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The Constituents of *Schizandra chinensis* Baill. V.[1] The Structures of Four New Lignans, Gomisin N, Gomisin O, Epigomisin O and Gomisin E, and Transformation of Gomisin N to Deangeloylgomisin B[2]

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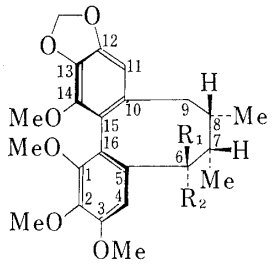
Four new dibenzocyclooctadiene lignans, gomisins N (**1**), O (**2**) and E (**4**), and epigomisin O (**3**), together with a known lignan (+)-deoxyschizandrin (**5**) were isolated from the fruits of *Schizandra chinensis* Baill. (Schizandraceae). The structures of the new lignans were elucidated by chemical and spectral studies.

The transformation of **1** to deangeloylgomisin B (debenzoylgomisin C) (**6**) is also described.

Keywords——*Schizandra chinensis* Baill.; Schizandraceae; dibenzocyclooctadiene lignan; gomisin E; gomisin N; gomisin O; epigomisin O; (+)-deoxyschizandrin; transformation of gomisin N to deangeloylgomisin B

The presence of a number of dibenzocyclooctadiene lignans in the fruits of *Schizandra chinensis* Baill. (Schizandraceae) has been reported by several workers.[4] In our previous papers, we reported the isolation of several new lignans, gomisins A—D, F—H, J and pre-gomisin, from the fruits of this plant.[1,2,5]

This paper deals with structure determination of additional new lignans named gomisin N(**1**),[2] gomisin O(**2**), epigomisin O(**3**) and gomisin E(**4**), as well as the isolation of a known lignan, (+)-deoxyschizandrin (**5**), and also describes the transformation of gomisin N to deangeloylgomisin B(debenzoylgomisin C) (**6**).[5b]



1 : $R_1=R_2=H$
1b : $R_1=D$, $R_2=H$
2 : $R_1=OH$, $R_2=H$
3 : $R_1=H$, $R_2=OH$

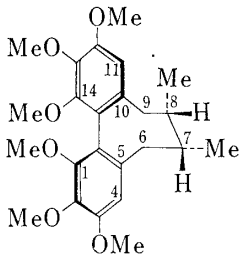


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Chart 1

Structure Determination of Gomisin N(1), Gomisin O(2) and Epigomisin O(3), and Isolation of (+)-Deoxyschizandrin (5)

Gomisin N(**1**) was isolated as colorless prisms, $C_{23}H_{28}O_6$, mp 105—107°, $[\alpha]_D^{23}$

1) Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), **27**, 1583 (1979).
2) *a*) A part of this work was presented in a preliminary communication; see Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), **26**, 3257 (1978).
3) Location: *a*) *Izumi 1421, Komae-shi, Tokyo 201, Japan*; *b*) *Hongo, Bunkyo-ku, Tokyo 113, Japan.*
4) *a*) N.K. Kochetkov, A. Khorlin, O.S. Chizhov, and V.I. Sheichenko, *Tetrahedron Letters*, **1961**, 730; *b*) N.K. Kochetkov, A. Khorlin, and O.S. Chizhov, *ibid.*, **1962**, 361; *c*) Y.Y. Chen, Z.B. Shu and L.N. Li, *Sci. Sin.*, **19**, 276 (1976) [*C.A.*, **86**, 29518*m* (1977)]; *d*) Y.Y. Chen and L.N. Li, *Hua Hsueh Hsueh Pao.*, **34**, 45 (1976) [*C.A.*, **86**, 167860*t* (1977)]; *e*) J.S. Liu, S.D. Fang, M.F. Huang, Y.L. Gao and J.S. Hsu, *ibid*, **34**, 229 (1976) [*C.A.*, **89**, 24193*d* (1978)].
5) *a*) Y. Ikeya, H. Taguchi, I. Yosioka, Y. Iitaka, and H. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), **27**, 1395 (1979); *b*) Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *ibid.*, **27**, 1383 (1979); *c*) *Idem*, *ibid.*, **27**, 1576 (1979).

TABLE I. PMR Spectral Data for **1**, **1a**, **1b**, **2**, **2a**, **3**, **8** (**5**), **6a**, **7**, **9** and **10** (in $CDCl_3$, δ Values)

Compd.	H-4, s H-11, s	$-OCH_2O-$ s	–OMe s	H-6α (J=Hz)	H-6β (J=Hz)	H-9α, dd (J=Hz)	H-9β, dd (J=Hz)	H-7 H-8	Me–$C_{(7)}$ d(J=Hz)	Me–$C_{(8)}$ d(J=Hz)
1	6.55 6.47	5.93	3.55, 3.82 3.93(×2)	2.57, center (2×H, m)		2.27 (13.5/8)	2.03 (13.5/1)	1.83 (2×H, m)	0.73 (7)	0.97 (7)
1a[a]	6.58 6.62	—	3.30, 3.50, 3.92(×2) 5.60, 2×H, br, s, OH[c]	2.58, center (2×H, m)		2.08, center (2×H, m)		1.85 (2×H, m)	0.75 (7)	0.97 (7)
1b	6.48 6.41	5.90	3.55, 3.81 3.88(×2)	2.56 d (8)	—	2.26 (13.5/8.5)	2.01 (13.5/2)	1.88 (2×H, m)	0.75 (7)	0.99 (7)
8(**5**[b])	6.55 (2×H)	—	3.58(×2) 3.90(×4)	2.58, center (2×H, m)		2.27 (13.5/9)	2.02 (13.5/1)	1.82(m)[e] 1.92(m)[d]	0.73[d] (7)	0.98[e] (7)
7	6.63 (2×H)	—	3.50(×2), 3.94(×2) 5.91, 2×H, s, OH[c]	2.48, center (2×H, m)		2.25 (13.5/8.5)	1.99 (13.5/1)	1.95 (2×H, m)	0.75 (7)	0.99 (7)
2	6.57 6.42	5.95	3.53 3.90(×3)	4.33 d (8)	1.63 s, OH[c]	1.92—2.47 (2×H, m)		1.75 (2×H, m)	0.92 (6×H, d, 7)	
2a[a]	7.57 6.47	6.00	3.45, 3.87 3.97(×2)	—	—	1.97—2.68 (2×H, m)		2.68(m)[d] 1.73(m)[e]	1.00[d] (7)	0.80[e] (7)
3	6.98 6.43	5.92	3.53, 3.82 3.90(×2)	1.93 s, OH[c]	4.53 s	2.13 (13/8)	1.93 (13/1)	1.87 (2×H, m)	0.70 (7)	1.00 (6)
6a[a]	6.70 6.40	5.93	3.70, 3.80 3.90, 3.93	—	—	2.53 (14/9)	2.20 (14/2)	1.92, s, OH[c] 1.70(m)	1.37 s	1.10 (7)
9	6.68 6.47	—	3.60, 3.77 3.85, 3.90, 3.93(×2)	—	—	2.53 (13.5/9)	2.28 (13.5/2)	1.92, s, OH[c] 1.77(m)	1.38 s	1.13 (7)
10[a]	6.60 6.45	6.02	3.60, 3.83 3.88, 3.92	—	—	2.37, center (2×H, m)		1.83, s, OH[c] 1.75(m)	1.37 s	1.13 (7)

a) These compounds were measured at 60 MHz.
b) Assignments for **5**: 2.58 (H-9), 2.25 (H-6α), 2.02 (H-6β), 1.92 (H-7), 1.82 (H-8), 0.98 (Me–$C_{(7)}$), 0.73 (Me–$C_{(8)}$).
c) Hydroxy signals were confirmed on addition of D_2O.
d, *e*) Assignments of the signals were confirmed by double resonance experiments.
f) d=doublet, m=multiplet, s=singlet.

$-84.7°$ (in $CHCl_3$) (yield 0.31%). The ultraviolet (UV) spectrum of **1** showed absorption maxima at 218 (log ε 4.73), 251 (sh 4.14) and 275—280 nm (sh 3.61) and the infrared (IR) spectrum showed no hydroxy band, indicating that **1** is a dibenzocyclooctadiene lignan and has no hydroxy group. The proton nuclear magnetic resonance (PMR) spectrum (Table I) indicated the presence of a methylenedioxy moiety and four methoxy groups on the aromatic rings, and also two secondary methyl and two benzylic methylene groups. A comparison of the PMR spectrum of **1** with those of gomisin J(**7**) and its dimethyl ether ((−)-deoxyschizandrin) (**8**)[1] suggests that **1** possesses the same conformational structure as **7** and **8**.

On treatment with lead tetraacetate [$Pb(OAc)_4$] in dry benzene, **1** afforded the diphenol (**1a**), $C_{22}H_{28}O_6$, mp 184.5—188°, $[\alpha]_D^{23}$ −129° (in $CHCl_3$), IR (in KBr), 3525, 3275 cm^{-1} (OH).[6] Methylation of **1a** [$(CH_3)_2SO_4/K_2CO_3$ in acetone] afforded a dimethyl ether as colorless plates, $C_{24}H_{32}O_6$, mp 116—117°, $[\alpha]_D^{22}$ −100° (in $CHCl_3$), which was identified as dimethylgomisin J(**8**) by direct comparison (IR, mixed mp, PMR and $[\alpha]_D$) (Chart 2).

These findings indicate that **1** possesses the same cyclooctadiene moiety as **7** (*cis*-dimethyl) and has an *S*-biphenyl configuration. The structure of **1** was confirmed by measurements of the intramolecular nuclear Overhauser effects (NOE) in **1** (in $CDCl_3$)[5a,b,7] As shown in Fig. 1, irradiations of the methoxy (δ 3.93) and higher field methyl (δ 0.73, $C_{(7)}$–CH_3) signals each caused a 14% increase in the integrated intensity of the lower field aromatic proton signal ($C_{(4)}$–H), while irradiation of each methoxy signal did not affect the higher field aromatic proton signal ($C_{(11)}$–H). These findings indicate that the $C_{(7)}$ methyl and $C_{(4)}$ aromatic protons are close to each other, and that the methylenedioxy moiety is located at the C-12 and -13 positions. In addition, irradiation of the lower field methyl signal (δ 0.97) did not affect the aromatic protons, while irradiation of the $C_{(9\beta)}$ proton signal (δ 2.03), which was assigned by comparison of the PMR spectrum with that of **7**, caused a 13% increase in the integrated intensity of the higher field aromatic proton signal. On the basis of the above results, the absolute structure of gomisin N was elucidated as **1**.

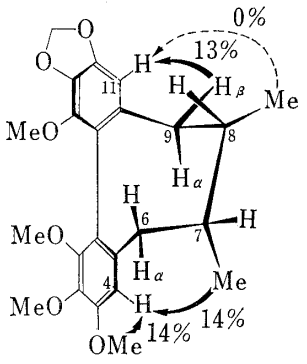


Fig. 1. NOE in **1** (in $CDCl_3$)

Gomisin O(**2**) was isolated as colorless prisms, $C_{23}H_{28}O_7$, mp 145—146.5°, $[\alpha]_D^{25}$ −33.9° (in $CHCl_3$). The UV, IR and circular dichroism (CD) spectra[5a,b] of **2** indicate that **2** is a dibenzocyclooctadiene lignan possessing a hydroxy group and an *S*-biphenyl configuration. The PMR spectrum (Table I) of **2** suggests the presence of two secondary methyl groups (δ 0.92, 6H, d, J=7 Hz) on the cyclooctadiene ring and also a methylenedioxy moiety and four methoxy groups on the aromatic rings. The doublet signal at δ 4.33 (1H, J=8 Hz, $C_{(6)}$–H), as well as the signal at δ 1.63 (1H, s), which disappeared on addition of D_2O, suggests that **2** possesses a secondary hydroxy group at the benzylic position. The partial structure of **2** was confirmed by measurements of the NOE (in $CDCl_3$) as shown in Fig. 2. Irradiation of the methoxy (δ 3.90) and methine (δ 4.33, $C_{(6)}$–H) signals caused 10.4% and 13.6% increases in the integrated intensity of the lower field aromatic proton signal (δ 6.57, $C_{(4)}$–H), respectively, while irradiation of each methoxy signal did not affect the higher field aromatic proton (δ 6.42, $C_{(11)}$–H). These findings indicate that the $C_{(4)}$ aromatic proton and benzylic methine ($C_{(6)}$–H) are close to each other, and that the methylenedioxy moiety is located at the C-12 and -13 positions. On the other hand, irradiation of the secondary methyl signals (δ 0.92,

6) Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **27**, 2536 (1979).
7) Y.P. Chen, R. Liu, H.Y. Hsu, S. Yamamura, Y. Shizuri, and Y. Hirata, *Bull. Chem. Soc. Japan*, **50**, 1824 (1977).

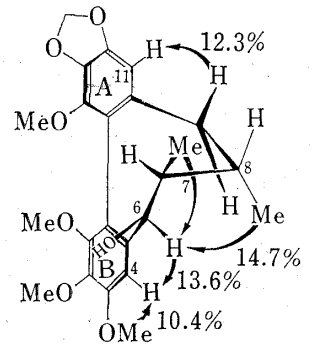
$C_{(7)}$–, $C_{(8)}$–CH_3) caused a 14.7% increase in the integrated intensity of the $C_{(6)}$ proton signal, but did not affect the aromatic protons. Irradiation at δ 2.43 (lower field methylene signal) caused a 12.3% increase in the integrated intensity of the higher field aromatic proton signal ($C_{(11)}$–H). These findings indicate that at least one methyl group and a $C_{(6)}$ proton are close to each other, and that the benzylic methylene and $C_{(11)}$ proton are in close proximity.

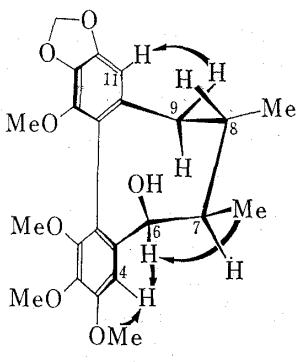
On the basis of the above NOE results, three structures were considered for gomisin O: **2**, **2′** ($C_{(8)}$ epimer of **2**) and **2″**. However, the structure **2″** was excluded by the $C_{(6)}$ proton J value (J=8 Hz) of gomisin O, because the Dreiding model shows that the dihedral angle between the $C_{(6)}$ and $C_{(7)}$ protons in **2″** is approximately 90°, so the J value of the $C_{(6)}$ proton should consequently be zero. Thus, gomisin O should correspond to **2** or **2′** ($\phi_{6,7}$=150—180°).

Next, catalytic hydrogenation of **2** over platinum oxide (PtO_2) in acetic acid afforded the hydrogenolysis product (**1**), $C_{23}H_{28}O_6$, mp 103—105°, $[\alpha]_D^{22}$ −72.9° (in $CHCl_3$), which was identical with natural gomisin N(**1**) on direct comparison (IR, mixed mp, PMR and $[\alpha]_D$). On the other hand, hydrogenolysis of **2** with deuterium in AcOH-d_4 by the same method afforded the deuterated compound (**1b**), $C_{23}H_{27}DO_6$ (M^+, m/e, 401, base peak), the PMR spectrum of which showed a doublet at δ 2.56 (J=8 Hz, ϕ=30°) assignable to the $C_{(6\alpha)}$ proton. These findings indicate that **2** possesses a *cis*-dimethyl configuration and a $C_{(6\beta)}$ hydroxy group. The structure of gomisin O was confirmed by its preparation from **1** (Chart 2). Treatment of **1** with $Pb(OAc)_4$ in AcOH followed by hydrolysis with 0.5 M methanolic KOH afforded **2** as colorless prisms, mp 145—146.5°, $[\alpha]_D^{23}$ −32.7° (in $CHCl_3$).

On the basis of the above results, the absolute structure of gomisin O was elucidated as **2**; this is the first lignan possessing a boat conformation of the cyclooctadiene ring to be isolated from this plant. Compound **2** must have such a conformation, since if **2** has a twist-boat-chair conformation[8] such as **1**, the steric interaction between ring A and the $C_{(6)}$ *ax*-hydroxy group and also that between ring B and the $C_{(7)}$ *ax*-methyl group would be extremely large.

Epigomisin O(**3**) was isolated as an amorphous powder, $C_{23}H_{28}O_7$, $[\alpha]_D^{23}$ −66.7° (in $CHCl_3$), and its UV and IR spectra indicate that **3** is a dibenzocyclooctadiene lignan possessing a hydroxy group. Although the PMR spectrum (Table I) of **3** shows that **3** possesses the same





OMe ---0%---> $C_{(11)}$–H

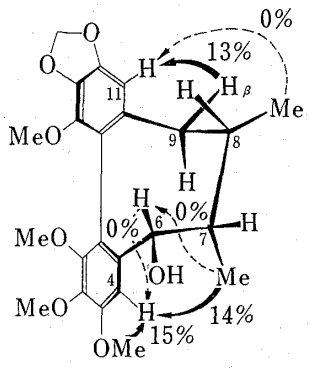
H–C(Me) ---0%---> $C_{(11)}$–H

2

2′ ($C_{(8)}$–epimer of **2**)

Fig. 2. NOE in **2** (in $CDCl_3$)

2″

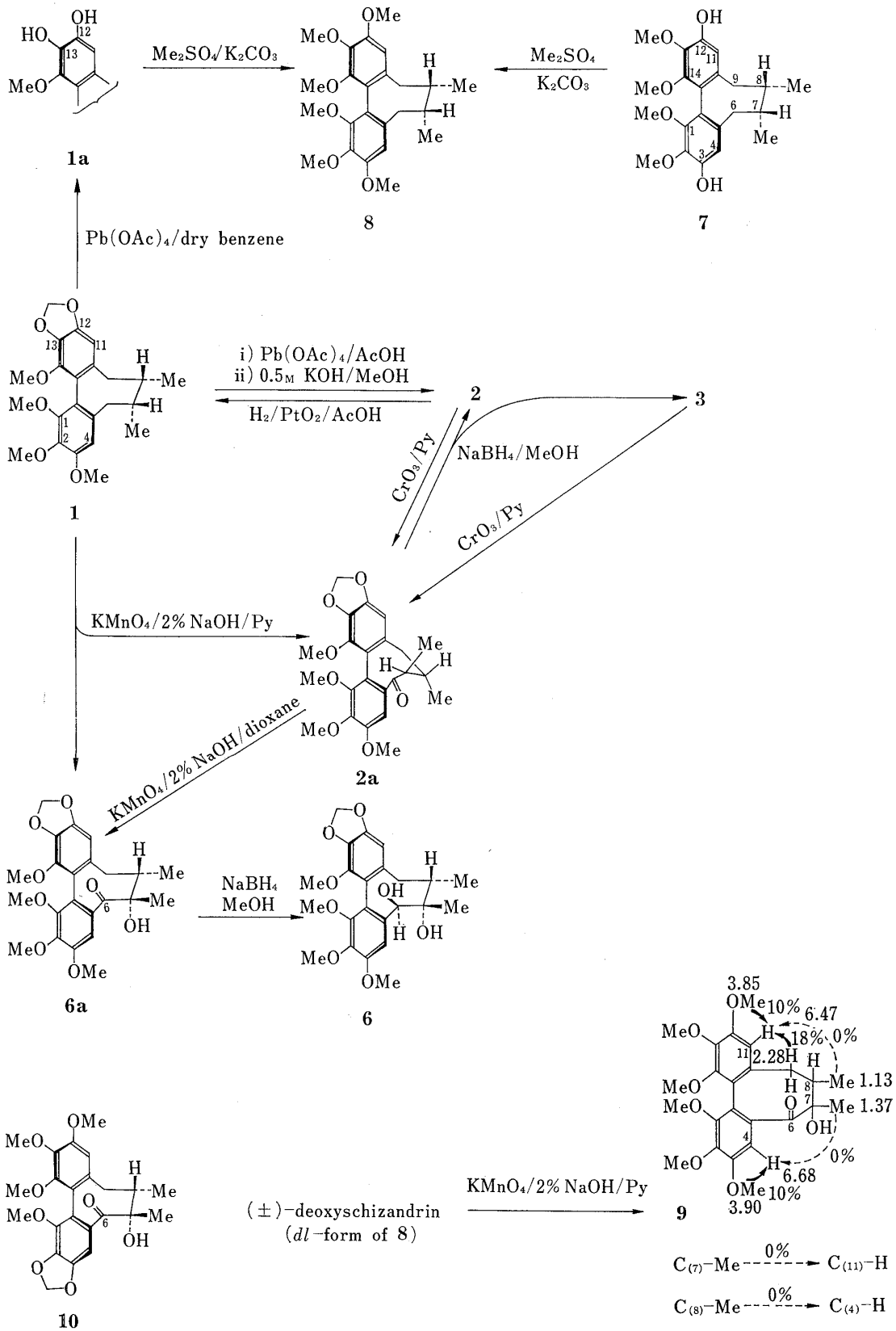


OMe ---0%---> $C_{(11)}$–H

$C_{(8)}$–Me ---0%---> $C_{(4)}$–H

Fig. 3. NOE in **3** (in $CDCl_3$)

8) F.A.L. Anet and I. Yavari, *Tetrahedron Lett.*, **1975**, 1567.



Ac=CH_3CO, Me=CH_3, Py=pyridine

NOE in **9** (δ value in $CDCl_3$)

(numbers on carbons are based on an *S*-biphenyl configuration)

Chart 2

functional groups as **2**, its behavior is quite different from that of **2**. The appearance of two distinct methyl and lower field aromatic proton signals suggests that **3** possesses a twist-boat-chair conformation, as well as a *cis* dimethyl configuration and $C_{(6\alpha)}$ hydroxy group [*vide*, PMR: $C_{(6)}$–H, br. s]. The structure of **3** was supported by measurements of the NOE (in $CDCl_3$) as shown in Fig. 3. In addition, the structure of **3** was confirmed by its preparation from **2**.

Oxidation of **2** with chromium trioxide (CrO_3) in pyridine afforded **2a**, $C_{23}H_{26}O_7$, mp 151.5—152°. The IR spectrum of **2a** showed a carbonyl band at 1658 cm^{-1} and the PMR spectrum showed an extreme downfield shift (δ 7.57) of one aromatic proton ($C_{(4)}$–H), indicating that the carbonyl group is coplanar with the adjacent aromatic ring and that the cyclooctadiene ring is in a boat conformation.[9] Treatment of **2a** with sodium borohydride ($NaBH_4$) in methanol afforded a pair of epimers, **2** and **3**, in almost equal amounts. The products were proved to be identical with natural gomisin O(**2**) and epigomisin O(**3**). On the other hand, oxidation of natural **3** with CrO_3 in pyridine afforded **2a**. The absolute structure of epigomisin O was thus elucidated as **3**.

(+)-Deoxyschizandrin (**5**) (mirror image of **8**)[10] was isolated as colorless prisms, $C_{24}H_{32}O_6$, mp 114—116°, $[\alpha]_D^{28}$ +92.1° (in $CHCl_3$). The structure of **5** was confirmed by CD, IR and UV spectral analyses, as well as by comparison of the PMR spectrum with those of (±)-deoxyschizandrin synthesized by Ghera *et al.*[11]

Transformation of Gomisin N(1) to Deangeloylgomisin B(6)

In the course of structure determination of the numerous lignans isolated from this plant, we have found that oxidation of (±)-deoxyschizandrin[10] with potassium permanganate ($KMnO_4$) in a mixture of 2% NaOH and pyridine afforded the ketoalcohol (**9**) (yield 38%), colorless prisms (from ethar–*n*-hexane), mp 166—167.5°, which showed a hydroxy (3440 cm^{-1}) and an unconjugated carbonyl (1693 cm^{-1}) bands in the IR spectrum. The PMR spectrum (Table I) of **9** showed the signals of a secondary methyl (δ 1.13, d, J=7 Hz), a tertiary methyl (δ 1.38, s) and a benzylic methylene (ABX octet, δ 2.28, 1H, d, d, J=13.5/2 Hz; δ 2.53, 1H, d, d, J=13.5/9 Hz) groups, and lacked one benzylic methylene signal, compared to **5** (and **8**) (δ 2.58, 2H, m). On the basis of comparison of the above spectral data with those of **6a** and **10**,[5b] **9** appears to have the same cyclooctadiene moiety as **6a** and **10**. The structure of **9** was confirmed by measurement of the NOE (in $CDCl_3$) as shown in Chart 2.

The above reaction indicated that the benzylic methylene group of the axial-methyl side was oxidized to a carbonyl group, and the methine carrying the axial methyl to a carbinol, accompanied by inversion of methyl orientation.

This finding prompted us to transform **1** to deangeloylgomisin B (**6**). Thus, **1** was oxidized in the same manner to give two compounds **2a** (6.8%) and **6a** (5.6%), $C_{23}H_{26}O_8$, mp 129—130.5°, together with unchanged **1** (22.5%). Compound **2a** obtained here was further oxidized with $KMnO_4$ in a mixture of 2% NaOH and dioxane to afford **6a** (14%). Finally, reduction of **6a** with $NaBH_4$ afforded the diol (82%), $C_{23}H_{28}O_8$, mp 209—211°, $[\alpha]_D^{22}$ −83.8° (in $CHCl_3$), which was identical with **6** on direct comparison (IR, mixed mp, PMR and $[\alpha]_D$). When **2a** was treated with $NaBH_4$, a pair of epimers, **2** and **3**, was obtained in almost equal amounts as mentioned above, but **6a** afforded only one product (**6**) in the same reaction. Transformation of **1** to **6** (and also that of **2** and **3** to **6**) was thus accomplished. The above reaction sequences are summarized in Chart 2.

9) M. Mervic and E. Ghera, *J. Am. Chem. Soc.*, **99**, 7673 (1977); A.S. Kende, L.S. Liebeskind, C. Kubiak, and R. Eisenberg, *ibid.*, **98**, 6389 (1976); B. Becker, L.R. Hughes, and R.A. Raphael, *J. Chem. Soc.* Parkin I., **1977**, 1674.

10) (±)-Deoxyschizandrin, mp 113.5—115°, $[\alpha]_D$ 0° (in $CHCl_3$), $CD[\theta]_{220-400\,nm}^{25}=0$ (in MeOH), had been isolated from the other source.

11) E. Ghera, Y. Ben David and D. Becker, *Tetrahedron Lett.*, **1977**, 463; T. Biftu, B.G. Hazra and R. Stevenson, *J. Chem. Soc. Chem. Commun.*, **1978**, 491.

The reaction mechanism of the inversion of $C_{(7)}$ methyl orientation during oxidation of **1** is not known, but it seems feasible that initial attack of the reagent at the $C_{(6)}$ position from the less hindered side yields **2a**, which forms an enolized intermediate **2a'** in the alkaline medium, and then $C_{(7)}$ is attacked by the reagent from the less hindered side to yield **6a** (Fig. 4).

Structure Determination of Gomisin E

Gomisin E (**4**) was isolated as an amorphous powder, $C_{28}H_{34}O_9$, $[\alpha]_D^{24}$ +28.1° (in $CHCl_3$). The IR, UV and CD spectra of **4** indicate that it is a dibenzocyclooctadiene lignan possessing a hydroxy group, an ester linkage and an *S*-biphenyl configuration. The PMR spectrum (in C_6D_6, Table II) indicates the presence of three methoxy groups, and one methylenedioxy and one methyleneoxy (▪–CH_2O–, around δ 3.98, 2H, m) moieties on the aromatic rings, and also three secondary methyl (δ 0.70, 0.92 and 1.13, each 3H, d, J=7 Hz), a tertiary methyl (δ 1.20, s, CH_3–Ċ–OH) and a benzylic methine (δ 5.13, 1H, d, J=7 Hz) groups. A comparison of the PMR spectrum of **4** with that of gomisin D(**11**)[5a] suggested **4** to be 7-deoxygomisin **D**. In fact, the presence of the partial structure [Ar–CH(OCOR)–ĊH–CH_3] was confirmed by a double resonance experiment: upon irradiation at δ 1.86, one doublet methyl at δ 0.92 and a doublet methine at δ 5.13 each changed to a sharp singlet.

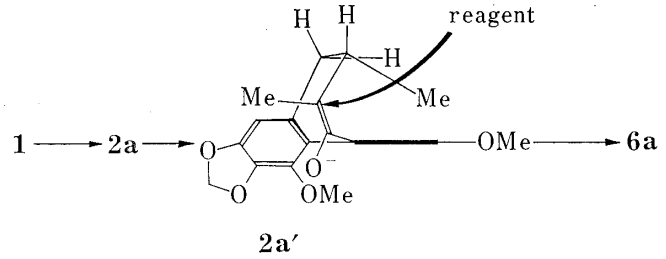
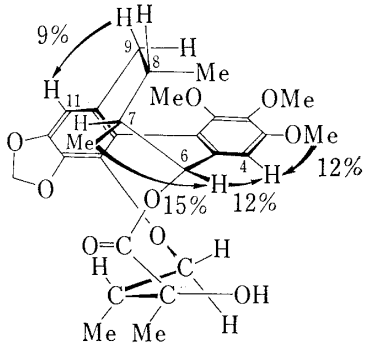


Fig. 4



H–Ċ–Me(×3) ---0%---> $C_{(4)}$–H, $C_{(11)}$–H

OMe(×3) ---0%---> $C_{(11)}$–H

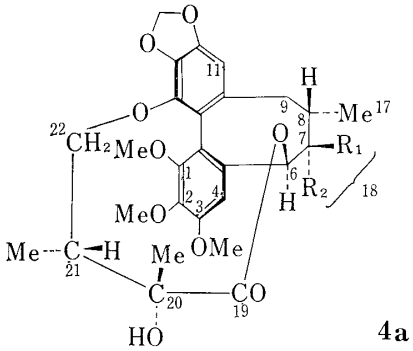
Fig. 5. NOE in **4** (in C_6D_6)

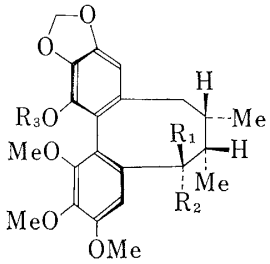
On hydrolysis with 3% ethanolic KOH followed by methylation with diazomethane, **4** afforded compound **4a** as an amorphous powder, $C_{29}H_{38}O_{10}$, $[\alpha]_D^{25}$ ≃0° (in $CHCl_3$). The high resolution mass spectrum of **4a** (Chart 4 and Table III) indicates that **4a** possesses the same side chain as **11a**, which was prepared from **11**.[5a] On the other hand, oxidation of **4a** with CrO_3 in pyridine smoothly afforded the ketoalcohol (**4b**), which gave a conjugated carbonyl band at 1660 cm^{-1} in the IR spectrum and showed a downfield shift of one aromatic proton (δ 7.23) as well as the absence of a benzylic methine signal in the PMR spectrum. These observations indicate that **4b** possesses a boat conformation of the cyclooctadiene ring, as mentioned above. The partial structure of **4** was confirmed by measurements of the NOE as shown in Fig. 5. Irradiations of the methoxy (δ 3.53) and methine (δ 5.13, $C_{(6)}$–H) signals each caused a 12% increase in the integrated intensity of the lower field aromatic proton signal (δ 6.88, $C_{(4)}$–H), while irradiation of each methoxy signal caused no enhancement of the signal intensity of the higher field aromatic proton (δ 6.42, $C_{(11)}$–H). On the other hand, irradiation of the doublet methyl signal at δ 0.92 ($C_{(7)}$–CH_3) caused a 15% increase of the integrated intensity of the $C_{(6)}$-methine signal. Irradiation at δ 2.33 (lower field methylene signal) caused a 9% increase of the integrated intensity of the $C_{(11)}$-proton signal, while

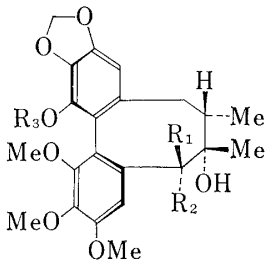
TABLE II. PMR Spectral Data for **4**, **4a—4f**, **11**, **11b** and **12** (in $CDCl_3$)

Compd.[a]	H-4, s H-11, s	$-OCH_2O-$ (J=Hz)	H-6, d (J=Hz)	Ar-CH_2O- H-22(J=Hz)	$-CH_2O-$ H-19(J=Hz)	OMe s	H-9 (2×H, m)	H–C–, m (H-7,-8, 21)	HO–C–Me. s H-18	 H-23	>C< Me, s Me, s	H–C–Me, d (J=7 Hz) (H-17,-18,-24)	OH s
4[b]	6.88 6.42	5.33, 5.47 each 1H, d (1.5)	5.13 (7)	3.90—4.20 m	—	3.53, 3.72 3.75	1.75—2.50	1.58(H-8) 1.86(H-7) 2.28(H-21)[f]	—	1.13	—	0.70(H-17) 0.92(H-18) 1.20(H-24)[f]	3.00
11	6.80 6.43	5.90, 5.99 each 1H, d (1)	5.71 s	3.4—4.0 m	—	3.56, 3.86 3.92	2.43, 1H, dd(14/8) 1.95, 1H, dd(14/1)	1.63, 1.72	1.20	1.26	—	1.02(H-17) 1.10(H-24)	1.73 3.10
4a	6.62 6.42	5.93 s	4.37 (8)	3.80—4.38 m	—	3.47, 3.67 3.92(×2)	2.00—2.50	1.77(×2) 2.17(H-21)	—	1.23	—	0.90 0.93 0.95	2.30, br. s 2.87, br. s
4b[b]	7.23 6.43	5.33 s	—	4.10, 1H, dd(9/7) 4.38, 1H, dd(9/5)	—	3.70, 3.72 3.75, 3.97	2.00—2.50	2.88(H-7)[f] 1.67(H-8) 2.20(H-21)	—	1.25	—	0.82(H-17) (J=6.5) 0.95(H-24) 1.12(H-18)[f]	3.13, br. s
4c	6.58 6.42	5.95 s	4.33 (8)	4.33 m	3.28 s	3.48 3.92(×2)	1.82—2.45	1.72(×3)	—	0.95	—	0.87 0.93(×2)	2.60(×3) bs. s
4d	6.58 6.43	5.95 s	4.33 (7)	3.95, 1H, dd(10/7) 4.37, 1H, dd(10/3.5)	3.48, 3.73 each 1H, d (9)	3.53 3.90(×2)	1.80—2.50	1.78(×3)	—	1.00	1.30 1.34	0.80 0.90 0.93	1.88
4e	7.57 6.47	6.00 s	—	3.80—4.12[d] 4.35, 1H, dd(9/3.5)	3.47, 3.75 each 1H, d (9)	3.45 3.95(×2)	1.82—2.68	2.67(H-7)[f] 1.85(×2)	—	1.03	1.34 (×2)	0.72 0.80 1.02(H-18)[f]	—
4f	6.70 6.40	5.93 s	—	3.79[d] 4.46, 1H, dd(9/3.5)	3.47, 3.74 each 1H, d (9)	3.68, 3.90 3.93	2.00—2.90	1.97(×2)	1.38	1.08	1.32 1.36	0.70, 1.12 (H-17, -24)	2.12
12	6.63 6.52	5.98 s	4.58[e] (10.5)	3.80[d] 4.42, 1H, dd(9/3.5)	3.45, 3.73 each 1H, d (9)	3.58 3.92(×2)	2.33, 1H, dd(13.5/9) 2.07, 1H, dd(13.5/1)	1.93(×2)	1.41	1.02	1.32 1.35	0.78, 1.12 (H-17, -24)	1.93(×2)
11b	6.62 6.55	6.00 s	4.57 br. s	3.80—4.40 m	3.31 s	3.55, 3.91 3.93	2.00—2.50	1.92(×2)	1.41	1.00	—	0.83, 1.12 (H-17, -24)	2.10(×4) br. s

a) Compounds **4** and **11** were measured at 100 MHz, and **4a—4f**, **11b** and **12** were measured at 60 MHz.
b) These compounds were measured in C_6D_6.
c) The signals changed into a singlet on addition of D_2O or irradiation of hydroxy signals (decoupling experiment).
d) The signals were unclear due to overlapping with methoxyl signals.
e) Hydroxy signals of all compounds were confirmed by addition of D_2O.
f) These signals were confirmed by decoupling experiments.
g) d=doublet, m=multiplet, s=singlet.







4 : R_1=H, R_2=Me

11 : R_1=Me, R_2=OH

4a : R_1=OH, R_2=H
4b : R_1=R_2=O
— R_3 = $-CH_2-C(H)(Me)-C(Me)(OH)-COOMe$

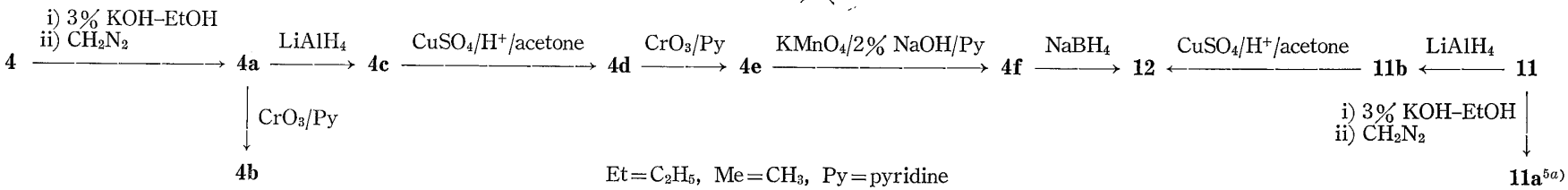
4c : R_1=OH, R_2=H, R_3 = $-CH_2-C(H)(Me)-C(Me)(OH)-CH_2OH$

4d : R_1=OH, R_2=H
4e : R_1=R_2=O
— R_3 = $-CH_2-C(H)(Me)-C(Me)(O_2C(Me)_2)-CH_2$

4f : R_1=R_2=O
12 : R_1=OH, R_2=H
— R_3 = $-CH_2-C(H)(Me)-C(Me)(O_2C(Me)_2)-CH_2$

11a : R_1=OH, R_2=H, R_3 = $-CH_2-C(H)(Me)-C(Me)(OH)-COOMe$

11b : R_1=OH, R_2=H, R_3 = $-CH_2-C(H)(Me)-C(Me)(OH)-CH_2OH$



Et=C_2H_5, Me=CH_3, Py=pyridine

Chart 3

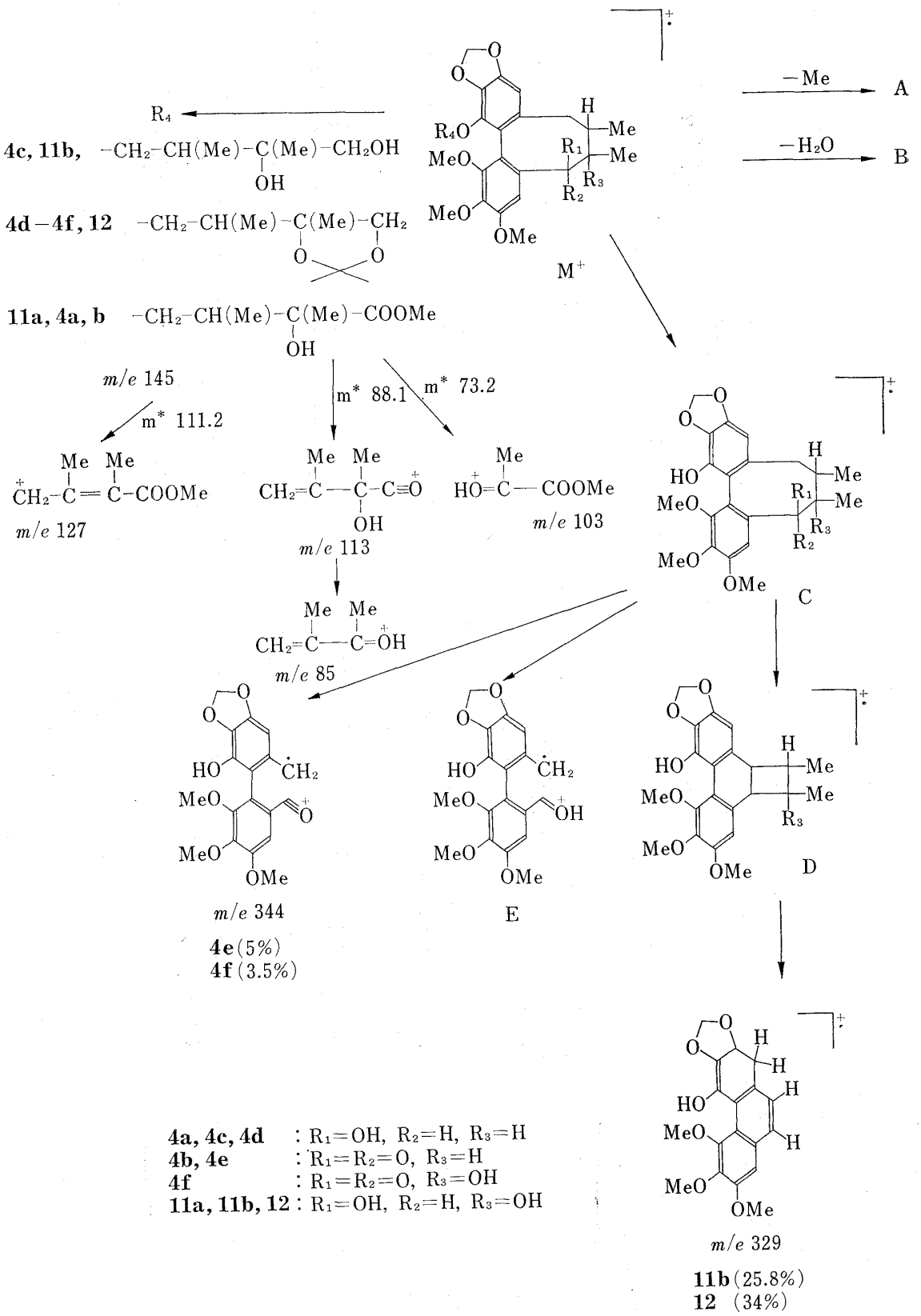
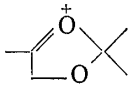


Chart 4. Mass Fragments for **4a**—**4f**, **11a**, **11b** and **12**

Table III. Mass Fragments for **4a**—**4f**, **11a**, **11b** and **12**

Compd.	Fragment *m/e* (%)						
	M^+	A	B	C	D	E	R_4
4a	546.244 (37)	—	528.236 (1.5)	400 (2)	384.155 (10)	346.109 (8)	145.086(100), 127.076(18), 113.061(18), 103.041(22), 85.069(31)
4b	544 (12)	—	—	400 (16)	—	—	145(100), 127(16), 113(18), 103(18), 85(31)
4c	518 (45)	—	500 (3)	—	384 (97)	346 (83)	—
4d	558 (100)	543 (6.5)	540 (5)	400 (12)	384 (58)	346 (49)	 115(40)
4e	556 (27)	541 (1.6)	—	400 (100)	—	—	115(23)
4f	572 (73)	557 (6.5)	—	416 (32)	—	—	115(43)
11b	534 (32)	—	516 (21)	418 (7.3)	400 (32)	346 (33)	$HO{=}C(Me){-}CH_2OH$ 75(15)
12	574 (39)	559 (5)	556 (20)	418 (4)	400 (30)	346 (27)	115(43)
11a							145.082(97), 127.076(18.7), 113.056(18.7), 103.038(18.7), 85.067(31.8)

irradiation of each doublet methyl signal did not affect the aromatic protons. The above NOE results suggest that gomisin E corresponds to one of the structures **4** or a C-8 epimer.

The structure of **4**, including the configurations at C-8, —20 and —21, was confirmed by correlation with **11**, the absolute structure of which has been elucidated by X-ray analysis,[5a] as mentioned below. Treatment of **4a** with $LiAlH_4$ in dry ether afforded **4c**, $C_{28}H_{38}O_9$ (M^+, 518) (yield 73%), $[\alpha]_D^{25}$ —5.1° (in $CHCl_3$) as an amorphous powder, which was converted to the acetonide (**4d**) (84%), $C_{31}H_{42}O_9$, $[\alpha]_D^{22} \simeq 0°$ (in $CHCl_3$) on treatment with $CuSO_4$ and 0.25% H_2SO_4 in dry acetone. On oxidation with CrO_3 in pyridine, **4d** afforded the carbonyl compound (**4e**), $C_{31}H_{40}O_9$, $[\alpha]_D^{22}$ +41.8° (in $CHCl_3$). The IR (1660 cm^{-1}) and PMR (chemical shift of an aromatic proton: δ 7.57) spectra of **4e** indicate that **4e** possesses a boat conformation.

Next, oxidation of **4e** with $KMnO_4$ in a mixture of 2% NaOH and pyridine afforded the ketoalcohol (**4f**) (19%), $C_{31}H_{40}O_{10}$, $[\alpha]_D^{24}$ —41.5° (in $CHCl_3$). The IR spectrum of **4f** showed an unconjugated carbonyl band (1700 cm^{-1}) and the PMR spectrum showed a higher field shift of one of the aromatic proton signals, compared with that of **4e** (**4e**, δ 7.57→**4f**, δ 6.70). These findings indicate that **4f** possesses a twist-boat-chair conformation. In addition, the appearance of a singlet methyl at δ 1.38 suggests the presence of the partial structure [CH_3–Ç–OH] in **4f** (*vide* IR 3450 cm^{-1}) and a 7-*S* configuration, as mentioned in the case of the transformation of **1** to **6**.

Finally, reduction of **4f** with $NaBH_4$ in MeOH afforded the diol (**12**) (76%), $C_{31}H_{42}O_{10}$, $[\alpha]_D^{24}$ —24.4° (in $CHCl_3$), which was identical with compound **12** on comparison of IR, PMR and mass spectra, and $[\alpha]_D$. An authentic sample of **12**, amorphous powder, $[\alpha]_D^{23}$ —23.8° (in $CHCl_3$), was prepared from gomisin D by the procedure shown in Chart 3 and described in the experimental section.

Thus, the absolute structure of gomisin E was elucidated as **4**. The PMR and mass spectral data of the reaction products are shown in Table II, and in Chart 4 and Table III, respectively.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus (a hot stage type) and are uncorrected. The UV spectra were recorded with a Hitachi 624 digital spectrophotometer and the IR spectra with a Hitachi EPI-G2 unit. The PMR spectra were recorded with Varian T-60 and JEOL PS-100 spectrometers with tetramethylsilane as an internal standard. The mass spectra (MS) were measured with Hitachi double-focusing and JEOL JMS-01SG-2 mass spectrometers. The specific rotations were measured with a JASCO DIP-SL unit and the CD spectra with a JASCO J-20 spectrophotometer. Silica gel (Kieselgel 60, Merck) was used for column chromatography. Thin layer chromatography (TLC) was carried out on Merck plates precoated with Kieselgel $60F_{254}$. Preparative layer chromatography (PLC) was carried out on plates (20×20 cm; 0.75 mm thick) coated with Kieselgel GF_{254} (Merck).

Isolation of 1, 2, 3, 4 and 5——In the previous papers,[5b] it was reported that the pet. ether and methanolic extracts of the fruits of *Schizandra chinensis* Baill. (4.67 kg) afforded twelve fractions (fr. 1—12) on silica gel column chromatography, developing with *n*-hexane, acetone–benzene and acetone solvent systems. Fr. 4 (12.5 g) was crystallized from ether–*n*-hexane to give **1** as colorless prisms (4.758 g). A portion (635 mg) of fr. 5 was subjected to PLC using benzene–ether (5: 1) and the zones with *Rf* 0.71 and 0.54 were extracted with $CHCl_3$–MeOH (4: 1). The extract of the zone with *Rf* 0.71 (169 mg) was further puried by PLC [*n*-hexane–AcOEt (4: 1), *Rf* 0.44] to give **1** (94 mg; the calculated yield from fr. 5 (64.89 g) is 9.62 g; total calcd. yield 14.39 g, 0.31%).

The extract of the zone with *Rf* 0.54 was further purified by PLC [*n*-hexane–AcOEt (4: 1), *Rf* 0.32] to give **5** (25 mg, calcd. yield 2.56 g, 0.055%). Fr. 7, 8 and 9 were combined and rechromatographed on silica gel using a benzene–ether solvent system to give nine fractions [fr. (7—9)-a—i] as described in the previous paper.[5c] Fr(7—9)-e (4.64 g) was subjected to silica gel column chromatography (SiO_2, 100 g, 3×26.5 cm) using a benzene–ether solvent system. The fractions eluted with benzene–ether (9: 1) were concentrated to give a residue (2.88 g), which was rechromatographed on silica gel (60 g, 2.5×25.5 cm) using an *n*-hexane–acetone solvent system. The fractions eluted with *n*-hexane–acetone (23: 2) were concentrated to give a residue (950 mg). Repeated PLC [i) *n*-hexane–acetone (7: 3), *Rf* 0.63; ii) ether–*n*-hexane (2: 1), *Rf* 0.30] of this residue gave **2** (47 mg). Fr. (7—9)-f and -g (total 28.5 g), after separating gomisin A,[5b] were subjected to silica gel column chromatography (SiO_2, 425 g, 5.5×39 cm) using an *n*-hexane–AcOEt solvent system, and the fractions eluted with *n*-hexane–AcOEt (4: 1) were concentrated to give a residue (1.138 g). Repeated PLC [i) *n*-hexane–AcOEt (1: 1), *Rf* 0.55; ii) ether–*n*-hexane (2: 1), *Rf* 0.30] of this residue gave a mixture of **2** and **3**. This mixture was purified by PLC [$CHCl_3$–EtOH (19: 1)] to give **2** (61 mg, total yield 108 mg, 0.0023%) and **3** (48 mg, 0.001%). Fr. (7—9)-d (5.11 g) was subjected to silica gel column chromatography (SiO_2, 120 g, 3×35 cm) using an *n*-hexane–acetone solvent system. The fractions eluted with *n*-hexane–acetone (9: 1) were concentrated to dryness. The residue (948 mg) was purified by PLC [ether–*n*-hexane (2: 1), *Rf* 0.47] to give **4** (313 mg, 0.0067%).

Gomisin N (1)——Pure gomisin N was obtained as colorless prisms (from ether–*n*-hexane), mp 105—107°, $[\alpha]_D^{23}$ −84.7° (c=2.171, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 218 (4.73), 251 (sh. 4.14), 275—280 (sh. 3.61). IR ν_{max}^{KBr} cm^{-1}: 1615, 1595, 1570 (aromatic). *Anal.* Calcd. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.92; H, 7.07.

Gomisin O (2)——Pure gomisin O was obtained as colorless prisms (from ether–*n*-hexane), mp 145—146.5°. $[\alpha]_D^{25}$ −33.9° (c=0.707, $CHCl_3$). CD (c=0.0298, MeOH). $[\theta]^{23}$ (nm): +40000 (227), −54000 (251), −10000 sh. (290). UV λ_{max}^{EtOH} nm (log ε): 214 (4.60), 253 (sh. 3.93), 282 (3.54). IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1615, 1595 (aromatic). MS, *m/e* (%): 416 (M^+, 100), 398 (M^+-H_2O, 15), 360 (M^+-CH_3–CH=CH–CH_3, 54). *Anal.* Calcd. for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.34; H, 6.70. High resolution MS, Calcd. for $C_{23}H_{28}O_7$(M^+): 416.184. Found: 416.187.

Epigomisin O (3)——Pure epigomisin O was obtained as a white amorphous powder, $[\alpha]_D^{23}$ −66.7° (c=1.50, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 218 (4.53), 253 (sh. 3.95), 275—279 (sh. 3.39), 288—289 (sh. 3.33). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1615, 1593 (aromatic). MS, *m/e* (%): 416 (M^+, 88), 398 (M^+-H_2O, 3.4), 224 (100). High resolution MS, Calcd. for $C_{23}H_{28}O_7$(M^+): 416.184. Found: 416.182.

Gomisin E (4)——Pure gomisin E was obtained as a white amorphous powder, $[\alpha]_D^{24}$ +28.1° (c=0.278, $CHCl_3$). CD (c=0.0165, MeOH), $[\theta]^{23}$ (nm): +47000 (228), −31000 (243), −19000 (288). UV λ_{max}^{EtOH} nm (log ε): 213 (4.77), 290 (3.62). IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 1727 (ester), 1618, 1595 (aromatic). MS, *m/e* (%): 514 (M^+, 82), 470 (43), 386 (57), 384 (40), 85 (57), 43 (100). High resolution MS, *m/e* (%), Calcd. for $C_{28}H_{34}O_9$(M^+): 514.221. Found: 514.222.

(+)-Deoxyschizandrin (5)——Pure (+)-deoxyschizandrin was obtained as colorless prisms (from ether–*n*-hexane), mp 114—116°, $[\alpha]_D^{23}$ +92.1° (c=2.73, $CHCl_3$) [Ref. 4*b*, mp 116—117°, $[\alpha]_D^{28}$ +107° (in $CHCl_3$)]. UV λ_{max}^{EtOH} nm (log ε): 218 (4.68), 248 (4.19), 284 (sh, 3.43). IR ν_{max}^{KBr} cm^{-1}: 1591, 1577 (aromatic). MS, *m/e* (%): 416 (M^+, 100), 181 (4). CD (c=0.0198, MeOH), $[\theta]^{23}$ (nm): −120000 (211), +79000 sh. (235), +100000 (247), +10000 sh. (274).[5b] *Anal.* Calcd. for $C_{24}H_{32}O_6$: C, 69.21; H, 7.71. Found: C, 68.71; H, 7.50. The IR and PMR spectra are the same as those of **8**.

Treatment of 1 with $Pb(OAc)_4$ in Dry Benzene, giving 1a——A solution of **1** (160 mg) and $Pb(OAc)_4$ (320 mg) in dry benzene (8 ml) was stirred at 52—54° for 30 hr then diluted with ether (80 ml). The total

mixture was washed 3 times with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (7: 3), *Rf* 0.75] to give **1a** (26 mg, 17%) and unchanged **1** (46 mg). **1a** was obtained as colorless prisms (from ether–*n*-hexane), mp 184.5—188°, $[\alpha]_D^{23}$ −129° (*c*=0.520, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3525, 3275 (OH), 1594 (aromatic). $FeCl_3$: dark green. *Anal.* Calcd. for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C, 67.82; H, 7.27.

Methylation of 1a——$(CH_3)_2SO_4$ (0.1 ml) and K_2CO_3 (100 mg) were added to a solution of **1a** (20 mg) in dry acetone. The reaction mixture was stirred at 46° for 4 hr, then diluted with H_2O (10 ml) and extracted with ether (15 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (2: 1), *Rf* 0.73] to give the dimethyl ether of **1a** (**8**) as colorless prisms (ether–*n*-hexane), mp 116—117°, $[\alpha]_D^{22}$ −100° (*c*=0.340, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1591, 1576 (aromatic). *Anal.* Calcd. for $C_{24}H_{32}O_6$: C, 69.21; H, 7.74. Found: C, 69.33; H, 7.82. The compound obtained here was identified as **8** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$).

Catalytic Reduction of 2 in AcOH (with H_2)——Compound **2** (30 mg) in AcOH was shaken with H_2 in the presence of PtO_2 (30 mg) as a catalyst at 22° for 5 hr. The catalyst was filtered off and the filtrate was concentrated to dryness under reduced pressure. The residue was purified by PLC [benzene–ether (4: 1)] to give **1** (9.6 mg, *Rf* 0.72) and unchanged **2** (5 mg, *Rf* 0.27). **1**: colorless prisms (from ether–*n*-hexane), mp 103—105°, $[\alpha]_D^{22}$ −72.9° (*c*=0.480, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.01; H, 6.84. The compound obtained here was identified as gomisin N (**1**) by direct comparison with an authentic sample (IR, mixed mp and $[\alpha]_D$).

Catalytic Reduction of 2 in AcOH-d_4 with D_2——Compound **2** (47 mg) in CD_3COOD (99%) was treated with D_2 as described for the hydrogenolysis of **2** with H_2 to give **1b** (8 mg) and unchanged **2** (26 mg). **1b** was obtained as a white amorphous powder, MS, *m/e* (%): $C_{23}H_{27}DO_6$, 401 (M^+, 100). PMR spectral data are given in Table I.

Treatment of 1 with $Pb(OAc)_4$ in AcOH followed by Hydrolysis with 0.5 M KaOH, giving 2——$Pb(OAc)_4$ (600 mg) was added to a solution of **1** (460 mg) in AcOH (10 ml) and the reaction mixture was stirred at 12—16° for 24 hr. $Pb(OAc)_4$ (400 mg) was added to the reaction mixture and the total mixture was further stirred at 12—16° for 72 hr, then diluted with ether. The ethereal solution was washed with 1 N NaOH, then with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (4: 1), *Rf* 0.58] to give unchanged **1** (25 mg) and a product (acetylgomisin O, 15.7 mg); PMR (δ in $CDCl_3$): 0.80 (3H, d, *J*=7 Hz, C<u>H</u>$_3$–CH), 0.90 (3H, d, *J*=6 Hz, C<u>H</u>$_3$–CH), 1.75 (2H, m, –CH), 1.82 (3H, s, OAc), 2.18 (2H, m, Ar–C<u>H</u>$_2$–), 3.52, 3.87, 3.89, 3.90 (each 3H, s, 4×OCH_3), 5.53 (1H, d, *J*=9 Hz, $C_{(6)}$–H), 6.13 (2H, s, OCH_2O), 6.40 (1H, s, $C_{(11)}$–H), 6.75 (1H, s, $C_{(4)}$–H). The product obtained here was dissolved in a mixture of dioxane (1 ml) and 0.5 M KOH–MeOH (1.5 ml). The reaction mixture was stirred at 23° for 3 hr and diluted with ether (30 ml). The total mixture was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [ether–*n*-hexane (2: 1), *Rf* 0.30] to give colorless prisms (from ether–*n*-hexane) (11.2 mg), mp 145—146.5°, $[\alpha]_D^{23}$ −32.7° (*c*=0.373, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.39; H, 6.79. The compound obtained here was identified as **2** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$).

Oxidation of 2 with CrO_3 in Pyridine——CrO_3 (50 mg) was added to a solution of **2** (15 mg) in dry pyridine (0.5 ml). The reaction mixture was stirred at 20° for 2.5 hr, then diluted with H_2O (10 ml) and extracted with ether (15 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [ether–*n*-hexane (2: 1), *Rf* 0.58] to give **2a** (9.8 mg) as colorless plates (from ether–*n*-hexane), mp 151.5—152°, $[\alpha]_D^{25}$ +38° (*c*=0.317, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 209 (4.52), 229 (4.51), 250 (sh. 4.20), 272 (sh. 4.02), 319 (3.62). IR ν_{max}^{KBr} cm^{-1}: 1658, 1587 (aromatic). *Anal.* Calcd. for $C_{23}H_{26}O_7$: C, 66.68; H, 6.32. Found: C, 66.59; H, 6.35.

Reduction of 2a with $NaBH_4$——$NaBH_4$ (160 mg) was added to a solution of **2a** (83 mg) in MeOH (6 ml). The reaction mixture was stirred at room temperature for 20 hr, then diluted with H_2O (30 ml) and extracted with ether (20 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [$CHCl_3$–EtOH (19: 1)] to give **2** (*Rf* 0.79, 39 mg, 47%) and **3** (*Rf* 0.69, 39 mg, 47%). **2**: colorless prisms (from ether–*n*-hexane), mp 146—147°, $[\alpha]_D^{22}$ −31.4° (*c*=1.73, $CHCl_3$). *Anal.* Calcd for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.56; H, 6.84. This compound was identified as **2** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$). **3**: a white amorphous powder, $[\alpha]_D^{22}$ −67.1° (*c*=1.52, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.46; H, 6.91. This compound was identified as **3** by direct comparison with an authentic sample (IR, TLC, PMR and $[\alpha]_D$).

Oxidation of 3 with CrO_3 in Pyridine——CrO_3 (20 mg) was added to a solution of **3** (20 mg) in dry pyridine (0.5 ml). The reaction mixture was stirred at 23° for 2 hr, diluted with H_2O and extracted with ether (25 ml×2). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (7: 3)] to give **2a** (*Rf* 0.73, 12 mg) and a minor product (*Rf* 0.68, 1 mg). **2a**: colorless needles (from ether–*n*-hexane), mp 151—152.5°, $[\alpha]_D^{24}$ +45.4° (*c*=0.507, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. Found: C, 66.89; H, 6.37. **2a** was identical

with an authentic sample prepared from **2** on direct comparison (IR, mixed mp, PMR and $[\alpha]_D$). The minor product has not yet been studied in detail, since insufficient material is available.

Oxidation of (±)-Deoxyschizandrin with $KMnO_4$——A solution of (±)-deoxyschizandrin (*dl* form of **8**) (127 mg) in a mixture of pyridine (2 ml) and 2% NaOH (4 ml) containing $KMnO_4$ was kept at 60° for 5 hr, then cooled and diluted with H_2O (10 ml). The reaction mixture was treated with $NaHSO_3$ until no color could be detected in the solution, then acidified with 10% H_2SO_4 and extracted with ether (30 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (3:2), *Rf* 0.38] to give **9** (53 mg, 38%) as colorless prisms (from ether–*n*-hexane), mp 166—167.5°, $[\alpha]_D^{25} \simeq 0°$ ($c=0.779$, $CHCl_3$). UV λ_{max}^{EtOH} (log ε): 216 (4.62), 243 (sh. 3.42), 290—292 (sh. 3.32). IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1693 (C=O). MS, *m/e* (%): 446 (M^+, 100), 403 (13), 374 ($M^+-CH_3CH=CH(CH_3)$–OH, 60). *Anal.* Calcd. for $C_{24}H_{30}O_8$: C, 64.56; H, 6.77. Found: C, 64.64; H, 6.80.

Oxidation of 1 with $KMnO_4$——A solution of **1** (1 g) and $KMnO_4$ (2 g) in a mixture of pyridine (21 ml) and 2% NaOH (42 ml) was stirred at 46—48° for 1.5 hr, then diluted with H_2O (40 ml). The solution was treated with $NaHSO_3$ until no color could be detected, then extracted with ether. The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (7:3)] to give unchanged **1** (*Rf* 0.90, 225 mg, 22.5%), **2a** (*Rf* 0.73, 70 mg, 6.8%) and **6a** (*Rf* 0.33, 60 mg, 5.6%). **2a**: colorless needles (from ether–*n*-hexane), mp 151—152°, $[\alpha]_D^{21}$ +46.5° ($c=0.753$, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. Found: 66.52; H, 6.36. This compound was identified as **2a** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$). **6a**: colorless needles (from ether–*n*-hexane), mp 129—130.5°, $[\alpha]_D^{23}$ −86.3° ($c=0.973$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 1690 (C=O). This compound was identified as **6a** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$).[5b]

Oxidation of 2a with $KMnO_4$——A solution of **2a** (60 mg) and $KMnO_4$ (240 mg) in a mixture of dioxane (3 ml) and 2% NaOH (4 ml) was stirred at 50° for 3 hr, then diluted with H_2O (20 ml). The solution was treated with $NaHSO_3$ until no color could be detected, then extracted with ether (15 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (7:3)] to give unchanged **2a** (*Rf* 0.73, 20 mg, 33%) and **6a** (*Rf* 0.33, 9 mg, 14%). **6a**: colorless needles (from ether–*n*-hexane), mp 130—131°, $[\alpha]_D^{22}$ −101° ($c=0.648$, $CHCl_3$). *Anal.* Calcd. for $C_{23}H_{26}O_8$: C, 64.17; H, 6.09. Found: C, 64.04; H, 6.22. This compound was identified as **6a** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$).

Reduction of 6a with $NaBH_4$——$NaBH_4$ (46 mg) was added to a solution of **6a** (23 mg) in MeOH. The reaction mixture was stirred at room temperature for 10 hr and then treated as described for the reduction of **2a**. The crude product was purified by PLC [benzene–ether (1:1), *Rf* 0.35] to give **6** (19 mg, 82%) as colorless needles (from ether–*n*-hexane), mp 209—211°, $[\alpha]_D^{22}$ −83.8° ($c=0.895$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3500, 3425 (OH), 1615, 1590 (aromatic). *Anal.* Calcd. for $C_{23}H_{28}O_8$: C, 63.88; H, 6.58. Found: C, 64.15; H, 6.59. This compound was identified as **6** by direct comparison with an authentic sample (IR, mixed mp, PMR and $[\alpha]_D$).[5b]

Preparation of 4a——A solution of **4** (116 mg) in 3% KOH–EtOH (5 ml) was stirred at 75° for 4 hr, then cooled, diluted with H_2O (10 ml) and extracted with ether (15 ml). No product was detected in the ethereal extract. The aqueous solution was acidified with 10% H_2SO_4 and extracted with ether (15 ml×3). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4, concentrated and treated with ethereal diazomethane. The reaction mixture was allowed to stand for 2 hr, then concentrated to dryness. The residue was purified by PLC [benzene–ether (3:2), *Rf* 0.28] to give **4a** as a white amorphous powder (79 mg), $[\alpha]_D^{25} \simeq 0°$ ($c=0.564$, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 214 (4.66), 255 (sh. 3.96), 283 (3.55). High resolution MS, Calcd. for $C_{29}H_{38}O_{10}(M^+)$: 546.247. Found: 546.244.

Oxidation of 4a with CrO_3 in Pyridine——CrO_3 (50 mg) was added to a solution of **4a** (36 mg) in pyridine (0.5 ml). The reaction mixture was stirred at room temperature for 2 hr, then diluted with H_2O (10 ml) and extracted with ether (15 ml×3). The combined ethereal extract was washed with 1 N HCl (5 ml) then with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (3:2), *Rf* 0.48] to give **4b** as a white amorphous powder (27 mg), $[\alpha]_D^{25}$ +55.7° ($c=0.287$, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 209 (4.49), 228 (4.49), 252 (sh. 4.16), 273 (sh. 3.98), 311—322 (sh. 3.60). IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1735 (ester), 1660 (C=O). MS, *m/e* (%), 544 ($C_{29}H_{26}O_{10}$, M^+, 12).

Reduction of 4a with $LiAlH_4$——$LiAlH_4$ (200 mg) was added to a solution of **4a** (388 mg) in dry ether (40 ml). The reaction mixture was stirred at room temperature for 2 hr, then wet ether was added and the mixture was filtered. The filtrate was concentrated to dryness and the residue was purified by PLC [*n*-hexane–acetone (3:2), *Rf* 0.25] to give **4c** as a white amorphous powder (270 mg, 73%), $[\alpha]_D^{25}$ −5.1° ($c=0.780$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3410 (OH), 1615, 1592 (aromatic). MS, *m/e* (%): 518 ($C_{28}H_{38}O_9$, M^+, 45).

Preparation of 4d——Anhydrous $CuSO_4$ (800 mg) and 0.25% H_2SO_4 (in acetone) (0.05 ml) were added to a solution of **4c** (230 mg) in dry acetone (20 ml). The reaction mixture was stirred at 25° for 1 hr, then diluted with H_2O (50 ml) and extracted with ether (40 ml×2). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (2:1), *Rf* 0.48] to give **4d** as a white amorphous powder (209 mg, 84%), $[\alpha]_D^{22} \simeq 0°$ ($c=1.45$, $CHCl_3$).

IR ν_{max}^{KBr} cm^{-1}: 3475 (OH), 1614, 1589 (aromatic). High resolution MS, Calcd. for $C_{31}H_{42}O_9(M^+)$: 558.283. Found: 558.284.

Oxidation of 4d with CrO_3 in Pyridine——CrO_3 (100 mg) was added to a solution of **4d** (209 mg) in dry pyridine (4 ml). The reaction mixture was stirred at 25° for 3 hr, diluted with H_2O and extracted with ether (35 ml×2). The combined ethereal extract was washed with 1 N HCl, then with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (2: 1), *Rf* 0.81] to give **4e** as a white amorphous powder (150 mg, 72%), $[\alpha]_D^{22}$ +41.8° (c=1.52, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 210 (4.55), 229 (4.52), 250 (sh. 4.17), 272 (sh. 3.99), 317—321 (sh. 3.58). IR ν_{max}^{KBr} cm^{-1}: 1660 (C=O), 1615, 1582 (aromatic). High resolution MS, Calcd. for $C_{31}H_{40}O_9(M^+)$: 556.267. Found: 556.269.

Oxidation of 4e with $KMnO_4$——A solution of **4e** (150 mg) and $KMnO_4$ (450 mg) in a mixture of pyridine (6 ml) and 2% NaOH (9 ml) was stirred at 50° for 3 hr, then diluted with H_2O (40 ml). The solution was treated with $NaHSO_3$ until no color could be detected in the solution, then extracted with ether (30 ml×2). The combined ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (3: 2)] to give unchanged **4e** (*Rf* 0.62, 35 mg) and **4f** (*Rf* 0.41, 29 mg, 19%). **4f**: A white amorphous powder, $[\alpha]_D^{24}$ −41.5° (c=1.06, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 216 (4.56), 250 (sh. 4.15), 294—295 (sh. 3.44). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1700 (C=O), 1615, 1590 (aromatic). High resolution MS, Calcd. for $C_{31}H_{40}O_{10}$: 572.262. Found: 572.261.

Reduction of 4f with $NaBH_4$——$NaBH_4$ (29 mg) was added to a solution of **4f** (29 mg) in MeOH (2 ml). The reaction mixture was allowed to stand at 23° for 20 hr, then diluted with ether. The total mixture was washed with H_2O (10 ml×3), dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [benzene–ether (1: 1), *Rf* 0.38] to give **12** (22 mg, 76%) as a white amorphous powder, $[\alpha]_D^{24}$ −24.4° (c=0.900, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3525, 3450 (OH), 1615, 1593 (aromatic). High resolution MS, Calcd. for $C_{31}H_{42}O_{10}(M^+)$: 574.278. Found: 574.278. This compound was identified as **12** by direct comparison with an authentic sample prepared from **11** (IR, MS, PMR and $[\alpha]_D$).

Preparation of 12 from 11——i) Preparation of **11b**:[12] $LiAlH_4$ (100 mg) was added to a solution of **11** (100 mg) in dry ether (6 ml). The reaction mixture was stirred at 24° for 4 hr, then wet ether was added and the mixture was allowed to stand for 10 min and filtered. The filtrate was concentrated to dryness and the residue was purified by PLC [*n*-hexane–acetone (4: 1), *Rf* 0.15] to give **11b** (42 mg, 42%) as a white amorphous powder, $[\alpha]_D^{23}$ −45.1° (c=1.73, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3430 (OH), 1618, 1597 (aromatic). High resolution MS, Calcd. for $C_{28}H_{38}O_{10}(M^+)$: 534.246. Found: 534.244.

ii) Preparation of **12** from **11b**: Anhydrous $CuSO_4$ (200 mg) and 0.25% H_2SO_4 (in acetone) (0.02 ml) were added to a solution of **11b** (42 mg) in dry acetone (4 ml). The reaction mixture was stirred at 22° for 1.5 hr, then diluted with H_2O (20 ml) and extracted with ether (15 ml×3). The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to dryness. The residue was purified by PLC [*n*-hexane–acetone (3: 2), *Rf* 0.38] to give **12** as a white amorphous powder, $[\alpha]_D^{23}$ −23.8° (c=1.43, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 214 (4.74), 256 (sh. 4.04), 278—288 (sh. 3.51). *Anal.* Calcd. for $C_{31}H_{42}O_{10}$: C, 64.79: H, 7.37. Found: C, 64.80; H, 7.31.

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12) Reduction of **11a**[5a] with $LiAlH_4$ in dry ether gave a complex mixture of products, and **11b** was obtained in very low yield.