Synthesis of (±)-Dibenzocyclooctadiene Lignans, (±)-Schizandrin, (±)-Gomisin A and Their Stereoisomers, Utilizing the Samarium-Grignard Reaction

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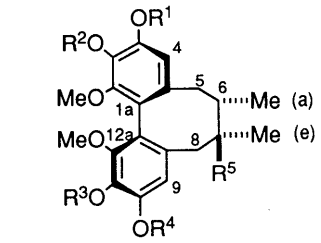
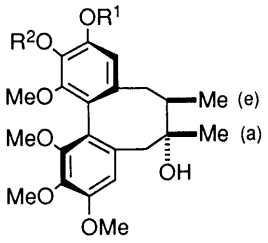
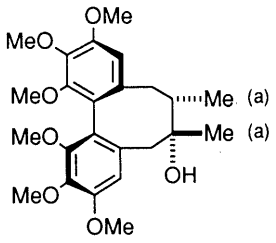
Several (±)-dibenzocyclooctadiene lignans, (±)-schizandrin (1a) (±)-gomisin A (1b), and their stereoisomers 2a and 2b, were synthesized by the samarium-Grignard reaction of the phenylpropyl bromides 4 and the phenylacetone derivative 5 to give the *erythro* and *threo*-butanols 6 and 7 followed by oxidative aryl–aryl coupling reaction of each butanol.

Keywords synthesis; lignan; dibenzocyclooctadiene; samarium-Grignard reaction; oxidative aryl–aryl coupling reaction

The fruits of *Schizandra chinesis* BAILLON (Schizandraceae) are very widely used in Asia as an antitussive and tonic, and more than three dozen dibenzocyclooctadiene lignans have been isolated from the plant since 1961.[1] These lignans can be classified into three types, namely, compounds in which the C-6 and C-7 methyl groups on dibenzocyclooctadiene ring (DBCO) have a *cis* relative configuration, such as schizandrin (**1a**) and gomisin A (**1b**), compounds having a *trans* configuration of the methyl groups such as **3a**, and deoxy-type compounds of **1a** or **1b** such as deoxyschizandrin (**1c**) and wuweizisu C (**1d**)[1a–c,o] (Chart 1). It is known that the DBCO ring of these lignans has a twist-boat-chair form (TBC) except for gomisin R, in which it has a twist-boat form (TB).[1o] These novel biaryl lignans offer attractive targets for synthesis[2] because of not only their unique structures, but also their





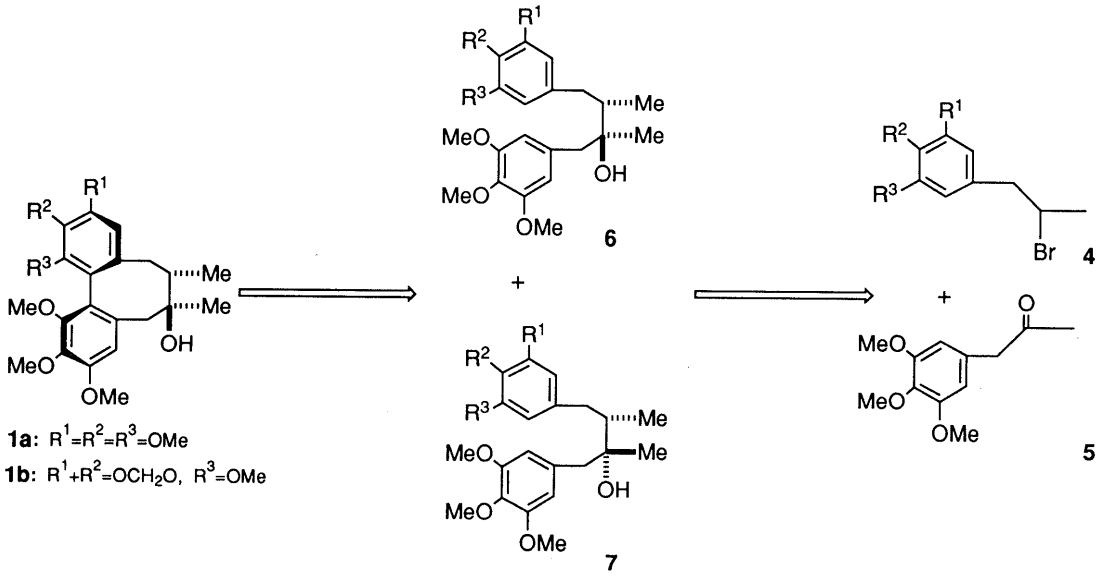


1a: $R^1=R^2=R^3=R^4=Me$, $R^5=OH$ (schizandrin)
1b: $R^1+R^2=CH_2$, $R^3=R^4=Me$, $R^5=OH$ (gomisin A)
1c: $R^1=R^2=R^3=R^4=Me$, $R^5=H$ (deoxyschizandrin)
1d: $R^1+R^2=R^3+R^4=CH_2$, $R^5=H$ (wuweizisu C)

2a: $R^1=R^2=Me$
2b: $R^1+R^2=CH_2$

3a (isoschizandrin)

Chart 1



1a: $R^1=R^2=R^3=OMe$
1b: $R^1+R^2=OCH_2O$, $R^3=OMe$

6

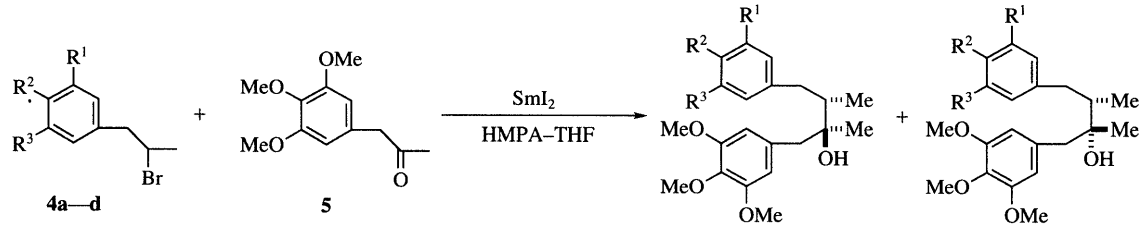
7

4

5

Chart 2

TABLE I. Cross Coupling Reactions of Phenylacetone and Phenylpropyl Bromides with the SmI_2–HMPA–THF System



Run	Bromide	Yield (%)	Product	Ratio (6:7)[a]
1	**4a**: $R^1=R^2=R^3=H$	61	**6a**+**7a**	(52:48)
2	**4b**: $R^1+R^2=OCH_2O$, $R^3=H$	50	**6b**+**7b**	(72:28)
3	**4c**: $R^1=R^2=R^3=OMe$	82	**6c**+**7c**	(58:42)
4	**4d**: $R^1+R^2=OCH_2O$, $R^3=OMe$	71	**6d**+**7d**	(46:54)

a) The *erythro*/*threo* ratios were determined by HPLC analysis.

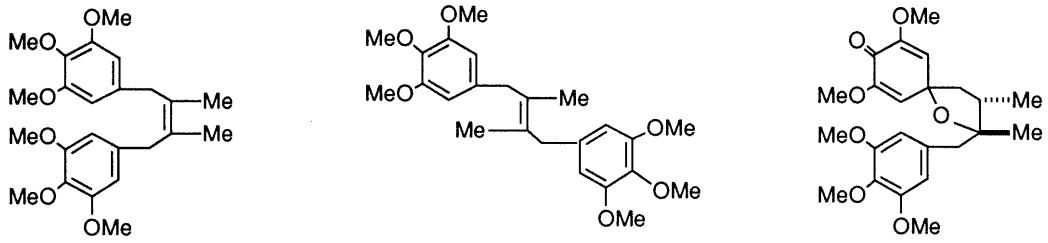


Chart 3

significant biological activities.[3] We report herein a new and concise synthesis of (±)-schizandrin (**1a**), (±)-gomisin A (**1b**) and their stereoisomers **2a** and **2b**, utilizing the recently developed samarium-Grignard reaction.[4]

The present synthetic strategy consists of reductive C–C coupling of the phenylpropyl bromides **4** and the phenylacetone derivative **5** to give the *erythro*- and *threo*-butanols **6** or **7**, followed by oxidative aryl–aryl coupling reaction of appropriate type to construct the target lignans, as shown in Chart 2.

The phenylpropyl bromides **4a** and **4b**[5a] were synthesized from the corresponding 1-phenyl-2-propenes by treatment with HBr gas, and **4c**[5c] and **4d** were prepared from the 1-phenyl-2-propanols obtained by the reduction of **5** and 1-(3-methoxy-4,5-methylenedioxyphenyl)-2-propanone[6] with $NaBH_4$, by treatment with PBr_3 in dimethylformamide (DMF). Although a number of C–C coupling reactions have been developed to date, we found that the samarium-Grignard reaction, consisting of the reaction of carbonyl compounds with *in situ*-formed alkylsamarium(III) reagents generated by the SmI_2 reduction of alkyl halides in the presence of hexamethylphosphoramide (HMPA) in tetrahydrofuran (THF),[4] is a suitable method for reductive coupling of **4** and **5** to yield the *erythro*- and *threo*-butanols **6** and **7**.

The results of the cross coupling reactions of **4a**—**4d** with **5** by using the SmI_2–HMPA–THF system are summarized in Table I. In these reactions, the cross coupling products were obtained in fairly good yields, but no stereoselectivity were observed and almost equal amounts of *erythro* and *threo* isomers **6** and **7** were obtained. The key intermediates **6c** and **7c** or **6d** and **7d** were separated by preparative HPLC using MeOH : H_2O = 6 : 4 as an eluent. We found that the *erythro* isomer **6c** (a suitable intermediate for the synthesis of the natural lignan schizandrin) and **6d** can be separated by two recrystallizations of the mixture from MeOH–H_2O (3 : 1). The structures of **6c** and **7c** were identified by direct comparison with authentic samples which were synthesized from the (*Z*)-butene **8** and the (*E*)-butene **9**[6] by hy-

TABLE II. Oxidative Aryl–Aryl Coupling Reaction of **11a** and **11b**

Run	Substrate	Reagent	Yield (%)	Product	Ratio (12:13)[a]
1	**11a**	A	36.0	**12a**±**13a**	(80:20)
2		B	21.0		
3		C	9.5		
4		D	5.0		
5		E	5.0		
6		F	Trace		
7		G	Trace		
8	**11b**	A	41.0	**12b**+**13b**	(80:20)
9		B	10.5		
10		C	10.0		
11		D	5.5		

a) The **12**/**13** ratios were determined by HPLC analysis. Reagent: A, $Fe(ClO_4)_3 \cdot 9H_2O$–CH_2Cl_2–MeCN; B, $Fe(ClO_4)_3 \cdot 9H_2O$–MeCN; C, $Fe(ClO_4)_3 \cdot 9H_2O$–CF_3CO_2H–CH_2Cl_2–MeCN; D, $FeCl_3$–MeCN; E, $FeCl_3$–Ac_2O; F, $Mn(ClO_4) \cdot 6H_2O$–$KMnO_4$–Ac_2O; G, VOF_3–CF_3CO_2H–CH_2Cl_2.

droboration with BH_3–THF followed by treatment with 30% H_2O_2 and aqueous 3 N NaOH. The structures of the related compounds **6a**, **7a**, **6b**, **7b**, **6d**, and **7d** were elucidated by analyses of their physical data in comparison with those of **6c** and **7c**.

Next, the oxidative aryl–aryl coupling reactions of the butanols **6** with various reagent systems (reagents A—C in Table II) were investigated. These oxidations were carried out with the isobutyrates **11** because direct oxidation of an alcohol such as **6c** with the reagent system $Fe(ClO_4)_3 \cdot 9H_2O$–MeCN gave only the spiro-dienone ether **10**. The results of the oxidation of the isobutyrate **11a** and **11b** with various reagent systems are summarized in Table II: the best results were obtained with both **11a** and **11b** by oxidation with the reagent system $Fe(ClO_4)_3 \cdot 9H_2O$–CH_2Cl_2–MeCN to give the biaryls **12a** and **12b** along with their stereoisomers **13a** and **13b** in the ratios of 8 : 2. Preferential formation of the stereoisomers **12a** and **13a** in these aryl–aryl coupling reactions may be due to the stereochemical stability differences between **11α** and **11β**; the **11β** form may be less stable than the **11α** form owing to the interaction between methyl and the bulky ester groups. Thus, **12a** and **12b** may result from the more favorable **11α** form in preference to **13a** and **13b**, as shown in Chart 5.

Finally, alkaline hydrolysis of **12a** and **12b** afforded (±)-schizandrin (**1a**), mp 129—130 °C, and (±)-gomisin A (**1b**), mp 165.5—166 °C. Similar treatment of **13a** and

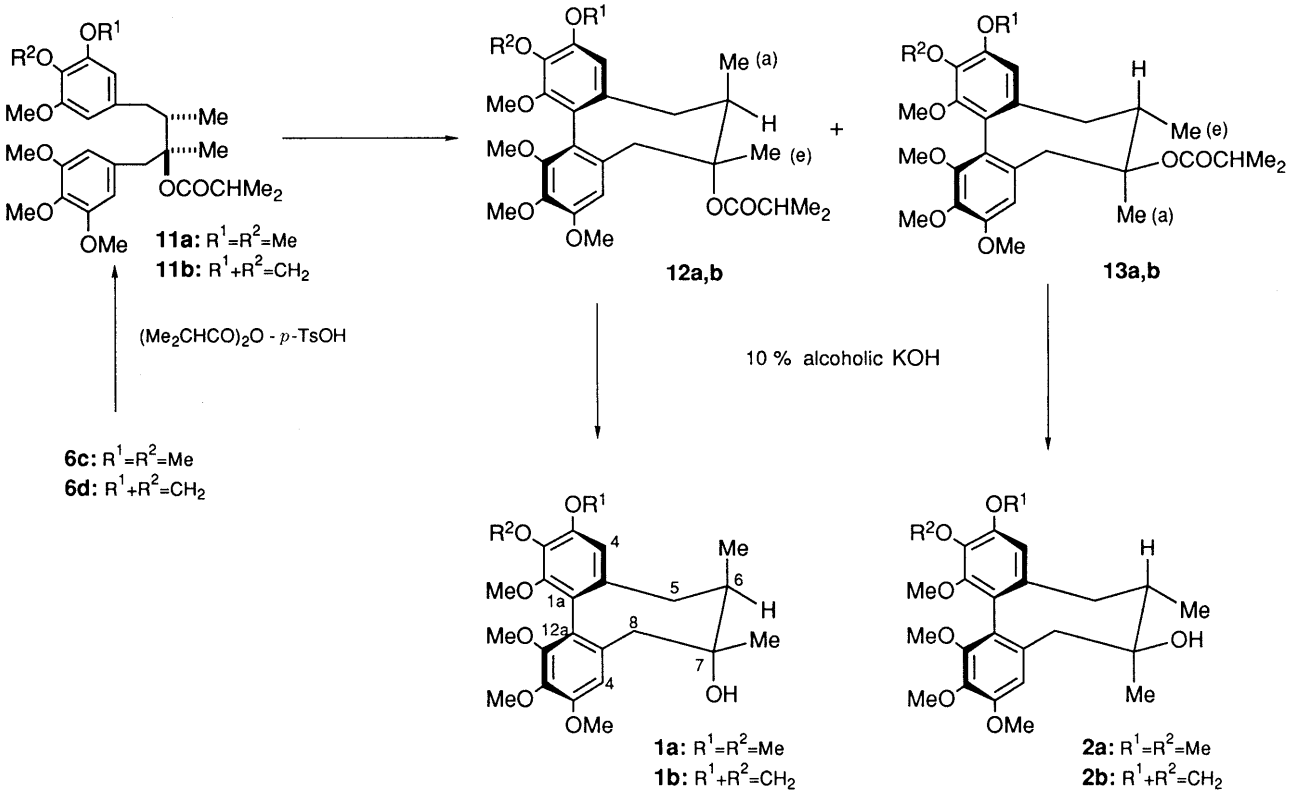


Chart 4

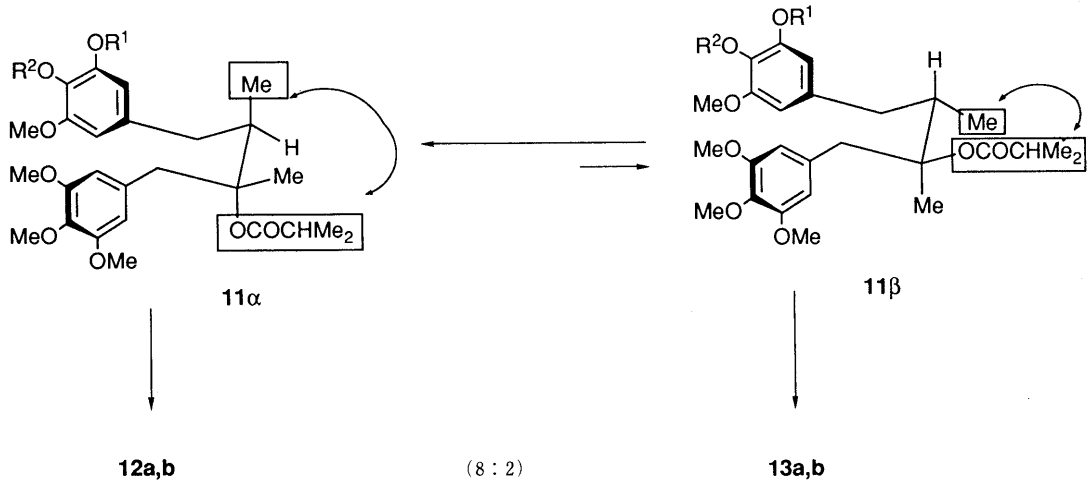


Chart 5

TABLE III. ^{1}H-NMR Spectral Data for the Lignans[a)]

	12a	12b	13a	13b	1a	1b	2a	2b
H-9	6.66	6.69	6.58	6.52	6.60	6.62	6.56	6.50
H-4	6.53	6.47	6.75	6.75	6.53	6.48	6.64	6.65
H-8α	2.60, d	2.62, d	2.84, d	2.89, d	2.36, d	2.34, d	2.61, d	2.62, d
(J=Hz)	(13.9)	(13.7)	(12.8)	(13.1)	(13.0)	(13.4)	(13.1)	(13.4)
H-8β	2.94, d	2.89, d	3.26, d	3.22, d	2.68, d	2.69, d	2.68, d	2.69, d
(J=Hz)	(13.9)	(13.7)	(12.8)	(13.1)	(13.0)	(13.4)	(13.1)	(13.4)
H-5α	2.86, d	2.79, d	2.16—2.20	2.16—2.19	2.67, dd	2.58, dd	2.20, dd	2.15, dd
(J=Hz)	(12.2)	(13.1)	(m)	(m)	(14.0)	(14.0)	(14.0)	(13.4)
					(1.5)	(1.5)	(9.7)	(9.4)
H-5β	2.22—2.48	2.16—2.44	2.16—2.20	2.16—2.19	2.38, dd	2.34, dd	2.18, d	2.12, d
(J=Hz)	(m)	(m)	(m)	(m)	(14.0)	(14.0)	(14.0)	(13.4)
					(7.3)	(7.3)		
H-6 (m)	2.22—2.48	2.26—2.44	2.16—2.20	2.21—2.31	1.80—1.88	1.83—1.93	1.64—1.75	1.65—1.75
C7-O<u>H</u> (s)	—	—	—	—	1.85	1.89	1.62	1.59
Me-7 (s)	1.60	1.59	1.31	1.30	1.25	1.26	1.07	1.06
Me-6	0.83, d	0.82, d	1.06, d	1.02, d	0.83, d	0.82, d	1.10, d	1.07, d
(J=Hz)	(6.9)	(7.0)	(6.1)	(6.7)	(7.3)	(7.3)	(7.3)	(5.8)
Ar-O<u>Me</u>	3.55	3.51	3.55	3.60	3.58	3.52	3.60	3.58
	3.58	3.806	3.62	3.79	(×2)	3.84	(×2)	3.83
	3.86	3.808	3.88	3.89	3.88	3.91	3.87	3.890
	3.875	3.875	(×2)	3.90	(×2)	(×2)	(×2)	3.891
	3.879		3.91		3.89		3.895	3.898
	3.89		(×2)		(×2)		3.90	
O<u>CH</u>$_2$O	—	5.96, s	—	5.95, s	—	5.97, d	—	5.95, s
(J=Hz)						(1.5)		
–CO<u>CH</u>–	2.22—2.48	2.26—2.44	2.16—2.20	2.38—2.49	—	—	—	—
–CH<u>Me</u>$_2$	0.98, d (7.0)	0.96, d (7.0)	1.13, d (7.0)	1.12, d (7.0)	—	—	—	—
	0.97, d (7.0)		1.12, d (7.0)	1.11, d (7.0)				

a) δ in $CDCl_3$, ^{1}H-NMR at 270 MHz.

TABLE IV. ^{1}H-NMR Spectral Data for the Lignans[a)]

	1a	1b	2a	2b
H-9	6.59	6.56	6.48	6.44
H-4	6.37	6.48	6.50	6.51
H-8α	2.32, d	2.28, d	2.47, d	2.42, d
(J=Hz)	(13.1)	(13.4)	(13.1)	(12.8)
H-8β	2.76, d	2.74, d	2.75, d	2.70, d
(J=Hz)	(13.1)	(13.4)	(13.1)	(12.8)
H-5α	2.80, dd	2.72, dd	2.29, dd	2.20, d
(J=Hz)	(14.2)	(14.0)	(13.4)	(13.4)
	(1.8)	(1.5)	(9.8)	(9.5)
H-5β	2.22, dd	2.16, dd	2.13, d	2.02, d
(J=Hz)	(14.2)	(14.0)	(13.4)	(13.4)
	(7.8)	(7.6)		
H-6 (m)	1.82—1.93	1.73—1.85	1.67—1.78	1.52—1.65
C7-O<u>H</u> (s)	1.75	1.73	1.35	1.56
Me-7 (s)	1.24	1.19	0.98	0.94
Me-6	0.72, d	0.70, d	1.07, d	0.98, d
(J=Hz)	(7.2)	(7.3)	(7.0)	(7.0)
Ar-OMe	3.40	3.39	3.46	3.43
	3.46	3.52	(×2)	3.60
	3.64	3.87	3.67	3.85
	3.70	3.89	3.70	3.88
	3.85		3.87	
	3.87		(×2)	
OCH_2O	—	5.35, d	—	5.34, d
(J=Hz)		(1.5)		(1.2)
		5.30, d		5.30, d
		(1.5)		(1.2)

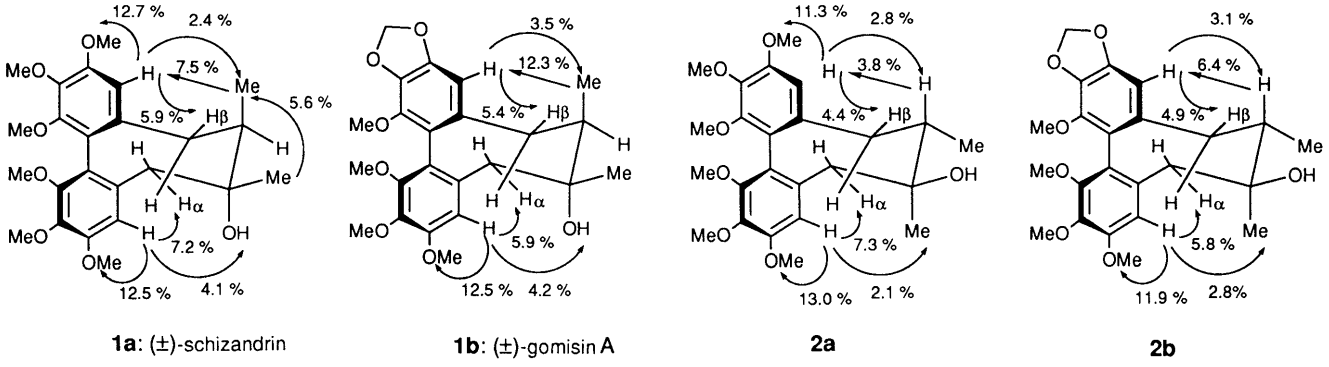
a) δ in C_6D_6, ^{1}H-NMR at 270 MHz.

13b gave **2a**, mp 164.5—165.5 °C, and a new compound **2b**, mp 155—156 °C (these two compounds have not yet been isolated from nature). All physical data for these synthetic lignans **1a** and **1b** were identical with those of the natural and synthetic products except for the optical rotations. Further, the physical data of **2a** were also identical with those of previously synthesized **2a**.[2b)] The structure of **2b** was elucidated by ^{1}H-NMR comparison of **2b** and **2a** and ^{1}H-nuclear Overhauser effect (^{1}H-NOE) experiments. As shown in Table II, the ^{1}H-NMR signals of **2a** and **2b** are almost identical except for protons belong to the methylenedioxy group. ^{1}H-NOE experiments were also done on **1a**, **1b**, **2a**, and **2b**, and the results are shown in Chart 6. When the signal of C(9)-H of **2b** at δ 6.50 was irradiated, 5.8% and 2.8% increments of the C(8)-αH and C(7)-Me signals, respectively, were observed, but the proton signal of C(7)-OH was not enhanced. Similarly, when the signal of C(4)-H of **2b** at δ 6.65 was irradiated, 4.9% and 3.1% increments of the C(5)-βH and C(6)-H signals, respectively, were obtained, but the proton of C(6)-Me showed no enhancement. The dihedral angle between C(5)-βH and C(6)-H may be about 90° because the coupling constant of these two protons was 0 Hz, and the dihedral angle between C(5)-αH and C(6)-H may be about 180° because the coupling constant of these two protons was 9.4 Hz. Thus, the DBCO ring of **2b** may have twist-boat-chair form and the conformations of the C(6)-Me, C(7)-Me, and C(7)-OH groups of **2b** may be equatorial, axial, and equatorial (Chart 6), respectively.

TABLE V. ^{13}C-NMR Spectral Data for the Lignans[a]

Carbon No.	12a	12b	13a	13b	1a	1b	2a	2b
1a	123.1	122.2	121.8	120.8	122.8	121.8	121.8	120.7
1	151.5	141.3	151.3	140.9	151.6	141.2	151.3	140.9
2	140.2	135.0	140.2	136.5	140.3	134.9	140.2	136.9
3	151.8	147.8	152.0	148.9	152.3	147.9	153.1	148.9
4a	133.7	132.6	137.7	135.1	133.8	132.5	138.2	134.8
4	110.3	105.9	107.3	103.7	110.1	106.0	107.2	102.9
5	34.4	33.7	41.3	36.3	34.4	33.7	37.1	37.0
6	38.3	38.3	44.8	44.6	41.8	42.0	48.0	48.0
7	84.3	84.1	85.7	85.6	71.8	71.6	73.8	73.7
8a	132.5	132.4	132.2	132.4	131.8	132.0	132.9	133.0
8	39.1	39.0	44.8	41.2	40.9	40.5	48.3	48.2
9	110.7	111.1	110.6	110.7	110.5	110.3	110.5	110.6
10	151.7	151.5	153.1	152.0	152.0	153.3	152.9	151.9
11	141.5	140.2	140.6	140.5	140.8	140.7	140.6	140.5
12a	123.4	123.4	123.4	123.4	124.2	124.1	123.4	123.3
12	151.5	151.5	151.5	151.6	151.9	152.1	151.5	151.6
C-6-Me	15.2	15.1	18.0	18.1	15.9	15.8	18.9	18.8
C-7-Me	25.2	25.5	18.7	18.6	29.7	30.1	20.8	20.6
C-1 OMe	60.58	59.63	60.9	59.6	60.5	59.66	60.61	59.6
C-12 OMe	60.71	60.71	(×2)	60.66	(×2)	60.60	(×2)	60.6
C-2 OMe	60.90	—	60.5	—	60.9	—	60.96	—
C-11 OMe	60.95	60.98	(×2)	60.96	(×2)	61.02	(×2)	61.0
C-3 OMe	55.67	—	55.9	—	56.0	—	55.97	—
C-10 OMe	55.91	55.65	(×2)	55.9	(×2)	55.95	(×2)	55.9
OCH_2O	—	100.8	—	100.8	—	100.8	—	100.8
–CO–	176.3	176.3	176.7	176.7	—	—	—	—
–COCH–	35.4	35.4	35.2	35.2	—	—	—	—
$-COCHMe_2$	18.8	18.8	19.0	19.0	—	—	—	—
	18.7	18.7	18.9	19.0				

a) δ in $CDCl_3$, ^{13}C-NMR at 125.65 MHz.



1a: (±)-schizandrin **1b**: (±)-gomisin A **2a** **2b**

Chart. 6. ^{1}H-NOE Data for Synthetic Dibenzocyclooctadiene Lignans **1a**, **1b**, **2a**, and **2b** in C_6D_6

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with JASCO IR-700 spectrometer, ^{1}H- and ^{13}C-NMR spectra with JEOL JNM-EX90, JNM-GX270, and JNM-GSX500 spectrometers, with tetramethylsilane as an internal standard ($CDCl_3$ and C_6D_6 solution). Mass spectra were recorded on JEOL JMS-D300 spectrometer. Elemental analyses were done using a Yanaco CHN-MT-3 apparatus. Wako silica gel C-200 (200 mesh) and Merck Kieselgel 60 F_{254} were used for column chromatography and thin-layer chromatography (TLC), respectively. The organic extract was dried over Na_2SO_4. High-performance liquid chromatography (HPLC) was performed on a Wakosil 5C4-200 column (25 cm × 4.6 mm i.d. for analytical scale or 25 cm × 20 mm i.d. for preparative scale) with aqueous methanol (40—60%), using a Shimadzu LC-6A apparatus for monitoring at 254 nm.

2-Bromo-1-(3-methoxy-4,5-methylenedioxyphenyl)propane (4d) DMF (20 ml) was added to a cooled solution of PBr_3 (5 g) in Et_2O (10 ml). The reaction was exothermic. Then, a solution of 1-(3-methoxy-4,5-methylenedioxyphenyl)-2-propanol (941 mg, 4.5 mol) [prepared from 1-(3-methoxy-4,5-methylenedioxyphenyl)-2-propanone[6] by reduction with $NaBH_4$] in DMF (20 ml) was added slowly. The mixture was heated at 50 °C for 7 h, then cooled, and H_2O (40 ml) was added. The aqueous layer was separated and extracted 4 times with Et_2O. The organic layer was combined with the ether extracts and the whole was washed with H_2O, dried and concentrated. The residue was subjected to silica gel column chromatography using hexane–$CHCl_3$ (8 : 2, v/v) to give 1.08 g (83%) of **4d**, mp 49.5—50 °C, as colorless crystals. IR (KBr): 1632 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.68 (3H, d, J=6.6 Hz, –Me), 2.80—3.27 (2H, m, Ar-CH_2), 3.90 (3H, s, Ar-OMe), 4.02—4.44 (1H, m, –CH-Br), 5.95 (3H, s, OCH_2O), 6.38 (2H, br s, Ar-H). MS m/z: 273 (M^+).

General Procedure for the Coupling Reactions of the Ketone (5) and the Bromides (4a—4d) with the SmI_2–HMPA–THF System The bromide (0.5 mmol) in anhydrous THF (1.5 ml) was added over 1—2 min to a 0.1 M solution of SmI_2 in THF (11 ml)[7] and HMPA (0.62 ml). After 5 min, the ketone (**5**)[6] in anhydrous THF (2 ml) was added, and the solution was stirred at 25 °C for 30—40 min. The reaction was quenched with 0.5 N HCl or saturated NH_4Cl and extracted with *n*-hexane–ether (1 : 1). The organic extracts were combined and washed with H_2O, aqueous 3% $Na_2S_2O_3$, and brine. The organic layer was dried, filtered, and concentrated. The residue was subjected to silica gel column chromatography, eluted successively with $CHCl_3$–hexane (8 : 2; giving a

mixture of **6a** and **7a**), $CHCl_3$–hexane (8 : 2; giving a mixture of **6b** and **7b**), $CHCl_3$–hexane (9 : 1; giving a mixture of **6c** and **7c**), and $CHCl_3$–hexane (9 : 1; giving a mixture of **6d** and **7d**). The mixtures were further separated by preparative HPLC using MeOH–H_2O.

***erythro*-2,3-Dimethyl-4-phenyl-1-(3,4,5-trimethoxyphenyl)-2-butanol (6a) and *threo*-2,3-Dimethyl-4-phenyl-1-(3,4,5-trimethoxyphenyl)-2-butanol (7a)** These compounds were prepared from **4a** and **5**.

6a: A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J=7.0 Hz, C3-Me), 1.17 (3H, s, C2-Me), 1.48 (1H, br s, C2-OH), 1.86—1.93 (1H, m, C3-H), 2.23 (1H, t, J=13.1 Hz, C4-H), 2.77 and 2.88 (each 1H, d, J=13.1 Hz, C1-H), 3.20 (1H, dd, J=13.1, 2.4 Hz, C4-H), 3.86 (9H, s, 3 × Ar-OMe), 6.49 (2H, s, Ar-H), 7.15—7.32 (5H, m, Ar-H). MS m/z: 344 (M^+).

7a: A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, d, J=7.0 Hz, C3-Me), 1.17 (3H, s, C2-Me), 1.48 (1H, br s, C2-OH), 1.86—1.93 (1H, m, C3-H), 2.22 (1H, t, J=13.1 Hz, C4-H), 2.74 and 2.80 (each 1H, d, J=13.1 Hz, C1-H), 3.21 (1H, dd, J=13.1, 2.4 Hz, C4-H), 3.86 (9H, s, 3 × Ac-OMe), 6.46 (2H, s, Ar-H), 7.15—7.32 (5H, m, Ar-H). MS m/z: 344 (M^+).

***erythro*-2,3-Dimethyl-4-(3,4-methylenedioxyphenyl)-1-(3,4,5-trimethoxyphenyl)-2-butanol (6b) and *threo*-2,3-Dimethyl-4-(3,4-methylenedioxyphenyl)-1-(3,4,5-trimethoxyphenyl)-2-butanol (7b)** These compounds were prepared from **4b** and **5**.

6b: A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, d, J=7.0 Hz, C3-Me), 1.15 (3H, s, C2-Me), 1.50 (1H, br s, C2-OH), 1.72—1.89 (1H, m, C3-H), 2.15 (1H, t, J=13.1 Hz, C4-H), 2.73 and 2.84 (each 1H, d, J=13.1 Hz, C1-H), 3.14 (1H, dd, J=13.1, 2.8 Hz, C4-H), 3.86 (9H, s, 3 × Ar-OMe), 5.92 (2H, s, OCH_2O), 6.48 (2H, s, Ar-H), 6.65 (1H, dd, J=2.0, 7.9 Hz, Ar-H), 6.67 (1H, d, J=2.0 Hz, Ar-H), 6.73 (1H, d, J=7.9 Hz, Ar-H). MS m/z: 388 (M^+).

7b: A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J=7.0 Hz, C3-Me), 1.14 (3H, s, C2-Me), 1.50 (1H, br s, C2-OH), 1.72—1.89 (1H, m, C3-H), 2.14 (1H, t, J=13.1 Hz, C4-H), 2.73 and 2.79 (each 1H, d, J=13.1 Hz, C1-H), 3.10 (1H, dd, J=13.1, 2.4 Hz, C4-H), 3.86 (9H, s, 3 × Ar-OMe), 5.92 (2H, s, OCH_2O), 6.46 (2H, s, Ar-H), 6.65 (1H, dd, J=2.0, 7.9 Hz, Ar-H), 6.67 (1H, d, J=2.0 Hz, Ar-H), 6.73 (1H, d, J=7.9 Hz, Ar-H). MS m/z: 388 (M^+).

***erythro*-2,3-Dimethyl-1,4-bis(3,4,5-trimethoxyphenyl)-2-butanol (6c) and *threo*-2,3-Dimethyl-1,4-bis(3,4,5-trimethoxyphenyl)-2-butanol (7c)** These compounds were prepared from **4c** and **5**.

6c: Colorless prisms, mp 138—139 °C (ether–hexane). IR (KBr): 3450, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, d, J=6.8 Hz, C3-Me), 1.17 (3H, s, C2-Me), 1.65 (1H, br s, C2-OH), 1.84—1.91 (1H, m, C3-H), 2.15 (1H, dd, J=13.1, 11.5 Hz, C4-H), 2.76 and 2.86 (each 1H, d, J=13.4 Hz, 2 × C1-H), 3.16 (1H, dd, J=13.1, 2.5 Hz, C4-H), 3.83 (3H, s, Ar-OMe), 3.84 (6H, s, 2 × Ar-OMe), 3.84 (3H, s, Ar-OMe), 3.86 (6H, s, 2 × Ar-OMe), 6.39 (2H, s, Ar-H), 6.51 (2H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 13.7 (C3-Me), 24.3 (C2-Me), 38.4 (C4), 44.7 (C3), 44.8 (C1), 56.0 (2 × Ar-OMe), 60.8 (4 × Ar-OMe), 74.4 (C2), 105.9, 107.7, 132.7, 136.1, 136.7, 137.2, and 152.9 (each Ar-C). *Anal.* Calcd for $C_{24}H_{34}O_7$: C, 66.34; H, 7.89. Found: C, 66.38; H, 8.00. MS m/z: 434 (M^+).

7c: Colorless prisms, mp 119—120 °C (ether–hexane): IR (KBr): 3450, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6.8 Hz, C3-Me), 1.15 (3H, s, C2-Me), 1.50 (1H, br s, C2-OH), 1.84—1.91 (1H, m, C3-H), 2.15 (1H, dd, J=13.5, 11.5 Hz, C4-H), 2.74 and 2.80 (each 1H, d, J=13.4 Hz, 2 × C1-H), 3.19 (1H, dd, J=13.1, 2.7 Hz, C4-H), 3.83 (3H, s, Ar-OMe), 3.84 (6H, s, 2 × Ar-OMe), 3.85 (3H, s, Ar-OMe), 3.86 (6H, s, 2 × Ar-OMe), 6.39 (2H, s, Ar-H), 6.47 (2H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 14.4 (C3-Me), 22.3 (C2-Me), 37.7 (C4), 44.8 (C3), 46.2 (C1), 55.9 (2 × Ar-OMe), 60.9 (4 × Ar-OMe), 74.3 (C2), 105.8, 107.6, 132.7, 136.9, 137.4, and 152.8 (each Ar-C). *Anal.* Calcd for $C_{24}H_{34}O_7$: C, 66.34; H, 7.89. Found: C, 66.15; H, 7.90. MS m/z: 434 (M^+).

***erythro*-4-(3-Methoxy-4,5-methylenedioxyphenyl)-2,3-dimethyl-1-(3,4,5-trimethoxyphenyl)-2-butanol (6d) and *threo*-4-(3-Methoxy-4,5-methylenedioxyphenyl)-2,3-dimethyl-1-(3,4,5-trimethoxyphenyl)-2-butanol (7d)** These compounds were prepared from **4d** and **5**.

6d: Colorless prisms, mp 128—128.5 °C ($CHCl_3$–ether). IR (KBr): 3530, 1628, 1588 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, J=7.0 Hz, C3-Me), 1.15 (3H, s, C2-Me), 1.60 (1H, br s, C2-OH), 1.79—1.87 (1H, m, C3-H), 2.12 (1H, dd, J=13.1, 11.6 Hz, C4-H), 2.73 and 2.84 (each 1H, d, J=13.5 Hz, 2 × C1-H), 3.11 (1H, dd, J=13.1, 2.4 Hz, C4-H), 3.85 (3H, s, Ar-OMe), 3.86 (6H, s, 2 × Ar-OMe), 3.88 (3H, s, Ar-OMe), 5.94 (2H, s, OCH_2O), 6.32 (1H, s, Ar-H), 6.37 (1H, s, Ar-H), 6.49 (2H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 13.7 (C3-Me), 24.3 (C2-Me), 38.2 (C4), 44.7 (C3), 44.8 (C1), 56.1, 56.6, and 60.8 (4 × Ar-OMe), 74.4 (C2), 103.0, 105.9, 107.7, 108.1, 133.0, 133.3, 136.2, 136.8, 143.4, 148.7 and 153.0 (each Ar-C). *Anal.* Calcd for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 65.85; H, 7.27. MS m/z: 418 (M^+).

7d: Colorless prisms, mp 86.5—87.0 °C ($CHCl_3$–ether). IR (KBr): 3494, 1632, 1593 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, d, J=7.0 Hz, C3-Me), 1.14 (3H, s, C2-Me), 1.65 (1H, br s, C2-OH), 1.77—1.85 (1H, m, C3-H), 2.11 (1H, dd, J=13.1, 11.3 Hz, C4-H), 2.72 and 2.79 (each 1H, d, J=13.4 Hz, 2 × C1-H), 3.15 (1H, dd, J=13.1, 2.8 Hz, C4-H), 3.85 (3H, s, Ar-OMe), 3.86 (6H, s, 2 × Ar-OMe), 3.89 (3H, s, Ar-OMe), 5.93 (2H, s, OCH_2O), 6.34 (1H, s, Ar-H), 6.38 (1H, s, Ar-H), 6.46 (2H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 14.5 (C3-Me), 22.5 (C2-Me), 37.6 (C4), 45.2 (C3), 46.4 (C3), 46.4 (C1), 56.1, 56.6, and 60.9 (4 × Ar-OMe), 74.4 (C2), 103.1, 107.7, 108.2, 132.8, 136.1, 136.7, 137.2, and 152.9 (each Ar-C). *Anal.* Calcd for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 66.00; H, 7.19. MS m/z: 418 (M^+).

Preparation of 6c from 8 A 1.0 M BH_3·THF solution (100 ml, Aldrich) was added under a nitrogen atmosphere to a solution of the (*Z*)-butene **8**[6] (14 g, 34 mmol) in anhydrous THF (135 ml) at 0 °C, and the whole was stirred at room temperature for 3 h. A solution prepared from aqueous 30% H_2O_2 (135 ml) and aqueous 3 M NaOH (27 ml) was added slowly, and the reaction mixture was stirred at room temperature for 2 h, then poured into saturated aqueous NaCl and extracted with $CHCl_3$–ether (1 : 3, v/v). The organic layer was washed with H_2O, then dried and concentrated. The residue was recrystallized from $CHCl_3$–ether to yield 10.18 g (70%) of **6c** as colorless prisms, mp 138.5—139 °C. *Anal.* Calcd for $C_{24}H_{34}O_7$: C, 66.34; H, 7.89. Found: C, 66.30; H, 7.86. MS m/z: 434 (M^+).

Preparation of 7c from 9 **7c**, colorless prisms, mp 119—120 °C, was synthesized from **9**[6] in 70% yield by a procedure similar to that used for **6c**. *Anal.* Calcd for $C_{24}H_{34}O_7$: C, 66.34; H, 7.89. Found: C, 66.29; H, 7.79. MS m/z: 434 (M^+).

Oxidation of *erythro*-2,3-Dimethyl-1,4-bis(3,4,5-trimethoxyphenyl)-2-butanol (6c) with $Fe(ClO_4)_3 \cdot 9H_2O$–CH_2Cl_2–MeCN A solution of the *erythro*-butanol **6c** (87 mg, 0.2 mmol) in anhydrous MeCN (1 ml) and CH_2Cl_2 (1 ml) was added to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (259 mg, 0.5 mmol) in anhydrous MeCN (1.5 ml) and CH_2Cl_2 (1.5 ml), and the whole was stirred at room temperature for 5 min. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with H_2O, then dried and concentration. The residue was subjected to silica gel chromatography. The eluate with CH_3CO_2Et–hexane (2 : 3, v/v) gave 32 mg (38%) of 7,9-dimethoxy-2,3-dimethyl-8-oxo-2-(3,4,5-trimethoxybenzyl)-1-oxospiro[4.5]deca-6,9-diene (**10**) as colorless crystal (ether–hexane), mp 139—140 °C. IR (KBr): 1680, 1660, 1620, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.21 (3H, d, J=6.8 Hz, C3-Me), 1.25 (3H, s, C2-Me), 2.20 (1H, t, J=12.7 Hz, C4-H), 2.28 (1H, dd, J=12.7, 6.6 Hz, C4-H), 2.47 and 2.85 (2H, each d, J=13.7 Hz, Ar-CH_2), 2.48—2.60 (1H, m, C3-H), 3.66 and 3.70 (6H, each s, Ar-OMe), 3.80 (3H, s, Ar-OMe), 3.82 (6H, s, 2 × Ar-OMe), 5.81 (2H, s, 2 × olefinic-H), 6.53 (2H, s, 2 × Ar-H). *Anal.* Calcd for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 66.13; H, 7.43. MS m/z: 418 (M^+).

***erythro*-2-Isopropylcarbonyl-2,3-dimethyl-1,4-bis(3,4,5-trimethoxyphenyl)butane (11a)** *p*-Toluenesulfonic acid (400 mg) was added to a solution of the *erythro*-butanol **6c** (868 mg, 2 mmol) in isobutyric anhydride (15 ml), and the mixture was stirred at room temperature for 1.5 h, poured into ice-water and extracted with ether. The ether layer was washed with saturated $NaHCO_3$ and H_2O, then dried and concentrated. The residue was recrystallized from ether–hexane to yield 847 mg (84%) of **11a** as colorless crystals, mp 78—79 °C (ether–hexane). IR (KBr): 1717 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, J=6.7 Hz, C3-Me), 1.14 and 1.16 (each 3H, d, J=7.0 Hz, CH-Me$_2$), 1.15 (3H, s, C2-Me), 2.15 (1H, dd, J=13.0 and 11.6 Hz, C4-H), 2.44—2.54 (1H, m, –CO–CH), 2.78—2.86 (1H, m, C3-H), 2.96 (1H, dd, J=13.0, 1.6 Hz, C4-H), 3.04 and 3.22 (each 1H, d, J=14.4 Hz, C1-H), 3.82 (3H, s, Ar-OMe), 3.83 (6H, s, 2 × Ar-OMe), 3.84 (9H, s, 3 × Ar-OMe), 6.32 and 6.47 (each 2H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 14.1 (C3-Me), 19.1 and 19.2 (–CHMe$_2$), 21.1 (C2-Me), 35.3 (–CO–CH), 41.3 (C3), 56.06, 56.08, 60.85, 60.88, and 60.8 (each Ar-OMe), 86.9 (C2), 105.9, 107.9, 132.8, 136.2, 136.8, 152.7, and 153.1 (each Ar-C), 176.4 (–CO–CH). *Anal.* Calcd for $C_{28}H_{40}O_8$: C, 66.64; H, 7.99. Found: C, 66.73; H, 8.01. MS m/z: 504 (M^+).

***erythro*-2-Isopropylcarbonyloxy-4-(3-methoxy-4,5-methylenedioxyphenyl)-2,3-dimethyl-1-(3,4,5-trimethoxyphenyl)butane (11b)** **11b**, colorless crystals, mp 103—103.5 °C, was synthesized from **6d** in 82% yield

by a procedure similar to that used for **11a**. IR (KBr): 1718, 1636, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, d, J=6.7 Hz, C3-Me), 1.13 and 1.15 (each 3H, d, J=7.0 Hz, CH-Me$_2$), 1.14 (3H, s, C2-Me), 2.13 (1H, dd, J=13.0, 11.6 Hz, C4-H), 2.43—2.53 (1H, m, –CO–CH), 2.74—2.81 (1H, m, C3-H), 2.93 (1H, dd, J=13.0, 2.1 Hz, C4-H), 2.99 and 3.23 (each 1H, d, J=14.0 Hz, C1-H), 3.88 (3H, s, Ar-OMe), 3.85 (9H, s, 3 × Ar-OMe), 5.93 (2H, s, OCH_2O), 6.27 and 6.33 (1H, s, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 13.9 (C3-Me), 19.1 and 19.2 (–CHMe$_2$), 21.1 (C2-Me), 35.2 (–CO–CH), 37.8 (C4-Me), 41.3 (C3), 41.4 (C1), 56.1, 56.5, and 60.9 (each Ar-OMe), 86.8 (C2), 103.1, 107.9, 108.1, 132.8, 133.4, 135.5, 136.7, 143.4, 148.7, and 152.7 (each Ar-C), 176.4 (–CO–CH). *Anal.* Calcd for $C_{27}H_{36}O_8$: C, 66.37; H, 7.43. Found: C, 66.47; H, 7.60. MS *m/z*: 488 (M^+).

Oxidation of *erythro*-2-Isopropylcarbonyloxy-2,3-dimethyl-1,4-bis(3,4,5-trimethoxyphenyl)butane (11a) Method A: With $Fe(ClO_4)_3 \cdot 9H_2O$–CH_2Cl_2–MeCN (Reagent A): A solution of the *erythro* compound **11a** (101 mg, 0.2 mmol) in anhydrous MeCN (1 ml) and CH_2Cl_2 (1 ml) was added to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (259 mg, 0.5 mmol) in anhydrous MeCN (1.5 ml) and CH_2Cl_2 (1.5 ml), and the whole was stirred at room temperature for 1 min. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with H_2O, then dried and concentrated. The residue was subjected to silica gel chromatography. The eluate with ether–hexane–$CHCl_3$ (1 : 4 : 1, v/v) gave 36 mg (36%) of a mixture **12a** and **13a**. The mixture was further subjected to preparative HPLC with MeOH–H_2O (60 : 40, v/v).

The first eluate gave 29 mg (80%) of 6(*RS*),7(*SR*)-5,6,7,8-tetrahydro-7-isopropylcarbonyloxy-1,2,3,10,11,12-hexamethoxy-6,7-dimethyldibenzo[*a,c*]cyclooctene, *RS*-biar (**12a**) as colorless prisms ($CHCl_3$–ether), mp 128.5—129 °C. IR (KBr): 1720, 1600, 1580 cm^{-1}. *Anal.* Calcd for $C_{28}H_{38}O_8$: C, 66.91; H, 7.62. Found: C, 66.77; H, 7.51. MS *m/z*: 502 (M^+).

The second eluate gave 7 mg (20%) of 6(*SR*), 7(*RS*)-5,6,7,8-tetrahydro-7-isopropylcarbonyloxy-1,2,3,10,11,12-hexamethoxy-6,7-dimethyldibenzo[*a,c*]cyclooctene, *RS*-biar (**13a**) as colorless prisms ($CHCl_3$–ether) mp 100—101 °C. IR (KBr): 1720, 1600, 1580 cm^{-1}: *Anal.* Calcd for $C_{28}H_{38}O_8$: C, 66.91; H, 7.62. Found: C, 66.80; H, 7.50. MS *m/z*: 502 (M^+). Physical data of **12a** and **13a** are listed in Tables III, IV, and V.

Method B: With $Fe(ClO_4)_3 \cdot 9H_2O$–MeCN (Reagent B): A solution of **11a** (101 mg, 0.2 mmol) in anhydrous MeCN (1 ml) was added to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (259 mg, 0.5 mmol) in anhydrous MeCN (3 ml), and the whole was stirred at room temperature for 1.5 min. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with saturated $NaHCO_3$ and H_2O, then dried and concentrated. The residue was purified as described in method A to give 21 mg (21%) of a mixture of **12a** and **13a**. The **12a**/**13a** ratios were determined by HPLC analysis.

Method C: With $Fe(ClO_4)_3 \cdot 9H_2O$–CF_3CO_2H–CH_2Cl_2–MeCN (Reagent C): A solution of **11a** (101 mg, 0.2 mmol) in anhydrous MeCN (1 ml) and CH_2Cl_2 (1 ml) was added to a solution of $Fe(ClO_4)_3 \cdot 9H_2O$ (259 mg, 0.5 mmol) in anhydrous MeCN (1.5 ml), CH_2Cl_2 (1.5 ml), and CF_3CO_2H (0.3 ml). The reaction mixture was stirred at room temperature for 1.5 min, then poured into ice-water and extracted with ether. The organic layer was washed with saturated $NaHCO_3$ and H_2O, then dried and concentrated. The residue was purified as described in method A to give 9.6 mg (9.5%) of a mixture of **12a** and **13a**.

Method D: With $FeCl_3$–MeCN (Reagent D): A solution of **11a** (101 mg, 0.2 mmol) in anhydrous MeCN (3 ml) was added to a solution of $FeCl_3$ (292 mg, 1.8 mmol) in anhydrous MeCN (3 ml). The reaction mixture was stirred at room temperature for 1 min, then poured into ice-water and extracted with ether. The organic layer was washed with H_2O, then dried and concentrated. The residue was purified as described in method A to give 5 mg (5.0%) of a mixture of **12a** and **13a**.

Method E: With $FeCl_3$–Ac_2O (Reagent E): A solution of **11a** (101 mg, 0.2 mmol) in Ac_2O (3 ml) was added to a solution of $FeCl_3$ (292 mg, 1.8 mmol) in Ac_2O (3 ml), and the whole was stirred at room temperature for 1 min. The reaction mixture was poured into ice-water and extracted with ether. The organic layer was washed with H_2O, then dried and concentrated. The residue was purified as described in method A to give 5 mg (5.0%) of a mixture of **12a** and **13a**.

Method F: With $Mn(ClO_4)_2 \cdot 6H_2O$–$KMnO_4$–Ac_2O (Reagent F): A solution prepared by addition of a solution of $KMnO_4$ (19.5 mg, 0.13 mmol) in Ac_2O (7.5 ml) to a solution of $Mn(ClO_4)_2 \cdot 6H_2O$ (168.0 mg, 0.50 mmol) in Ac_2O (0.5 ml) was added to a solution of **11a** (60.4 mg, 1.2 mmol) in Ac_2O (10 ml) with stirring at room temperature. The reaction mixture was stirred for 20 min, then worked up as described in method B to give a mixture of **12a** and **13a** (trace).

Method G: With VOF_3–CF_3CO_2H–CH_2Cl_2 (Reagent G): VOF_3 (300 mg) was added to a solution of **11a** (130 mg, 0.26 mmol) in CF_3CO_2H (5 ml) and CH_2Cl_2 (40 ml) at −78 °C under a nitrogen atmosphere, and the whole was stirred at −78 °C for 30 min, then at room temperature for an additional 30 min. Saturated Na_2CO_3 was added to the solution, and the organic layer was successively washed with saturated Na_2CO_3, brine and H_2O, then dried and concentrated. The residue was purified as described in method A to give a mixture of **12a** and **13a** (trace).

Oxidation of *erythro*-3-Isopropylcarbonyloxy-4-(3-methoxy-4,5-methylenedioxyphenyl)-2,3-dimethyl-1-(3,4,5-trimethoxyphenyl)butane (11b) Method A: With $Fe(ClO_4)_3 \cdot 9H_2O$–CH_2Cl_2–MeCN (Reagent A): Oxidation of **11b** was carried out by the procedure described for the oxidation of **11a** with reagent A, to give 6(*RS*),7(*SR*)-5,6,7,8-tetrahydro-7-isopropylcarbonyloxy-1,10,11,12-tetramethoxy-6,7-dimethyl-2,3-methylenedioxydibenzo[*a,c*]cyclooctene, *RS*-biar (**12b**) and 6(*SR*),7(*RS*)-5,6,7,8-tetrahydro-7-isopropylcarbonyloxy-1,10,11,12-tetramethoxy-6,7-dimethyl-2,3-methylenedioxydibenzo[*a,c*]cyclooctene, *RS*-biar (**13b**).

12b: Colorless prisms ($CHCl_3$–ether), mp 146.5—147 °C. IR (KBr): 1724, 1616, 1594 cm^{-1}. *Anal.* Calcd for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.81; H, 7.14. MS *m/z*: 486 (M^+).

13b: Colorless prisms ($CHCl_3$–ether), mp 150.5—151 °C. IR (KBr): 1715, 1618, 1597 cm^{-1}. *Anal.* Calcd for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.70; H, 7.00. MS *m/z*: 486 (M^+). Yields and physical data of **12b** and **13b** are listed in Tables II, III, IV, and V.

Method B: With $Fe(ClO_4)_3 \cdot 9H_2O$–MeCN (Reagent B): Oxidation of **11b** was carried out by the procedure described for the oxidation of **11a** with reagent B, to give **12b** and **13b**. The **12b**/**13b** ratios were determined by HPLC analysis (Table II).

Method C: With $Fe(ClO_4)_3 \cdot 9H_2O$–CF_3CO_2H–CH_2Cl_2–MeCN (Reagent C): Oxidation of **11b** was carried out by the procedure described for the oxidation of **11a** with reagent C, to give **12b** and **13b**.

Method D: With $FeCl_3$–MeCN (Reagent D): Oxidation of **11b** was carried out by the procedure described for the oxidation of **11a** with reagent D, to give **12b** and **13b**.

General Procedure for Hydrolysis of 12a, 12b, 13a, and 13b A solution of the coupling products (0.1 mmol) in 10% alcoholic KOH (20 ml) was refluxed for 40 h. The reaction mixture was poured into ice-water, acidified with aqueous 10% HCl and then extracted with chloroform. The organic layer was washed with H_2O, dried and concentrated. The crude products were purified by column chromatography on silica gel in the designated solvents. ^{1}H- and ^{13}C-NMR data for **1a**, **1b**, **2a**, and **2b** are listed in Tables III—V.

6(*RS*),7(*SR*)-5,6,7,8-Tetrahydro-7-hydroxy-1,2,3,10,11,12-hexamethoxy-6,7-dimethyldibenzo[*a,c*]cyclooctene, *RS*-Biar, (±)-Schizandrin (1a) Compound **1a** was prepared from **12a** and was purified by silica gel column chromatography in CH_3CO_2Et–$CHCl_3$ (1 : 9, v/v) to give 37 mg (85%), as colorless needles ($CHCl_3$–ether–hexane), mp 128—129 °C. IR (KBr): 3450, 1590 cm^{-1}. *Anal.* Calcd for $C_{24}H_{32}O_7$: C, 66.65; H, 7.46. Found: C, 66.85; H, 7.56. MS *m/z*: 432 (M^+).

6(*SR*),7(*RS*)-5,6,7,8-Tetrahydro-7-hydroxy-1,2,3,10,11,12-hexamethoxy-6,7-dimethyldibenzo[*a,c*]cyclooctene, *RS*-Biar (2a) Compound **2a** was prepared from **13a** and was purified by silica gel column chromatography in CH_3CO_2Et–$CHCl_3$ (1 : 9, v/v) to give 41 mg (95%), as colorless plates ($CHCl_3$–ether–hexane), mp 164.5—165.5 °C. IR (KBr): 3450, 1590 cm^{-1}. *Anal.* Calcd for $C_{24}H_{32}O_7$: C, 66.65; H, 7.46. Found: C, 66.58; H, 7.48. MS *m/z*: 432 (M^+).

6(*RS*),7(*SR*)-5,6,7,8-Tetrahydro-7-hydroxy-1,10,11,12-tetramethoxy-6,7-dimethyl-2,3-methylenedioxydibenzo[*a,c*]cyclooctene, *RS*-Biar, (±)-Gomisin A (1b) Compound **1b** was prepared from **12b** and was purified by silica gel column chromatography in CH_3CO_2Et–$CHCl_3$(1 : 9, v/v) to give 35 mg (84%), as colorless needles ($CHCl_3$–ether–hexane), mp 165.5—166 °C. IR (KBr): 3566, 1614, 1591 cm^{-1}. *Anal.* Calcd for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.34; H, 6.94. MS *m/z*: 416 (M^+).

6(*SR*),7(*RS*)-5,6,7,8-Tetrahydro-7-hydroxy-1,10,11,12-tetramethoxy-6,7-dimethyl-2,3-methylenedioxydibenzo[*a,c*]cyclooctene, *RS*-Biar (2b) Compound **2b** was prepared from **13b** and was purified by silica gel column chromatography in CH_3CO_2Et–$CHCl_3$ (1 : 9, v/v) to give 40 mg (95%), as colorless crystals ($CHCl_3$–ether–hexane), mp 155—156 °C. IR (KBr): 3520, 1614, 1590 cm^{-1}. *Anal.* Calcd for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.43; H, 6.85. MS *m/z*: 416 (M^+).

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