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The Constituents of *Schizandra chinensis* Baill. VI.[1] ^{13}C Nuclear Magnetic Resonance Spectroscopy of Dibenzocyclooctadiene Lignans

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The ^{13}C NMR spectra of thirteen dibenzocyclooctadiene lignans, isolated from the fruits of *Schizandra chinensis* Baill. (Schizandraceae), were analyzed and their carbon shifts assigned. Several important chemical shift trends are described.

Keywords——*Schizandra chinensis* Baill.; Schizandraceae; dibenzocyclooctadiene; lignans; gomisins; ^{13}C NMR

We have already isolated eighteen new dibenzocyclooctadiene lignans from the fruits of *Schizandra chinensis* Baill. (Schizandraceae) and elucidated their structures on the basis of proton nuclear magnetic resonance (^1H NMR), infrared (IR), mass and ultraviolet (UV) spectral analysis as well as chemical studies.[3,4]

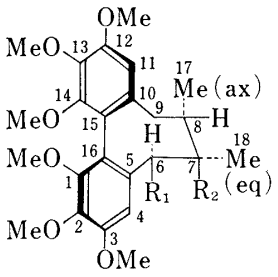
The present paper describes carbon (^{13}C) NMR spectral studies of the dibenzocyclooctadiene lignans isolated from this source. The lignans isolated from *Schizandra chinensis* can be classified into the following five groups: i) (+)-deoxyschizandrin (**1**) group, with an *R*-biphenyl configuration;[5] ii) gomisin N (**2**) group, with an *S*-biphenyl configuration [(−)-gomisin K_1 (**3**),[6] dimethylgomisin J (**4**)[3d] and gomisin J (**5**)]; iii) schizandrin (**7**) group, with an *R*-biphenyl configuration and a hydroxy group at C-7 [gomisins A(**6**) and H(**8**)]; iv) gomisin O (**9**) group, with an *S*-biphenyl configuration and a hydroxy group at C-6 [epigomisin O (**10**)] and v) gomisin B group, with an *S*-biphenyl configuration and two hydroxy groups at C-6 and C-7 [deangeloylgomisins B (**11**) and F (**12**), and gomisin P (**13**)]. Among the above lignans, gomisin O (**9**) possesses a boat conformation of the cyclooctadiene ring,[1] while the others possess a twist-boat-chair conformation.[1,3] The assignments of the carbon shifts were based on the proton coupled spectra, single frequency off-resonance decoupling (SFORD) experiments [graphical method and proton selective decoupling (PSD) technique],[7] specific deuteration experiments[7d] and spin-lattice relaxation time (T_1) measurements[8] as well as comparisons with the chemical shifts of model compounds [1,2,3-trimethoxybenzene (**14**),[9] 2,3-dimethoxy-

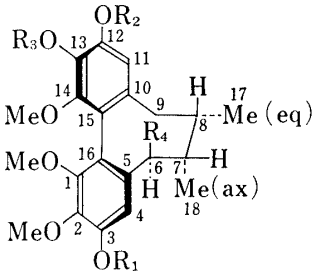
1) Part V: Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **27**, 2695 (1979).
2) Location: *Honcho 1-9-9, Izumi, Komae-shi, Tokyo, 201, Japan.*
3) *a*) Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **27**, 1383 (1979); *b*) Y. Ikeya, H. Taguchi, I. Yosioka, Y. Iitaka, and H. Kobayashi, *ibid.*, **27**, 1395 (1979); *c*) Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *ibid.*, **27**, 1576 (1979); *d*) *Idem*, *ibid.*, **27**, 1583 (1979).
4) Studies on the biological activities of these lignans are in progress in our laboratory. Details will be reported elsewhere in the near future.
5) The other lignans in this group will be described in the following paper.
6) The isolation and structure elucidation of **3** will be reported in the following paper.
7) *a*) R. Freeman and H.D.W. Hill, *J. Chem. Phys.*, **54**, 3367 (1971); *b*) B. Birdsall, N.J.M. Birdsall, and J. Feeney, *J. Chem. Soc. Chem. Commun.*, **1972**, 316; *c*) F.W. Wehrli and T. Wirthlin, "Interpretation of Carbon-13 NMR Spectra," Heyden and Son Ltd., London, 1976, pp. 64—82; *d*) *Idem*, *ibid.*, pp. 107—110.
8) F.W. Wehri, "Topics in Carbon-13 NMR Spectroscopy," Vol. II, ed. by G.C. Levy, John Wiley and Sons Inc., New York, London·Sydney·Toront, 1976, p. 362.
9) E. Wenkert, H.E. Gottlieb, O.T. Gottlieb, M.O.S. Pereira, and M.D. Formig, *Phytochemistry*, **15**, 1547 (1976).

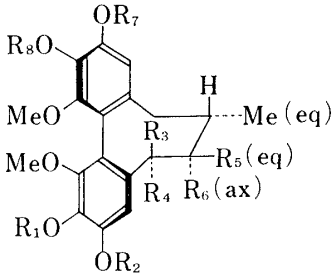
phenol (**15**),[9] 2,6-dimethoxyphenol (**16**),[9] 2,3-methylenedioxyanisole (**17**), 2,3-methylenedioxyphenol (**18**) and 1-acetoxy-2,3-methylenedioxybenzene (**19**)].

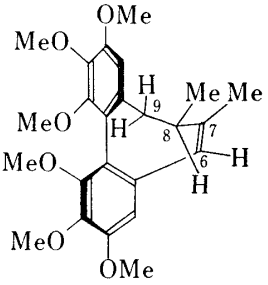
Methyl Carbons (C-17 and C-18)

The chemical shifts of two methyl carbons of the lignans in groups i and ii [**2**, **3**, **3a** (acetate of **3**), **4**(**1**) and **5**] appeared over narrow ranges, δ 12.7±0.2 and δ 21.7±0.2, On







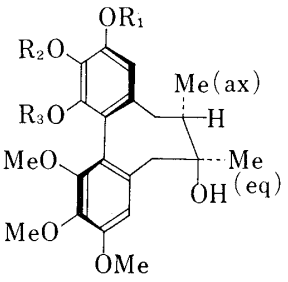


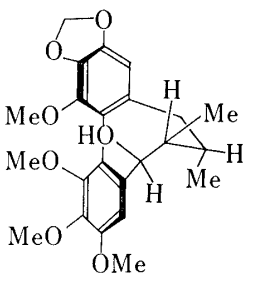
1 : $R_1=R_2=H$ (antipode of **4**)
1a : $R_1=R_2=D$

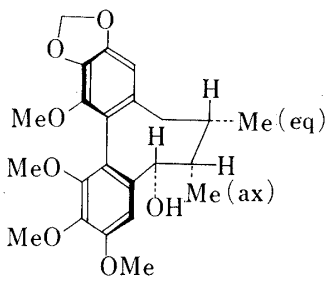
2 : $R_1=Me$, $R_2+R_3=CH_2$, $R_4=H$
2a : $R_1=Me$, $R_2+R_3=CH_2$, $R_4=D$
3 : $R_1=R_3=Me$, $R_2=R_4=H$
3a : $R_1=R_3=Me$, $R_2=COCH_3$, $R_4=H$
4 : $R_1=R_2=R_3=Me$, $R_4=H$
5 : $R_1=R_2=R_4=H$, $R_3=Me$

11 : $R_1=R_2=R_5=Me$, $R_3=R_6=OH$, $R_4=H$, $R_7+R_8=CH_2$
12 : $R_1+R_2=CH_2$, $R_3=R_6=OH$, $R_4=H$, $R_5=R_7=R_8=Me$
13 : $R_1=R_2=R_6=Me$, $R_3=H$, $R_4=R_5=OH$, $R_7+R_8=CH_2$

20







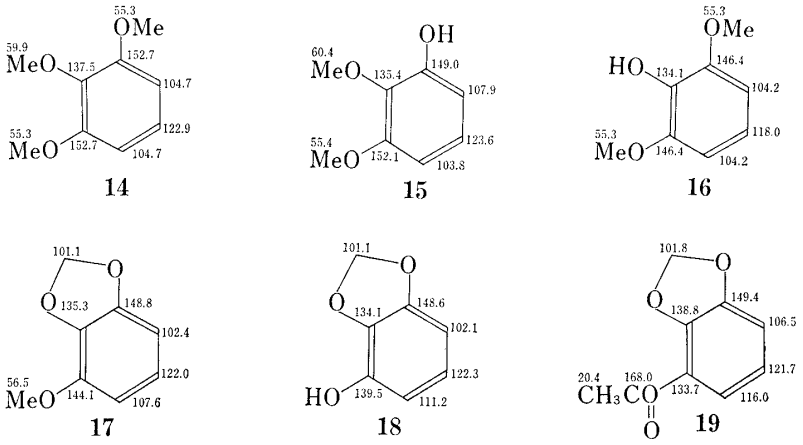
6 : $R_1+R_2=CH_2$, $R_3=Me$
7 : $R_1=R_2=R_3=Me$
8 : $R_1=R_2=Me$, $R_3=H$

9

10

(ax=axial; eq=equatorial)

Chart 1



14 **15** **16**

17 **18** **19**

Chart 2

^{13}C NMR Spectra of **17**, **18** and **19** were measured in $CDCl_3$ at 25° (20 MHz). Data for **14**, **15** and **16** are those reported by Wenkert *et al.*[9]

Table I. ^{13}C NMR Spectral Data for the Lignans in Groups i and ii
[δ in $CDCl_3$, ^{13}C: 20 MHz at 25°]

Carbon	Group i	T_1 (sec)	Compound(*R*-biphenyl configuration) Group iii		
	1		**6**	**7**[a]	**8**
1	151.6[b]	17.0	152.1	151.9[b]	152.6[b]
2	140.3[c]	17.7	140.8[b]	140.8[c]	140.8
3	153.0	10.0	152.3	152.3	152.6
4	107.3		110.4	110.5[d]	110.6
5	139.1	4.2	132.1	131.8	132.5
6	35.7		40.6	40.9	41.1
7	40.9		71.7	71.8	72.0
8	33.8		42.1	41.8	41.8
9	39.2		33.8	34.4	34.5
10	133.9	4.0	132.5	133.8	134.3
11	110.6		105.9	110.1[d]	107.3
12	151.7	10.0	147.9	152.0	150.7[b]
13	139.9[c]	18.4	135.0	140.3[c]	134.0
14	151.5[b]	17.8	141.3[b]	151.6[b]	146.9
15	123.5	12.6	121.9	122.8	116.5
16	122.4	13.1	124.2	124.2	123.2
17	12.7		15.8	15.9	15.9
18	21.8		30.1	29.7	29.7
OCH_3 C—1, 14	60.3(×2)		60.6, 59.6	60.5(×2)	61.1, —
OCH_3 C—2, 13	60.7(×2)		61.0 —	60.9(×2)	61.0(×2)
OCH_3 C—3, 12	55.7(×2)		56.0 —	56.0(×2)	55.8, 56.0
OCH_2O	—		100.8	—	—

a) Measured at 15.04 MHz.
b, *c*, *d*) Assignments within any vertical column may be reversed.

the basis of SFORD experiments with **1**, the upfield signal was assigned to an axial methyl carbon and the downfield one to an equatorial methyl carbon. Two methyl carbons of the lignans in group iii (**6**—**8**) [axial secondary methyl (C-17): δ 15.8±0.1; equatorial tertiary methyl (C-18): δ 29.8±0.1] were also assigned by SFORD experiments with **7**.[10] The equatorial methyl carbon (C-17, δ 22.0) of epigomisin O (**10**) was assigned by comparison with those of the lignans in groups i and ii, and an upfield methyl carbon signal at δ 7.8 was thus assigned to axial methyl (C-18). The upfield shift of *ca.* 5 ppm of the axial methyl carbon in **10**, compared with those of the lignans in groups i and ii (δ 12.7±0.2), can be explained by the γ-effect of the $C_{(6\alpha)}$ hydroxy group. On the other hand, two methyl carbons of gomisin O (**9**) appeared at δ 16.6 and 17.5. These chemical shifts differ from those of the other lignans possessing a twist-boat-chair conformation of the cyclooctadiene ring. This observation seems to support the view that **9** possesses a boat conformation of the cyclooctadiene ring.

The methyl carbons at δ 18.8 and δ 16.0 of gomisin P (**13**) were assigned to C-17 (equatorial methyl) and C-18 (axial methyl), respectively, by the PSD technique (^1H NMR: $C_{(17)}$-H, δ 1.07, d; $C_{(18)}$-H, δ 1.00, s). On comparison with the methyl carbon shift of **10**, C-17 of **13** showed an upfield shift of 3.2 ppm (γ-gauche effect) and C-18 showed a downfield shift of 8.2 ppm (β-shift) due to the influence of the $C_{(7)}$ equatorial hydroxy group. On the other hand, when the methyl carbon shifts of the lignans in group iii were compared with those of the compounds in groups i and ii, C-18 showed the expected downfield shift (*ca.* +8.0 ppm) due to the β-effect of the $C_{(7)}$ axial hydroxy group, but C-17 showed an unexpected downfield shift (+3.2 ppm) in spite of the γ-*trans* position relative to the hydroxy group. The

10) ^1H NMR spectral data for **1** and **7** (δ in $CDCl_3$). **1**: $C_{(17)}$–H, 0.73, d; $C_{(18)}$–H, 0.98, d; $C_{(6)}$–H, 2.13 (center), ABX octet; $C_{(9)}$–H, 2.58, m. **7**: $C_{(17)}$–H, 0.82, d; $C_{(18)}$–H, 1.25, s.

Table II. ^{13}C NMR Spectral Data for the Lignans in Groups ii, iv and v [δ in $CDCl_3$, ^{13}C: 20 MHz at 25°]

Carbon	Compound (*S*-biphenyl configuration)									
	Group ii					Group iv		Group v		
	2	**3**	**3a**	**4**[b]	**5**	**9**[a]	**10**	**11**[a]	**12**	**13**[a]
1	151.7	151.6[c]	151.5[c]	151.3[c]	150.3[c]	151.9	151.2	151.9	141.5[c]	150.9
2	140.2[c]	140.3	140.3	140.0[d]	137.8[d]	141.7[c]	140.8[c]	141.5[c]	136.5	140.8[c]
3	151.6	151.7	152.0	151.3	147.6[e]	152.1	152.3	152.1	148.1	152.4
4	110.7	110.8	110.7	110.3	113.3	110.2	106.4	110.3	106.0	106.4
5	134.1	134.1	133.9	133.5	134.9	137.0[d]	136.5[d]	133.6[d]	132.2	135.4
6	39.2	39.3	39.1	39.1	38.9	81.4	73.4	86.0	85.9	75.0
7	33.6	33.8	33.7	33.7	33.8	40.1	42.6	73.6	73.8	76.2
8	40.8	40.9	40.9	40.7	41.0	37.2	39.3	41.6	41.6	46.6
9	35.6	35.3	35.1	35.5	35.3	38.1	34.7	36.3	36.4	36.9
10	137.8	140.0	139.5	138.8	140.2	135.5[d]	137.9[d]	135.0[d]	136.7	136.9
11	102.9	110.0	117.5	107.0	110.2	102.5	102.8	103.2	107.7	102.7
12	148.7	148.8	143.7	152.7	148.8[e]	149.2	149.2	149.8	154.2	149.1
13	134.6	137.5	142.4	139.6[d]	137.5[d]	134.6	134.6	135.5	140.5[c]	134.9
14	141.1[c]	150.3[c]	151.6[c]	151.5[c]	150.5[c]	141.5[c]	140.9[c]	140.7[c]	151.4	141.1[c]
15	121.4	121.6	128.0	122.2	121.5	120.7	119.6	119.6	120.5	119.5
16	123.4	123.4	122.9	123.3	122.5	122.2	121.3	122.1	120.6	122.2
17	21.5	21.7	21.7	21.8	21.7	17.5[e]	22.0	18.8	18.9	18.8
18	12.9	12.8	12.6	12.7	12.6	16.6[e]	7.8	28.5	28.7	16.0
OCH_3 C-1, 14	60.5, 59.6	60.5, 60.1	60.6, 60.3	60.4 (×2)	60.1 (×2)	60.3, 59.5	60.6, 59.6	60.7, 59.8	59.7, 60.6	60.5, 59.8
OCH_3 C-2, 13	61.0 —	61.0, 60.9	61.0, 60.8	60.8 (×2)	61.0 (×2)	60.8 —	61.0 —	60.8 —	— 61.0	60.9 —
OCH_3 C-3, 12	55.9 —	56.0 —	56.0 —	55.7 (×2)	—	56.0 —	56.0 —	56.0 —	— 55.9	56.0 —
OCH_2O	100.7	—	—	—	—	100.7	100.8	101.0	101.3	100.8
$COCH_3$	—	—	169.0, 20.8	—	—	—	—	—	—	—

a) Measured at 15.04 MHz.
b) Measured at 25.15 MHz.
c, *d*, *e*) Assignments within any vertical column may be reversed.

methyl signals at around δ 18.8—18.9 and δ 28.5—28.7 in the spectra of deangeloylgomisins B (**11**) and F (**12**) were assigned to C-17 and C-18, respectively, by comparison with data for **13** and the lignans in group iii.

Benzylic Methylene (C-6 and C-9) and Methine (C-7 and C-8) Carbons

The benzylic methylene carbons of the lignans in groups i and ii appeared over narrow ranges, δ 35.4±0.2 and δ 39.1±0.2. On the basis of SFORD experiments with **1**, the upfield signal was assigned to the methylene carbon of the equatorial methyl side and the downfield one to the methylene carbon of the axial methyl side. The above assignments were confirmed by the noise-decoupled spectrum of $C_{(6\beta)}$-deuterogomisin N[1] (**2a**, C-6 is on the axial methyl side), which showed no signal at δ 39.2. The methylene carbons of the lignans in group iii appearing at δ 34.2±0.4 and δ 40.9±0.3 were assigned to C-9 and C-6, respectively, because the C-9 signal was expected to be shifted upfield due to the γ-effect and that of C-6 downfield due to the β-effect of the $C_{(7)}$ axial hydroxy group, compared with those of **1** (C-9: $\Delta\delta$, −4.7∼−5.4; C-6: $\Delta\delta$, +4.9∼+5.4).

The methine carbons of the lignans in groups i and ii appeared over the ranges, δ 33.7±0.1 and δ 40.8±0.2. On the basis of the following experiments, the upfield signal was assigned to the methine carbon carrying an axial methyl group and the downfield one to the methine carbon carrying an equatorial methyl group. The noise-decoupled spectrum of $C_{(6\delta),(7\beta)}$-

dideuterodeoxyschizandrin (**1a**), which was prepared from schizandrin (see "Experimental"), lacked two signals at δ 35.7 and δ 40.9 (very low intensity signals were observed near δ 35.7 and δ 40.9), compared with the spectrum of **1** [δ 33.8(d), 35.7(t), 39.2(t) and 40.9(d)]. The above results indicate that the signal at δ 40.9 was ascribable to C-7 and that at δ 33.8 to C-8. In addition, the assignments of the methylene carbons at δ 35.7 (C-6) and δ 39.2 (C-9) in **1** were confirmed.

Aromatic Carbons

The assignments for the protonated aromatic carbons were based on comparison with the chemical shifts of model compounds (**14**—**19**). The protonated aromartic carbons (C-4 and C-11) of lignans (**2**, **6**, **9**—**13**) possessing a methylenedioxy moiety at C-12 and -13 or C-2 and -3 were easily assigned, as shown in Tables I and II, because the protonated aromatic carbons adjacent to the methylenedioxy moiety appear consistently at higher field by *ca.* 4 ppm than those adjacent to the methoxy group (Chart 2).[9,11]

The protonated aromatic carbons of the lignans [**3**, **4**(**1**), **5**, **7** and **8**], which possess the same functional groups at C-3 and C-12 (*i.e.*: OCH_3 or OH) were assigned as described below. C-4(δ 107.3) and C-11 (δ 110.6) of **1** were distinguished by comparison of the proton coupled spectra of **1** and **1a**: in the spectrum of **1**, they appeared as doublet-triplets due to the couplings with their α-protons and methylene protons ($^1J_{C-4,H-4}=^1J_{C-11,H-11}=155$ Hz, $^3J_{C-4,H-6}=^3J_{C-11,H-9}=6$ Hz), however the signal at δ 107.3 in **1a** appeared as a double-doublet. This finding indicated that the signal at δ 107.3 could be ascribed to C-4 and that at δ 110.6 to C-11 (for **4**: C-4, δ 110.3; C-11, δ 107.0). On the other hand, it is clear that the replacement of the methoxy group adjacent to the protonated aromatic carbon by the hydroxy group produces a downfield shift of *ca.* 3 ppm for the *ortho* protonated aromatic carbon signal, as shown in the ^{13}C NMR data for **17** and **18**, and those for the other lignans,[9,11] so the protonated aromatic carbons of gomisin J (**5**) (C-4: δ 113.3 and C-11: δ 110.2) and (—)-gomisin K_1 (**3**) (C-4: δ 110.8 and C-11: δ 110.0) were assigned by comparison with those of **4**. The above assignments were confirmed by the expected shift of C-11 of (—)-gomisin K_1 acetate (**3a**) (+10.5 ppm *vs.* **4** and +7.5 ppm *vs.* **3**)[9,12]. The assignments of C-4 and C-11 of gomisin H (**8**) were based on a comparison with data for schizandrin (**7**). The signal at δ 107.3 in **8**, which appeared at higher field (*ca.* —3 ppm) than in **7**, was identified as C-11 (*para* position relative to OH) and the other signal at δ 110.6 was identified as C-4.

In conclusion, four predictions were made for the chemical shifts of the protonated aromatic carbons of lignans possessing the partial structure [A] (Chart 3) and the twist-boat-chair conformation of the cyclooctadiene ring. a) When the methyl group is in an axial orientation, the protonated aromatic carbon appears at δ 110.6 $\pm$0.3 [**2**, **3**, **3a** and **4**(**1**)], and when the methyl group is equatorial, it appears at δ 107.3$\pm$0.3 [**4**(**1**) and **12**]; b) The replacement of OMe(x) by the hydroxy group or acetoxy group produces a downfield shift of *ca.* 3 ppm or *ca.* 10 ppm, respectively, for the protonated aromatic carbon (**3**, **3a** and **5**); c) The replacement of OMe(z) by the hydroxy group produces an upfield shift of *ca.* 3 ppm for the protonated aromatic carbon (**8** *vs.* **7**); d) The replacement of OMe (x and y) by the methylenedioxy moiety produces an upfield shift of *ca.* 4 ppm for the protonated aromatic carbon (**2**, **6**, **9**—**13**) [see Table III for b), c) and d)].

The assignments for the aromatic quaternary carbons of the lignans were also based on a comparison with the chemical shifts of model compounds (**14**—**19**) as well as T_1 measurements, proton coupled spectra and the use of PSD techniques.

For example, in the case of **1**, the five pairs of signals between δ 122.4 and δ 153.0 were expected to be the ten aromatic quaternary carbons. Among them, the three pairs of low

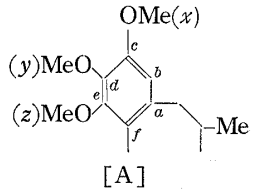
11) R.S. Ward, P. Satyanarayana, L. Ramanchandra Raw, and B.V. Gopala Rao, *Tetrahedron Lett.*, **1979**, 3043.

12) J.S. Craigie, A.G. McInnes, M.A. Ragan, and J.A. Walter, *Can. J. Chem.*, **55**, 1575 (1977).

intensity signals at δ 122.4 and 123.5, δ 139.9 and 140.3, and δ 151.5 and 151.6 could be ascribed to the carbons with no *ortho* protons (C-1, -2, -13, -14, -15 and -16) in view of their T_1 values (Table I).[8] The pair of signals at δ 122.4 and 123.5 was assigned to C-16 and C-15 on the basis of their multiplicities (broad quartets due to the coupling with benzylic methylene and aromatic protons) in the proton coupled spectrum. The individual signals were identified by PSD techniques as mentioned below. Irradiation at the frequency (δ 2.58) of the $C_{(9)}$ methylene protons[10] caused increases of the signal intensities at δ 110.6 (C-11) and δ 123.5 with loss of the long range couplings, while irradiation at the frequency (δ 2.13) of the $C_{(6)}$ methylene protons caused increases of the signal intensities at δ 107.3 (C-4) and δ 122.4, indicating that the signal at δ 122.4 was due to C-16 and that at δ 123.5 was due to C-15. In the above experiments, the signals for C-15 and C-16 appeared as doublets due to the remaining three-bond couplings with the aromatic protons ($^3J_{C-15,H-11}=^3J_{C-16,H-4}=7$ Hz).

The other two pairs of signals at δ 139.9 and δ 140.3 and δ 151.5 and 151.6 were assigned to C-2 and C-13 and to C-1 and C-14, respectively, by comparison with the data for **14** (*vide* T_1 values) and their multiplicities. In the proton coupled spectrum, the signals for C-2 and C-13 appeared as finely split multiplets due to the couplings with their methoxy groups and the aromatic protons, and the signals for C-1 and C-14 appeared as quartets due to the couplings with their methoxy groups ($^3J_{C,\,OCH_3}=4$ Hz). On irradiation at the frequency (δ 3.85) of the methoxy protons [OCH_3: δ 3.90 ($\times 4$) and δ 3.58 ($\times 2$)], the C-2 and C-13 signals changed to doublets due to the remaining three-bond couplings with the aromatic protons ($^3J_{C-2,H-4}=^3J_{C-13,H-11}=7$ Hz), and the C-1 and C-14 signals changed to singlets due to loss of the long range couplings with their methoxy groups. Although the individual signals in each pair could not be identified, the assignments for the above pairs of signals were thus confirmed.

The remaining two pairs of signals at δ 151.7 and 153.0 [T_1 (sec): each 10.0] and δ 133.9 (T_1: 4.0) and 139.1 (T_1: 4.2) were assigned to C-12 and C-13 and to C-10 and C-5, respectively, because the former were expected to be carbons carrying methoxy groups in view of their chemical shifts and the latter were expected to be carbons having three adjacent protons in view of their small T_1 values. In the proton coupled spectrum, the signal at δ 153.0 appeared as a quintet due to the couplings with the methoxy group ($^3J_{C,\,OCH_3}=4$ Hz) and two-bond coupling with the aromatic proton ($^2J_{C-3,H-4}=4$ Hz). On irradiation at the frequency (δ 6.55) of the aromatic protons, this signal changed to a quartet due to loss of the two-bond coupling (the signal at δ 151.7 was not clear because of overlapping). The signal at δ 133.9 was assignable to C-10, because it was expected to appear



[A]

Chart 3

Table III. Effects of Replacement of OMe on the Aromatic Ring by OH, OAc or OCH_2O for the Aromatic Carbon Shifts (see Chart 3)

Aromatic carbon	δ (ppm) [OMe(*x*)→OH] **4→3, 5 3→5**	[OMe(*x*)→OAc] **4→3a**	[OMe(*z*)→OH] **7→8**	[OMe(*x*,*y*)→OCH_2O]	[OH(*x*)→OAc] **3→3a**
C-(*a*)	+1.2±0.4	+0.7	+0.5	−0.9∼−2.0	−0.5
C-(*b*) (protonated aromatic carbon)	+2.8±0.3	+10.5	−2.8	−4.1± 0.5	+7.5
C-(*c*)	−3.9±0.2	−9.0	−1.3	−3.5± 0.5	−5.1
C-(*d*)	−2.4±0.3	+2.8	−6.7	−4.5± 0.5	+4.9
C-(*e*)	−1.2±0.2	+0.1	−4.7	−10.4± 0.4	+1.3
C-(*f*)	−0.8±0.2	+5.8	−6.3	−0.8∼−2.7	+6.4

Plus and minus signals denote downfield and upfield shifts, respectively.

at higher field than C-5 (δ 139.1) due to the influence of the $C_{(8)}$ axial methyl group [the upfield shift ($\Delta\delta$ −6.6∼−7.3) of the C-5 signal of the lignans in group iii, compared with **1**, can also be explained by the influence of the $C_{(7)}$ axial OH].

The aromatic quaternary carbons of **1** were thus assigned and these data were used for the assignments for the aromatic carbons of the other lignans. The results are listed in Tables I and II. The effects of replacements of the aromatic ring methoxyls by hydroxyl, acetoxyl and methylenedioxy moieties on the aromatic quaternary carbon signals are shown in Table III. These effects should be useful for elucidation of the positions of functional groups on the aromatic rings.

Methoxy Carbons

As is clear from Tables I and II, methoxy groups (at C-3 and C-12) adjacent to an aromatic proton are consistently observed at δ 55.9±0.2 and the other methoxy groups at C-1, -2, -13 and -14 are observed at δ 60.5±1.0. These values should also be useful for predicting the positions of functional groups on the aromatic rings.

In conclusion, the structure elucidation of the dibenzocyclooctadiene lignans was mainly based on measurements of intramolecular Overhauser effects in the ^1H NMR spectra, as described in the previous papers,[1,3] but it appears now that ^{13}C NMR analysis may be more useful for the structure elucidation of lignans of this type.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus (a hot-stage type) and are uncorrected. The IR spectra were recorded with a Hitachi EPI-G2 spectrometer. ^1H NMR spectra were recorded with a Varian T-60 spectrometer and ^{13}C NMR spectra with Varian FT-80A (20 MHz, spectral width 5000 Hz, acquisition time 1.6 sec, flip angle 40°, internal ^2H pulse lock, 16K data points), JEOL FX-100 and JEOL FX-60 spectrometers with tetramethylsilane as an internal standard. T_1 values for the aromatic quaternary carbons of **1** were determined in $CDCl_3$ (1 M solution, at 25°, not degassed) by the inversion recovery method with a reproducibility of ±10%. The mass spectrum (MS) was measured with a Hitachi double-focusing mass spectrometer. Preparative layer chromatography (PLC) was carried out on plates (20×20 cm, 0.75 mm thick) coated with Kieselgel PF_{254} (Merck) and preparative high performance liquid chromatography (prep. HPLC) was done on a JASCO Trirotar II chromatograph with a UVIDEC-100-II detecter.

Preparation of 2,3-Methylenedioxyphenol (18)——Methylene iodide (2.68 g, 10 mmol) and K_2CO_3 (1.5 g) were added to a solution of pyrogallol (1.26 g, 10 mmol, Kokusan Chemical Works Ltd., Tokyo) in dry dimethylsulfoxide (10 ml), and the reaction mixture was stirred at 60° for 5 hr, cooled, diluted with H_2O (50 ml), then extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by PLC [acetone–hexane (2: 3), *Rf* 0.71] to give 2,3-methylenedioxyphenol (**18**, 285 mg, 21%) as colorless needles (from ether–hexane), mp 65—65.5°, IR ν_{max}^{KBr} cm^{-1}: 3290 (OH), 1640, 1628, 1615 (aromatic), 922 (OCH_2O). ^1H NMR (δ in $CDCl_3$): 5.33 (1H, s, OH), 5.90 (2H, s, OCH_2O), 6.33—6.83 (3H, m, 3×arom.-H). *Anal.* Calcd for $C_7H_6O_3$: C, 60.87; H, 4.38. Found: C, 60.59; H, 4.31.

Preparation of 2,3-Methylenedioxyanisole (17)——$(CH_3)_2SO_4$ (0.5 ml) and K_2CO_3 (1 g) were added to a solution of **18** (225 mg) in dry acetone (8 ml) and the reaction mixture was stirred at 50° for 5 hr, then diluted with H_2O (30 ml) and extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by PLC [acetone–hexane (3: 7), *Rf* 0.78] to give 2,3-methylenedioxyanisole (**17**, 180 mg) as colorless needles (from ether–hexane), mp 41.5—42°. ^1H NMR (δ in $CDCl_3$): 3.88 (3H, s, OCH_3), 5.92 (2H, s, OCH_2O), 6.38—6.90 (3H, m, 2×arom.-H).

Preparation of 1-Acetoxy-2,3-Methylenedioxybenzene (19)——A solution of **18** (150 mg) in a mixture of Ac_2O (0.4 ml) and pyridine (0.8 ml) was allowed to stand at room temperature overnight, then diluted with H_2O (20 ml) and extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by PLC [acetone–hexane (3: 7)] to give 1-acetoxy-2,3-methylenedioxybenzene (**19**, 190 mg) as colorless plates (from ether–hexane), mp 47—48°. ^1H NMR (δ in $CDCl_3$): 2.30 (3H, s, $COCH_3$), 5.98 (2H, s, OCH_2O), 6.55—6.85 (3H, m, 3×arom.-H).

Dehydration of Schizandrin (7)——A solution of **7** (718 mg) and phosphorous oxychloride (1 ml) in anhydrous pyridine (4 ml) was heated at 100° for 2 hr. After cooling, the reaction mixture was diluted with ether (70 ml) and poured into ice-water. The ethereal solution was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [ether–hexane (2: 3)] to give dehydrated schizandrin (**20**) as a pale yellow oil (513 mg, 74.5%), $[\alpha]_D^{23}$ −92.5° (c=2.67, $CHCl_3$). ^1H NMR (δ in $CDCl_3$): 1.07 (3H, d, J=6.5 Hz, $C\underline{H}_3$–CH–), 1.63 (3H, br s, $C\underline{H}_3$–C=CH), 2.80 (1H, m, –CH), 2.97 (center) (2H, m, $ArC\underline{H}_2$–), 3.50 (3H, s), 3.65 (3H, s), 3.87 (6H, s), 3.88 (3H, s), 3.90 (3H, s) (6×OCH_3), 6.20 (1H, br s, H–C=C–), 6.47 (2H, s, 2×arom.-H). IR ν_{max}^{KBr} cm^{-1}: no OH, 1590, 1570 (aromatic).

Catalytic Hydrogenation of Dehydrated Schizandrin (20) with H_2——Compound **20** (120 mg) in MeOH (3 ml) was shaken with H_2 in the presence of PtO_2 (50 mg) as a catalyst at 23° for 5 hr. The catalyst was filtered off and the filtrate was concentrated to dryness under reduced pressure. The residue (83 mg) was purified by prep. HPLC to give **1** (55 mg) and a minor product (15 mg).[13] Prep. HPLC conditions: column, semi prep. μ-Bondapak C_{18} (8 mm i.d.×30 cm); mobile phase, MeOH–H_2O (2: 1); flow rate, 3 ml/min; temp., room temperature; detection, UV 290 nm. Compound **1**: t_R(min), 18.0; minor product: t_R(min), 16.5.

Compound **1**: colorless prisms (from ether–hexane), mp 115.5—117°, $[\alpha]_D^{23}$ +98.6° (c=0.923, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1591, 1576 (aromatic). This compound was identified as (+)-deoxyschizandrin (**1**) by direct comparison with an authentic sample (IR, mixed mp, ^1H NMR and $[\alpha]_D$).

Catalytic Hydrogenation of Dehydrated Schizandrin (20) with D_2——Compound **20** (120 mg) in methanol-d_4 (3 ml) was shaken with D_2 in the presence of PtO_2 as a catalyst at 23° for 5 hr. The catalyst was filtered off and the filtrate was concentrated to dryness. The residue (88 mg) was purified by prep. HPLC under the conditions described for purification of the product of catalytic hydrogenation of **20** with H_2 to give 6β,7β-dideuterodeoxyschizandrin [**1a**, 59 mg, t_R(min), 18.0] and a minor product [14 mg, t_R(min), 16.5].

Compound **1a**: a white amorphous powder, MS, m/e (%): 418 ($C_{24}H_{30}D_2O_6$, M^+, 100). ^1H NMR (δ in $CDCl_3$): 0.73 (3H, d, J=7 Hz, $C\underline{H}_3$–$\overset{|}{C}_{(8)}$–H), 0.98 (3H, s, $C\underline{H}_3$–$\overset{|}{C}_{(7)}$–D), 1.83 (1H, m, H–$\overset{|}{C}_{(8)}$–), 2.25 (1H, br s, $C_{(6a)}$–H), 2.55 (center) (2H, m, $C_{(9)}$–H), 3.60 (6H, s), 3.90 (12H, s) (6×OCH_3), 6.55 (2H, s, 2×arom.–H).

13) Although detailed examination of the minor product has not been carried out, it may be 7-*epi*-deoxyschizandrin formed by addition of H_2 from the α side of **20**.