reaction solution was stirred at 0 °C for 1.5 h before addition of saturated aqueous $NaHCO_3$ solution. The organic solution was separated, washed with saturated aqueous $CuSO_4$ solution, saturated aqueous $NaHCO_3$ solution, and brine, and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc/hexane, 1:3) to give the silyl ether **26** (0.29 g, 0.41 mmol, 87%) as a colorless oil: $[\alpha]^{20}_D$ −37° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98−1.09 (21H, m, *i*-Pr), 2.24 (1H, dd, *J* = 13.7, 7.3 Hz, C*H*HAr-3), 2.42 (1H, dd, *J* = 13.7, 8.3 Hz, CH*H*Ar-3), 2.46 (1H, d, *J* = 5.4 Hz, H-2), 2.99 (1H, m, H-3), 3.76 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 3.97 (1H, dd, *J* = 8.6, 4.9 Hz, H-4), 4.36 (1H, dd, *J* = 8.6, 8.6 Hz, H-4), 5.06 (1H, d, *J* = 12.2 Hz, OC*H*HPh), 5.09 (1H, d, *J* = 12.2 Hz, OC*H*HPh), 5.10 (1H, d, *J* = 12.2 Hz, OCH*H*Ph), 5.14 (1H, d, *J* = 12.2 Hz, OCH*H*Ph), 5.47 (1H, s, ArCHOTIPS), 6.25 (1H, d, *J* = 8.3 Hz, ArH), 6.33 (1H, s, ArH), 6.64 (1H, s, ArH), 6.74 (1H, d, *J* = 8.3 Hz, ArH), 6.78 (1H, d, *J* = 8.8 Hz, ArH), 6.83 (1H, s, ArH), 7.25−7.35 (6H, m, ArH), 7.39−7.42 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6, 18.0, 35.8, 39.6, 54.5, 55.8, 71.0, 71.1, 72.6, 73.7, 109.2, 112.4, 113.7, 114.0, 117.5, 120.5, 127.3, 127.4, 127.7, 127.8, 128.5, 131.1, 135.6, 137.0, 137.2, 146.8, 147.4, 149.5, 177.9; *anal*. C, 72.62%, H 7.64%, calcd for $C_{43}H_{54}O_7Si$, C 72.64%, H 7.66%.

(2*S*,3*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-2-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-butanolide (27): colorless oil; 65% yield; $[\alpha]^{20}_D$ −50° (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00−1.05 [18H, m, $(CH_3)_2$CH], 1.05−1.15 [3H, m, $(CH_3)_2$C*H*], 2.51 (1H, dd, *J* = 13.2, 10.3 Hz, ArC*H*H), 2.60 (1H, m, H-3), 2.88 (1H, dd, *J* = 7.1, 3.7 Hz, H-2), 3.12 (1H, dd, *J* = 13.2, 4.4 Hz, ArCH*H*), 3.44 (1H, dd, *J* = 9.1, 7.3 Hz, *H*H-4), 3.71 (1H, dd, *J* = 9.1, 6.3 Hz, H*H*-4), 3.836 (3H, s, OCH_3), 3.845 (3H, s, OCH_3), 5.11 (4H, s, OCH_2Ph), 5.45 (1H, d, *J* = 3.4 Hz, ArCHOTIPS), 6.56 (1H, d, *J* = 8.3 Hz, ArH), 6.60 (1H, s, ArH), 6.77 (1H, d, *J* = 8.2 Hz, ArH), 6.84 (1H, d, *J* = 8.3 Hz, ArH), 6.89 (1H, d, *J* = 8.3 Hz, ArH), 6.99 (1H, s, ArH), 7.27−7.37 (6H, m, ArH), 7.41−7.43 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1, 17.98, 18.05, 38.0, 39.5, 54.8, 55.91, 55.94, 71.1, 71.2, 71.6, 73.2, 110.0, 112.4, 113.8, 114.4, 118.4, 120.5, 127.2, 127.4, 127.8, 127.9, 128.48, 128.52, 128.6, 131.8, 133.9, 137.0, 137.2, 147.0, 147.7, 149.4, 149.8, 176.6; HRFABMS *m/z* 733.3529 (calcd for $C_{43}H_{54}O_7SiNa$, 733.3536).

(2*S*,3*R*)-2,3-Bis[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-butanolide (28): colorless oil: 84% yield; $[\alpha]^{20}_D$ +11° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.84−1.06 (42H, m, *i*-Pr), 2.57 (1H, dd, *J* = 4.9, 2.0 Hz, H-2), 3.18 (1H, m, H-3), 3.72 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 4.40 (1H, dd, *J* = 8.8, 4.9 Hz, *H*H-4), 4.46 (1H, dd,

J = 8.8, 8.8 Hz, H*H*-4), 4.56 (1H, d, J = 4.4 Hz, ArCHOSi-3), 5.04 (1H, d, J = 11.7 Hz, PhC*H*HO), 5.08 (1H, d, J = 11.7 Hz, PhCH*H*O), 5.09 (1H, d, J = 12.2 Hz, PhC*H*HO), 5.13 (1H, d, J = 12.2 Hz, PhCH*H*O), 5.44 (1H, d, J = 2.0 Hz, ArCHOSi), 6.12 (1H, d, J = 8.3 Hz, ArH), 6.47 (1H, s, ArH), 6.58 (1H, d, J = 8.3 Hz, ArH), 6.63−6.77 (3H, m, ArH), 7.26−7.35 (6H, m, ArH), 7.39−7.40 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 12.6, 17.88, 17.90, 18.0, 42.0, 50.8, 55.71, 55.75, 69.4, 70.9, 71.0, 73.8, 75.3, 109.2, 110.1, 113.1, 113.6, 117.6, 118.9, 127.26, 127.34, 127.7, 127.8, 128.41, 128.44, 133.6, 135.7, 137.1, 147.4, 147.5, 149.2, 149.4, 178.2; *anal*. C 70.91%, H 8.48%, calcd for $C_{52}H_{74}O_8Si_2$, C 70.71%, H 8.44%.

(2*S*,3*R*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-3-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-butanolide (29): colorless oil; 100% yield; $[\alpha]^{20}_D$ −2.7° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81−0.89 (21H, m, *i*-Pr), 0.96−1.06 (21H, m, *i*-Pr), 2.51 (1H, dd, J = 3.4, 1.4 Hz, H-2), 2.83 (1H, m, H-3), 3.73 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.17 (1H, d, J = 6.4 Hz, ArCHOSi), 4.28 (1H, dd, J = 8.8, 8.3 Hz, *H*H-4), 4.64 (1H, dd, J = 8.8, 3.4 Hz, H*H*-4), 5.05−5.17 (4H, m, OCH_2Ph), 5.43 (1H, d, J = 1.4 Hz, ArCHOSi), 6.33 (1H, d, J = 8.3 Hz, ArH), 6.47 (1H, s, ArH), 6.61−6.66 (2H, m, ArH), 6.73 (1H, s, ArH), 6.78 (1H, dd, J = 8.3, 2.0 Hz, ArH), 7.26−7.35 (6H, m, ArH), 7.41−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5, 12.6, 17.87, 17.93, 18.0, 43.5, 52.5, 55.6, 55.7, 68.8, 70.8, 70.9, 74.0, 75.5, 109.1, 109.5, 113.1, 113.3, 117.5, 118.5, 127.4, 127.8, 128.42, 128.44, 135.07, 135.10, 137.0, 137.1, 147.4, 147.5, 149.3, 178.1; *anal*. C 70.80%, H 8.49%, calcd for $C_{52}H_{74}O_8Si_2$, C 70.71%, H 8.44%.

(2*R*,3*R*)-2-(4-Benzyloxy-3-methoxybenzyl)-3-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-1,4-butanediol (30). To an ice-cooled suspension of $LiAlH_4$ (15 mg, 0.40 mmol) in THF (5 mL) was added a solution of the lactone **26** (0.28 g, 0.39 mmol) in THF (10 mL). After stirring at room temperature for 30 min, saturated aqueous $MgSO_4$ solution and K_2CO_3 were added. The mixture was stirred at room temperature for 30 min and then filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane, 2:3) to give the diol **30** (0.20 g, 0.28 mmol, 72%) as a colorless oil: $[\alpha]^{20}_D$ −42° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95−0.96 (21H, m, *i*-Pr), 1.63 (1H, s, OH), 1.91 (1H, m), 2.25 (1H, m), 2.53 (1H, dd, J = 13.7, 7.8 Hz, C*H*HAr-2), 2.77 (1H, dd, J = 13.7, 8.3 Hz, CH*H*Ar-2), 2.85−3.09 (1H, br, OH), 3.39 (1H, dd, J = 11.2, 5.4 Hz, C*H*HOH), 3.48 (1H, dd, J = 11.0, 4.6 Hz, CH*H*OH), 3.61 (1H dd, J = 11.2, 2.9 Hz, C*H*HOH), 3.80 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.85 (1H, dd, J = 11.0, 5.4 Hz, CH*H*OH), 5.01 (1H, d, J = 6.4 Hz, ArCHOTIPS), 5.11 (2H, s, OCH_2Ph), 5.12 (2H, s, OCH_2Ph), 6.55 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.63 (1H, d, J = 2.0 Hz, ArH), 6.71−6.79 (3H, m, ArH), 6.86 (1H, s, ArH), 7.27−7.37 (6H, m, ArH), 7.42−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5, 18.0, 36.6, 40.2, 50.3, 55.85, 55.93, 59.7, 61.2, 71.1, 71.2, 75.3, 110.7, 112.7, 113.5, 114.2, 119.3, 121.0, 127.3, 127.4, 127.7, 127.8, 128.5, 133.7, 136.2, 137.1, 137.4, 146.5, 147.4, 149.4, 149.6; *anal*. C, 72.13%; H, 8.19%, calcd for $C_{43}H_{58}O_7Si$, C 72.23%, H 8.18%.

(2*R*,3*R*)-2-(4-Benzyloxy-3-methoxybenzyl)-3-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-1,4-butanediol (31): colorless oil; 84% yield; $[\alpha]^{20}_D$ +39° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91−0.98 (21H, m, *i*-Pr), 1.71 (1H, m, H-2 or H-3), 1.80 (1H, m, H-2 or H-3), 2.52 (1H, dd, J = 14.1, 8.3 Hz, ArC*H*H), 2.65 (1H, dd, J = 14.1, 7.1 Hz, ArCH*H*), 2.80 (1H, br s), 3.20 (1H, br s), 3.48 (1H, dd, J = 11.2, 5.4 Hz, HOC*H*H), 3.63 (1H, dd, J = 11.2, 3.4 Hz, HOCH*H*), 3.746 (3H, s, OCH_3), 3.751 (3H, s, OCH_3), 3.89 (1H, dd, J = 11.2, 4.4 Hz, HOC*H*H), 4.05 (1H, dd, J = 11.2, 2.9 Hz, HOCH*H*), 4.99 (1H, d, J = 8.3 Hz, ArCHOTIPS), 5.10 (2H, s, OCH_2Ar), 5.12 (2H, s, OCH_2Ar), 6.40 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.47 (1H, d, J = 1.5 Hz, ArH), 6.63 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.70−6.75 (3H, m, ArH), 7.28−7.37 (6H, m, ArH), 7.41−7.43 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.7, 17.9, 18.1, 36.5, 41.1, 49.7, 55.79, 55.81, 60.0, 62.4, 71.0, 71.1, 77.2, 110.5, 112.7, 113.4, 114.0, 119.8, 120.9, 127.2, 127.3, 127.7, 127.8, 128.5, 133.3, 136.7, 137.1, 137.4, 146.4, 147.5, 149.5, 149.6; HRFABMS *m/z* 737.3868 (calcd for $C_{43}H_{58}O_7SiNa$, 737.3849).

(2*R*,3*R*)-2,3-Bis[(*S*)-(4-Benzyloxy-3-methoxyphenyl)-(triisopropylsilyloxy)methyl]-1,4-butanediol (32). To a solution of the lactone **28** (1.50 g, 1.70 mmol) in CH_2Cl_2 (30 mL) was added DIBAL-H (2.04 mL, 1 M in toluene, 2.04 mmol) at −70 °C. The reaction solution was stirred at −70 °C for 30 min before addition of 6 M aqueous HCl solution. The organic solution was separated, washed with saturated aqueous $NaHCO_3$ solution and brine, and dried (Na_2SO_4). Concentration gave a crude hemiacetal. To a solution of $LiBH_4$ (0.17 g, 7.80 mmol) in THF (10 mL) was added a solution of this hemiacetal in THF (10 mL) at 0 °C. After the reaction solution was stirred at room temperature for 20 h, saturated aqueous NH_4Cl solution was added. The mixture was concentrated, and then the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane, 1:6 and 1:4) gave the diol **32** (0.87 g, 0.98 mmol, 58%) as a colorless oil: $[\alpha]^{20}_D$ −49° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88−0.97 (42H, m, *i*-Pr), 2.35 (2H, m, H-2, H-3), 3.44 (2H, br s, OH), 3.47 (2H, dd, J = 11.0, 6.8 Hz, C*H*HOH), 3.72 (2H, dd, J = 11.0, 4.2 Hz, CH*H*OH), 3.79 (6H, s, OCH_3), 4.92 (2H, d, J = 5.4 Hz, ArCHOSi), 5.09 (2H, d, J = 12.2 Hz, OC*H*HPh), 5.14 (2H, d, J = 12.2 Hz, OCH*H*Ph), 6.56 (2H, d, J = 8.3 Hz, ArH), 6.69 (2H, d, J = 8.3 Hz, ArH), 6.74 (2H, s, ArH), 7.26−7.37 (6H, m, ArH), 7.43−7.45 (4H, m, ArH); ^{13}CNMR ($CDCl_3$, 100 MHz) δ 12.5, 18.0, 46.2, 55.6, 60.4, 70.9, 76.3, 109.9, 113.1, 118.8, 127.4, 127.8, 128.4, 135.9, 137.2, 147.1, 149.2; *anal*. C, 70.54%; H, 8.92%, calcd for $C_{52}H_{78}O_8Si_2$, C 70.39%, H 8.86%.

(2*R*,3*R*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-3-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-1,4-butanediol (33). To a solution of $LiBH_4$ (1.11 g, 51.0 mmol) in THF (15 mL) was added a solution of the lactone **29** (3.00 g, 3.40 mmol) in THF (15 mL) at 0 °C. After the reaction solution was stirred at room temperature for 2 days, saturated aqueous NH_4Cl solution was added. The mixture was concentrated, and then the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane, 1:6 and 1:4) gave the diol **33** (1.95 g, 2.21 mmol, 65%) as a colorless oil: $[\alpha]^{20}_D$ +7.3° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87−0.90 (42H, m, *i*-Pr), 1.86 (1H, m, C*H*CH_2OH), 2.19 (1H, m, C*H*CH_2OH), 2.88 (1H, s, OH), 2.95 (1H, s, OH), 3.41 (1H, dd, J = 10.7, 4.4 Hz, C*H*HOH), 3.46 (1H, dd, J = 11.2, 5.4 Hz, CH*H*OH), 3.62 (1H, dd, J = 10.7, 5.9 Hz, C*H*HOH), 3.78 (1H, dd, J = 11.2, 7.8 Hz, CH*H*OH), 3.81 (6H, s, OCH_3), 4.78 (1H, d, J = 9.3 Hz, ArCHOSi), 4.81 (1H, d, J = 4.9 Hz, ArCHOSi), 5.07−5.15 (4H, m, OCH_2Ph), 6.62−6.67 (2H, m, ArH), 6.73−6.79 (4H, m, ArH), 7.29−7.37 (6H, m, ArH), 7.42−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 12.6, 17.8, 17.9, 18.1, 46.8, 47.4, 55.8, 55.9, 60.3, 60.6, 70.96, 71.01, 77.1, 78.1, 110.6, 113.2, 119.1, 120.0, 127.3, 127.5, 127.8, 128.45, 128.47, 135.2, 136.6, 137.1, 147.4, 147.7, 149.2; *anal*. C 70.33%, H 8.95%, calcd for $C_{52}H_{78}O_8Si_2$, C 70.39%, H 8.86%.

(3*R*,4*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-tetrahydrofuran (34). To an ice-cooled solution of the diol **30** (0.37 g, 0.52 mmol) and pyridine (0.08 mL, 0.99 mmol) in CH_2Cl_2 (20 mL) was added *p*-TsCl (0.10 g, 0.52 mmol). The reaction solution was stirred at room temperature for 21 h before addition of H_2O. The organic solution was separated, washed with 1 M aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and dried (Na_2SO_4). After concentration, the residue was purified by silica gel column chromatography (EtOAc/hexane, 1:4) to give the tetrahydrofuran derivative **34** (0.28 g, 0.40 mmol, 77%) as a colorless oil: $[\alpha]^{20}_D$ −53° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90−0.99 (21H, m, *i*-Pr), 2.32 (1H, m, H-4), 2.48 (1H, dd, J = 12.7, 10.3 Hz, C*H*HAr-3), 2.55 (1H, m, H-3), 2.82 (1H, dd, J = 12.7, 4.4 Hz, CH*H*Ar-3), 3.48−3.54 (2H, m, *H*H-2, *H*H-5), 3.65 (1H, dd, J = 8.6, 6.8 Hz, H*H*-2), 3.71 (1H, dd, J = 8.6, 7.8 Hz,

H*H*-5), 3.86 (6H, s, OCH_3), 4.62 (1H, d, J = 7.3 Hz, ArCHOTIPS), 5.12 (2H, s, OCH_2Ph), 5.13 (2H, s, OCH_2Ar), 6.62 (1H, d, J = 7.3 Hz, ArH), 6.70−6.72 (2H, m, ArH), 6.78−6.80 (2H, m, ArH), 6.97 (1H, s, ArH), 7.27−7.37 (6H, m, ArH), 7.41−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6, 18.0, 18.1, 40.1, 43.3, 54.2, 55.9, 56.0, 69.7, 71.2, 73.0, 76.5, 110.8, 112.7, 113.6, 114.2, 119.4, 120.7, 127.3, 127.4, 127.7, 127.8, 128.5, 134.0, 136.8, 137.1, 137.4, 146.6, 147.6, 149.5, 149.6; HRFABMS *m/z* 719.3736 (calcd for $C_{43}H_{56}O_6SiNa$, 719.3744).

(3*R*,4*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-tetrahydrofuran (35): colorless oil; 62% yield; $[\alpha]^{20}_D$ −6.9° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90−0.98 (21H, m, *i*-Pr), 2.05 (1H, m, H-4), 2.15−2.24 (1H, m, H-3), 2.18 (1H, dd, J = 13.4, 5.6 Hz, ArC*H*H), 2.27 (1H, dd, J = 13.4, 9.5 Hz, ArCH*H*), 3.46 (1H, dd, J = 8.8, 5.4 Hz, *H*H-5), 3.68−3.83 (2H, m, H_2-2), 3.77 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.98 (1H, dd, J = 6.8, 3.4 Hz, H*H*-5), 4.49 (1H, d, J = 7.8 Hz, ArCHOTIPS), 5.09 (2H, s, OCH_2Ar), 5.11 (1H, d, J = 12.2, OC*H*HAr), 5.15 (1H, d, J = 12.2 Hz, OCH*H*Ar), 6.30 (1H, dd, J = 7.8, 2.0 Hz, ArH), 6.36 (1H, d, J = 2.0 Hz, ArH), 6.67 (1H, d, J = 7.8 Hz, ArH), 6.68 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.78 (1H, d, J = 8.3 Hz, ArH), 6.84 (1H, d, J = 2.0 Hz, ArH), 7.25−7.35 (6H, m, ArH), 7.40−7.42 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5, 17.9, 39.5, 43.6, 54.2, 55.77, 55.84, 71.06, 71.08, 71.13, 73.5, 77.2, 110.5, 112.4, 113.4, 114.0, 119.2, 120.4, 127.2, 127.29, 127.34, 127.7, 127.8, 128.4, 133.8, 137.0, 137.2, 137.4, 146.4, 147.5, 149.4, 149.6; *anal*. C 74.10%, H 8.10%, calcd for $C_{43}H_{56}O_6Si$, C 73.82%, H 8.10%.

(3*R*,4*R*)-3,4-Bis[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]tetrahydrofuran (36): colorless oil; 50% yield; $[\alpha]^{20}_D$ −6.1° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94−1.01 (42H, m, *i*-Pr), 2.85 (2H, m, H-3, H-4), 3.50 (2H, dd, J = 9.3, 3.4 Hz, OC*H*H), 3.58 (2H, dd, J = 9.3, 6.8 Hz, OCH*H*), 3.86 (6H, s, OCH_3), 4.51 (2H, d, J = 8.3 Hz, ArCHOSi), 5.13 (4H, s, OCH_2Ph), 6.71 (2H, dd, J = 8.3, 1.5 Hz, ArH), 6.78 (2H, d, J = 8.3 Hz, ArH), 6.95 (2H, d, J = 1.5 Hz, ArH), 7.25−7.37 (6H, m, ArH), 7.42−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5, 18.0, 18.2, 50.2, 55.7, 69.3, 71.0, 76.0, 110.6, 113.2, 119.9, 127.3, 127.8, 128.4, 137.09, 137.14, 147.5, 149.5; *anal*. C 72.00%, H 8.92%, calcd for $C_{52}H_{76}O_7Si_2$, C 71.84%, H 8.81%.

(3*R*,4*R*)-3-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]tetrahydrofuran (37): colorless oil; 52% yield; $[\alpha]^{20}_D$ +13° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87−0.97 (42H, m, *i*-Pr), 2.39−2.47 (2H, m, H-3, H-4), 3.50 (1H, dd, J = 8.8, 6.8, *H*H-2), 3.72−3.74 (2H, m, H*H*-2, *H*H-5), 3.83 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.95 (1H, dd, J = 9.0, 5.1 Hz, H*H*-5), 4.35 (1H, d, J = 6.5 Hz, ArCHOSi-3), 4.67 (1H, d, J = 6.3 Hz, ArCHOSi-4), 5.13 (4H, s, OCH_2Ph), 6.63 (1H, dd, J = 10.3, 1.5 Hz, ArH), 6.67−6.82 (4H, m, ArH), 6.86 (1H, dd, J = 10.3, 1.5 Hz, ArH), 7.28−7.45 (6H, m, ArH), 7.42−7.75 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 12.6, 17.9, 18.0, 18.06, 18.10, 50.3, 50.5, 55.8, 69.7, 70.1, 71.0, 71.1, 76.2, 76.8, 110.4, 111.0, 113.1, 113.4, 119.0, 119.7, 127.34, 127.37, 127.75, 127.80, 128.4, 128.5, 136.3, 137.1, 137.5, 147.4, 147.5, 149.2, 149.4; *anal*. C 71.85%, H 8.93%, calcd for $C_{52}H_{76}O_7Si_2$, C 71.84%, H 8.81%.

(3*R*,4*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]tetrahydrofuran (38). A reaction solution of the silyl ether **34** (0.84 g, 1.21 mmol) and (n-Bu)$_4$NF (1.05 mL, 1 M in THF, 1.05 mmol) in THF (30 mL) was stirred at room temperature for 1 h before addition of saturated aqueous NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration and silica gel column chromatography (EtOAc/benzene, 3:7) gave the benzyl alcohol **38** (0.50 g, 0.92 mmol, 76%) as colorless crystals: mp 124 °C; $[\alpha]^{20}_D$ −47° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.05 (1H, br s, OH), 2.29 (1H, m, H-4), 2.52 (1H, dd, J = 13.2, 9.5 Hz, C*H*HAr-3), 2.59 (1H, m, H-3), 2.78 (1H, dd, J = 13.2, 5.4 Hz, CH*H*Ar-3), 3.49−3.52 (2H, m, *H*H-2, *H*H-5), 3.69 (1H, dd, J = 9.3, 7.3 Hz, H*H*-2), 3.83−3.86 (1H, m, H*H*-5), 3.84 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.52 (1H, d, J = 7.8 Hz, ArC*H*OH), 5.11 (2H, s, OCH_2-Ph), 5.13 (2H, s, OCH_2Ar), 6.59 (1H, d, J = 8.3 Hz, ArH), 6.67 (1H, d, J = 1.5 Hz, ArH), 6.71−6.87 (4H, m, ArH), 7.25−7.36 (6H, m, ArH), 7.41−7.45 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.9, 43.5, 52.0, 55.9, 70.5, 71.0, 71.1, 73.5, 76.3, 109.9, 112.7, 113.8, 114.2, 118.5, 120.7, 127.2, 127.7, 127.8, 128.4, 128.5, 133.8, 136.3, 137.0, 137.3, 146.5, 147.7, 149.5, 149.7; HRFABMS *m/z* 563.2413 (calcd for $C_{34}H_{36}O_6Na$, 563.2409).

(3*R*,4*R*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-[(*R*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]tetrahydrofuran (39): colorless crystals; mp 128 °C (EtOH); 87% yield; $[\alpha]^{20}_D$ −14° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03−2.12 (2H, m, H-4, OH), 2.18−2.23 (1H, m, H-3), 2.20 (1H, dd, J = 13.7, 6.3 Hz, ArC*H*H), 2.35 (1H, dd, J = 13.7, 8.8 Hz, ArCH*H*), 3.44 (1H, dd, J = 8.8, 5.9 Hz, *H*H-2), 3.76 (3H, s, OCH_3), 3.80−3.84 (1H, m, *H*H-5), 3.82 (3H, s, OCH_3), 3.92−3.99 (2H, m, H*H*-2, H*H*-5), 4.35 (1H, dd, J = 8.3, 2.5 Hz, ArC*H*OH), 5.08 (2H, s, OCH_2Ar), 5.11 (1H, d, J = 12.3, OC*H*HAr), 5.14 (1H, d, J = 12.3 Hz, OCH*H*Ar), 6.33 (1H, d, J = 8.3 Hz, ArH), 6.37 (1H, s, ArH), 6.67−6.69 (2H, m, ArH), 6.79−6.80 (2H, m, ArH), 7.25−7.35 (6H, m, ArH), 7.40−7.41 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.3, 43.8, 52.0, 55.8, 55.9, 70.8, 71.0, 71.1, 73.5, 76.4, 110.0, 112.5, 113.8, 114.1, 118.7, 120.4, 127.21, 127.23, 127.4, 127.7, 127.8, 128.4, 128.5, 133.5, 136.4, 137.0, 137.3, 146.5, 147.8, 149.5, 149.9; HRFABMS *m/z* 541.2592 (calcd for $C_{34}H_{37}O_6$, 541.2591).

(3*R*,4*R*)-Bis[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]tetrahydrofuran (40): colorless crystals; mp 148−150 °C; 100% yield; $[\alpha]^{20}_D$ −11° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.55 (2H, m, H-3, H-4), 3.31 (2H, dd, J = 8.2, 6.8 Hz, OC*H*H), 3.48 (2H, dd, J = 8.2, 7.8 Hz, OCH*H*), 3.88 (6H, s, OCH_3), 4.35 (2H, d, J = 9.3 Hz, ArC*H*OH), 4.40 (2H, s, OH), 5.13 (4H, s, OCH_2Ph), 6.74 (2H, d, J = 8.3 Hz, ArH), 6.81 (2H, d, J = 8.3 Hz, ArH), 6.90 (2H, s, ArH), 7.25−7.37 (6H, m, ArH), 7.42−7.44 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 52.6, 56.0, 71.0, 71.7, 76.8, 110.0, 113.7, 119.0, 127.2, 127.8, 128.5, 136.0, 137.0, 148.0, 149.9; HRFABMS *m/z* 557.2537 (calcd for $C_{34}H_{37}O_7$, 557.2539).

(3*R*,4*R*)-3-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-4-[(*R*)-(4-benzyloxy-3-methoxyphenyl)-(hydroxy)methyl]tetrahydrofuran (41): colorless oil; 70% yield; $[\alpha]^{20}_D$ −12° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.38 (1H, m, H-3), 2.62 (1H, m, H-4), 3.21 (1H, brs, OH), 3.37−3.48 (1H, br, OH), 3.39 (1H, dd, J = 9.3, 5.9 Hz, *H*H-2), 3.46 (1H, dd, J = 9.3, 8.3 Hz, H*H*-2), 3.72 (1H, dd, J = 8.0, 6.8 Hz, *H*H-5), 3.79 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.86 (1H, dd, J = 8.0, 7.8 Hz, H*H*-5), 4.36 (1H, d, J = 7.8 Hz, ArC*H*OH-4), 4.55 (1H, br s, ArC*H*OH-3), 5.06−5.13 (4H, m, OCH_2Ph), 6.62 (1H, d, J = 6.8 Hz, ArH), 6.64 (1H, d, J = 9.8 Hz, ArH), 6.67−6.79 (3H, m, ArH), 6.85 (1H, d, J = 1.5 Hz, ArH), 7.25−7.35 (6H, m, ArH), 7.39−7.42 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.1, 49.5, 55.8, 55.9, 70.4, 70.87, 70.91, 70.95, 74.0, 76.1, 109.8, 110.3, 113.4, 113.6, 118.4, 118.9, 127.19, 127.22, 127.8, 128.4, 135.4, 135.8, 136.97, 136.99, 147.5, 147.6, 149.4, 149.5; *anal*. C 73.17%, H 6.65%, calcd for $C_{34}H_{36}O_7$, C 73.36%, H 6.52%.

(3*R*,4*R*)-3-(4-Benzyloxy-3-methoxybenzoyl)-4-(4-benzyloxy-3-methoxybenzyl)tetrahydrofuran (42). A reaction mixture of the benzyl alcohol **38** (0.10 g, 0.18 mmol), PCC (47 mg, 0.22 mmol), and MS 4A (10 mg) in CH_2Cl_2 (10 mL) was stirred at room temperature for 16 h before addition of dry diethyl ether (20 mL). After filtration, the filtrate was concentrated. The residue was subjected to silica gel column chromatography (EtOAc/hexane, 1:2) to give the ketone **42** (90 mg, 0.17 mmol, 94%) as a colorless oil: $[\alpha]^{20}_D$ −17° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.71 (2H, d, J = 7.8 Hz, ArCH_2CH), 3.01 (1H, m, H-4), 3.65 (1H, dd, J = 8.8, 5.9 Hz, *H*H-2), 3.72 (1H, m, H-3), 3.78 (3H, s, OCH_3), 3.88 (1H, dd, J = 8.3, 6.3 Hz, *H*H-5), 3.90 (3H, s, OCH_3), 3.94 (1H, dd, J = 8.8, 6.8 Hz, H*H*-2), 4.19 (1H, dd, J = 8.3, 8.3 Hz, H*H*-5), 5.07 (2H, s, OCH_2Ph), 5.20 (2H, s, OCH_2Ph), 6.60 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.66 (1H, d, J = 2.0 Hz, ArH), 6.73 (1H, d, J = 8.3 Hz, ArH), 6.80 (1H, d, J = 8.3 Hz, ArH), 7.20 (1H, dd, J = 8.3, 2.0 Hz, ArH), 7.25−7.45 (11H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.7, 45.0, 51.5, 55.8, 56.0, 70.7, 71.0, 71.1, 73.2,

110.8, 111.9, 112.5, 114.1, 120.9, 122.6, 127.1, 127.2, 127.4, 127.7, 128.1, 128.4, 128.5, 128.6, 130.0, 132.9, 136.1, 137.2, 146.7, 149.58, 149.62, 152.6, 198.0; HRFABMS *m/z* 539.2441 (calcd for $C_{34}H_{35}O_6$, 539.2433).

(3*R*,4*R*)-3,4-Bis(4-benzyloxy-3-methoxybenzoyl)tetrahydrofuran (43): colorless crystals; mp 134−136 °C (EtOAc); 78% yield; $[\alpha]^{20}_D$ +12° (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.92 (6H, s, OCH_3), 3.92−3.97 (2H, m, H-3, H-4), 4.27 (2H, dd, *J* = 8.3, 7.8 Hz, OC*H*H), 4.59 (2H, dd, *J* = 5.4, 5.4 Hz, OCH*H*), 5.21 (4H, s, OCH_2Ph), 6.89 (2H, d, *J* = 8.3 Hz, ArH), 7.26−7.42 (10H, m, ArH), 7.49−7.54 (4H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.2, 56.0, 70.8, 72.0, 111.0, 112.2, 123.2, 127.2, 128.1, 128.7, 129.4, 136.1, 149.6, 152.9, 197.1; *anal*. C 73.50%, H 5.56%, calcd for $C_{32}H_{32}O_7$, C 73.89%, H 5.84%.

(2*R*,3*R*)-2,3-Bis(4-hydroxy-3-methoxybenzyl)-4-butanolide (Matairesinol) (1). A reaction mixture of the benzyl alcohols **22** and **23** (1.40 g, 2.52 mmol) and $Pd(OH)_2$ (1.2 g) in EtOAc (10 mL) was stirred at ambient temperature for 22 h under H_2 gas. After filtration, the filtrate was concentrated. The residue was subjected to silica gel column chromatography (EtOAc/hexane, 1:1) to give matairesinol (**1**) (0.57 g, 1.59 mmol, 63%) as a colorless oil: $[\alpha]^{20}_D$ −61° (*c* 0.3, $CHCl_3$) {lit.[9] $[\alpha]^{20}_D$ −42.2° (*c* 1, acetone)}. NMR data were in agreement with reported data.[10] Benzyl alcohol (0.64 g, 1.78 mmol, 37%) was recovered.

(3*R*,4*R*)-3,4-Bis(4-hydroxy-3-methoxybenzyl)tetrahydrofuran (2): 78% yield; colorless crystals; mp 107−109 °C; $[\alpha]^{20}_D$ −43° (*c* 1.0, THF) {lit.[11] mp 105−107 °C; $[\alpha]^{20}_D$ −43° (*c* 0.9, THF)}. NMR data were in agreement with reported data.

(3*R*,4*R*)-4-[(*S*)-(Hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]-3-(4-hydoxy-3-methoxybenzyl)tetrahydrofuran (3). A reaction mixture of the benzyl ether **38** (95 mg, 0.18 mmol) and 5% Pd/C (20 mg) in EtOAc (10 mL) was stirred under H_2 gas at ambient temperature for 2 h before filtration. The filtrate was concentrated, and then the residue was subjected to silica gel column chromatography (EtOAc/hexane, 3:2) to give the *trans* isomer, **3** (43 mg, 0.12 mmol, 67%), as a colorless oil: $[\alpha]^{20}_D$ −49° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.97 (1H, br s, OH), 2.30 (1H, m, H-4), 2.54 (1H, dd, *J* = 12.2, 8.8 Hz, C*H*HAr-3), 2.52−2.44 (1H, m, H-3), 2.78 (1H, dd, *J* = 12.2, 5.4 Hz, CH*H*Ar-3), 3.51−3.56 (2H, m, *H*H-2, *H*H-5), 3,72 (1H, dd, *J* = 9.3, 7.3 Hz, H*H*-2), 3.85 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.88 (1H, dd, *J* = 9.3, 8.8 Hz, H*H*-5), 4.54 (1H, d, *J* = 7.8 Hz, ArC*H*OH), 5.49 (1H, s, ArOH), 5.59 (1H, s, ArOH), 6.59 (1H, d, *J* = 1.5 Hz, ArH), 6.62 (1H, d, *J* = 8.3 Hz, ArH), 6.77−6.81 (3H, m, ArH), 6.85 (1H, d, *J* = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.0, 43.6, 51.9, 55.8, 55.9, 70.6, 73.6, 76.5, 108.6, 111.2, 114.1, 119.1, 121.4, 128.3, 132.4, 135.1, 143.9, 145.3, 146.4, 146.6; EIMS *m/z* 360 [M^+] (21), 342 ($M^+ - H_2O$, 8), 208 [M^+ − (4-HO-3-$CH_3OC_6H_3$)C(OH)H, 5], 153 [(4-HO-3-$CH_3OC_6H_3$)C(OH)H, 100], 137 [(4-HO-3-$MeOC_6H_3$)CH_2, 32]; HREIMS *m/z* 360.1562 (calcd for $C_{20}H_{24}O_6$, 360.1570).

(3*R*,4*R*)-4-[(*R*)-(Hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]-3-(4-hydoxy-3-methoxybenzyl)tetrahydrofuran (4): colorless oil; 92% yield; $[\alpha]^{20}_D$ −41° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.96 (1H, s, OH), 2.06 (1H, m, H-4), 2.19−2.25 (1H, m, H-3), 2.23 (1H, dd, *J* = 13.4, 7.6 Hz, ArC*H*H), 2.40 (1H, dd, *J* = 13.4, 8.1 Hz, ArCH*H*), 3.48 (1H, dd, *J* = 8.5, 5.1 Hz, *H*H-2), 3.74 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.87 (1H, dd, *J* = 7.8, 7.8 Hz, *H*H-5), 3.95−4.03 (2H, m, H*H*-2, H*H*-5), 4.36 (1H, d, *J* = 8.8 Hz, ArC*H*OH), 5.47 (1H, s, ArOH), 5.63 (1H, s, ArOH), 6.23 (1H, s, ArH), 6.41 (1H, d, *J* = 7.3 Hz, ArH), 6.67 (1H, s, ArH), 6.68−6.73 (2H, m, ArH), 6.84 (1H, d, *J* = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.6, 43.9, 51.8, 55.6, 55.7, 70.8, 73.5, 76.6, 108.4, 110.9, 113.7, 113.9, 119.8, 121.3, 132.1, 135.2, 143.8, 145.4, 146.3, 146.8; EIMS *m/z* 361 [M^+ + 1] (100), 360 [M^+] (95), 343 (M^+ − OH, 5), 208 [M^+ − (4-HO-3-$MeOC_6H_3$)C(OH)H, 23], 153 [(4-HO-3-$MeOC_6H_3$)C(OH)H, 82], 137 [(4-HO-3-$MeOC_6H_3$)CH_2, 93]; HREIMS *m/z* 360.1566 (calcd for $C_{20}H_{24}O_6$, 360.1572).

(3*R*,4*R*)-3,4-Bis[(*S*)-(Hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofuran (7): colorless crystals; mp 184−186 °C; 84% yield; $[\alpha]^{20}_D$ −18° (*c* 0.7, C_5H_5N); ^{1}H NMR (C_5D_5N, 400 MHz) δ 3.11 (2H, m, H-3, H-4), 3.77 (6H, s, OCH_3), 3.78 (2H, dd, *J* = 8.8, 7.3 Hz, OC*H*H), 3.88 (2H, dd, *J* = 8.8, 7.3 Hz, OCH*H*), 4.90 (2H, d, *J* = 8.8 Hz, ArC*H*OH), 5.01 (2H, br s, OH), 7.20 (2H, dd, *J* = 7.8, 2.0 Hz, ArH), 7.26 (2H, d, *J* = 7.8 Hz, ArH), 7.41 (2H, d, *J* = 2.0 Hz, ArH), 7.87 (2H, br s, OH); ^{13}C NMR (C_5D_5N, 100 MHz) δ 53.7, 55.9, 72.2, 77.0, 111.3, 116.2, 120.5, 136.4, 147.8, 148.7; EIMS *m/z* 376 [M^+] (7), 358 ($M^+ - H_2O$, 15), 340 ($M^+ - 2H_2O$, 32), 279 ($M^+ - 2OCH_3$ − 2OH, 8), 259 ($M^+ - 3H_2O - 2OCH_3$ − H, 29), 206 [$M^+ - H_2O$ − (4-HO-3-$CH_3OC_6H_3$)C(H)OH, 48], 153 [(4-HO-3-$CH_3OC_6H_3$)C(H)OH, 100]; HREIMS *m/z* 376.1524 (calcd for $C_{20}H_{24}O_7$, 376.1522).

(3*R*,4*R*)-3-[(*S*)-(Hydroxy)(4-hydroxy-3-methoxyphenyl)methyl]-4-[(*R*)-(hydroxy)(4-hydroxy-3-methoxyphenyl)-methyl]tetrahydrofuran (8): colorless crystals; mp 150−152 °C; 80% yield; $[\alpha]^{20}_D$ −11° (*c* 0.5, C_5H_5N); ^{1}H NMR (C_5D_5N, 400 MHz) δ 3.23 (1H, m, H-3), 3.35 (1H, m, H-4), 3.68 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 4.02 (1H, dd, *J* = 8.5, 5.6 Hz, *H*H-5), 4.09 (1H, dd, *J* = 15.4, 7.6 Hz, *H*H-2), 4.23 (1H, dd, *J* = 15.4, 8.1 Hz, H*H*-2), 4.54 (1H, dd, *J* = 8.5, 6.1 Hz, H*H*-5), 4.95 (1H, d, *J* = 7.8 Hz, ArC*H*OH-4), 5.01 (2H, br s, OH), 5.38 (1H, d, *J* = 5.4 Hz, ArC*H*OH-3), 7.05 (1H, br s, OH), 7.16−7.30 (6H, m, ArH, OH), 7.47 (1H, d, *J* = 1.5 Hz, ArH); ^{13}C NMR (C_5D_5N, 100 MHz) δ 50.1, 51.1, 55.7, 55.8, 70.3, 71.4, 74.1, 76.0, 111.1, 111.2, 116.0, 120.0, 120.2, 136.8, 137.1, 147.0, 147.3, 148.47, 148.49; EIMS *m/z* 376 [M^+] (19), 358 ($M^+ - H_2O$, 49), 340 ($M^+ - 2H_2O$, 62), 279 ($M^+ - 2OCH_3 - 2OH$, 16), 259 ($M^+ - 3H_2O - 2OCH_3$ − H, 85), 206 [$M^+ - H_2O$ − (4-HO-3-$CH_3OC_6H_3$)C(H)OH, 99], 153 [(4-HO-3-$CH_3OC_6H_3$)C(H)OH, 100], 137 [(4-HO-3-$CH_3OC_6H_3$)CH_2, 58]; HREIMS *m/z* 376.1524 (calcd for $C_{20}H_{24}O_7$, 376.1522).

(3*R*,4*R*)-3-(4-Hydroxy-3-methoxybenzoyl)-4-(4-hydroxy-3-methoxybenzyl)tetrahydrofuran (6): colorless oil; 66% yield; $[\alpha]^{20}_D$ +5.0° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.72 (2H, d, *J* = 8.3 Hz, $ArCH_2$-4), 3.00 (1H, m, H-4), 3.67 (1H, dd, *J* = 8.3, 5.4 Hz, *H*H-2), 3.72−3.80 (1H, m, H-3), 3.79 (3H, s, OCH_3), 3.89−3.93 (1H, m, *H*H-5), 3.92 (3H, s, OCH_3), 3 95 (1H, dd, *J* = 8.3, 6.8 Hz, H*H*-2), 4.22 (1H, dd, *J* = 8.3, 8.3 Hz, H*H*-5), 5.53 (1H, s, OH), 6.18 (1H, s, OH), 6.62 (1H, s, ArH), 6.64 (1H, d, *J* = 8.3 Hz, ArH), 6.78 (1H, d, *J* = 8.3 Hz, ArH), 6.87 (1H, d, *J* = 8.3 Hz, ArH), 7.23 (1H, dd, *J* = 8.3, 2.0 Hz, ArH), 7.42 (1H, d, *J* = 2.0 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 38.8, 45.3, 51.4, 55.8, 56.0, 71.1, 73.2, 110.1, 111.3, 113.7, 114.3, 121.6, 123.5, 129.6, 131.6, 144.1, 146.5, 146.8, 150.6, 198.1; EIMS *m/z* 358 [M^+] (67), 222 [M^+ − (4-HO-3-$CH_3OC_6H_3$)CH_2, 5], 163 [(4-HO-3-$CH_3OC_6H_3$)C(=O)C, 69], 151 [(4-HO-3-$CH_3OC_6H_3$)C=O, 100]; HREIMS *m/z* 358.1417 (calcd for $C_{20}H_{22}O_6$, 358.1416).

(3*R*,4*R*)-3,4-Bis(4-hydroxy-3-methoxybenzoyl)tetrahydrofuran (9): colorless crystals; mp 168−169 °C; 100% yield; $[\alpha]^{20}_D$ +69° (*c* 0.4, C_5H_5N); ^{1}H NMR (C_5D_5N, 400 MHz) δ 3.74 (6H, s, OCH_3), 4.28 (2H, dd, *J* = 8.3, 5.9 Hz, H-3, H-4), 4.54 (2H, dd, *J* = 8.3, 7.8 Hz, OC*H*H), 5.01−5.05 (4H, m, OCH*H*, OH), 7.20 (2H, d, *J* = 8.3 Hz, ArH), 7.84 (2H, dd, *J* = 8.3, 2.4 Hz, ArH), 7.88 (2H, d, *J* = 2.4 Hz, ArH); ^{13}C NMR (C_5D_5N, 100 MHz) δ 49.9, 55.7, 72.3, 112.1, 116.2, 124.6, 128.6, 148.7, 154.0, 197.2; EIMS *m/z* 372 [M^+] (5), 220 [M^+ − (4-HO-3-$CH_3OC_6H_3$)C=O, 10], 194 [(4-HO-3-$CH_3OC_6H_3$)(C=O)$CHCH_2O$, 27], 151 [(4-HO-3-$CH_3OC_6H_3$)C=O, 100], 123 [(4-HO-3-$CH_3OC_6H_3$), 11]; MREIMS *m/z* 372.1208 (calcd for $C_{20}H_{20}O_7$, 372.1209).

(4*S*)-4-Benzyl-3-{(*R*)-2-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-4-pentenoyl}-2-oxazolidinone (45). A reaction mixture of the acylated oxazolidinone **44** (7.62 g, 29.4 mmol), 4-benzyloxy-3-methoxybenzaldehyde (8.54 g, 35.2 mmol), $MgCl_2$ (2.80 g, 29.4 mmol), Et_3N (8.20 mL, 58.8 mmol), and Me_3SiCl (5.60 mL, 44.1 mmol) in EtOAc (100 mL) was stirred at room temperature for 16 h before filtration through silica gel with diethyl ether. After the filtrate was concentrated, the residue was dissolved in MeOH (100 mL), and then a few drops of CF_3CO_2H were added. The reaction mixture was stirred at room temperature for 1 h. After addition of a few drops of Et_3N, the mixture was concentrated. The residue was recrystallized from EtOH to give the *anti*-aldol product **45** (14.7 g, 29.3 mmol, 99%) as colorless crystals: mp 124 °C; $[\alpha]^{20}_D$ −5.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.33 (1H, m, CH_2=CH−C*H*H), 2.45 (1H, m,

CH_2═CH−CH*H*), 2.56 (1H, dd, J = 13.7, 9.3 Hz, ArC*H*H), 3.11 (1H, dd, J = 13.7, 3.4 Hz, ArCH*H*), 3.19 (1H, d, J = 7.8 Hz, OH), 3.90 (3H, s, OCH_3), 4.06−4.14 (2H, m, H_2-5), 4.56 (1H, m, O═CCH), 4.63 (1H, m, H-4), 4.81 (1H, dd, J = 7.8, 7.3 Hz, ArC*H*OH), 4.98−5.07 (2H, m, CH_2═CH), 5.12 (2H, s, $ArCH_2O$), 5.74 (1H, m, CH_2═C*H*), 6.85 (1H, d, J = 8.3 Hz, ArH), 6.90 (1H, d, J = 8.3 Hz, ArH), 7.02 (1H, s, ArH), 7.09−7.11 (2H, m, ArH), 7.25−7.34 (6H, m, ArH), 7.40−7.42 (2H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 34.3, 37.5, 48.7, 55.3, 56.0, 65.8, 71.0, 75.5, 109.8, 113.7, 117.4, 118.6, 127.2, 127.3, 127.8, 128.5, 128.9, 129.4, 134.5, 135.1, 135.3, 137.0, 147.8, 149.8, 153.5, 175.5; *anal*. C, 71.97%, H 6.20%, N 2.64%, calcd for $C_{30}H_{31}O_6N$, C 71.84%, H 6.23%, N 2.79%.

(4*S*)-4-Benzyl-3-{(*R*)-2-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-pentenoyl}-2-oxazolidinone (46). To an ice-cooled solution of the alcohol **45** (5.47 g, 10.9 mmol) and 2,6-lutidine (2.54 mL, 21.8 mmol) in CH_2Cl_2 (60 mL) was added TIPSOTf (5.00 mL, 14.9 mmol). The resulting solution was stirred on an ice-bath for 1.5 h before addition of saturated aqueous $NaHCO_3$ solution. The organic solution was separated, washed with saturated aqueous $CuSO_4$ solution and brine, and dried (Na_2SO_4). After concentration, the residue was recrystallized from MeOH to give the silyl ether **46** (5.57 g, 8.47 mmol, 78%) as colorless crystals: mp 115 °C; $[\alpha]^{20}_D$ −27° (c 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.91−0.99 (21H, m, i-Pr), 1.90 (1H, m, CH_2═CH−C*H*H), 2.13 (1H, m, CH_2═CH−CH*H*), 2.61 (1H, dd, J = 11.2, 3.2 Hz, ArC*H*H), 3.53 (1H, dd, J = 13.2, 2.9 Hz, ArCH*H*), 3.92 (3H, s, OCH_3), 4.06 (1H, dd, J = 8.8, 8.8 Hz, *H*H-5), 4.11 (1H, dd, J = 8.8, 2.4 Hz, H*H*-5), 4.54 (1H, m, O═CCH), 4.60 (1H, m, H-4), 4.87−4.94 (2H, m, CH_2═CH), 5.04 (1H, d, J = 8.8 Hz, ArC*H*OH), 5.14 (2H, s, $ArCH_2O$), 5.57 (1H, m, CH_2═C*H*), 6.82 (2H, s, ArH), 7.08 (1H, s, ArH), 7.25−7.30 (5H, m, ArH), 7.33−7.37 (3H, m, ArH), 7.42−7.44 (2H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 12.6, 17.9, 18.1, 34.3, 38.4, 51.4, 56.0, 65.9, 71.0, 111.0, 113.3, 116.8, 120.1, 127.2, 127.3, 127.8, 128.4, 128.9, 129.3, 134.9, 135.5, 135.9, 137.0, 147.9, 149.7, 153.4, 174.6; *anal*. C 71.32%, H 8.10%, N 2.10%, calcd for $C_{39}H_{51}O_6NSi$, C 71.20%, H 7.81%, N 2.13%.

(2*S*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-penten-1-ol (47). To an ice-cooled solution of $LiBH_4$ (2.79 g, 0.13 mol) and MeOH (5.36 mL, 0.13 mol) in THF (150 mL) was added a solution of the acyl oxazolidinone **46** (36.3 g, 55.2 mmol) in THF (200 mL). The reaction solution was stirred at room temperature for 16 h before addition of saturated aqueous NH_4Cl solution. After concentration, the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration and subsequent silica gel column chromatography (EtOAc/hexane, 1:9) gave the alcohol **47** (16.2 g, 33.4 mmol, 61%) as a colorless oil: $[\alpha]^{20}_D$ −45° (c 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.96−1.02 (21H, m, i-Pr), 1.83−1.96 (2H, m, H-2, OH), 2.18 (1H, m, CH_2═CH−C*H*H), 2.65 (1H, m, CH_2═CH−CH*H*), 3.58 (1H, m, *H*H-1), 3.79 (1H, m, H*H*-1), 3.88 (3H, s, OCH_3), 4.85 (1H, d, J = 5.4 Hz, ArCHOTIPS), 4.98−5.14 (2H, m, CH_2═CH), 5.14 (2H, s, $ArCH_2O$), 5.73 (1H, m, CH_2═C*H*), 6.57 (1H, dd, J = 8.3, 1.5 Hz, ArH), 6.82 (1H, d, J = 8.3 Hz, ArH), 6.95 (1H, d, J = 1.5 Hz, ArH), 7.28−7.31 (1H, m, ArH), 7.34−7.37 (2H, m, ArH), 7.42−7.44 (2H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 12.5, 17.9, 18.0, 32.4, 48.4, 55.9, 63.1, 71.1, 78.3, 110.5, 113.4, 116.4, 119.2, 127.3, 127.8, 128.5, 136.5, 136.8, 137.1, 147.5, 149.5; *anal*. C 72.03%, H 9.12%, calcd for $C_{29}H_{44}O_4Si$, C 71.85%, H 9.15%.

(2*S*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-4-pentenyl pivaloate (48). To an ice-cooled solution of the alcohol **47** (16.2 g, 33.4 mmol) and pyridine (5.41 mL, 66.9 mmol) in CH_2Cl_2 (20 mL) was added PivCl (5.41 mL, 43.9 mmol). After the reaction mixture was stirred at room temperature for 2 h, EtOAc and H_2O were added. The organic solution was separated, washed with 6 M aqueous HCl solution and brine, and dried (Na_2SO_4). Concentration and silica gel column chromatography (5% EtOAc in hexane) gave the pivaloyl ester **48** (19.1 g, 33.5 mmol, 100%) as a colorless oil: $[\alpha]^{20}_D$ −8.9° (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96−1.01 (21H, m, i-Pr), 1.23 (9H, s, t-Bu), 1.54 (1H, m, H-4), 2.21 (1H, m, *H*H-3), 2.36 (1H, m, H*H*-3), 3.81 (1H, dd, J = 11.2, 8.3 Hz, pivOC*H*H), 3.86 (3H, s, OCH_3), 4.16 (1H, dd, J = 11.2, 4.4 Hz, pivOC*H*H), 4.91−4.98 (3H, m, H_2-1, H-5), 5.13 (2H, s, $ArCH_2O$), 5.72 (1H, m, H-2), 6.69 (1H, dd, J = 8.3, 2.0 Hz, ArH), 6.81 (1H, d, J = 8.3 Hz, ArH), 6.89 (1H, d, J = 2.0 Hz, ArH), 7.26−7.38 (3H, m, ArH), 7.43−7.45 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 18.0, 18.1, 27.3, 30.2, 38.8, 45.8, 55.9, 63.9, 71.1, 73.9, 110.8, 113.4, 116.4, 119.3, 127.4, 127.8, 128.5, 135.0, 136.6, 137.2, 147.4, 149.3, 178.2; *anal*. C 71.89%, H 9.37%, calcd for $C_{34}H_{52}O_5Si$, C 71.79%, H 9.21%.

(2*S*)-2-[(*S*)-(4-Benzyloxy-3-methoxyphenyl)(triisopropylsilyloxy)methyl]-3-formylpropyl pivaloate (49). A reaction mixture of the olefin **48** (14.5 g, 25.5 mmol), NMO (3.69 g, 31.5 mmol), and OsO_4 (2 mL, 2% aqueous solution) in acetone (150 mL), t-BuOH (40 mL), and H_2O (40 mL) was stirred at room temperature for 16 h under N_2 gas in the dark. After addition of $Na_2S_2O_3$, the mixture was filtered. The filtrate was concentrated, and then the residue was dissolved in H_2O and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was dissolved in MeOH (100 mL). To this solution was added $NaIO_4$ (6.25 g, 29.2 mmol), and then the reaction mixture was stirred at room temperature for 1 h before concentration. The residue was dissolved in H_2O and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc/hexane, 1:8) to give the aldehyde **49** (13.6 g, 21.9 mmol, 86%) as a colorless oil: $[\alpha]^{20}_D$ −9.5° (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95−1.01 (21H, m, i-Pr), 1.22 (9H, s, t-Bu), 2.05 (1H, ddd, J = 16.6, 6.1, 1.0 Hz, *H*H-2), 2.50 (1H, ddd, J = 16.6, 6.6, 2.7 Hz, H*H*-2), 2.89 (1H, m, H-3), 3.88 (3H, s, OCH_3), 3.88 (1H, dd, J = 11.2, 8.3 Hz, pivOC*H*H), 3.98 (1H, dd, J = 11.2, 5.9 Hz, pivOCH*H*), 4.97 (1H, d, J = 5.4 Hz, ArCHOTIPS), 5.13 (2H, s, $ArCH_2O$), 6.66 (1H, dd, J = 8.3, 1.5 Hz, ArH), 6.82 (1H, d, J = 8.3 Hz, ArH), 6.87 (1H, d, J = 1.5 Hz, ArH), 7.26−7.38 (3H, m, ArH), 7.42−7.44 (2H, m, ArH), 9.73 (1H, dd, J = 2.7, 1.0 Hz, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 17.9, 18.0, 27.2, 38.8, 41.1, 41.3, 55.9, 64.4, 71.1, 73.9, 110.7, 113.4, 119.2, 127.3, 127.8, 128.5, 133.6, 137.0, 147.7, 149.5, 178.0, 200.9; *anal*. C 69.51%, H 8.65%, calcd for $C_{37}H_{50}O_6Si$, C 69.43%, H 8.83%.

(3*S*,4*S*)-4-(4-Benzyloxy-3-methoxyphenyl)-3-pivaloyloxymethyl-4-butanolide (50). To an ice-cooled solution of the silyl ether **49** (12.3 g, 19.9 mmol) in THF (80 mL) was added (n-Bu)$_4$NF (22.2 mL, 1 M in THF, 22.2 mmol). After the reaction solution was stirred in an ice-bath for 1 h, saturated aqueous NH_4Cl solution was added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was subjected to silica gel column chromatography (EtOAc/hexane, 1:2) to give a hemiacetal (7.76 g, 18.8 mmol, 94%) as a colorless oil. A reaction mixture of this hemiacetal (7.76 g, 18.8 mmol), PCC (4.62 g, 21.4 mmol), and MS 4A (0.3 g) in CH_2Cl_2 (40 mL) was stirred at room temperature for 16 h before addition of dry diethyl ether. After the mixture was filtered, the filtrate was concentrated. The residue was subjected to silica gel column chromatography (EtOAc/hexane, 1:4) to give the lactone **50** (6.78 g, 16.4 mmol, 82%) as colorless crystals: mp 94 °C (i-Pr_2O); $[\alpha]^{20}_D$ −34° (c 1.1, CHCl); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (9H, s, t-Bu), 2.57 (1H, dd, J = 17.3, 4.2 Hz, *H*H-2), 2.82 (1H, dd, J = 17.3, 8.5 Hz, H*H*-2), 3.04 (1H, m, H-3), 3.64 (1H, dd, J = 11.5, 6.6 Hz, pivOC*H*H), 3.86 (1H, dd, J = 11.5, 5.4 Hz, pivOCH*H*), 3.87 (3H, s, OCH_3), 5.13 (2H, s, $ArCH_2O$), 5.62 (1H, d, J = 6.8 Hz, H-4), 6.75 (1H, dd, J = 7.8, 2.0 Hz, ArH), 6.81 (1H, d, J = 2.0 Hz, ArH), 6.88 (1H, d, J = 7.8 Hz, ArH), 7.27−7.38 (3H, m, ArH), 7.42−7.44 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.0, 32.5, 38.6, 39.3, 56.1, 62.7, 71.0, 82.0, 109.0, 114.0, 117.6, 127.2, 127.86, 127.89, 128.5, 136.8, 148.3, 149.9, 175.6, 177.9; *anal*. C 69.94%, H 6.95%, calcd for $C_{24}H_{28}O_6$, C 69.88%, H 6.84%.

(2*S*,3*S*,4*S*)-4-(4-Benzyloxy-3-methoxyphenyl)-2-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]-3-pivaloyloxymethyl-4-butanolide (51). To a solution of KHMDS (64.7 mL, 0.5 M in toluene, 32.4 mmol) in THF (150 mL) was

added a solution of the lactone **50** (8.90 g, 21.6 mmol) in THF (80 mL) at −75 °C. After stirring at −75 °C for 15 min, a solution of 4-benzyloxy-3-methoxybenzaldehyde (6.27 g, 25.9 mmol) in THF (40 mL) was added. The reaction solution was stirred at −75 °C for 1 h before addition of saturated aqueous NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration and silica gel column chromatography (10% EtOAc in hexane) gave the *erythro* aldol product **51** (12.1 g, 18.5 mmol, 86%) as a colorless oil: $[\alpha]^{20}_D$ −48° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (9H, s, *t*-Bu), 2.72−2.89 (1H, br, OH), 2.91 (1H, dd, J = 3.9, 3.4 Hz, H-2), 3.08 (1H, m, H-3), 3.46−3.50 (2H, m, pivOCH_2), 3.86 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 5.11 (2H, s, ArCH_2O), 5.13 (2H, s, ArCH_2O), 5.40 (1H, d, J = 2.9 Hz, ArC*H*OH), 5.70 (1H, d, J = 7.3 Hz, H-4), 6.72 (1H, d, J = 8.3 Hz, ArH), 6.76 (1H, s, ArH), 6.84 (1H, d, J = 8.3 Hz, ArH), 6.88−6.91 (2H, m, ArH), 6.96 (1H, s, ArH), 7.16−7.18 (1H, m, ArH), 7.23−7.42 (9H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 26.9, 38.5, 39.3, 51.7, 56.1, 56.2, 62.8, 71.1, 72.8, 82.1, 109.2, 114.0, 114.1, 117.5, 117.9, 125.3, 127.2, 127.3, 127.9, 128,2, 128.4, 128.5, 129.0, 134.1, 136.8, 136.9, 148.0, 148.2, 149.8, 150.0, 177.3, 177.8; *anal*. C 71.63%, H 6.50%, calcd for $C_{39}H_{42}O_9$, C 71.54%, H 6.47%.

(2*R*,3*S*,4*S*)-2-(4-Benzyloxy-3-methoxybenzyl)-4-(4-benzyloxy-3-methoxyphenyl)-3-pivaloyloxymethyl-4-butanolide (52). To a solution of the aldol product **51** (12.1 g, 18.5 mmol) and Et_3SiH (11.8 mL, 73.9 mmol) in CH_2Cl_2 (550 mL) was added $BF_3{\cdot}OEt_2$ (1.17 mL, 9.23 mmol) at 3 °C. After the reaction solution was stirred at 3 °C for 2 h, saturated aqueous $NaHCO_3$ solution was added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). The solvent was concentrated, and then the residue was applied to silica gel column chromatography (6% EtOAc in toluene) to give the benzyl lactone **52** (6.68 g, 10.5 mmol, 57%) as colorless crystals: mp 108 °C (*i*-Pr_2O), $[\alpha]^{20}_D$ +30 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.09 (9H, s, *t*-Bu), 2.79 (1H, m, H-3), 2.87 (1H, m, H-2), 3.02 (1H, dd, J = 14.2, 4.9 Hz, ArC*H*H), 3.08 (1H, dd, J = 14.2, 6.8 Hz, ArCH*H*), 3.62 (1H, dd, J = 11.5, 6.4 Hz, pivOC*H*H), 3.77 (1H, dd, J = 11.5, 5.9 Hz, pivOCH*H*), 3.86 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 5.13 (4H, s, PhCH_2O), 5.32 (1H, d, J = 6.8 Hz, 4-H), 6.66 (1H, d, J = 8.3 Hz, ArH), 6.72−6.75 (2H, m, ArH), 6.82−6.85 (3H, m, ArH), 7.26−7.41 (10H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.1, 29.7, 34.8, 38.7, 42.9, 44.4, 56.1, 56.2, 62.5, 71.1, 80.5, 109.3, 113.0, 114.0, 114.3, 117.9, 121.4, 127.2, 127.3, 127.8, 127.9, 128.1, 128.5, 128.6, 130.2, 136.8, 137.1, 147.4, 148.3, 149.9, 177.7, 177.8; *anal*. C 73.56%, H 6.69%, calcd for $C_{39}H_{42}O_8$, C 73.33%, H 6.63%.

(3*R*,4*S*)-3-(4-Benzyloxy-3-methoxybenzyl)-4-[(*S*)-(4-benzyloxy-3-methoxyphenyl)(hydroxy)methyl]tetrahydrofuran (53). To an ice-cooled suspension of $LiAlH_4$ (0.18 g, 4.74 mmol) in THF (10 mL) was added a solution of the lactone **52** (1.53 g, 2.40 mmol) in THF (10 mL). After stirring at room temperature for 30 min, saturated aqueous $MgSO_4$ solution and K_2CO_3 were added. On stirring further at room temperature for 30 min, the mixture was filtered, and then the filtrate was concentrated. To an ice-cooled suspension of NaH (0.12 g, 60% oil suspension, 3.00 mmol) in THF (10 mL) was added the residue in THF (10 mL). After stirring at −20 °C for 30 min, *N*-TsIm (0.62 g, 2.79 mmol) in THF (20 mL) was added. On stirring at −20 °C for 24 h, saturated aqueous NH_4Cl solution and EtOAc were added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc/hexane, 1:3) to give the tetrahydrofuran derivative **53** (0.79 g, 1.47 mmol, 31%) as a colorless oil: $[\alpha]^{20}_D$ −2.7° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04 (1H, d, J = 2.0 Hz, OH), 2.30 (1H, m, H-4), 2.55 (1H, dd, J = 13.7, 11.2 Hz, ArC*H*H), 2.71 (1H, m, H-3), 2.80 (1H, dd, J = 13.7, 4.4 Hz, ArCH*H*), 3.66−3.70 (2H, m, *H*H-2, *H*H-5), 3.80 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 3.98 (1H, dd, J = 8.8, 7.3 Hz, H*H*-2), 4.01 (1H, dd, J = 8.8, 7.3 Hz, H*H*-5), 4.81 (1H, dd, J = 7.3, 2.0 Hz, ArC*H*OH), 5.09 (2H, s, PhCH_2O), 5.14 (2H, s, PhCH_2O), 6.49 (1H, d, J = 8.3 Hz, ArH), 6.54 (1H, s, ArH), 6.74 (1H, d, J = 8.3 Hz, ArH), 6.83 (1H, d, J = 8.3 Hz, ArH), 6.87 (1H, d, J = 8.3 Hz, ArH), 6.95 (1H, s, ArH), 7.25−7.44 (10H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.9, 43.0, 48.8, 55.9, 56.0, 70.0, 71.0, 71.1, 72.5, 73.5, 109.9, 112.5, 113.8, 114.2, 118.5, 120.5, 127.2, 127.69, 127.72, 127.8, 128.45, 128.52, 133.8, 135.5, 136.6, 137.0, 137.2, 146.4, 147.8, 149.5, 149.9; HRFABMS *m/z* 540.2506 (calcd for $C_{34}H_{36}O_6$, 540.2512).

(2a*S*,3*R*,8a*R*)-5-Benzyloxy-3-(4-benzyloxy-3-methoxyphenyl)-6-methoxy-2,2a,8,8a-tetrahydronaphthalene-[2,3-*c*]tetrahydrofuran (54). The tetrahydrofuran derivative **53** (0.30 g, 0.55 mmol) was stood at room temperature for 48 h before application to a silica gel column (10% EtOAc in hexane). The compound **54** (0.29 g, 0.55 mmol, 100%) was obtained as colorless crystals: mp 133−134 °C; $[\alpha]^{20}_D$ +14° (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.52 (1H, dd, J = 13.4, 9.8 Hz, *H*H-8), 2.55−2.70 (2H, m, H-2a, H-8a), 2.85 (1H, dd, J = 13.4, 5.1 Hz, H*H*-8), 3.49−3.53 (1H, dd, *H*H-9), 3.52 (1H, d, J = 9.3 Hz, H-3), 3.63 (1H, dd, J = 8.8, 4.9 Hz, *H*H-2), 3.75−3.79 (1H, dd, H*H*-2), 3.77 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.00 (1H, dd, J = 8.3, 6.8 Hz, H*H*-9), 4.89 (2H, s, PhCH_2O), 5.20 (2H, s, PhCH_2O), 6.22 (1H, s, ArH), 6.62 (1H, d, J = 8.3 Hz, ArH), 6.65 (1H, s, ArH), 6.73 (1H, s, ArH), 6.87 (1H, d, J = 8.3 Hz, ArH), 7.18−7.25 (5H, m, ArH), 7.29−7.32 (1H, m, ArH), 7.36−7.40 (2H, m, ArH), 7.49−7.51 (2H, m, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.2, 39.2, 46.0, 47.2, 55.9, 56.2, 71.1 × 2, 73.6, 74.7, 111.5, 112.6, 113.7, 114.0, 121.0, 127.28, 127.30, 127.6, 127.9, 128.3, 128.6, 130.5, 133.6, 134.7, 137.2, 137.3, 146.2, 146.9, 147.8, 149.7; HRFABMS *m/z* 523.2482 (calcd for $C_{34}H_{34}O_5$, 523.2484).

(2a*S*,3*S*,8a*R*)-5-Hydroxy-3-(4-hydroxy-3-methoxyphenyl)-6-methoxy-2,2a,8,8a-tetrahydronaphthalene[2,3-*c*]tetrahydrofuran (5): colorless crystals; mp 175−176 °C; 100% yield, $[\alpha]^{20}_D$ −9.7° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.54 (1H, dd, J = 13.4, 9.8 Hz, *H*H-8), 2.61 (1H, m, H-2a), 2.71 (1H, m, H-8a), 2.85 (1H, dd, J = 13.4, 5.1 Hz, H*H*-8), 3.55 (1H, dd, J = 9.0, 4.4 Hz, *H*H-9), 3.56 (1H, d, J = 9.3 Hz, H-3), 3.64 (1H, dd, J = 8.8, 4.9 Hz, *H*H-2), 3.80 (1H, dd, J = 9.0, 7.1 Hz, H*H*-9), 3.85 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.02 (1H, dd, J = 8.8, 6.8 Hz, H*H*-2), 5.44 (1H, s, ArOH), 5.60 (1H, s, ArOH), 6.31 (1H, s, ArH), 6.71 (1H, s, ArH), 6.72−6.73 (2H, m, ArH), 6.90 (1H, d, J = 8.8 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 32.4, 39.3, 46.0, 47.3, 55.9, 56.1, 73.6, 74.7, 110.2, 111.5, 113.6, 114.5, 121.8, 129.4, 133.4, 134.6, 143.7, 144.4, 144.7, 146.7; FABMS *m/z* 342 [M^+] (25), 136 [(4-HO-3-MeOC_6H_3)CH_2, 100]; HRFABMS *m/z* 342.1472 (calcd for $C_{26}H_{22}O_5$, 342.1468).

Antioxidant Activity of Compounds 1−9 in a Tween 20 Micelle System. The method of Masuda et al.[18] was slightly modified. To 160 μL of the DMSO solution of a test sample (5.0 mM) were added freshly purified ethyl linoleate (139 μL) and 0.3 M Tween 20−0.05 M phosphate buffer (pH 7.4, 8 mL). The mixture was stirred vigorously using a vortex mixer for 2 min and then sonicated in a bath sonicator (Branson model 2210) for 3 min to give a clear micelle solution. Two milliliters of this micelle solution was put into a straight vial (35 mm diameter; 75 mm height), and 100 μL of 0.2 M AAPH aqueous solution was added to the solution. After stirring again with the vortex mixer, the vial was incubated at 37 °C in the dark while continuously shaking (82 shakes/min; Taitec P-11 water bath shaker). After 3 h of incubation, a 20 μL aliquot was taken from the solution and poured into 380 μL of a methanolic solution of trolox (0.2 mM). Ten microliters of the diluted solution was injected into the HPLC instrument to analyze ethyl linoleate hydroperoxide under the following conditions: column, YMC-Pack ODS-A (4.6 × 150 mm); solvent, CH_3CN/H_2O = 9:1; flow rate, 1.0 mL/min; detection, 234 nm. The concentration of the hydroperoxide was calculated from the peak area obtained by the following equation: $Y = 2.29X \times 10^{-6} - 4.38 \times 10^{-4}$, where Y is the concentration of ethyl linoleate hydroperoxide (mM) and X is the peak area of hydroperoxide.

Measurement for Antiradical Activity Using DPPH (1,1-Diphenyl-2-picrylhydrazyl).[19] To the appropriate amount of sample in methanol solution (4.9 mL) was added 100 μL of 5 mM DPPH in methanol solution. After the solution stood at 25 °C for 0.5 h, the absorbance at 517 nm was measured. The

antiradical activity was evaluated from the decreased value of 517 nm absorption, which was calculated by the following equation: decrease of absorbance = (absorbance of DPPH solution) − (absorbance of DPPH solution + sample solution) + (absorbance of sample solution).

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Supporting Information Available: ^{1}H NMR spectra of compounds **1**−**9** are available free of charge via the Internet at http://pubs.acs.org.

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