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Total Syntheses of the Metabolites of Schizandrin

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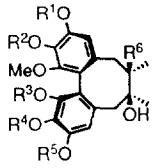
Abstract: The total syntheses of the metabolites of schizandrin were achieved. The tetracyclic lactone intermediates (**13a-e**) were prepared in optically pure form by the oxidative coupling reaction of the corresponding 3-benzyl-2-benzylidenebutyrolactones. Mukaiyama hydration of **13b** afforded hydroxylactone (**14**), which was converted into SZ-M3 (**4**). The introduction of C6,7-diol moiety, which is common to the metabolites (**4-11**), was carried out by the successive double bond migration to **15a-e**, lactone ring reduction to the allylic diols (**32a-e**), and glycol formation. Then, reduction of the mesylates **33** completed the syntheses of the metabolites.

Schizandrin (**1**) is the major lignan component of the fruits of *Schisandra chinensis* Bail. (Schisandraceae),[1] and pharmacologically **1** shows a restorative effect on functional depression of brain.[2] By the study of the metabolisms of **1** *in vitro*[3a] and *in vivo*[3b] by several groups, the metabolic transformations have been found to cause the demethylation of aromatic methyl ether and/or hydroxylation of eight membered ring affording the variety of metabolites (SZ-M1 (**2**), SZ-M2 (**3**), SZ-M3 (**4**), M_1 (**5**), SZ-M4 (M_{2b}) (**6**), SZ-M5 (**7**), SZ-MD2 (**8**), SZ-M7 (M_{2a}) (**9**), SZ-M8 (**10**), and SZ-M10 (**11**)). In this paper we report the total syntheses of the representative eight metabolites (SZ-M3 (**4**), M_1 (**5**), SZ-M4 (M_{2b}) (**6**), SZ-M5 (**7**), SZ-MD2 (**8**), SZ-M7 (M_{2a}) (**9**), SZ-M8 (**10**), and SZ-M10 (**11**)) in optically pure form.[4b,5]



1: R^1=R^2=R^3=R^4=R^5=Me, R^6=H; schizandrin
2: R^1=H, R^2=R^3=R^4=R^5=Me, R^6=H; SZ-M1
3: R^2=H, R^1=R^3=R^4=R^5=Me, R^6=H; SZ-M2
4: R^4=H, R^1=R^2=R^3=R^5=Me, R^6=H; SZ-M3
5: R^1=R^2=R^3=R^4=R^5=Me, R^6=OH; M_1
6: R^4=H, R^1=R^2=R^3=R^5=Me, R^6=OH; SZ-M4 (M_{2b})
7: R^1=H, R^2=R^3=R^4=R^5=Me, R^6=OH; SZ-M5
8: R^2=H, R^1=R^3=R^4=R^5=Me, R^6=OH; SZ-MD2
9: R^5=H, R^1=R^2=R^3=R^4=Me, R^6=OH; SZ-M7 (M_{2a})
10: R^4=R^5=H, R^1=R^2=R^3=Me, R^6=OH; SZ-M8
11: R^3=R^4=H, R^1=R^2=R^5=Me, R^6=OH; SZ-M10

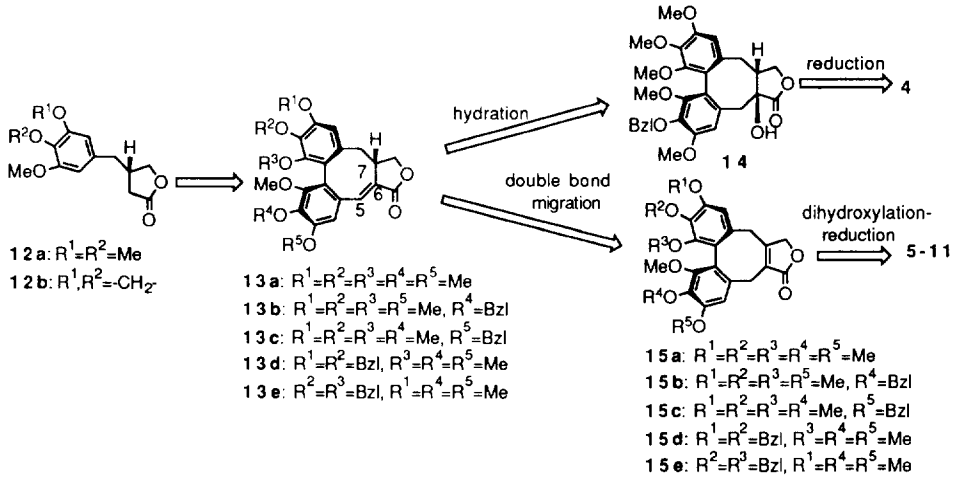
The syntheses were planned based on the strategy which was utilized for the syntheses of racemic deoxyschizandrin[5f] and wide variety of homochiral dibenzocyclooctene lignans.[4b,5g,j,k,n,o,q] In this strategy, the homochiral tetracyclic lactones (**13a-e**) were used as the key intermediates, and by the hydration or the successive double bond migration and dihydroxylation, C6-hydroxy group or C6,7-dihydroxyl groups were introduced as shown in Scheme 1.

The Syntheses of the Tetracyclic Key Intermediates

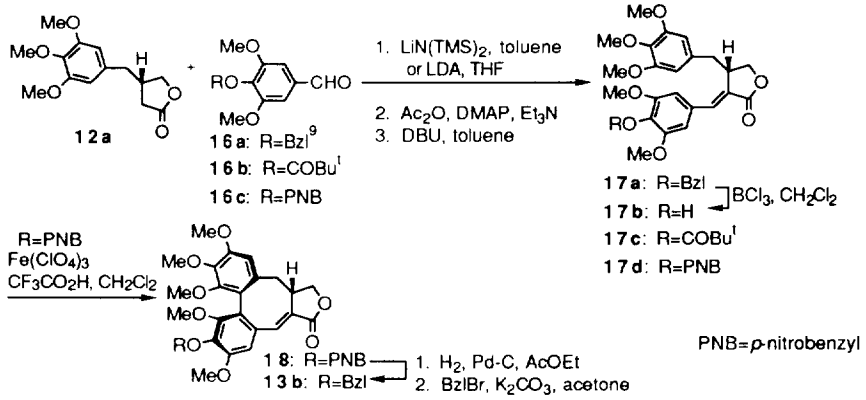
Total syntheses started with the preparation of the optically pure key tetracyclic lactones (**13a-e**) from the readily available optically pure benzylbutyrolactones (**12a, 12b**).[5j,n,6,7] Among **13a-e**, the syntheses of **13a** and **13d** had been already reported.[4b,5j,n] Thus, the intermediates for the syntheses of **5** and **10** were already in our hands. The syntheses of the other tetracyclic lactones (**13b, c, e**) will be discussed below.

13b was the intermediate required for the syntheses of SZ-M3 (**4**), SZ-M4 (**6**), and SZ-MD2 (**8**). At first, the synthesis of **13b** was attempted by the oxidative coupling of benzyl ether **17a** with the iron(III) perchlorate-trifluoroacetic acid condition (Scheme 2).[8] However, the reaction did not afford the desired product

at all. The failure of the attempt was probably due to the acid catalyzed debenzylation of **17a**. The oxidative coupling of the phenolic compound **17b** also failed. The undesired removal of the protecting group of the phenolic hydroxyl group was again observed with the acyl protected substrate **17c** providing no trace of the desired product. This problem was overcome by the introduction of the acid stable *p*-nitrobenzyl protecting group. Aldol condensation of **12a** with **16c** followed by the dehydration afforded **17d**, which was subjected to the iron(III) perchlorate mediated oxidative coupling reaction providing the lactone **18** without the deprotection of *p*-nitrobenzyl group. Thus, the exchange of the protecting group provided **13b**.



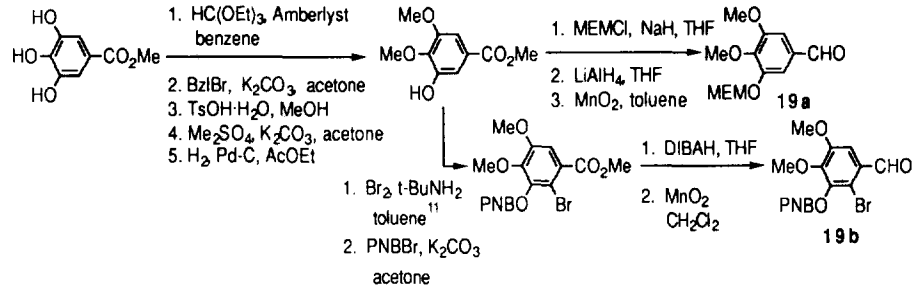
Scheme 1. Strategy for the synthesis of the metabolites of schizandrin



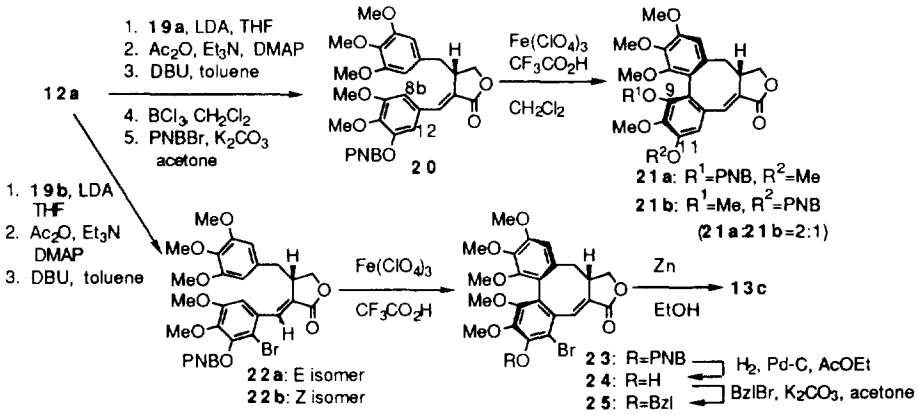
Scheme 2. The synthesis of the tetracyclic intermediate **13b**.

For the synthesis of **13c** (the intermediate for SZ-M5 (7) and SZ-M7 (**9**)) and **13e** (the intermediate for SZ-M10 (**11**)), the regioselectivity of the oxidative coupling was the major concern. The oxidative coupling reaction of *p*-nitrobenzyl ether **20** was attempted at first (Scheme 4). Aldol condensation of **12a** with **19a** (Scheme 3) followed by the exchange of methoxyethoxymethyl group to *p*-nitrobenzyl group provided **20** (Scheme 4). The oxidative coupling reaction of **20** with iron(III) perchlorate proceeded in 85% yield, however, provided the undesired 9-nitrobenzyloxy isomer (**21a**) preferentially over 11-nitrobenzyloxy isomer (**21b**) in the ratio of 2:1 (Scheme 4).[15] The observed regioselectivity could be understood as shown in Scheme 5.[10] At

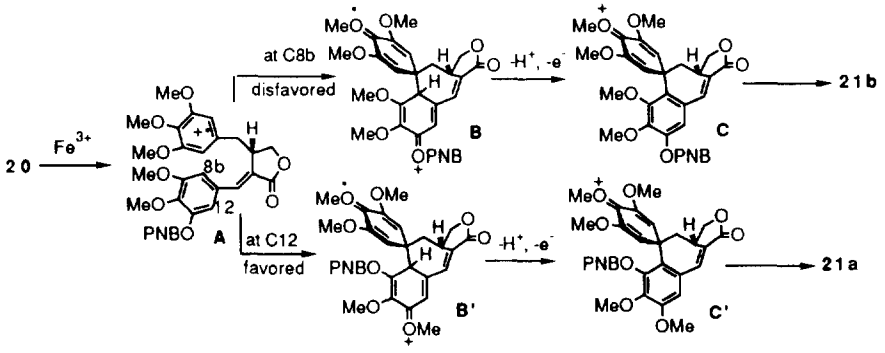
the first stage of the oxidative coupling reaction, the electrophilic intramolecular aromatic substitution with initially formed cation radical (**A**) took place at C8b or C12 position affording the intermediates **B** or **B'**, respectively. Because of the presence of the electron withdrawing *p*-nitrobenzyl group on the cationic oxygen, **B** could be expected to be less stable relative to **B'** providing the undesired isomer (**21a**) as the major product.



Scheme 3. The synthesis of the aldehydes **19a** and **19b**.



Scheme 4. The regiocontroled synthesis of the tetracyclic intermediate **13c**.

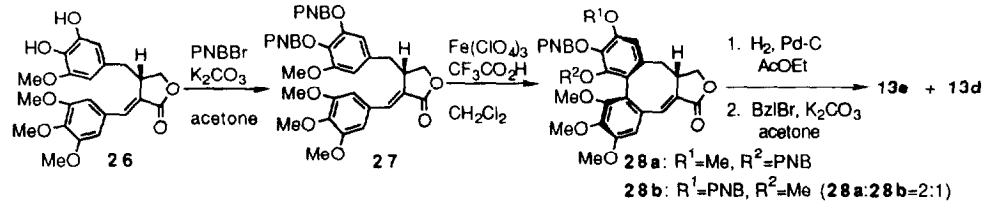


Scheme 5. The mechanistic explanation for the regioselectivity of the oxidative coupling of **20**.

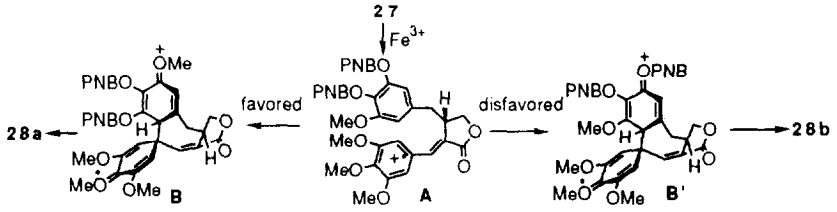
The control of the regioselectivity for the production of the desired 11-nitrobenzyloxy isomer was achieved by the introduction of bromine atom preventing the participation of the C12 position during the

oxidative coupling reaction. The bromoaldehyde (**19b**) was prepared from methyl gallate in 9 steps (Scheme 3). Aldol condensation and dehydration of **19b** with **12a** afforded two isomeric products, in which the compound with *E* configuration (**22a**) was the major product. Although **22b** with *Z* configuration did not react with iron(III) perchlorate at all, **22a** afforded **23** in 55% yield on the treatment with iron(III) perchlorate in trifluoroacetic acid.[12] *p*-Nitrobenzyl protecting group was exchanged to benzyl group (**25**), and then bromine atom was removed by zinc reduction of **25** in ethanol providing **13c** in 88% yield from **23** (Scheme 4).

For the synthesis of **13e**, the oxidative coupling of **27** was carried out (Scheme 6). The known catechol (**26**)[5j,n,8] was *p*-nitrobenzylated to **27** in 87% yield and **27** was treated with iron(III) perchlorate in a usual manner. The regioselectivity of this reaction favored the formation of the desired isomer (**28a**) over the compound (**28b**) in the ratio of 2:1 (the ratio was determined based on the peak area ratio of the characteristic peaks of the NMR spectrum of the isomeric mixture). The regioselectivity observed here would be explained again by the relative stability of the intermediates, **B** and **B'** (Scheme 7).[10] Then, the coupled products mixture was converted into benzyl ethers and separated into **13e** and the aforementioned **13d**[4b] completing the preparation of the key tetracyclic lactones.



Scheme 6. The regioselective synthesis of the tetracyclic intermediate **13e**.



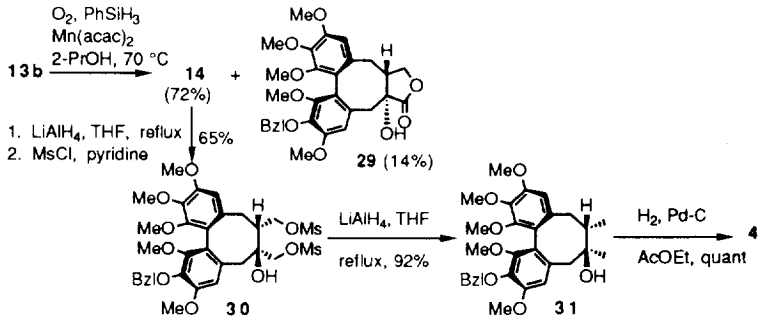
Scheme 7. The mechanistic explanation for the regioselectivity of the oxidative coupling of **27**.

The Syntheses of the metabolites

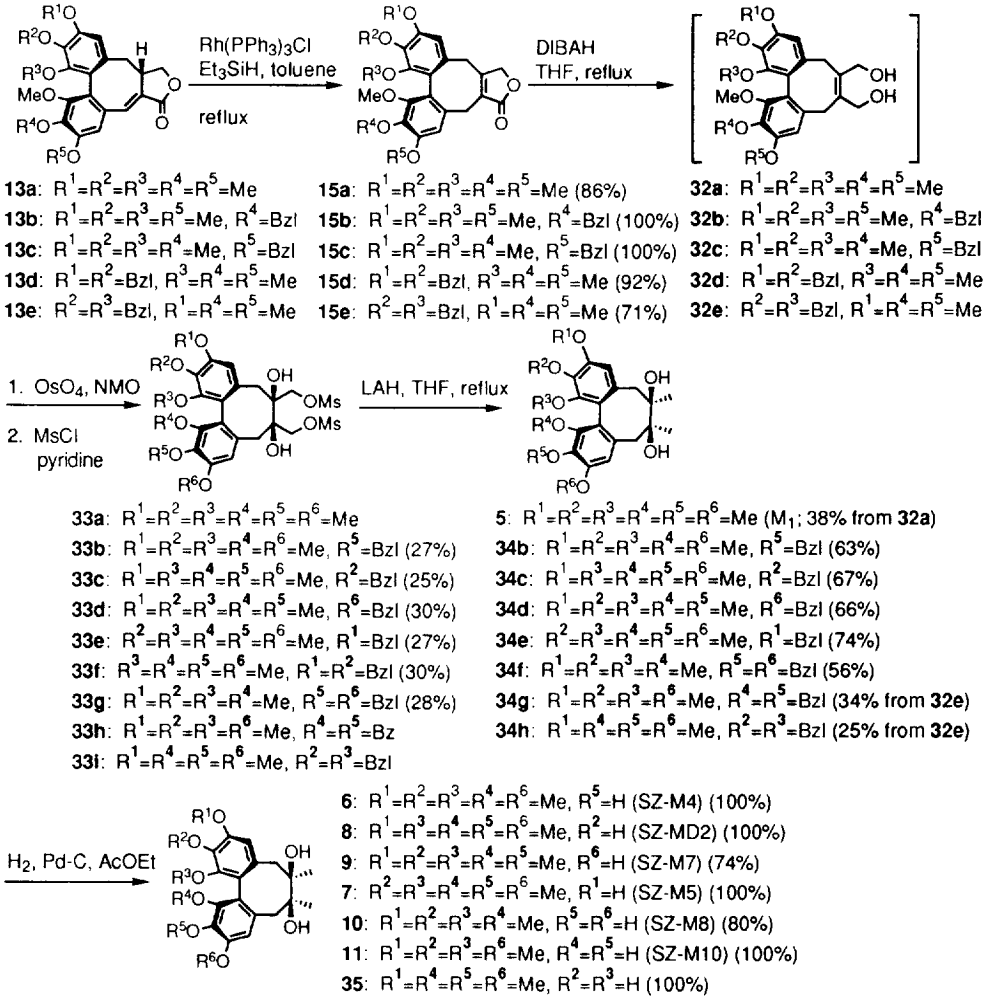
With the tetracyclic intermediates (**13a-e**) in hand, the transformation of them to the metabolites were achieved according to the methodology reported in the total synthesis of the metabolites of gomisin A.[4b] The introduction of hydroxyl group at C13a position of **13b** for the synthesis of SZ-M3 (**4**) was carried out utilizing the Mukaiyama hydration reaction providing **14** and **29** in 72% and 14% yields, respectively (Scheme 8).[13,16] The reduction of lactone ring of **14** to dimethyl groups afforded benzyl ether of SZ-M3 (**31**), which was debenzylated to complete the total synthesis of **4**. The physical data of synthetic **4** were completely identical with those of SZ-M3 which was obtained from rat.[3b]

For the syntheses of M_1 (**5**), SZ-M4 (**6**), SZ-M5 (**7**), SZ-MD2 (**8**), SZ-M7 (**9**), SZ-M8 (**10**), and SZ-M10 (**11**), the lactones (**13a-e**) were isomerized to the corresponding butenolides (**15a-e**) in 71-100% yield by the rhodium complex-triethylsilane catalyzed reaction developed by our group (Scheme 9).[14]

15a-e were reduced to the corresponding allylic diols (**32a-e**), which were treated with osmium tetroxide followed by the methanesulfonylation to the mesylates in the nonstereoselective manners (**32b** to **33b** and **33c**, **32c** to **33d** and **33e**, **32d** to **33f** and **33g**, and **32e** to **33h** and **33i**). Since **32a** has the axis of C2 symmetry, the product (**33a**) of this treatment was obtained as a single isomer.



Scheme 8. The total synthesis of **4**.



13a: R^1=R^2=R^3=R^4=R^5=Me
13b: R^1=R^2=R^3=R^5=Me, R^4=Bzl
13c: R^1=R^2=R^3=R^4=Me, R^5=Bzl
13d: R^1=R^2=Bzl, R^3=R^4=R^5=Me
13e: R^2=R^3=Bzl, R^1=R^4=R^5=Me

15a: R^1=R^2=R^3=R^4=R^5=Me (86%)
15b: R^1=R^2=R^3=R^5=Me, R^4=Bzl (100%)
15c: R^1=R^2=R^3=R^4=Me, R^5=Bzl (100%)
15d: R^1=R^2=Bzl, R^3=R^4=R^5=Me (92%)
15e: R^2=R^3=Bzl, R^1=R^4=R^5=Me (71%)

32a: R^1=R^2=R^3=R^4=R^5=Me
32b: R^1=R^2=R^3=R^5=Me, R^4=Bzl
32c: R^1=R^2=R^3=R^4=Me, R^5=Bzl
32d: R^1=R^2=Bzl, R^3=R^4=R^5=Me
32e: R^2=R^3=Bzl, R^1=R^4=R^5=Me

33a: R^1=R^2=R^3=R^4=R^5=R^6=Me
33b: R^1=R^2=R^3=R^4=R^6=Me, R^5=Bzl (27%)
33c: R^1=R^3=R^4=R^5=R^6=Me, R^2=Bzl (25%)
33d: R^1=R^2=R^3=R^4=R^5=Me, R^6=Bzl (30%)
33e: R^2=R^3=R^4=R^5=R^6=Me, R^1=Bzl (27%)
33f: R^3=R^4=R^5=R^6=Me, R^1=R^2=Bzl (30%)
33g: R^1=R^2=R^3=R^4=Me, R^5=R^6=Bzl (28%)
33h: R^1=R^2=R^3=R^6=Me, R^4=R^5=Bz
33i: R^1=R^4=R^5=R^6=Me, R^2=R^3=Bzl

5: R^1=R^2=R^3=R^4=R^5=R^6=Me (M_1; 38% from **32a**)
34b: R^1=R^2=R^3=R^4=R^6=Me, R^5=Bzl (63%)
34c: R^1=R^3=R^4=R^5=R^6=Me, R^2=Bzl (67%)
34d: R^1=R^2=R^3=R^4=R^5=Me, R^6=Bzl (66%)
34e: R^2=R^3=R^4=R^5=R^6=Me, R^1=Bzl (74%)
34f: R^1=R^2=R^3=R^4=Me, R^5=R^6=Bzl (56%)
34g: R^1=R^2=R^3=R^6=Me, R^4=R^5=Bzl (34% from **32e**)
34h: R^1=R^4=R^5=R^6=Me, R^2=R^3=Bzl (25% from **32e**)

6: R^1=R^2=R^3=R^4=R^6=Me, R^5=H (SZ-M4) (100%)
8: R^1=R^3=R^4=R^5=R^6=Me, R^2=H (SZ-MD2) (100%)
9: R^1=R^2=R^3=R^4=R^5=Me, R^6=H (SZ-M7) (74%)
7: R^2=R^3=R^4=R^5=R^6=Me, R^1=H (SZ-M5) (100%)
10: R^1=R^2=R^3=R^4=Me, R^5=R^6=H (SZ-M8) (80%)
11: R^1=R^2=R^3=R^6=Me, R^4=R^5=H (SZ-M10) (100%)
35: R^1=R^4=R^5=R^6=Me, R^2=R^3=H (100%)

Scheme 9. The total syntheses of **5**, **6**, **7**, **8**, **9**, **10**, and **11**.

Finally, the reductive removal of mesyloxy group of **33a** finished the synthesis of M_1 (**5**) (38% from **32a**). Similarly, the reductive removal of mesyloxy group and benzyl group of **33b**, **33c**, **33d**, **33e**, and **33g** provided SZ-M4 (**6**) (63%), SZ-MD2 (**8**) (67%), SZ-M7 (**9**) (49%), SZ-M5 (**7**) (74%), and SZ-M8 (**10**) (45%), respectively. The mixture of **33h** and **33i** was reduced with lithium aluminum hydride at first, and then the products were separated by chromatography affording **34g** and **34h** in the yield of 34% and 25% from **32e**, respectively . On catalytic debenzylation, each isomer afforded SZ-M10 (**11**) (100%) and its isomer (**35**) (100%). The physical data of the synthetic metabolites (**5**-**11**) of **1** were identical with those of the naturally derived materials.[3b]

Experimental[18]

(*S*)-3-(3,4,5-Trimethoxybenzyl)butanolide (12a). A solution of $Rh(COD)_2BF_4$ (550 mg, 1.34 mmol) and (*R,R*)-MOD-DIOP[6] (1.12 g, 1.55 mmol) in freshly distilled MeOH (500 ml) was stirred under argon at room temperature for 10 min. The resultant solution was added to a solution of (*E*)-3-methoxycarbonyl-4-(3,4,5-trimethoxyphenyl)but-3-enoic acid[5f] (257 g, 0.83 mol) and Et_3N (115 ml, 0.80 mol) in freshly distilled MeOH (1 l). The resultant solution was stirred at room temperature under a hydrogen atmosphere for 42 h. 0.5N NaOH was added, and the mixture was extracted with CH_2Cl_2. The aqueous layer was made acidic with 6N HCl and extracted with CH_2Cl_2. The combined extracts from the acidic solution were dried over $MgSO_4$. After evaporation of the solvent, (*S*)-3-methoxycarbonyl-4-(3,4,5-trimethoxyphenyl)butanoic acid was obtained as a pale yellow oil (250 g). A mixture of (*S*)-3-methoxycarbonyl-4-(3,4,5-trimethoxy-phenyl)butanoic acid (250 g), KOH (85%, 52.5 g, 0.80 mmol), $CaCl_2$ (100 g, 0.90 mol), and $NaBH_4$ (68 g, 1.8 mol) in EtOH (2.7 l) was stirred at 0 °C for 12 h. The reaction was quenched with 6N HCl and extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and evaporated to afford **12a** as a colorless solid (201 g, 91% from (*E*)-3-methoxycarbonyl-4-(3,4,5-trimethoxyphenyl)but-3-enoic acid). mp 101.5-103 °C (colorless prisms from AcOEt). $[\alpha]_D^{25}$ -8.50° (c 1.13, $CHCl_3$). NMR δ: 2.31 (1H, dd, J = 7, 17 Hz), 2.63 (1H, dd, J = 8, 17 Hz), 2.71 (2H, d, J = 9 Hz), 2.79-2.94 (1H, m), 3.84 (3H, s), 3.85 (6H, s), 4.06 (1H, dd, J = 6, 9 Hz), 4.36 (1H, dd, J = 7, 9 Hz), 6.36 (2H, s). IR (KBr): 1766, 1592 cm^{-1}. MS m/z: 266 (M^+). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.02; H, 6.87. The reported optical rotation for the antipode of **12a**; $[\alpha]_D$ +6.6° (c 0.76, $CHCl_3$).[7]

(*S*)-3-[5-Methoxy-3,4-(methylenedioxy)benzyl]butanolide (12b). (*E*)-3-Methoxycarbonyl-4-[5-methoxy-3,4-(methylenedioxy)phenyl]but-3-enoic acid[17] was hydrogenated as described above providing (*S*)-3-methoxycarbonyl-4-[5-methoxy-3,4-(methylenedioxy)phenyl]butanoic acid as a colorless solid (87.1 g, >94% e.e.) [enantio excess was determined by the HPLC analysis as its morpholine amide (eluent; 2-PrOH-hexane 1:2 at 1.35 ml/min, stationary phase; daicel chiralcell OC, 5 mm Φ x 25 cm, UV detection at 250 nm], which was taken up into MeOH (200 ml) and stirred at room temperature for 4 h. The precipitate was removed by filtration and the filtrate was concentrated to give (*S*)-3-methoxycarbonyl-4-[5-methoxy-3,4-(methylenedioxy)-phenyl]butanoic acid as a colorless solid (53.8 g, >99% e.e.). The precipitate (37.7 g) was taken up into MeOH (70 ml) again and stirred at room temperature for 12 h. The filtration and concentration of the filtrate gave additional (*S*)-3-methoxycarbonyl-4-[5-methoxy-3,4-(methylenedioxy)phenyl]butanoic acid as a colorless solid (19.0 g, >99% e.e.; total amount 72.8 g, 84% from (*E*)-3-methoxycarbonyl-4-[5-methoxy-3,4-(methylene-dioxy)phenyl]but-3-enoic acid). mp 96.5-97.0 °C (colorless prisms from MeOH). $[\alpha]_D^{23}$ -26.6° (c 1.18, $CHCl_3$). NMR δ: 2.46 (1H, dd, J = 4.5, 17 Hz), 2.62-2.77 (2H, m), 2.93-3.13 (2H, m), 3.69 (3H, s), 3.88 (3H, s), 5.94 (2H, s), 6.31 (1H, s), 6.34 (1H, s). IR (KBr): 3136, 2912, 1724, 1680, 1638 cm^{-1}. MS m/z: 296 (M^+). Anal. Calcd for $C_{14}H_{16}O_7$: C, 56.75; H, 5.44. Found: C, 56.89; H, 5.29. (*S*)-3-Methoxycarbonyl-4-[5-methoxy-3,4-(methylenedioxy)phenyl]butanoic acid was converted into **12b** as described above in 93% yield. mp 88.5-89.5 °C (colorless prisms from AcOEt-hexane). $[\alpha]_D^{23}$ -6.82° (c 1.12, $CHCl_3$). NMR δ: 2.27 (1H, dd, J = 7, 17 Hz), 2.55-2.89 (4H, m), 3.90 (3H, s), 4.03 (1H, dd, J = 6, 9 Hz), 4.34 (1H, dd, J = 7, 9 Hz), 5.95 (2H, s), 6.30 (1H, d, J = 2 Hz), 6.34 (1H, d, J = 2 Hz). IR (KBr):

1784, 1768, 1632 cm^{-1}. MS m/z: 250 (M^+). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.38; H, 5.69.

(3a*S*,*R*-Biar)-3a,4-Dihydro-6,7,8,9,10,11-hexamethoxydibenzo[4,5:6,7]cycloocta[1,2-*c*]-furan-1(3*H*)-one (13a). To a solution of diisopropylamine (6.5 ml, 46 mmol) in THF (40 ml) at -70 °C was added *n*-BuLi (1.6 M in hexane, 28 ml, 45 mmol). Stirring at -70°C was continued for 10 min, followed by the addition of **12a** (10.0 g, 38 mmol) in THF (100 ml). The resultant solution was stirred at -70 °C for 30 min, followed by the addition of the 3,4,5-trimethoxybenzaldehyde (8.8 g, 45 mmol) in THF (20 ml). The resultant solution was stirred at -70 °C for 5 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The combined extracts were washed with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (100 ml). Et_3N (8.0 ml, 58 mmol), Ac_2O (5.0 ml, 53 mmol), and DMAP (200 mg, 1.6 mmol) were added, and the resultant solution was stirred at room temperature for 1 h. The solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (100 ml) and DBU (10 ml, 64.5 mmol) was added. The resultant solution was stirred at 80 °C for 1.5 h. The reaction solution was dissolved in AcOEt, and the resultant solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 2:3) to afford (*S*)-(*E*)-3-(3,4,5-trimethoxybenzyl)-2-(3,4,5-trimethoxybenzylidene)butanolide (15.2 g, 91%) as a colorless solid. mp 88.5-90.0 °C (colorless needles from AcOEt-hexane). $[\alpha]_D^{24}$ +82.9° (c 0.92, $CHCl_3$). NMR δ: 2.65 (1H, dd, J = 10, 14 Hz), 3.11 (1H, dd, J = 5, 14 Hz), 3.82 (3H, s), 3.83 (6H, s), 3.89 (6H, s), 3.91 (3H, s), 3.82-3.91 (1H, m), 4.29-4.31 (2H, m), 6.38 (2H, s), 6.82 (2H, s), 7.53 (1H, d, J = 2 Hz). IR ($CHCl_3$): 2940, 1748, 1648, 1588 cm^{-1}. MS m/z: 444 (M^+). Anal. Calcd for $C_{24}H_{28}O_8$: C, 64.85; H, 6.35. Found: C, 64.71; H, 6.35. A mixture of (*S*)-(*E*)-3-(3,4,5-trimethoxybenzyl)-2-(3,4,5-trimethoxybenzylidene)butanolide (491 mg, 1.1 mmol), $Fe(ClO_4)_3 \cdot 6H_2O$ (1.47 g, 3.2 mmol), and CF_3CO_2H (0.44 ml) in CH_2Cl_2 (5 ml) was stirred at room temperature for 2 h. The reaction mixture was washed successively with 6N HCl, water, and saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give **13a** as a pale yellow oil (441 mg, 90%). $[\alpha]_D^{26}$ -284° (c 0.895, $CHCl_3$). NMR δ: 2.46 (1H, d, J = 14 Hz), 3.07 (1H, dd, J = 7, 14 Hz), 3.40-3.60 (1H, m), 3.59 (3H, s), 3.64 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 4.11 (1H, dd, J = 8, 10 Hz), 4.47 (1H, t, J = 8 Hz), 6.41 (1H, s), 6.59 (1H, s), 7.53 (1H, d, J = 3 Hz). IR ($CHCl_3$): 2940, 1754, 1668, 1596 cm^{-1}. MS m/z: 442 (M^+). HRMS m/z: Calcd for $C_{24}H_{26}O_8$ (M^+): 442.16277. Found: 442.16347.

(3a*S*,*R*-Biar)-6,7-Dibenzyloxy-3a,4-dihydro-8,9,10,11-tetramethoxydibenzo[4,5:6,7]cyclo-octa[1,2-*c*]furan-1(3*H*)-one (13d) To solution of diisopropylamine (3.5 ml, 24 mmol) in THF (20 ml) at -70 °C was added *n*-BuLi (1.66 M in hexane, 14.8 ml, 24.6 mmol). Stirring at -70 °C was continued for 10 min, followed by the addition of **12b** (5.0 g, 20 mmol) in THF (50 ml). The resultant solution was stirred at -70 °C for 30 min, followed by the addition of the 3,4,5-trimethoxybenzaldehyde (4.7 g, 20 mmol) in THF (20 ml). The resultant solution was stirred at -70 °C for 5 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The combined extracts were washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (50 ml). Et_3N (7 ml), Ac_2O (5 ml), and DMAP (100 mg) were added, and the resultant solution was stirred at room temperature for 1 h. The reaction mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (70 ml), and DBU (6.5 ml) was added. The resultant solution was stirred at 80 °C for 1.5 h. The reaction mixture was dissolved in AcOEt and washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to afford (*S*)-(*E*)-3-[5-methoxy-3,4-(methylenedioxy)benzyl]-2-(3,4,5-trimethoxybenzylidene)butanolide (8.0 g, 94%) as a pale yellow solid. mp 79-81 °C (colorless prisms from AcOEt-hexane). $[\alpha]_D^{24}$ +67.5° (c 0.835, $CHCl_3$). NMR δ: 2.64 (1H, dd, J =

10, 14 Hz), 3.01 (1H, dd, J = 5, 14 Hz), 3.83-3.90 (1H, m), 3.86 (3H, s), 3.89 (6H, s), 3.90 (3H, s), 4.22-4.36 (2H, m), 5.93 (2H, s), 6.28 (1H, d, J = 1.5 Hz), 6.33 (1H, d, J = 1.5 Hz), 6.77 (2H, s), 7.51 (1H, d, J = 1.7 Hz). IR ($CHCl_3$): 1746, 1644, 1582 cm^{-1}. MS m/z: 428 (M^+). Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.20; H, 5.66. To a stirred solution of (*S*)-(*E*)-3-[5-methoxy-3,4-(methylenedioxy)-benzyl]-2-(3,4,5-trimethoxybenzylidene)butanolide (0.84 g, 1.96 mmol) in CH_2Cl_2 (10 ml) was added BCl_3 (1.0 M in CH_2Cl_2, 4 ml, 4 mmol), and the resultant solution was stirred at 0 °C for 30 min. After evaporation of the solvent, the residue was dissolved in MeOH (20 ml), and 2N HCl (6 ml) was added. After stirring at room temperature for 2 h, the reaction mixture was extracted with AcOEt and the organic layer was washed successively with water and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, (*S*)-(*E*)-3-(3,4-dihydroxy-5-methoxybenzyl)-2-(3,4,5-trimethoxybenzylidene)butanolide (**26**) was obtained as a colorless amorphous solid (790 mg, 97%). $[\alpha]_D^{27}$ +50.3° (c 0.7, $CHCl_3$). NMR δ: 2.60 (1H, dd, J = 10, 14 Hz), 3.04 (1H, dd, J = 5, 14 Hz), 3.83 (3H, s), 3.89 (6H, s), 3.90 (3H, s), 3.78-3.90 (1H, m), 4.24-4.30 (2H, m), 5.31 (1H, s), 5.36 (1H, s), 6.43 (1H, d, J = 2 Hz), 6.23 (1H, d, J = 2 Hz), 6.79 (2H, s), 7.51 (1H, d, J = 2 Hz). IR ($CHCl_3$): 3556, 1746, 1646, 1620, 1582 cm^{-1}. MS m/z: 416 (M^+). HRMS m/z: Calcd for $C_{22}H_{24}O_8$ (M^+): 416.14702. Found: 416.14652. A mixture of **26** (1.15 g, 2.76 mmol), $Fe(ClO_4)_3 \cdot 6H_2O$ (3.0 g, 6.5 mmol), CF_3CO_2H (30 ml) in CH_2Cl_2 (30 ml) was stirred at room temperature for 30 min. AcOEt was added, and the organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was heated with benzyl bromide (1.7 ml, 14.3 mmol) and K_2CO_3 (3.6 g, 26 mmol) in acetone (30 ml) under reflux for 3 h. The reaction was quenched with Et_3N and the solvent was removed under reduced pressure. The residue was taken up into AcOEt and the organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **13d** as a colorless oil (1.18 g, 72%). $[\alpha]_D^{24}$ -222° (c 0.46, $CHCl_3$). NMR δ: 2.38 (1H, d, J = 14 Hz), 3.03 (1H, dd, J = 7, 14 Hz), 3.38-3.60 (1H, m), 3.61 (3H, s), 3.63 (3H, s), 3.83 (3H, s), 3.92 (3H, s), 3.82 (1H, dd, J = 9, 10 Hz), 4.34 (1H, t, J = 9 Hz), 5.00-5.18 (4H, m), 6.39 (1H, s), 6.59 (1H, s), 7.26-7.42 (10H, m), 7.52 (1H, d, J = 3 Hz). IR ($CHCl_3$): 3012, 1754, 1674, 1594 cm^{-1}. MS m/z: 594 (M^+). HRMS m/z: Calcd for $C_{36}H_{34}O_8$ (M^+): 594.22537. Found: 594.22506.

(*S*)-(*E*)-2-(4-Benzyloxy-3,5-dimethoxybenzylidene)-3-(3,4,5-trimethoxybenzyl)butanolide (17a). Lithium hexamethyldisilazide (1.0 M in hexane, 5.0 ml, 5.0 mmol) was added to a toluene (20 ml) solution of **12a** (1.0 g, 3.76 mmol) and **16a** (1.2 g, 4.4 mmol) at 0 °C. The resultant mixture was stirred at 0 °C for 20 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (4 ml). Ac_2O (2.0 ml, 21.2 mmol), Et_3N (2 ml, 14 mmol), and DMAP (50 mg, 0.41 mmol) were added and the resultant solution was stirred at room temperature for 45 min. The reaction mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (20 ml). DBU (1.2 ml, 8.05 mmol) was added and the resultant solution was stirred at 60 °C for 1 h. The solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:3) to give **17a** as a colorless oil (1.41 g, 72%). $[\alpha]_D^{26}$ +65.3° (c 0.56, $CHCl_3$). NMR δ: 2.57-2.74 (1H, m), 3.10 (1H, dd, J = 6, 14 Hz), 3.70-3.90 (1H, m), 3.82 (3H, s), 3.83 (6H, s), 3,85 (6H, s), 4.28-4.21 (2H, m), 5.07 (2H, s), 6.38 (2H, s), 6.82 (2H, s), 7.31 (6H, m). IR ($CHCl_3$): 1748, 1648, 1588 cm^{-1}. MS m/z: 520 (M^+). HRMS m/z: Calcd for $C_{30}H_{32}O_8$ (M^+): 520.20972. Found: 520.20825.

(*S*)-(*E*)-2-(4-Hydroxy-3,5-dimethoxybenzylidene)-3-(3,4,5-trimethoxybenzyl)butanolide (17b). BCl_3 (1.0 M in CH_2Cl_2, 3.0 ml, 3.0 mmol) was added to a solution of **17a** (1.30 g, 2.5 mmol) in CH_2Cl_2 (30 ml) and the resultant solution was stirred at 0 °C for 1.25 h. After addition of MeOH (20 ml), the resultant solution was concentrated and chromatographed (AcOEt-hexane 1:1) to give **17b** as a yellow solid

(0.79 g, 73%). mp 105.5-107 °C (colorless prisms from AcOEt-hexane). $[\alpha]_D^{24}$ +78.3° (c 1.13, $CHCl_3$). NMR δ: 2.66 (1H, dd, J = 11, 14 Hz), 3.12 (1H, dd, J = 6, 14 Hz), 3.75-3.90 (1H, m), 3.81 (3H, s), 3.83 (6H, s), 3.92 (6H, s), 4.29-4.32 (2H, m), 5.83 (1H, s), 6.38 (2H, s), 6.84 (2H, s), 7.52 (1H, d, J = 1.7 Hz). IR (KBr): 1740, 1642, 1590 cm^{-1}. MS m/z: 430 (M^+). Anal. Calcd for $C_{23}H_{26}O_8 \cdot 1/3H_2O$: C, 63.29; H, 6.16. Found: C, 63.29; H, 6.41.

3,5-Dimethoxy-4-pivaloyloxybenzaldehyde (16b). A solution of syringaldehyde (5.0 g, 27.5 mmol) and pivaloyl chloride (4.0 ml, 32.5 mmol) in pyridine (40 ml) was stirred at room temperature for 1 h. After addition of water, precipitated solid was collected by filtration to give **16b** (6.17 g, 84%). mp 109.5-110 °C (colorless needles from AcOEt-hexane). NMR δ: 1.39 (9H, s), 3.88 (6H, s), 7.26 (2H, s), 9.90 (1H, s). IR (KBr): 1752, 1694, 1610 cm^{-1}. MS m/z: 266 (M^+). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.27; H, 6.80.

(*S*)-(*E*)-2-(3,5-Dimethoxy-4-pivaloyloxybenzylidene)-3-(3,4,5-trimethoxybenzyl)butanolide (17c). Lithium hexamethyldisilazide (1.0 M in hexane, 4.5 ml, 4.5 mmol) was added to a toluene (20 ml) solution of **12a** (1.0 g, 3.76 mmol) and **16b** (1.1 g, 4.14 mmol) at 0 °C. The resultant mixture was stirred at 0 °C for 20 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in pyridine (5 ml). pivaloyl chloride (1.0 ml, 8.1 mmol), and DMAP (100 mg, 0.82 mmol) were added and the resultant solution was stirred at room temperature for 20 h. The reaction mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (10 ml). DBU (0.75 ml, 5 mmol) was added and the resultant solution was stirred at 60 °C for 1 h. The solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **17c** as a colorless oil (1.23 g, 64%). $[\alpha]_D^{24}$ +47.3° (c 0.37, $CHCl_3$). NMR δ: 1.38 (9H, s), 2.66 (1H, dd, J = 11, 16 Hz), 3.12 (1H, dd, J = 6, 16 Hz), 3.70-3.90 (1H, m), 3.81 (3H, s), 3.82 (6H, s), 3.823 (6H, s), 4.28-4.32 (2H, m), 6.35 (2H, s), 6.82 (2H, s), 7.55 (1H, d, J = 1.7 Hz). IR ($CHCl_3$): 1752, 1650, 1594 cm^{-1}. MS m/z: 514 (M^+). HRMS m/z: Calcd for $C_{28}H_{34}O_9$ (M^+): 514.22028. Found: 514.22133.

3,5-Dimethoxy-4-(4-nitrobenzyloxy)benzaldehyde (16c). A mixture of syringaldehyde (10 g, 55 mmol), *p*-nitrobenzyl bromide (13 g, 60 mmol), and K_2CO_3 (9.0 g, 65 mmol) in acetone (40 ml) was heated under reflux for 4 h. After evaporation of the solvent, the residue was taken up into CH_2Cl_2 and the organic layer was washed with water, and dried over $MgSO_4$. After evaporation of the solvent, the residue was washed with Et_2O to give **16c** as a colorless solid (16.7 g, 93%). mp 148-149 °C (colorless needles from AcOEt). NMR δ: 3.92 (6H, s), 5.22 (2H, s), 7.14 (2H, s), 7.68 (2H, d, J = 9 Hz), 8.21 (2H, d, J = 9 Hz), 9.88 (1H, s). IR ($CHCl_3$): 1694, 1594 cm^{-1}. MS m/z: 317 (M^+). Anal. Calcd for $C_{16}H_{15}NO_6$: C, 60.56; H, 4.77; N, 4.41. Found: C, 60.36; H, 4.86; N, 4.57.

(*S*)-(*E*)-2-[3,5-Dimethoxy-4-(4-nitrobenzyloxy)benzylidene]-3-(3,4,5-trimethoxybenzyl)-butanolide (17d). To solution of diisopropylamine (13 ml, 93 mmol) in THF (80 ml) at -60 °C was added *n*-BuLi (1.66 M in hexane, 56 ml, 93 mmol). Stirring at -70 °C was continued for 10 min, followed by the addition of **12a** (20 g, 75 mmol) in THF (200 ml). The resultant solution was stirred at -70 °C for 30 min, followed by the addition of the **16c** (30 g, 95 mmol) in THF (400 ml). The resultant solution was stirred at -70 °C for 3 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The combined extracts were washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (200 ml). Ac_2O (10 ml, 106 mmol), Et_3N (15 ml, 108 mmol), and DMAP (500 mg, 4 mmol) were added and the resultant solution was stirred at room temperature for 9 h. The reaction mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (200 ml). DBU (20 ml) was added and the resultant solution was stirred at 80

°C for 1 h. The reaction mixture was dissolved in AcOEt and washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **17d** as a colorless oil (41.16 g, 97%). $[\alpha]_D^{26}$ +49.2° (c 0.895, $CHCl_3$). NMR δ: 2.66 (1H, dd, J = 10, 14 Hz), 3.08 (1H, dd, J = 5, 14 Hz), 3.60-3.80 (1H, m), 3.81 (3H, s), 3.82 (6H, s), 3.87 (6H, s), 4.29-4.32 (2H, m), 5.17 (2H, s), 6.37 (2H, s), 6.81 (2H, s), 7.53 (1H, d, J = 1.5 Hz), 7.67 (2H, d, J = 9 Hz), 8.22 (2H, d, J = 9 Hz). IR ($CHCl_3$): 1748, 1648, 1588, 1522 cm^{-1}. MS m/z: 565 (M^+). MS m/z: Calcd for $C_{30}H_{31}NO_{10}$ (M^+): 565.19480. Found: 565.19649.

(3a*S*,*R*-Biar)-3a,4-Dihydro-6,7,8,9,11-pentamethoxy-10-(4-nitrobenzyloxy)dibenzo-[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (18). A mixture of **17d** (27.0 g, 47.8 mmol), $Fe(ClO_4)_3 \cdot 6H_2O$ (53.0 g, 115 mmol), and CF_3CO_2H (50 ml) in CH_2Cl_2 (500 ml) was stirred at room temperature for 3 h. AcOEt was added, and the organic layer was washed with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **18** as a pale yellow solid (25.6 g, 95%). mp 170.5-171.5 °C (colorless prisms from AcOEt). $[\alpha]_D^{29}$ -257° (c 1.01, $CHCl_3$). NMR δ: 2.47 (1H, dd, J = 1.5, 14 Hz), 3.02 (1H, dd, J = 7, 14 Hz), 3.40-3.64 (1H, m), 3.56 (3H, s), 3.60 (3H, s), 3.88 (6H, s), 3.89 (3H, s), 4.11 (1H, dd, J = 8, 10 Hz), 4.48 (1H, t, J = 8 Hz), 5.20 (2H, s), 6.42 (1H, s), 6.61 (1H, s), 7.52 (1H, d, J = 3.4 Hz), 7.68 (2H, d, J = 9 Hz), 8.23 (2H, d, J = 9 Hz). IR (KBr): 1754, 1672, 1596 cm^{-1}. MS m/z: 563 (M^+). Anal. Calcd for $C_{30}H_{29}NO_{10}$: C, 63.94; H, 5.19; N, 2.49. Found: C, 63.73; H, 5.09; N, 2.57.

(3a*S*,*R*-Biar)-10-Benzyloxy-3a,4-dihydro-6,7,8,9,11-pentamethoxydibenzo[4,5:6,7]cyclo-octa[1,2-*c*]furan-1(3*H*)-one (13b). **18** (20.0 g, 35.5 mmol) was hydrogenated over 10% Pd-C (400 mg) in AcOEt (400 ml) under a hydrogen atmosphere for 1 h. The catalyst was filtered off, and the filtrate was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. The solvent was evaporated to give (3a*S*,*R*-Biar)-3a,4-dihydro-10-hydroxy-6,7,8,9,11-pentamethoxydibenzo[4,5:6,7]cycloocta-[1,2-*c*]furan-1(3*H*)-one (15.2 g, 100%). mp 194-196 °C (colorless prisms from AcOEt-hexane). $[\alpha]_D^{29}$ -415° (c 0.78, $CHCl_3$). NMR δ: 2.46 (1H, dd, J = 2, 14 Hz), 3.09 (1H, dd, J = 7, 14 Hz), 3.44-3.63 (1H, m), 3.51 (3H, s), 3.57 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.93 (3H, s), 4.10 (1H, dd, J = 9, 10 Hz), 4.47 (1H, t, J = 9 Hz), 5.74 (1H, s), 6.42 (1H, s), 6.60 (1H, s), 7.52 (1H, d, J = 3.4 Hz). IR (KBr): 1744, 1662, 1598 cm^{-1}. MS m/z: 428 (M^+). Anal. Calcd for $C_{23}H_{24}O_8$: C, 54.48; H, 5.65. Found: C, 64.18; H, 5.74. The (3a*S*,*R*-Biar)-3a,4-dihydro-10-hydroxy-6,7,8,9,11-pentamethoxydibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (15.2 g, 35.5 mmol) was heated under reflux with benzyl bromide (8.5 ml, 72 mmol) and K_2CO_3 (14 g, 100 mmol) in acetone (100 ml) for 2.5 h. The reaction was quenched with Et_3N. After addition of AcOEt, the resultant mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was recrystallized from AcOEt-hexane to give **13b** as colorless needles (17.4 g, 95% from **18**). mp 144-144.5 °C. $[\alpha]_D^{26}$ +204° (c 0.972, $CHCl_3$). NMR δ: 2.45 (1H, dd, J = 1.5, 14 Hz), 3.04 (1H, dd, J = 7, 14 Hz), 3.50-3.60 (1H, m), 3.56 (3H, s), 3.64 (3H, s), 3.86 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 4.10 (1H, dd, J = 8, 10 Hz), 4.47 (1H, t, J = 8 Hz), 5.05 (1H, d, J = 11 Hz), 5.10 (1H, d, J = 11 Hz), 6.41 (1H, s), 6.56 (1H, s), 7.26-7.54 (6H, m). IR (KBr): 1758, 1674, 1594 cm^{-1}. MS m/z: 518 (M^+). Anal. Calcd for $C_{30}H_{30}O_8$: C, 69.48; H, 5.83. Found: C, 69.28; H, 6.01.

Methyl 3-Benzyloxy-4,5-dihydroxybenzoate. A mixture of methyl gallate (100 g, 54 mmol), triethyl orthoformate (250 ml), and Amberlyst 15 (5 g) in benzene (300 ml) was heated under reflux for 24 h, and the insoluble material was removed by filtration. After evaporation of the solvent, the residue was dissolved into DMF (500 ml). K_2CO_3 (160 g, 1.16 mol) and benzyl bromide (107 ml, 0.89 mol) were added and the resultant mixture was heated at 70 °C for 1.5 h. The reaction was quenched with Et_3N and extracted with AcOEt. The organic layer was washed with 10% H_2SO_4, water, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved into MeOH (500 ml), and *p*-TsOH (1 g) was added. The resultant solution was stirred at room temperature for 12 h. The solution was concentrated, and the residue was dissolved into AcOEt. The organic layer was washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated to give methyl 3-benzyloxy-4,5-dihydroxybenzoate as a colorless solid (112 g, 75%). mp 145.5-147 °C (colorless

prisms from AcOEt). NMR δ: 3.87 (3H, s), 5.13 (2H, s), 5.45 (1H, s), 5.89 (1H, s), 7.31 (1H, d, J = 1.7 Hz), 7.36 (1H, d, J = 1.7 Hz), 7.38-7.44 (5H, m). IR (KBr): 1690, 1616, 1600 cm^{-1}. MS m/z: 274 (M^+). Anal. Calcd for $C_{15}H_{14}O_5 \cdot 1/10H_2O$: C, 65.69; H, 5.15. Found: C, 65.28; H, 5.22.

Methyl 3-Benzyloxy-4,5-dimethoxybenzoate. A mixture of methyl 3-benzyloxy-4,5-dihydroxybenzoate (103 g, 0.38 mol), K_2CO_3 (150 g, 1.09 mol), and dimethyl sulfate (80 ml, 0.84 mol) in acetone (600 ml) was heated under reflux for 1.5 h, and the reaction was quenched with Et_3N. After evaporation of the solvent, the residue was dissolved into AcOEt, and the resultant solution was washed successively with 2N HCl, water, brine, and dried over $MgSO_4$. After evaporation of the solvent, methyl 3-benzyloxy-4,5-dimethoxy-benzoate was obtained as a colorless solid (109.7 g, 97%). Analytical sample was obtained by the bulb to bulb distillation (bp 230-240 °C/0.5 mmHg). mp 71.5-72.5 °C. NMR δ: 3.89 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 5.16 (2H, s), 7.26-7.49 (7H, m). IR (KBr): 1710, 1590 cm^{-1}. MS m/z: 302 (M^+). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.57; H, 6.24.

Methyl 3-Hydroxy-4,5-dimethoxybenzoate. Methyl 3-benzyloxy-4,5-dimethoxybenzoate (10.0 g) was hydrogenated over 10% Pd-C (100 mg) in MeOH (100 ml) under a hydrogen atmosphere for 20 h. After removal of the catalyst and solvent, methyl 3-hydroxy-4,5-dimethoxybenzoate was obtained as a colorless solid (7.0 g, 100%). mp 72.5-73.0 °C (colorless prisms from AcOEt-hexane). NMR δ: 3.89 (3H, s), 3.91 (3H, s), 3.96 (3H, s), 5.86 (1H, br), 7.20 (1H, d, J = 2 Hz), 7.31 (2H, d, J = 2 Hz). IR (KBr): 1708, 1598 cm^{-1}. MS m/z: 212 (M^+). Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.76; H, 5.80.

3,4-Dimethoxy-5-[(2-methoxyethoxy)methoxy]benzaldehyde (19a). NaH (60% in oil, 7.5 g, 0.19 mol) and MEMCl (20 ml, 0.17 mol) were added to a stirred solution of methyl 3-hydroxy-4,5-dimethoxy-benzoate (30.5 g, 0.14 mol) in THF (200 ml), and the resultant mixture was heated under reflux for 2 h. Saturated NH_4Cl and AcOEt were added, and the organic layer was successively washed with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:5) to give methyl 3,4-dimethoxy-5-[(2-methoxyethoxy)methoxy]benzoate as a colorless oil (34.33 g, 80%). NMR δ: 3.40 (3H, s), 3.50-3.70 (2H, m), 3.90-4.00 (11H, m), 5.40 (2H, s), 7.25-7.60 (2H, m). A solution of methyl 3,4-dimethoxy-5-[(2-methoxyethoxy)methoxy]benzoate (34 g, 0.11 mol) in THF (50 ml) was added to a stirred suspension of $LiAlH_4$ (3.0 g, 80 mmol) in THF (50 ml) and the resultant mixture was stirred at 0 °C for 4 h. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$. The insoluble material was filtered off, and the filtrate was concentrated to give a colorless oil (30.45 g, 99%). A mixture of this oil (30 g) and MnO_2 (100 g, 1.1 mol) in toluene (300 ml) was stirred at room temperature for 22 h, and the insoluble material was filtered off. The filtrate was concentrated to give **19a** as a colorless oil (27.9 g, 94%). NMR δ: 3.40 (3H, s), 3.50-3.68 (2H, m), 3.88-4.00 (8H, m), 5.40 (2H, s), 7.16-7.30 (2H, m), 9.92(1H, s). IR (neat): 2984, 1694, 1588 cm^{-1}. MS m/z: 270 (M^+).

Methyl 2-Bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzoate. Br_2 (1.7 ml, 33 mmol) and a solution of methyl 3-hydroxy-4,5-dimethoxybenzoate (5.95 g, 28.1 mmol) in CH_2Cl_2 (25 ml) were added successively to a solution of *t*-$BuNH_2$ (6.7 ml, 64 mmol) in toluene (140 ml) at -70 °C. The resultant solution was stirred at -70 °C for 30 min, warmed up to room temperature during 3.5 h, and stirred at room temperature for 4 h. AcOEt (100 ml) was added, and the mixture was washed with 2N HCl, water, saturated $NaHCO_3$, and dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved into acetone (100 ml). K_2CO_3 (6.2 g, 44.9 mmol) and *p*-nitrobenzyl bromide (9.1 g, 42.1 mmol) were added and the resultant mixture was heated under reflux for 3 h. The reaction was quenched with Et_3N and concentrated. The residue was taken up into CH_2Cl_2, and the organic layer was washed with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was triturated in Et_2O to give methyl 2-bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzoate as a colorless solid (6.95 g, 58%). mp 154-154.5 °C (colorless needles from AcOEt). NMR δ: 3.905 (3H, s), 3.911 (3H, s), 3.94 (3H, s), 5.15 (2H, s), 7.21 (1H, s), 7.73 (2H, d, J = 9 Hz), 8.26 (2H, d, J = 9 Hz). IR (KBr): 1740, 1608, 1570 cm^{-1}. MS m/z: 425 (M^+), 427 (M^++2). Anal. Calcd for $C_{17}H_{16}BrNO_7$: C, 47.90; H, 3.78; N, 3.29. Found: C, 47.89; H, 3.84; N, 3.51.

2-Bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzyl alcohol. DIBAH (1.5 M in toluene, 30 ml, 45 mmol) was added to a solution of methyl 2-bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzoate (6.85 g, 16.1 mmol) in THF (200 ml) at 0 °C and the resultant solution was stirred at 0 °C for 15 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$. After removal of the insoluble material by filtration, the filtrate was concentrated to give 2-bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzyl alcohol as a colorless solid (6.40 g, 100%). mp 149.5-150 °C (colorless needles from AcOEt). NMR δ: 1.50-1.90 (1H, br), 3.86 (3H, s), 3.91 (3H, s), 4.73 (2H, s), 5.17 (2H, s), 6.96 (1H, s), 7.72 (2H, d, J = 9 Hz), 8.24 (2H, d, J = 9 Hz). IR (KBr): 1608, 1572 cm^{-1}. MS m/z: 397 (M^+), 399 (M^++2). Anal. Calcd for $C_{16}H_{16}BrNO_6$: C, 48.26; H, 4.05; N, 3.52. Found: C, 48.21; H, 4.15; N, 3.75.

2-Bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzaldehyde (19b). A mixture of 2-bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)benzyl alcohol (6.4 g, 16.1 mmol) and MnO_2 (5.0 g) in CH_2Cl_2 (100 ml) was heated under reflux for 16.5 h, and the insoluble material was removed by filtration. Concentration of the filtrate gave **19b** as a colorless solid (6.0 g, 94%). mp 163-164 °C (colorless needles from AcOEt). NMR δ: 3.94 (3H, s), 3.96 (3H, s), 5.18 (2H, s), 7.36 (1H, s), 7.73 (2H, d, J = 9 Hz), 8.28 (2H, d, J = 9 Hz), 10.3 (1H, s). IR (KBr): 1688, 1578 cm^{-1}. MS m/z: 395 (M^+), 397 (M^++2). Anal. Calcd for $C_{16}H_{14}BrNO_6$: C, 48.50; H, 3.56; N, 3.53. Found: C, 48.45; H, 3.68; N, 3.72.

(*S*)-(*E*)-2-[3,4-Dimethoxy-5-(4-nitrobenzyloxy)benzylidene]-3-(3,4,5-trimethoxybenzyl)-butanolide (20). To a solution containing diisopropylamine (6.6 ml, 47 mmol) in THF (50 ml) at -60 °C was added *n*-BuLi (1.66 M in hexane, 28 ml, 47 mmol). Stirring at -70°C was continued for 10 min, followed by the addition of (10 g, 37.6 mmol) in THF (60 ml). The resultant solution was stirred at -70 °C for 30 min, followed by the addition of the **19a** (11.2 g, 41.5 mmol) in THF (20 ml). The resultant solution was stirred at -70 °C for 3 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The combined extracts were washed with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (100 ml). Ac_2O (5 ml, 53 mmol), Et_3N (8 ml, 57.8 mmol), and DMAP (200 mg, 1.6 mmol) were added and the resultant solution was stirred at room temperature for 30 min. The solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (60 ml) and DBU (10 ml, 64.5 mmol) was added. The resultant solution was stirred at 70 °C for 1 h. The reaction solution was dissolved into AcOEt, and the resultant solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. The solvent was evaporated to give colorless oil (18.75 g). BCl_3 (1.0 M in CH_2Cl_2, 50 ml, 50 mmol) was added to a solution of above mentioned product (1.30 g, 2.5 mmol) in CH_2Cl_2 (190 ml) and the resultant solution was stirred at 0 °C for 10 min. After addition of saturated $NaHCO_3$, the organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give (*S*)-(*E*)-2-(5-hydroxy-3,4-dimethoxybenzylidene)-3-(3,4,5-trimethoxybenzyl)butanolide as a colorless oil (10.1 g, 62.5%). NMR δ: 2.58 (1H, dd, J = 12, 15 Hz), 3.04 (1H, dd, J = 6, 15 Hz), 3.70-3.90 (1H, m), 3.86 (3H, s), 3.93 (6H, s), 3.94 (3H, s), 4.00 (3H, s), 4.22-4.40 (2H, m), 5.93 (1H, br), 6.50 (2H, s), 6.66 (1H, d, J = 2 Hz), 7.03 (1H, d, J = 2 Hz), 7.52 (1H, d, J = 2 Hz). IR ($CHCl_3$): 3532, 1746, 1648, 1590 cm^{-1}. MS m/z: 430 (M^+). A mixture of (*S*)-(*E*)-2-(5-hydroxy-3,4-dimethoxybenzylidene)-3-(3,4,5-trimethoxybenzyl)-butanolide (7.5 g, 17.4 mmol), *p*-nitrobenzyl bromide (4.6 g, 21.3 mmol), and K_2CO_3 (3.0 g, 22 mmol) in acetone (100 ml) was heated under reflux for 3.5 h. After evaporation of the solvent, the residue was taken up into AcOEt, and the organic layer was washed with water, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give **20** as a colorless oil (9 g, 91%). $[\alpha]_D^{24}$ +45.6° (c 0.645, $CHCl_3$). NMR δ: 2.58-2.73 (1H, m), 3.01 (1H, dd, J = 4, 14 Hz), 3.75-3.90 (1H, m), 3.80 (6H, s), 3.81 (3H, s), 3.90 (3H, s), 3.93 (3H, s), 4.25-4.40 (2H, m), 5.20 (2H, s), 6.36 (2H, s), 6.77 (1H, d, J = 1.7 Hz), 6.86 (1H, d, J = 1.7 Hz), 7.48 (1H, d, J = 1.7 Hz), 7.59 (2H, d, J = 9 Hz), 8.23 (2H, d, J = 9 Hz). IR ($CHCl_3$): 3012, 2968, 1746, 1648, 1590, 1524, 1348 cm^{-1}. MS m/z: 565 (M^+). HRMS m/z: Calcd for $C_{30}H_{31}NO_{10}$ (M^+): 565.19480. Found: 565.19656.

(3a*S*,*R*-Biar)-3a,4-Dihydro-6,7,8,10,11-pentamethoxy-9-(4-nitrobenzyloxy)dibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (21a) and (3a*S*,*R*-Biar)-3a,4-Dihydro-6,7,8,9,10-pentamethoxy-11-(4-nitrobenzyloxy)dibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (21b). A mixture of **20** (91 mg, 0.16 mmol), $Fe(ClO_4)_3 \cdot 6H_2O$ (190 mg, 0.41 mmol), and CF_3CO_2H (0.2 ml) in CH_2Cl_2 (2 ml) was stirred at room temperature for 1.25 h. AcOEt was added and the mixture was washed with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give an inseparable mixture of **21a** and **21b** as a colorless oil (77 mg, 85%).[15] NMR δ: 2.27 (2/3 x 1H, d, J = 14 Hz), 2.46 (1/3 x 1H, d, J = 14 Hz), 3.85 (2/3 x 1H, dd, J = 7,14 Hz), 3.09 (1/3 x 1H, dd, J = 7, 14 Hz), 3.40-3.60 (1H, m), 3.58 (2/3 x 3H, s), 3.60 (1/3 x 3H, s), 3.66 (1/3 x 3H, s), 3.79 (2/3 x 3H, s), 3.88 (1/3 x 3H, s), 3.89 (1/3 x 3H, s), 3.90 (2/3 x 3H, s), 3.92 (2/3 x 6H, s), 3.95 (1/3 x 3H, s), 4.08 (1H, q, J = 9 Hz), 4.41-4.49 (1H, m), 4.86 (2/3 x 1H, d, J = 13 Hz), 5.09 (2/3 x 1H, d, J = 13 Hz), 5.24 (1/3 x 2H, s), 6.33 (2/3 x 1H, s), 6.49 (1/3 x 1H, s)), 6.61 (1/3 x 1H, s), 6.64 (2/3 x 1H, s), 7.13 (2/3 x 2H, d, J = 9 Hz), 7,48 (1/3 x 1H, d, J = 3 Hz), 7.52 (2/3 x 1H, d, J = 4 Hz), 7.67 (1/3 x 2H, d, J = 9 Hz), 8.03 (2/3 x 2H, d, J = 9 Hz), 8.29 (1/3 x 2H, d, J = 9 Hz). IR ($CHCl_3$): 1754, 1676, 1594 cm^{-1}. MS m/z: 563 (M^+). HRMS m/z: Calcd for $C_{30}H_{29}NO_{10}$ (M^+): 563.17915. Found: 563.17905.

(*S*)-(*E*)-2-[2-Bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)-benzylidene]-3-(3,4,5-trimethoxybenzyl)butanolide (22a) and (*S*)-(*Z*)-2-[2-Bromo-4,5-dimethoxy-3-(4-nitrobenzyloxy)-benzylidene]-3-(3,4,5-trimethoxybenzyl)butanolide (22b). To a solution containing diisopropylamine (0.73 ml, 5.2 mmol) in THF (10 ml) at -70 °C was added *n*-BuLi (1.66 M in hexane, 2.6 ml, 3.76 mmol). Stirring at -70°C was continued for 10 min, followed by the addition of **12a** (1.0 g, 3.76 mmol) in THF (10 ml). The resultant solution was stirred at -70 °C for 30 min, followed by the addition of **19b** (1.62 g, 4.1 mmol) in THF (20 ml). The resultant solution was stirred at -70 °C for 3 min. The reaction was quenched with a saturated NH_4Cl and extracted with AcOEt. The combined extracts were washed with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (20 ml). Ac_2O (0.6 ml, 5.9 mmol), Et_3N (1.0 ml, 7 mmol), and DMAP (50 mg, 0.41 mmol) were added and the resultant solution was stirred at room temperature for 30 min. The solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in toluene (30 ml) and DBU (1.5 ml, 10 mmol) was added. The resultant solution was stirred at 80 °C for 1.5 h. The reaction solution was dissolved into AcOEt, and the resultant solution was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **22b** as a pale yellow solid (400 mg, 16%) and **22a** as a pale yellow oil (1.14 g, 47%). **22a**: $[\alpha]_D^{26}$ +43.2° (c 0.43, $CHCl_3$). NMR δ: 2.63 (1H, dd, J = 9, 14 Hz), 2.76 (1H, dd, J = 6, 14 Hz), 3.70-3.96 (1H, m), 3.78 (3H, s), 3.79 (6H, s), 3.88 (3H, s), 3.91 (3H, s), 4.24 (1H, dd, J = 2, 10 Hz), 4.40 (1H, dd, J = 7, 10 Hz), 5.18 (2H, s), 6.22 (2H, s), 6.88 (1H, s), 7.71 (2H, d, J = 9 Hz), 8.25 (2H, d, J = 9 Hz). IR ($CHCl_3$): 1756, 1592 cm^{-1}. MS m/z: 643 (M^+), 645 (M^++2). HRMS m/z: Calcd for $C_{30}H_{30}BrNO_{10}$ (M^+): 643.10531. Found: 643.10359. **22b**: mp 139-141 °C (colorless needles from AcOEt-hexane). $[\alpha]_D^{26}$ +10.2° (c 0.325, $CHCl_3$). NMR δ: 2.87 (1H, dd, J = 9, 15 Hz), 3.02 (1H, dd, J = 7, 15 Hz), 3.40-3.60 (1H, m), 3.84 (3H, s), 3.86 (6H, s), 3.90 (6H, s), 4.16 (1H, dd, J = 4, 9 Hz), 4.41 (1H, dd, J = 9, 7 Hz), 5.15 (2H, s), 6.44 (2H, s), 7.02 (1H, d, J = 1.7 Hz), 7.51 (1H, s), 7.72 (2H, d, J = 9 Hz), 8.26 (2H, d, J = 9 Hz). IR (KBr): 1758, 1592 cm^{-1}. MS m/z: 643 (M^+), 645 (M^++2). HRMS m/z: Calcd for $C_{30}H_{30}BrNO_{10}$ (M^+): 643.10531, 645.10339. Found: 643.10442, 645.10662.

(3a*S*,*R*-Biar)-12-Bromo-3a,4-dihydro-6,7,8,9,10-pentamethoxy-11-(4-nitrobenzyloxy)-dibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (23). A mixture of **22a** (1.1 g, 1.71 mmol) and $Fe(ClO_4)_3 \cdot 6H_2O$ (1.9 g, 4.1 mmol) in CF_3CO_2H (10 ml) was stirred at room temperature for 3.5 h. AcOEt was added, and the mixture was washed with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give **23** as a

colorless amorphous solid (605 mg, 55%). $[\alpha]_D^{26}$ -164° (c 0.70, $CHCl_3$). NMR δ: 2.47 (1H, d, J = 14 Hz), 2.97 (1H, dd, J = 14, 7 Hz), 3.44-3.66 (1H, m), 3.62 (3H, s), 3.64 (3H, s), 3.88 (3H, s), 3,90 (3H, s), 3.93 (3H, s), 4.10 (1H, t, J = 9 Hz), 4.51 (1H, t, J = 9 Hz), 5.28 (2H, s), 6.42 (1H, s), 7.45 (1H, d, J = 3.4 Hz), 7.76 (2H, d, J = 9 Hz), 8.28 (2H, d, J = 9 Hz). IR ($CHCl_3$): 1756, 1676, 1600 cm^{-1}. MS m/z: 641 (M^+), 643(M^++2). HRMS m/z: Calcd for $C_{30}H_{28}NBrO_{10}$ (M^+): 643.08774, 641.08966. Found: 643.08827, 641.08984.

(3a*S*,*R*-Biar)-12-Bromo-3a,4-dihydro-11-hydroxy-6,7,8,9,10-pentamethoxydibenzo-[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (24). **23** (50 mg, 0.078 mmol) was hydrogenated over 10% Pd-C (5 mg) in AcOEt (3 ml) under a hydrogen atmosphere for 1 h. The catalyst was filtered off, and the filtrate was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. Evaporation of the solvent gave **24** as a colorless solid (38 mg, 96%). mp 228-230 °C (colorless needles from AcOEt-hexane). $[\alpha]_D^{26}$ -181° (c 0.615, $CHCl_3$). NMR δ: 2.46 (1H, d, J = 14 Hz), 3.00 (1H, dd, J = 7, 14 Hz), 3.50-3.60 (1H, m), 3.58 (3H, s), 3.61 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.98 (3H, s), 4.04-4.15 (1H, m), 4.50 (1H, t, J = 9 Hz), 6.19 (1H, s), 6.42 (1H, s), 7.45 (1H, d, J = 3.4 Hz). IR (KBr): 1748, 1670, 1598 cm^{-1}. MS m/z: 506 (M^+), 508 (M^++2). Anal. Calcd for $C_{23}H_{23}BrO_8$: C, 54.45; H, 4.57. Found: C, 54.38; H, 4.78.

(3a*S*,*R*-Biar)-11-Benzyloxy-12-bromo-3a,4-dihydro-6,7,8,9,10-pentamethoxydibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (25). **24** (38 mg, 0.075 mmol) was heated at 60 °C with benzyl bromide (0.1 ml, 0.84 mmol) and K_2CO_3 (125 mg, 0.91 mmol) in DMF (2 ml) for 2 h. The reaction was quenched with Et_3N and taken up into AcOEt. The organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give **25** as a colorless solid (46 mg, 100%). mp 165-167.5 °C (colorless prisms from Et_2O). $[\alpha]_D^{26}$ -196° (c 0.44, $CHCl_3$). NMR δ: 2.46 (1H, d, J = 14 Hz), 2.97 (1H, dd, J = 7, 14 Hz), 3.44-3.65 (1H, m), 3.60 (3H, s), 3.63 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.95 (3H, s), 4.09 (1H, dd, J = 9, 10 Hz), 4.49 (1H, t, J = 9 Hz), 5.17 (2H, s), 6.41 (1H, s), 7.35-7.60 (6H, m). IR (KBr): 1762, 1670, 1598 cm^{-1}. MS m/z: 596 (M^+), 598 (M^++2). Anal. Calcd for $C_{30}H_{29}BrO_8$: C, 60.31; H, 4.89. Found: C, 60.30; H, 4.82.

(3a*S*,*R*-Biar)-11-Benzyloxy-3a,4-dihydro-6,7,8,9,10-pentamethoxydibenzo[4,5:6,7]cyclo-octa[1,2-*c*]furan-1(3*H*)-one (13c). **25** (431 mg, 0.72 mmol) and zinc powder (1.5 g) in EtOH (30 ml) was heated under reflux for 34 h. After filtration of the insoluble material, the filtrate was concentrated and dissolved in AcOEt. The resultant solution was washed with water and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (CH_2Cl_2) to give **13c** as a colorless solid (343 mg, 92%). mp 172.5-173.5 °C (colorless plates from AcOEt-hexane). $[\alpha]_D^{26}$ -301° (c 0.475, $CHCl_3$). NMR δ: 2.42 (1H, d, J = 14 Hz), 3.06 (1H, dd, J = 7, 14 Hz), 3.46-3.70 (1H, m), 3.58 (3H, s), 3.66 (3H, s), 3.87 (3H, s), 3.88 (3H, s), 3.93 (3H, s), 4.10 (1H, dd, J = 8, 9 Hz), 4.46 (1H, t, J = 9 Hz), 5.14 (2H, s), 6.40 (1H, s), 6.64 (1H, s), 7.34-7.50 (6H, m). IR (KBr): 1750, 1672, 1592 cm^{-1}. MS m/z: 518 (M^+). Anal. Calcd for $C_{30}H_{30}O_8$: C, 69.48; H, 5.83. Found: C, 69.32; H, 5.98.

(*S*)-(*E*)-2-(3,4,5-Trimethoxybenzylidene)-3-[3-methoxy-4,5-bis(4-nitrobenzyloxy)benzyl]-butanolide (27). A mixture of **26** (2.g, 4.8 mmol), *p*-nitrobenzyl bromide (3.05 g, 14.1 mmol), and K_2CO_3 (2.03 g, 14.7 mmol) in acetone (70 ml) was heated under reflux for 2.5 h. After evaporation of the solvents, the residue was taken up into CH_2Cl_2. The organic layer was washed with water and dried over $MgSO_4$. After evaporation of the solvent, the residue was triturated in Et_2O to give **27** as a yellow solid (2.88 g, 87%). mp 171-172 °C (colorless needles from AcOEt). $[\alpha]_D^{27}$ -20.4° (c 0.495, $CHCl_3$). NMR δ: 2.74 (1H, dd, J = 9, 14 Hz), 3.00 (1H, dd, J = 5, 14 Hz), 3.70-3.90 (1H, m), 3.82 (3H, s), 3.87 (6H, s), 3.90 (3H, s), 4.20-4.37 (2H, m), 5.07 (2H, s), 5.11 (2H, s), 6.36 (1H, d, J = 1.7 Hz), 6.42 (1H, d, J = 1.7 Hz), 6.78 (2H, s), 7.52 (1H, d, J = 2 Hz), 7.53 (2H, d, J = 9 Hz), 7.61 (2H, d, J = 9 Hz), 8.18 (2H, d, J = 9 Hz), 8.22 (2H, d, J = 9 Hz). IR (KBr): 2940, 1748, 1646, 1584, 1514, 1346 cm^{-1}. MS m/z: 686 (M^+). Anal. Calcd for $C_{36}H_{34}N_2O_{12}$: C, 62.97; H, 4.99; N, 4.08. Found: C, 62.73; H, 5.01; N, 4.31.

(3a*S*,*R*-Biar)-3a,4-Dihydro-6,9,10,11-tetra-methoxy-7,8-bis(4-nitrobenzyloxy)dibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (28a) and (3a*S*,*R*-Biar)-3a,4-Dihydro-8,9,10,11-tetra-methoxy-6,7-bis(4-nitrobenzyloxy)dibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (28b). A mixture of **27** (2.50 g, 3.64 mmol), $Fe(ClO_4)_3 \cdot 6H_2O$ (4.0 g, 8.65 mmol), and CF_3CO_2H (6 ml) in CH_2Cl_2 (60 ml) was stirred at room temperature for 4 h. AcOEt was added, and the organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give an inseparable mixture of **28b** and **28a** as a pale yellow oil (1.45 g, 58%). NMR δ: 2.42-2.50 (1H, m), 3.02-3.18 (1H, m), 3.40-3.64 (1H, m), 3.57 (1/3 x 3H, s), 3.58 (2/3 x 3H, s), 3.63 (1/3 x 3H, s), 3.83 (2/3 x 3H, s), 3.88 (2/3 x 3H, s), 3.90 (2/3 x 3H, s), 3.91 (1/3 x 3H, s), 3.92 (1/3 x 3H, s), 4.07 (1H, dd, J = 8, 10 Hz), 4.40-4.58 (1H, m), 4.64 (2/3 x 1H, d, J = 12 Hz), 5.02 (2/3 x 1H, d, J = 12 Hz), 5.14-5.30 (2/3 x 4H, m), 6.46 (1/3 x 1H, s), 6.49 (2/3 x 1H, s), 6.54 (2/3 x 1H, s), 6.61 (1/3 x 1H, s), 7.06 (2/3 x 2H, d, J = 9 Hz), 7.37 (2/3 x 1H, d, J = 2.6 Hz), 7.56-7.63 (1/3 x 5H + 2/3 x 2H, m), 8.02 (2/3 x 2H, d, J = 9 Hz), 8.17 (2/3 x 2H, d, J = 9 Hz), 8.25 (1/3 x 4H, d, J = 9 Hz). IR ($CHCl_3$): 1754, 1674, 1604, 1348 cm^{-1}. MS m/z: 684 (M^+). HRMS m/z: Calcd for $C_{36}H_{32}N_2O_{12}$ (M^+): 684.19552. Found: 684.19850.

(3a*S*,*R*-Biar)-7,8-Dibenzyloxy-3a,4-dihydro-6,9,10,11-tetramethoxydibenzo[4,5:6,7]cyclo-octa[1,2-*c*]furan-1(3*H*)-one (13e) and (3a*S*,*R*-Biar)-6,7-Dibenzyloxy-3a,4-dihydro-8,9,10,11-tetramethoxydibenzo[4,5:6,7]-cycloocta[1,2-*c*]furan-1(3*H*)-one (13d). A solution of an above described mixture of **28b** and **28a** (1.4 g, 2.05 mmol) in AcOEt (50 ml) was hydrogenated over 10% Pd-C (100 mg) under a hydrogen atmosphere at room temperature for 2.5 h. After filtration of the catalyst, the filtrate was concentrated and the residue was dissolved into AcOEt. The organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was heated with benzyl bromide (1.7 ml, 21.4 mmol) and K_2CO_3 (3.6 g, 26.1 mmol) in acetone (30 ml) for 4 h. The reaction was quenched with Et_3N. AcOEt was added, and the organic layer was washed successively with 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:3) to give **13e** as a colorless oil (644 mg, 53%) and **13d** as a colorless oil (238 mg, 20%; physical data were shown before). **13e**: $[\alpha]_D^{25}$ -139° (c 1.20, $CHCl_3$). NMR δ: 2.47 (1H, dd, J = 1, 14 Hz), 3.08 (1H, dd, J = 7, 14 Hz), 3.43-3.60 (1H, m), 3.62 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.91 (3H, s), 4.11 (1H, dd, J = 9, 10 Hz), 4.47 (1H, t, J = 9 Hz), 4.52 (1H, d, J = 11 Hz), 4.91 (1H, d, J = 11 Hz), 5.03 (1H, d, J = 10 Hz), 5.13 (1H, d, J = 10 Hz), 6.44 (1H, s), 6.54 (1H, s), 6.86-6.94 (2H, m), 7.16-7.20 (3H, m,), 7.29-7.37 (3H, m), 7.43-7.48 (2H, m). IR ($CHCl_3$): 1752, 1674, 1594 cm^{-1}. MS m/z: 594 (M^+). HRMS m/z: Calcd for $C_{36}H_{34}O_8$ (M^+): 594.22537. Found: 594.22550.

(3a*S*,13a*S*,*R*-Biar)-10-Benzyloxy-3a,4,13,13a-tetrahydro-13a-hyxroxy-6,7,8,9,11-penta-methoxydibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (14) and (3a*S*,13a*R*,*R*-Biar)-10-Benzyloxy-3a,4,13,13a-tetrahydro-13a-hyxroxy-6,7,8,9,11-pentamethoxydibenzo[4,5:6,7]-cycloocta[1,2-*c*]furan-1(3*H*)-one (29). A mixture of **13b** (100 mg, 0.193 mmol), $Mn(acac)_2$ (20 mg, 0.08 mmol), and $PhSiH_3$ (0.1 ml, 0.81 mmol) in 2-PrOH (5 ml) was stirred at 70 °C under an oxygen atmosphere for 20 h. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:1) to give **29** as a colorless foam (15 mg, 14%) and **14** as a colorless oil (75 mg, 72%). **14**: $[\alpha]_D^{25}$ +0.38° (c 0.26, $CHCl_3$). NMR δ: 2.68-2.90 (6H, m), 3.60 (3H, s), 3.65 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 3.85-3.95 (1H, m), 4.40 (1H, dd, J = 8, 9 Hz), 5.11 (1H, d, J = 11 Hz), 5.04 (1H, d, J = 11 Hz), 6.38 (1H, s), 6.71 (1H, s), 7.31-7.52 (5H, m). IR ($CHCl_3$): 1778, 1596 cm^{-1}. MS m/z: 536 (M^+). HRMS m/z: Calcd for $C_{30}H_{32}O_9$ (M^+): 536.20463. Found: 536.20439. **29**: $[\alpha]_D^{25}$ +123° (c 0.22, $CHCl_3$). NMR δ: 1.88 (1H, br), 2.00-2.15 (1H, m), 2.56 (1H, d, J = 13 Hz), 2.69 (1H, dd, J = 11, 16 Hz), 2.96 (1H, dd, J = 7, 16 Hz), 3.43 (1H, d, J = 13 Hz), 3.53 (3H, s), 3.73 (3H, s), 3.80 (3H, s), 3.88 (3H, s), 4.04 (1H, dd, J = 8, 10 Hz), 4.17 (1H, t, J = 8 Hz), 5.08 (2H, s), 6.38 (1H, s), 6.55 (1H, s), 7.26-7.49 (5H, m). IR ($CHCl_3$): 1776, 1598 cm^{-1}. HS m/z: 536 (M^+). HRMS m/z: Calcd for $C_{30}H_{32}O_9$ (M^+): 536.20463. Found: 536.20576.

(6*S*,7*R*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,3,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6-ol (30). A solution of **14** (180 mg, 0.34 mmol) in THF (5 ml) was added to a refluxing solution of $LiAlH_4$ (150 g, 4.0 mmol) in THF (5 ml) and the resultant mixture was heated under reflux for 10 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (2.0 ml). Pyridine (1 ml) and methanesulfonyl chloride (0.5 ml) were added and the resultant mixture was stirred at 0 °C for 1 h. AcOEt was added, and the mixture was washed with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 2:1) to give **30** as a colorless solid (153 mg, 65%). mp 170.0-171.0 °C (colorless plates from AcOEt-hexane). $[\alpha]_D^{23}$ +111° (c 0.14, $CHCl_3$). NMR δ: 2.20-2.43 (3H, m), 2.55-2.82 (3H, m), 3.04 (3H, s), 3.14 (3H, s), 3.57 (3H, s), 3.62 (3H, s), 3.86 (3H, s), 3.90 (3H, s), 3.93 (3H, s), 4.19-4.21 (4H, m), 5.07 (1H, d, J = 12 Hz), 5.09 (1H, d, J = 12 Hz), 6.50 (1H, s), 6.76 (1H, s), 7.31-7.45 (5H, m). IR (KBr): 1594 cm^{-1}. MS m/z: 600 (M^+-$MeSO_3H$). Anal. Calcd for $C_{32}H_{40}S_2O_{13}$: C, 55.16; H, 5.79. Found: C, 54.91; H, 5.98.

(6*S*,7*S*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-1,3,10,11,12-pentamethoxy-6,7-dimethyldibenzo[*a*,*c*]cyclooctene-6-ol (31). A solution of **30** (125 mg, 0.18 mmol) in THF (5 ml) was added to a refluxing solution of $LiAlH_4$ (100 mg, 2.63 mmol) in THF (5 ml) and the resultant mixture was heated under reflux for 5 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 1:2) to give **31** as a colorless oil (84 mg, 92%). $[\alpha]_D^{23}$ +66.0° (c 0.16, $CHCl_3$). NMR δ: 0.82 (3H, d, J = 7 Hz), 1.25 (3H, s), 1.70-1.90 (2H, m), 2.35 (1H, d, J = 13 Hz), 2.37 (1H, dd, J = 7, 14.4 Hz), 2.63 (1H, dd, J = 14.4, 1.7 Hz), 2.67 (1H, d, J = 13 Hz), 3.55 (3H, s), 3.62 (3H, s), 3.85 (3H, s), 3.89 (6H, s), 5.04 (1H, d, J = 11 Hz), 5.10 (1H, d, J = 11 Hz), 6.54 (1H, s), 6.58 (1H, s), 7.26-7.58 (5H, m). IR (KBr): 1594 cm^{-1}. MS m/z: 508 (M^+). HRMS m/z: Calcd for $C_{30}H_{36}O_7$ (M^+): 508.24610. Found: 508.24800.

SZ-M3 (4). **31** (77 mg, 0.15 mmol) was hydrogenated over 10% Pd-C (7 mg) in AcOEt (5 ml) under a hydrogen atmosphere for 2.5 h. After filtration of the catalyst, the filtrate was concentrated to give **4** as a colorless solid (66 mg, 100%). mp 138.5-139 °C (colorless prisms from Et_2O). $[\alpha]_D^{24}$ +105° (c 0.385, $CHCl_3$). NMR δ: 0.83 (3H, d, J = 7 Hz), 1.26 (3H, s), 1.60-1.96 (2H, m), 2.36 (1H, d, J = 14 Hz), 2.39 (1H, dd, J = 7.5, 14 Hz), 2.67 (1H, d, J = 14 Hz), 2.68 (1H, dd, J = 14, 2 Hz), 3.41 (3H, s), 3.56 (3H, s), 3.90 (6H, s), 3.95 (3H, s), 5.64 (1H, s), 6.56 (1H, s), 6.63 (1H, s). IR (KBr): 1602, 1494 cm^{-1}. MS m/z: 418 (M^+). Anal. Calcd for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 65.81; H, 7.11.

General Procedure for the conversion of 13a-e to 15a-e. A solution of **13** (0.03 M), $Rh(PPh_3)_3Cl$ (0.0025 M), and Et_3SiH (0.005 M) in toluene was heated under reflux for 13 - 24 h. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane) to give **15**.

(*R*-Biar)-4,13-Dihydro-6,7,8,9,10,11-hexamethoxydibenzo[4,5:6,7]cycloocta[1,2-*c*]furan-1(3*H*)-one (15a). **15a** was obtained from **13a** as a pale brown amorphous solid (86%). $[\alpha]_D^{26}$ +267° (c 0.25, $CHCl_3$). NMR δ: 2.98 (1H, dd, J = 3, 16 Hz), 3.14 (1H, d, J = 16 Hz), 3.38 (1H, d, J = 3, 16 Hz), 3.55 (1H, d, J = 16 Hz), 3.69 (3H, s), 3.72 (3H, s), 3.86 (3H, s), 3.89 (6H, s), 3.90 (3H, s), 4.70 (2H, d, J = 3 Hz), 6.48 (1H, s), 6.56 (1H, s). IR ($CHCl_3$): 1746, 1668, 1598 cm^{-1}. MS m/z: 442 (M^+). HRMS m/z: Calcd for $C_{24}H_{26}O_8$ (M^+): 442.16277. Found: 442.16317.

(*R*-Biar)-10-Benzyloxy-4,13-dihydro-6,7,8,9,11-pentamethoxydibenzo[4,5:6,7]cycloocta-[1,2-*c*]furan-1(3*H*)-one (15b). **15b** was obtained from **13b** as a colorless solid (100%). mp 177.5-178 °C (colorless needles from AcOEt-hexane). $[\alpha]_D^{26}$ +252° (c 0.74, $CHCl_3$). NMR δ: 3.00 (1H, dd, J = 3, 15 Hz), 3.14 (1H, d, J = 16 Hz), 3.34 (1H, dd, J = 3, 15 Hz), 3.54 (1H, d, J = 16 Hz), 3.66 (3H, s), 3.72 (3H, s), 3.83 (3H, s), 3.88 (3H, s), 3,90 (3H, s), 4.69 (2H, dd, J = 3 Hz), 5.04 (1H, d, J = 11 Hz), 5.07 (1H, d, J = 11 Hz), 6.48 (1H, s), 6.55 (1H, s), 7.29-7.51 (5H, m). IR (KBr): 1748, 1672, 1596 cm^{-1}. MS m/z: 518 (M^+). Anal. Calcd for $C_{30}H_{30}O_8$: C, 69.48; H, 5.83. Found: C, 69.47; H, 6.02.

(*R*-Biar)-11-Benzyloxy-4,13-dihydro-6,7,8,9,10-pentamethoxydibenzo[4,5:6,7]cycloocta-[1,2-*c*]furan-1(3*H*)-one (15c). **15c** was obtained from **13c** as a pale brown amorphous solid (100%).

$[\alpha]_D^{26}$ +216° (c 0.615, $CHCl_3$). NMR δ: 2.96 (1H, dq, J = 16, 3 Hz), 3.15 (1H, d, J = 16 Hz), 3.36 (1H, dd, J = 16, 3 Hz), 3.54 (1H, d, J = 16 Hz), 3.69 (3H, s), 3.74 (3H, s), 3.88 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 4.69 (2H, d, J = 3 Hz), 5.09 (2H, s), 6.48 (1H, s), 6.65 (1H, s), 7.33-7.50 (5H, s). IR ($CHCl_3$): 1746, 1670, 1596 cm^{-1}. MS m/z: 518 (M^+). HRMS m/z: Calcd for $C_{30}H_{30}O_8$ (M^+): 518.19407. Found: 518.19360.

(*R*-Biar)-6,7-Dibenzyloxy-4,13-dihydro-8,9,10,11-tetramethoxydibenzo[4,5:6,7]cycloocta-[1,2-*c*]furan-1(3*H*)-one (15d). **15d** was obtained from **13d** as a colorless oil (92%). $[\alpha]_D^{24}$ +214° (c 0.655, $CHCl_3$). NMR δ: 2.92 (1H, dd, J = 4, 15 Hz), 3.11 (1H, d, J = 16 Hz), 3.32 (1H, dd, J = 4, 15 Hz), 3.55 (1H, d, J = 16 Hz), 3.70 (3H, s), 3.71 (3H, s), 3.86 (3H, s), 3.89 (3H, s), 4.67 (2H, d, J = 3 Hz), 5.03-5.30 (4H, m), 6.56 (1H, s), 6.54 (1H, s), 7.25-7.56 (10H, m). IR ($CHCl_3$): 1746, 1668, 1596 cm^{-1}. MS m/z: 594 (M^+). HRMS m/z: Calcd for $C_{36}H_{34}O_8$ (M^+): 594.22537. Found: 594.22665.

(*R*-Biar)-7,8-Dibenzyloxy-4,13-dihydro-6,9,10,11-tetramethoxydibenzo[4,5:6,7]cycloocta-[1,2-*c*]furan-1(3*H*)-one (15e). **15e** was obtained from **13e** as a colorless oil (71%). $[\alpha]_D^{25}$ +263° (c 1.65, $CHCl_3$). NMR δ: 3.16 (1H, d, J = 16 Hz), 3.36 (1H, d, J = 16 Hz), 3.40 (1H, d, J = 16 Hz), 3.76 (1H, d, J = 16 Hz), 3.70 (3H, s), 3.83 (3H, s), 3.86 (3H, s), 3.88 (3H, s), 4.70-4.73 (2H, br), 4.71 (1H, d, J = 11 Hz), 4.98 (1H, d, J = 11 Hz), 5.07 (1H, d, J = 11 Hz), 5.14 (1H, d, J = 11 Hz), 6.50 (2H, s), 6.90-6.95 (2H, m), 7.11-7.21 (3H, m), 7.30-7.38 (3H, m), 7.45-7.78 (3H, m). IR ($CHCl_3$): 1746, 1670, 1598 cm^{-1}. MS m/z: 594 (M^+). HRMS m/z: Calcd for $C_{36}H_{34}O_8$ (M^+): 594.22537. Found: 594.22675.

M_1 (5). A solution of **15a** (200 mg, 0.45 mmol) in THF (5 ml) was added to a refluxing solution of DIBAH (1.5 M in toluene, 2 ml, 3 mmol) in THF (10 ml) and the resultant solution was heated under reflux for 20 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. After evaporation of the solvent, the residue was dissolved in acetone (10 ml) and water (3 ml). OsO_4 (15 mg) and *N*-methylmorpholine *N*-oxide (NMO) (100 mg, 0.86 mmol) were added and the resultant solution was stirred at room temperature for 66 h. After addition of AcOEt, the organic layer was washed successively with water, 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in pyridine (2 ml). Methanesulfonyl chloride (0.5 ml) was added and the resultant mixture was stirred at room temperature for 1 h. AcOEt was added, and the mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue (211 mg) in THF (4 ml) was added to a refluxing suspension of $LiAlH_4$ (200 mg, 5.26 mmol) in THF (6 ml) and the resultant mixture was heated under reflux for 20 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. The filtrate was concentrated and chromatographed (AcOEt-hexane 1:1) to give **5** as a colorless solid (76 mg, 38%). mp 162.5-163.5 °C (colorless needles from Et_2O). $[\alpha]_D^{26}$ +115° (c 0.565, $CHCl_3$). NMR δ: 1.12 (3H, s),1.32 (3H, s), 1.40-2.00 (2H, m), 2.40 (1H, d, J = 14 Hz), 2.55 (1H, d, J = 14 Hz), 2.68 (1H, d, J = 14 Hz), 2.76 (1H, d, J = 14 Hz), 3.58 (3H, s), 3.61 (3H, s), 3.88 (3H, s), 3.90 (6H, s), 3.92 (3H, s), 6.61 (1H, s), 6.67 (1H, s). IR (KBr): 1596, 1490 cm^{-1}. MS m/z: 448 (M^+). Anal. Calcd for $C_{24}H_{32}O_8$: C, 64.27; H, 7.19. Found: C, 64.09; H, 7.21.

Typical procedure for the conversion of 15b-d to 33b-g.

(6*R*,7*S*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,3,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33b) and (6*S*,7*R*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,3,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33c). A solution of **15b** (16.9 g, 32.6 mmol) in THF (50 ml) was added to a refluxing solution of DIBAH (1.5 M in toluene, 80 ml, 120 mmol) in THF (50 ml) and the resultant mixture was heated under reflux for 20 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. After evaporation of the solvent, the residue was dissolved in acetone (200 ml) and water (50 ml). OsO_4 (150 mg) and NMO (6.0 g, 51.3 mmol) were added and the resultant mixture was stirred at room temperature for 70 h. The reaction was quenched with saturated $NaHSO_3$ and extracted with AcOEt. The combined extracts were successively washed with water, 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, the residue was dissolved in

pyridine (50 ml). Methanesulfonyl chloride (20.0 ml) was added and the resultant mixture was stirred at room temperature for 2 h. AcOEt was added, and the mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 3:2) to give **33b** (6.33 g, 27%, colorless oil) and **33c** (5.80 g, 25%, colorless oil). These materials were used in the next reaction without further purification. **33b**: NMR δ: 1.40-1.92 (2H, br), 2.66-2.91 (4H, m), 3.12 (3H, s), 3.14 (3H, s), 3.60 (3H, s), 3.64 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 3.94 (3H, s), 4.20-4.42 (4H, m), 5.08 (1H, d, J = 11 Hz), 5.10 (1H, d, J = 11 Hz), 6.55 (1H, s), 6.97 (1H, s), 7.28-7.54 (5H, m). **33c**: NMR δ: 1.40-1.92 (2H, br), 2.60-2.92 (4H, m), 3.16 (6H, s), 3.59 (3H, s), 3.66 (3H, s), 3.92 (3H, s), 3.93 (3H, s), 3.95 (3H, s), 4.21 (2H, s), 4.30 (1H, d, J = 11 Hz), 4.40 (1H, d, J = 11 Hz), 5.08 (1H, d, J = 11 Hz), 5.14 (1H, d, J=11 Hz), 6.63 (1H, s), 6.95 (1H, s), 7.28-7.54 (5H, m).

(6*R*,7*S*,*R*-Biar)-3-Benzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,2,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33d) and (6*S*,7*R*,*R*-Biar)-3-Benzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,2,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33e). **33d** (30%, colorless oil) and **33e** (27%, colorless oil) was obtained from **15c** as described above. **33d**: $[\alpha]_D^{28}$ +90.8° (c 0.065, $CHCl_3$). NMR δ: 1.64 (2H, br), 2.60-2.83 (4H, m), 3.08 (3H, s), 3.12 (3H, s), 3.60 (3H, s), 3.63 (3H, s), 3.89 (3H, s), 3.93 (6H, s), 4.20 (1H, d, J = 10 Hz), 4.20-4.21 (2H, m), 4.34 (1H, d, J = 10 Hz), 5.18 (2H, s), 6.62 (1H, s), 6.94 (1H, s), 7.33-7.51 (5H, m). IR ($CHCl_3$): 1594, 1490, 1462 cm^{-1}. MS m/z: 616 (M^+-$MeSO_3H$). **33e**: $[\alpha]_D^{24}$ +92.1° (c 0.18, $CHCl_3$). NMR δ: 1.40-2.10 (2H, br), 2.64-2.92 (4H, m), 3.12 (6H, s), 3.61 (3H, s), 3.63 (3H, s), 3.90 (3H, s), 3.92 (6H, s), 4.23 (2H, s), 4.25 (1H, d, J = 10 Hz), 4.41 (1H, d, J = 10 Hz), 5.16 (1H, d, J=12 Hz), 5.24 (1H, d, J = 12 Hz), 6.58 (1H, s), 7.01 (1H, s), 7.32-7.54 (5H, m). IR ($CHCl_3$): 1594, 1490, 1462 cm^{-1}. MS m/z: 520 (M^+-2 x $MeSO_3H$).

(6*S*,7*R*,*R*-Biar)-10,11-Dibenzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,2,3,12-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33g) and (6*R*,7*S*,*R*-Biar)-10,11-Dibenzyloxy-5,6,7,8-tetrahydro-6,7-bis(methanesulfonyloxymethyl)-1,2,3,12-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (33f). **33g** (28%, colorless oil) and **33f** (30%, colorless oil) was obtained from **15d** as described above. These materials were used in the next reaction without further purification. **33g**: NMR δ: 1.40-2.10 (2H, br), 2.52-2.84 (4H, m), 3.08 (3H, s), 3.12 (3H, s), 3.58 (3H, s), 3.65 (3H, s), 3.90 (3H, s), 3.93 (3H, s), 4.21 (1H, d, J = 10 Hz), 4.22 (2H, s), 4.35 (1H, d, J = 10 Hz), 5.07 (1H, d, J = 11 Hz), 5.12 (1H, d, J = 11 Hz), 5.13 (2H, s), 6.61 (1H, s), 6.95 (1H, s), 7.26-7.52 (10H, m). MS m/z: 692 (M^+-$MeSO_3H$). **33f**: NMR δ: 1.30-1.90 (2H, br), 2.04-2.89 (4H, m), 3.11 (3H, s), 3.12 (3H, s), 3.57 (3H, s), 3.65 (3H, s), 3.91 (3H, s), 3.92 (3H, s), 4.19 (2H, s), 4.26 (1H, d, J = 10 Hz), 4.37 (1H, d, J = 10 Hz), 5.10 (2H, s), 5.12 (1H, d, J = 10 Hz), 5.21 (1H, d, J = 10 Hz), 6.58 (1H, s), 7.00 (1H, s), 7.27-7.49 (10H, m). MS m/z: 692 (M^+-$MeSO_3H$).

Typical procedure for the conversion of 33b-e,g to 34b-f.

(6*S*,7*R*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,3,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-M4 benzyl ether) (34b). A solution of **33b** (6.33 g, 8.9 mmol) in THF (50 ml) was added to a refluxing suspension of $LiAlH_4$ (4.0 g, 0.1 mol) in THF (100 ml) over 10 min and the resultant mixture was heated under reflux for 20 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. The evaporation and chromatography (AcOEt-hexane 2:3) of the filtrate afforded **34b** as a colorless oil (2.92 g, 63%). $[\alpha]_D^{26}$ +94.3° (c 0.28, $CHCl_3$). NMR δ: 1.13 (3H, s), 1.32 (3H, s), 1.60 (2H, br), 2.40 (1H, d, J = 14 Hz), 2.54 (1H, d, J = 14 Hz), 2.63 (1H, d, J = 14 Hz), 2.76 (1H, d, J = 14 Hz), 3.57 (3H, s), 3.62 (3H, s), 3.86 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 5.02 (1H, d, J = 11 Hz), 5.10 (2H, d, J = 11 Hz), 6.57 (1H, s), 6.67 (1H, s), 7.26-7.49 (5H, m). IR ($CHCl_3$): 3544, 3008, 2940, 1594, 1488 cm^{-1}. MS m/z: 524 (M^+). HRMS m/z: Calcd for $C_{30}H_{36}O_8$ (M^+): 524.24102. Found: 524.24111.

(6*R*,7*S*,*R*-Biar)-2-Benzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,3,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-MD2 benzyl ether) (34c). **34c** was obtained from **33c** as a colorless oil (67%). $[\alpha]_D^{26}$ +101° (c=0.33, $CHCl_3$). NMR δ: 1.09 (3H, s), 1.32 (3H, s), 1.60 (2H, br), 2.40 (1H, d, J = 13 Hz), 2.54 (1H, d, J = 14 Hz), 2.67 (1H, d, J = 13 Hz), 2.73 (1H, d, J = 14 Hz), 3.54 (3H, s), 3.64 (3H, s), 3.85 (3H, s), 3.91 (3H, s), 3.92 (3H, s), 5.05 (1H, d, J = 11 Hz), 5.07 (1H, d, J = 11 Hz), 6.41 (1H, s), 6.64 (1H, s), 7.17-7.78 (5H, m). IR ($CHCl_3$): 3544, 3008, 2940, 1594, 1488 cm^{-1}. MS m/z: 524 (M^+). HRMS m/z: Calcd for $C_{30}H_{36}O_8$ (M^+): 524.24102. Found: 524.24023.

(6*S*,7*R*,*R*-Biar)-3-Benzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,2,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-M7 benzyl ether) (34d). **34d** was obtained from **33d** as a colorless oil (66%). $[\alpha]_D^{27}$ +94.4° (c 0.32, $CHCl_3$). NMR δ: 1.12 (3H, s), 1.31 (3H, s), 1.80-2.20 (2H, br), 2.40 (1H, d, J = 14 Hz), 4.52 (1H, d, J = 14 Hz), 2.68 (1H, d, J = 14 Hz), 2.75 (1H, d, J = 14 Hz), 3.60 (3H, s), 3.61 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 5.16 (2H, s), 6.67 (1H, s), 6.69 (1H, s), 7.34-7.51 (5H, m). IR ($CHCl_3$): 1594 cm^{-1}. MS m/z: 524 (M^+). HRMS m/z: Calcd for $C_{30}H_{36}O_8$ (M^+): 594.24102. Found: 524.24127.

(6*R*,7*S*,*R*-Biar)-3-Benzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,2,10,11,12-pentamethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-M5 benzyl ether) (34e). **34e** was obtained from **33e** as a colorless oil (74%). $[\alpha]_D^{24}$ +88.6° (c 0.22, $CHCl_3$). NMR δ: 0.92 (3H, s), 1.28 (3H, s), 1.70-2.20 (2H, br), 2.32 (1H, d, J = 14 Hz), 2.52 (1H, d, J = 14 Hz), 2.63 (1H, d, J = 14 Hz), 2.72 (1H, d, J = 14 Hz), 3.57 (3H, s), 3.64 (3H, s), 3.90 (3H, s), 3.916 (3H, s), 3.923 (3H, s), 5.15 (1H, d, J = 12 Hz), 5.22 (1H, d, J = 12 Hz), 6.60 (1H, s), 6.66 (1H, s), 7.26-7.48 (5H, m). IR ($CHCl_3$): 1594 cm^{-1}. MS m/z: 524 (M^+). HRMS m/z: Calcd for $C_{30}H_{36}O_8$ (M^+): 524.24102. Found: 524.24197.

(6*R*,7*S*,*R*-Biar)-10,11-Dibenzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,2,3,12-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-M8 dibenzyl ether) (34f). **34f** was obtained from **33g** as a colorless solid (56%). mp 145-147 °C (colorless needles from AcOEt-hexane). $[\alpha]_D^{27}$ +115° (c 0.245, $CHCl_3$). NMR δ: 1.13 (3H, s), 1.31 (3H, s), 1.58 (2H, br), 2.41 (1H, d, J = 14 Hz), 2.52 (1H, d, J = 14 Hz), 2.65 (1H, d, J = 14 Hz), 2.76 (1H, d, J = 14 Hz), 3.58 (3H, s), 3.63 (3H, s), 3.90 (3H, s), 3.90 (3H, s), 5.06 (1H, d, J = 11 Hz), 5.09 (1H, d, J = 12 Hz), 5.11 (1H, d, J = 11 Hz), 5.12 (1H, d, J = 12 Hz), 6.68 (2H, s), 7.26-7.34 (4H, m), 7.35-7.47 (6H, m). IR (KBr): 1594 cm^{-1}. MS m/z: 600 (M^+). Anal. Calcd for $C_{36}H_{40}O_8$: C, 71.98; H, 6.71. Found: C, 71.75; H, 6.76.

(6*R*,7*S*,*R*-Biar)-11,12-Dibenzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,2,3,10-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (SZ-M10 dibenzyl ether) (34g) and (6*S*,7*R*,*R*-Biar)-11,12-Dibenzyloxy-5,6,7,8-tetrahydro-6,7-dimethyl-1,2,3,10-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7-diol (34h). A solution of **15e** (400 mg, 0.67 mmol) in THF (10 ml) was added to a refluxing solution of DIBAH (1.5 M in toluene, 4 ml, 6 mmol) in THF (10 ml) and the resultant mixture was heated under reflux for 10 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. After evaporation of the solvent, to the residue (450 mg) in acetone (5 ml) and water (1 ml) were added OsO_4 (10 mg) and NMO (130 mg, 1.11 mmol), and the resultant mixture was stirred at room temperature for 20 h. The reaction was quenched with saturated $NaHSO_3$ and extracted with AcOEt. The combined extracts were washed successively with water, 2N HCl, water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$. After evaporation of the solvent, to the residue (450 mg) in pyridine (3 ml) was added methanesulfonyl chloride (1 ml), and the resultant mixture was stirred at 0 °C for 2.5 h. AcOEt was added, and the mixture was washed successively with 2N HCl, water, saturated $NaHCO_3$, brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (AcOEt-hexane 2:1) to give a mixture of **33h** and **33i** (202 mg, colorless oil). A solution of a mixture of **33h** and **33i** (202 mg, 0.256 mmol) in THF (10 ml)was added to a refluxing suspension of $LiAlH_4$ (200 mg, 5.3 mmol) in THF (10 ml) over 10 min and the resultant mixture was heated under reflux for 30 min. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ and the insoluble material was filtered off. The concentration and chromatography (AcOEt-hexane 1:1) of the filtrate gave **34g** as a colorless oil (52 mg, 34%) and **34h** as a colorless oil (38 mg, 25%). **34g**: NMR δ: 1.11 (3H,

s), 1.32 (3H, s), 1.60-2.10 (2H, br), 2.30 (1H, d, J = 14 Hz), 2.54 (1H, d, J = 14 Hz), 2.55 (1H, d, J = 14 Hz), 2.78 (1H, d, J = 14 Hz), 3.59 (3H, s), 3.80 (3H, s), 3.88 (3H, s), 3.92 (3H, s), 4.45 (1H, d, J = 10.5 Hz), 4.89 (1H, d, J = 10.5 Hz), 5.06 (1H, d, J = 11 Hz), 5.16 (1H, d, J = 11 Hz), 6.63 (1H, s), 6.64 (1H, s), 6.84-6.89 (2H, m), 7.14-7.21 (3H, m), 7.26-7.41 (3H, m), 7.46-7.50 (2H, m). **34h**: NMR δ: 1.10 (3H, s), 1.30 (3H, s), 1.50-2.10 (2H, br), 2.41 (1H, d, J = 14 Hz), 2.42 (1H, d, J = 13 Hz), 2.60 (1H, d, J = 14 Hz), 2.69 (1H, d, J = 13 Hz), 3.57 (3H, s), 3.81 (3H, s), 3.86 (3H, s), 3.94 (3H, s), 4.53 (1H, d, J = 10.7 Hz), 4.91 (1H, d, J = 10.7 Hz), 5.07 (1H, d, J = 10.7 Hz), 5.15 (1H, d, J = 10.7 Hz), 6.57 (1H, s), 6.70 (1H, s), 6.86-6.91 (2H, m), 7.14-7.20 (3H, m), 7.26-7.40 (3H, m), 7.46-7.60 (2H, m).

Typical procedure for the conversion of 34b-h to 6-11 and 35.

SZ-M4 (6). **34b** (386 mg, 0.73 mmol) was hydrogenated over 10% Pd-C (30 mg) in AcOEt (20 ml) under a hydrogen atmosphere for 3.5 h. The catalyst was filtered off, and the filtrate was concentrated to give **6** as a colorless solid (320 mg, 100%). mp 156-157.5 °C (colorless needled from Et_2O). $[\alpha]_D^{30}$ +122° (c 1.47, $CHCl_3$). NMR δ: 1.13 (3H, s), 1.32 (3H, s), 2.06 (1H, s), 2.42 (1H, d, J = 13 Hz), 2.54 (1H, d, J = 14 Hz), 2.69 (1H, d, J = 13 Hz), 2.76 (1H, d, J = 14 Hz), 3.25 (1H, s), 3.41 (3H, s), 3.58 (3H, s), 3.90 (3H, s), 3.903 (3H, s), 3.96 (3H, s), 5.68 (1H, s), 6.62 (1H, s), 6.68 (1H, s). IR (KBr): 1600, 1494 cm^{-1}. MS m/z: 434 (M^+). Anal. Calcd for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96. Found: C, 63.40; H, 6.95.

SZ-M5 (7). **7** was obtained from **34e** as a colorless solid (100%). mp 159.0-160.0 °C (colorless prisms from Et_2O-hexane). $[\alpha]_D^{25}$ +117° (c 0.515, $CHCl_3$). NMR δ: 1.13 (3H, s), 1.32 (3H, s), 2.08 (1H, s), 2.38 (1H, d, J = 14 Hz), 2.55 (1H, d, J = 14 Hz), 2.64 (1H, d, J = 14 Hz), 2.78 (1H, d, J = 14 Hz), 3.22 (1H, s), 3.55 (3H, s), 3.57 (3H, s), 3.91 (3H, s), 3.92 (6H, s), 5.87 (1H, s), 6.63 (1H, s), 6.75 (1H, s). IR (KBr): 1586, 1488 cm^{-1}. MS m/z: 434 (M^+). Anal. Calcd for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96. Found: C, 63.52; H, 6.89.

SZ-MD2 (8). **8** was obtained from **34c** as a colorless solid (100%). mp 203.5-204.5 °C (colorless needles from AcOEt). $[\alpha]_D^{26}$ +129° (c 0.565, $CHCl_3$). NMR δ: 1.13 (3H, s), 1.32 (3H, s), 2.06 (1H, s), 2.38 (1H, d, J = 13 Hz), 2.56 (1H, d, J = 14 Hz), 2.67 (1H, d, J = 13 Hz), 2.78 (1H, d, J = 14 Hz), 3.20 (1H, s), 3.46 (3H, s), 3.54 (3H, s), 3.91 (3H, s), 3.93 (6H, s), 5.57 (1H, s), 6.63 (1H, s), 6.67 (1H, s). IR (KBr): 1598, 1494 cm^{-1}. MS m/z: 434 (M^+). Anal. Calcd for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96. Found: C, 63.41; H, 6.88.

SZ-M7 (9). **9** was obtained from **34d** as a colorless solid (74%). mp 196.5-198.5 °C (colorless prisms from Et_2O). $[\alpha]_D^{26}$ +144° (c 0.135, $CHCl_3$). NMR δ: 1.12 (3H, s), 1.30 (3H, s), 1.60 (2H, br), 2.40 (1H, d, J = 14 Hz), 2.50 (1H, d, J = 14 Hz), 2.72 (1H, d, J = 14 Hz), 2.72 (1H, d, J = 14 Hz), 3.53 (3H, s), 3.59 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 3.95 (3H, s), 5.81 (1H, br), 6.68 (1H, s), 6.70 (1H, s). IR (KBr): 1586, 1488 cm^{-1}. MS m/z: 434 (M^+). Anal. Calcd for $C_{23}H_{30}O_8 \cdot 1/10H_2O$: C, 63.33; H, 6.98. Found: C, 63.20; H, 6.78.

SZ-M8 (10). **10** was obtained from **34f** as a colorless solid (80%). mp 250-252 °C (colorless needles from AcOEt). $[\alpha]_D^{26}$ +136° (c 0.32, $CHCl_3$). NMR δ: 1.14 (3H, s), 1.31 (3H, s), 2.12 (1H, br), 2.42 (1H, d, J = 13 Hz), 2.50 (1H, d, J = 14 Hz), 2.72 (1H, d, J = 14 Hz), 2.75 (1H, d, J = 13 Hz), 3.26 (3H, s), 3.34 (1H, br), 3.53 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 5.55 (1H, s), 5.72 (1H, s), 6.70 (1H, s), 6.71 (1H, s). IR (KBr): 1598, 1492 cm^{-1}. MS m/z: 420 (M^+). Anal. Calcd for $C_{22}H_{28}O_8 \cdot 1/10H_2O$: C, 62.57; H, 6.73. Found: C, 62.42; H, 6.65.

SZ-M10 (11). **11** was obtained from **34g** as a colorless solid (100%). $[\alpha]_D^{27}$ +70.6° (c 0.225, $CHCl_3$). NMR δ: 1.16 (3H, s), 1.32 (3H, s), 1.60-2.20 (2H, br), 2.41 (1H, d, J = 14 Hz), 2.55 (1H, d, J = 14 Hz), 2.65 (1H, d, J = 14 Hz), 2.72 (1H, d, J = 14 Hz), 3.60 (3H, s), 3.906 (3H, s), 3.913 (3H, s), 3.96 (3H, s), 5.68 (1H, br), 5.75 (1H, br), 6.51 (1H, s), 6.76 (1H, s). IR ($CHCl_3$): 1622, 1596, 1498 cm^{-1}. MS m/z: 420 (M^+).

(6*S*,7*R*,*R*-Biar)-5,6,7,8-Tetrahydro-6,7-dimethyl-1,2,3,10-tetramethoxydibenzo[*a*,*c*]cyclooctene-6,7,11,12-tetraol (35). **35** was obtained from **34h** as a colorless solid (100%). $[\alpha]_D^{27}$ +71.1° (c 0.17, $CHCl_3$). NMR δ: 1.16 (3H, s), 1.32 (3H, s), 1.60-2.20 (2H, br), 2.40 (1H, d, J = 14 Hz), 2.54 (1H,

d, J = 14 Hz), 2.66 (1H, d, J = 14 Hz), 2.76 (1H, d, J = 14 Hz), 3.57 (3H, s), 3.93 (9H, s), 5.58 (1H, br), 5.63 (1H, br), 6.56 (1H, s), 6.69 (1H, s). IR ($CHCl_3$): 1596, 1498 cm^{-1}. MS m/z: 420 (M^+). HRMS m/z: Calcd for $C_{22}H_{28}O_8$ (M^+): 420.17842. Found: 420.17792.

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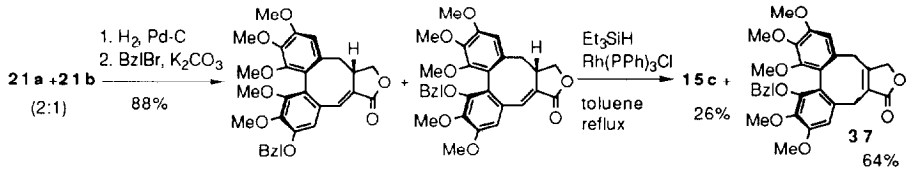
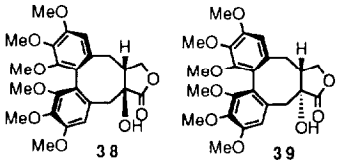


16. The structures of **14** and **29** were determined by the comparison of the NMR spectra of each product with those of the known hydroxylactones (**38** and **39**), the structures of which were confirmed by the correlation of them with schizandrin and isoschizandrin. **38**: NMR ($CDCl_3$) δ: 2.68 (6H, m), 3.637 (3H, s), 3.643 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 3.85-3.95 (1H, m), 4.40 (1H, dd, J = 8, 9 Hz), 6.37 (1H, s), 6.72 (1H, s). **39**: NMR ($CDCl_3$) δ: 1.86 (1H, br), 2.10-2.30 (1H, m), 2.57 (1H, d, J = 13 Hz), 2.73 (1H, dd, J = 12, 15 Hz), 3.01 (1H, dd, J = 7, 15 Hz), 3.44 (1H, d, J = 13 Hz), 3.57 (3H, s), 3.72 (3H, s), 3.84 (3H, s), 3.88 (3H, s), 3.89 (6H, s), 4.05 (1H, dd, J = 8, 10 Hz), 4.19 (1H, t, J = 8 Hz), 6.41 (1H, s), 6.55 (1H, s). See ref. 5n.



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18. Melting Points were measured using Buchi 535 melting point apparatus and are not corrected. Optical rotations were taken with a JASCO DIP-360 polarimeter. Ir spectra (IR) were obtained with a Hitachi 270-30 spectrophotometer. NMR spectra were measured in deuteriochloroform with a JEOL FX-200 Spectrometer at 200 MHz. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra (MS) and high resolution mass spectra (HRMS) were measured with a KRATOS CONCEPT 32 1H and 1S mass spectrometers. Flash chromatography was performed with silica gel 60 (230-400 mesh).

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