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The Constituents of *Schizandra chinensis* Baill. The Structures of Three New Lignans, Angeloylgomisin H, Tigloylgomisin H and Benzoylgomisin H, and the Absolute Structure of Schizandrin

Three new lignans named angeloylgomisin H(I), tigloylgomisin H(II) and benzoylgomisin H(III), which possess dibenzocyclooctadiene skeleton, have been isolated from the fruits of *Schizandra chinensis* Baill (Schizandraceae). Their structures including the absolute configurations were established by chemical and spectral evidence.

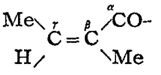
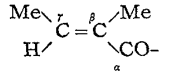
The absolute structure of schizandrin was also established by spectral studies (nuclear Overhauser effects and circular dichroism spectrum).

Keywords——*Schizandra chinensis*; Schizandraceae; lignan; angeloylgomisin H; tigloylgomisin H; benzoylgomisin H; schizandrin; NOE; CD spectrum

In the preceding papers of this series, it was reported that the petroleum ether extract of the fruits of *Schizandra chinensis* Baill. (Schizandraceae) contains six new lignans possessing dibenzocyclooctadiene skeleton.[1] This paper concerns with isolation and characterization of three additional lignans named angeloylgomisin H(I, yield, 0.031%), tigloylgomisin H(II, 0.014%) and benzoylgomisin H(III, 0.003%), and the absolute structure of schizandrin(V).[2] The physical and spectral data of three new compounds are shown below and in Table I.

Table I. PMR Spectral Data of I—V, VIII and IX (in $CDCl_3$, δ Value)

Compound	C_4-H,s C_{11}-H,s	$C_{6\alpha}$-H (J=Hz)	$C_{6\beta}$-H (J=Hz)	$C_{9\alpha}$-H (J=Hz)	$C_{9\beta}$-H (J=Hz)	$C\underline{H}_3\text{-}\overset{|}{\underset{|}{C}}\text{-}\underline{H}$ (d,J=Hz)	m	$C\underline{H}_3\text{-}\overset{|}{\underset{|}{C}}\text{-}O\underline{H}$ s	s	OCH_3 s
I[a]	6.67 6.56	2.75, d (13.5)	2.30, d (13.5)	2.37, d,d (13.5/7)	2.75, d,d (13.5/2)	0.83(7)	1.83	1.23	1.83	3.53, 3.83(×2) 3.88, 3.90
II[a]	6.68 6.57	2.75, d (13.5)	2.30, d (13.5)	2.35, d,d (13.5/7)	2.75, d,d (13.5/2)	0.84(7)	1.93	1.23	1.93	3.50, 3.83(×2) 3.89, 3.90
III[a]	6.77 6.53	2.80, d (13.5)	2.33, d (13.5)	2.40, d,d (13.5/7)	2.78, d,d (13.5/2)	0.88(7)	1.87	1.27	1.87	3.53, 3.67, 3.80 3.87, 3.95
IV	6.63 6.35	2.70, d (13.5)	2.33, d (13.5)	2.31, d,d (13.5/7)	2.68, d,d (13.5/2)	0.83(7)	1.83	1.25	1.83	3.63, 3.90(×2) 3.92(×2)
V	6.62 6.56	2.70, d (14)	2.32, d (14)	2.33, d,d (14/7)	2.68, d,d (14/2)	0.82(7)	1.80	1.25	1.86	3.59(×2) 3.90(×4)
VIII	6.62, s[b] 6.72, s 6.75, s	2.1—2.9(4H, m)				0.87(7)	1.80	1.25	1.82	3.49, 3.86 3.91(×3)
IX	6.59, s (C_4-H)	2.78, d (15)	2.45, d (15)	2.97, d,d (15/9)	2.12, d,d (15/2)	0.87(7)	1.87	1.27	1.68	3.78, 3.87 3.92, 4.05(×2)

a) Other signals: I, 
$$\overset{\text{Me}}{\underset{\text{H}}{}}\!\diagdown\overset{\gamma}{C}=\overset{\beta}{C}\overset{\alpha\ \text{CO-}}{\underset{\text{Me}}{}}$$
1.73 (6H, m, β and γ- Me), 5.88 (1H, m, γ -H); II, 
$$\overset{\text{Me}}{\underset{\text{H}}{}}\!\diagdown\overset{\gamma}{C}=\overset{\beta}{C}\overset{\text{Me}}{\underset{\text{CO-}\ \alpha}{}}$$
1.70 (6H, m, β and γ -Me), 6.78 (1H, m, γ -H); III, 7.38 (3H, m), 7.98 (2H, d,d) (C_6H_5CO-).

b) in D_6-acetone: 6.70, 6.77 and 6.85 (each singlet).

c) Confirmed by decoupling experiments.

d) d=doublet, m=multiplet, s=singlet.

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1) *a*) H. Taguchi and Y. Ikeya, *Chem. Pharm. Bull.* (Tokyo), **23**, 3296 (1975); *b*) H. Taguchi and Y. Ikeya, *ibid.*, **25**, 364 (1977); *c*) Y. Ikeya, H. Taguchi and Y. Iitaka, *Tetrahedron Lett.*, 1976, 1357.

2) N.K. Kochetkov, A. Khorlin, O.S. Chizov and V.I. Sheichenko, *Tetrahedron Lett.*, 1961, 730; N.K. Kochetkov, A. Khorlin, O.S. Chizov, *ibid.*, 1962, 361.

Angeloylgomisin H(I), $C_{28}H_{36}O_8$(M^+, *m/e*, Calcd.: 500.240; Observed: 500.237), amorphous, $[\alpha]_D^{22}$ +19.4°(c=1.60, $CHCl_3$), Ultraviolet (UV) spectrum: λ_{max}^{EtOH} nm (log ε): 215 (4.72), 248 (sh, 4.18), 286 (sh, 3.14). Infrared (IR) spectrum: ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1735 (ester), 1645 ($\rangle C=C\langle$). Mass spectrum (MS), *m/e* (%): 500 (M^+, 51), 482 (M^+-H_2O, 5), 83[$CH_3CH=C(CH_3)$-CO, 100], 55[$CH_3CH=C(CH_3)$, 54].

Tigloylgomisin H(II), $C_{28}H_{36}O_8$(M^+, *m/e*, Calcd.: 500.240; Observed: 500.237), amorphous, $[\alpha]_D^{23}$ +67.7°(c=1.30, $CHCl_3$), UV λ_{max}^{EtOH} nm(log ε): 215 (4.75), 248 (sh, 4.21), 285 (sh, 3.47). IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1725 (ester), 1645 ($\rangle C=C\langle$), MS, *m/e* (%): 500 (M^+, 57), 482 (M^+-H_2O, 4), 418 (19), 83 [$CH_3CH=C(CH_3)CO$, 100], 55[$CH_3CH=C(CH_3)$, 85].

Benzoylgomisin H(III), $C_{30}H_{34}O_8$(M^+, *m/e*, Calcd.: 522.225, Observed: 522.224), amorphous, $[\alpha]_D^{24}$ +96.8°(c=1.25, $CHCl_3$), UV λ_{max}^{EtOH} nm (log ε): 217 (4.66), 250 (sh, 4.20), 282 (sh, 3.56). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1735 (ester), 1595, 705 (aromatic), MS, *m/e* (%): 522 (M^+, 47), 504 (M^+-H_2O, 5), 105 (C_6H_5CO, 100), 77 (C_6H_5, 25).

These spectral data suggested that three compounds are lignans possessing dibenzocyclooctadiene skeleton and have five methoxyl groups attached to the aromatic rings, a tertiary methyl group attached to the carbon atom having the hydroxyl group and a secondary methyl group.[1] Their proton magnetic resonance (PMR), infrared (IR) and mass spectra indicate that I, II and III possess angeloyl, tigloyl and benzoyl groups respectively. These compounds (I—III), on hydrolysis with 3% ethanolic potassium hydroxide, afforded the same phenolic

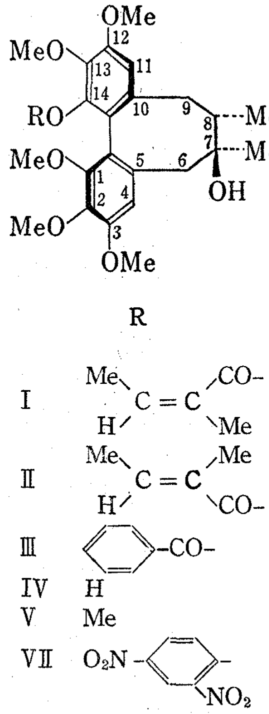
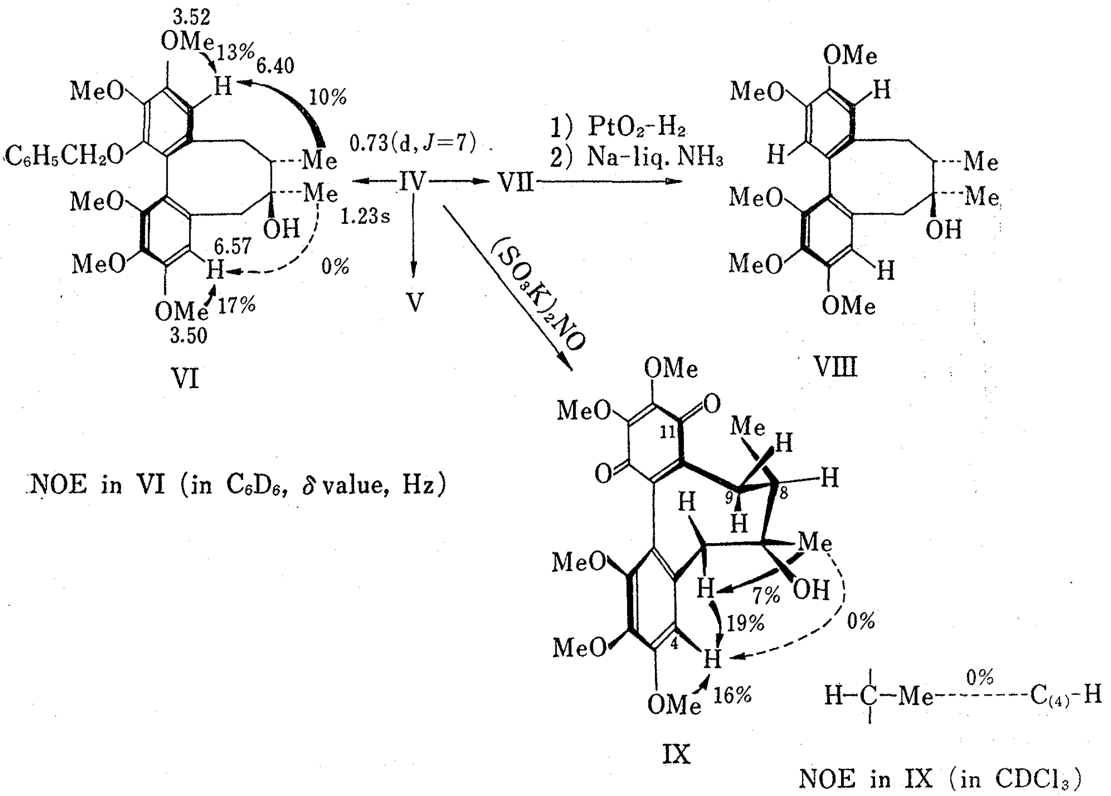


Chart 1



NOE in VI (in C_6D_6, δ value, Hz)

NOE in IX (in $CDCl_3$)

Chart 2

compound (IV, named gomisin H), $C_{23}H_{30}O_7$(M^+, m/e, 418), colourless plates (ether-*n*-hexane), mp 145—146.5°, $[\alpha]_D^{24}$ +44.5° (c=0.97, $CHCl_3$), UV λ_{max}^{EtOH} nm (log ε): 219 (4.81), 247—249 (sh, 4.32), 276 (3.72), 285 (sh, 3.65). IR ν_{max}^{KBr} cm^{-1}: 3530, 3350 (OH), 1630, 1600 (aromatic) and corresponding acids.[3] Methylation of IV with dimethyl sulfate and potassium carbonate in acetone gave monomethyl ether (V), colourless needles, mp 129—131°, $[\alpha]_D^{21}$ +86.9°(c=0.35, $CHCl_3$), which was identified with schizandrin obtained from the same source by the direct comparison (mixed mp, IR and TLC), indicating that IV corresponds to norschizandrin.

The following experiments were thus carried out to confirm the position of the phenolic hydroxyl group in IV. At first, the intramolecular nuclear Overhauser effects (NOE) in benzyl ether of IV(VI) were measured. As shown in chart 2, the both aromatic protons were effected by irradiation of two methoxyl signals, indicating that two methoxyl groups are attached to C_3 and C_{12} positions.

Next, treatment of IV with 2,4-dinitrofluorobenzene in benzene-dimethylformamide mixture in the presence of sodium hydride as a catalyst afforded 2,4-dinitrophenyl ether (VII) (yield, 71.5%), $C_{29}H_{32}N_2O_{11}$(M^+, m/e, 584), amorphous, $[\alpha]_D^{26}$ +49.9° (c=1.02, $CHCl_3$), UV λ_{max}^{EtOH} nm (log ε): 212 (4.70), 250 (4.31), 284 (4.06), 300 (sh, 3.98). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1602 (aromatic), 1532, 1343 (NO_2). Catalytic hydrogenation of VII over platinum oxide in tetrahydrofuran-methanol mixture followed by cleavage with sodium in liquid ammonia (−60——65°) afforded compound VIII (yield, 52.5%), $C_{23}H_{30}O_6$(M^+, m/e, 402), colourless plates, mp 121—122.5°, $[\alpha]_D^{24}$ +86.0° (c=0.43, $CHCl_3$), UV λ_{max}^{EtOH} nm (log ε): 213 (4.63), 254 (4.14), 282 (3.76), 293 (sh, 3.67). IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1600 (aromatic).[4] The PMR spectrum of VIII shows three singlet signals assignable to the aromatic protons in the region δ 6.60—7.00, indicating that the hydroxyl group in IV is located at the *para*-position (C_1 or C_{14}) to the aromatic proton. On the other hand, oxidation of IV with Fremy salts [$(SO_3K)_2$-NO][5] afforded *p*-quinoid compound (IX) (yield, 97%), $C_{23}H_{28}O_8$(M^+, m/e, 432), reddish needles, mp 65—66°, $[\alpha]_D^{23}$ +85.0° (c=0.64, $CHCl_3$), UV λ_{max}^{EtOH} nm (log ε): 216 (4.59), 241 (sh, 4.16), 274 (4.01), 365 (3.44). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1655, 1645 ($>$C=O), indicating that the hydroxyl group in IV is located at C_{14} position. The structure of IX was confirmed by the measurements of NOE(in $CDCl_3$) as shown in chart 2.[1] Irradiation of a methoxyl signal (δ 3.78) and a methylene proton signal (δ 2.45) caused 16% and 19% increase in the integrated intensity of the aromatic proton signal, respectively. Irradiation of the tertiary methyl signal caused 7% increase of the integrated intensity of a methylene proton signal at δ 2.45 (d, J=15), while the aromatic proton showed no effect by irradiation of the both methyl signals. Thus, the relative structure of IX including conformation is expressed by the formula IX. These facts agree with J value between C_8-proton and C_9-methylene protons, which show extreme down field (α-proton) and high field (β-proton) shifts by influence of the carbonyl group, in the PMR spectrum ($J_{8,9\alpha}$=9 Hz, $\phi_{8,9\alpha}$≒30°; $J_{8,9\beta}$=2 Hz, $\phi_{8,9\beta}$≒90°).

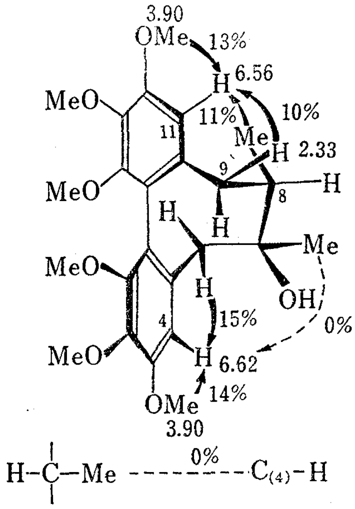


Fig. 1. NOE in V (in $CDCl_3$, δ value)

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3) Tiglic acid and benzoic acid were identified by mixed mp, gas chromatography (GLC) and IR spectra. Angelic acid was identified by GLC.

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Next, the absolute structure of schizandrin (V)[2,6] was determined by the measurements of NOE(in $CDCl_3$) and circular dichroism (CD) spectrum. As shown in Fig. 1, the results of NOE indicated that schizandrin has the same conformational structure as IX. On the other hand, the CD spectrum of V(in MeOH) showed two positive Cotton effects at 250 ([θ] +95000) and 235 nm ([θ] +75000), and a negative at 214 nm ([θ] −100000), indicating that V possesses *R*-biphenyl configuration.[1b,c]

On the basis of the above observations, the absolute structures of angeloylgomisin H, tigloylgomisin H, benzoylgomisin H and schizandrin are expressed by the formulae I, II, III and V, respectively.

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[6] Quite recently, Y.P. Chen, *et al.* suggested that schizandrin has *trans*-dimethyl groups at C_7 and C_8(Yuh-Pan Chen, Rolan Liu, Hon-Yen Hsu, S. Yamamura, Y. Shizuri and Y. Hirata, *Bull. Chem. Soc. Japan*, **50**, 1824 (1977)). However, we believe that our assumption should be correct considering the results of spectral analyses as described above together with the results of C. Yan-Yang, *et al.* supporting that schizandrin has *cis*-dimethyl groups (Chen Yan-Yang, Shu Zeng-Bao and Li Lianf-Nianf, *Scientia Scinica* (Peking), **19**, 276 (1976)).

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Structure of Gilvanol, a New Triterpene isolated from *Quercus gilva* BLUME

A new triterpene named Gilvanol (Ia), $C_{30}H_{50}O_4$, mp 212—215°, which have been elucidated to be hopan-3β-ol-17(21)-ozonide by chemical evidence and X-ray analysis, was isolated from *Quercus gilva* BLUME.

Keywords——triterpene; hopane; gilvanol; ozonide; X-ray analysis; *Quercus gilva* BLUME.

Previously, we reported about nine triterpenes isolated from *Quercus gilva* BLUME.[1,2] One of them named as D-20 was not yet elucidated structurally. Now, we wish to report the structure of D-20 named as Gilvanol.

Gilvanol (Ia), $C_{30}H_{50}O_4$, mp 212—215°, possessed one hydroxy function (3410 cm^{-1}) by its infrared spectrum (IR), six tertiary methyls, two secondary methyls by its proton magnetic resonance (PMR) using $Eu(dpm)_3$ as a shift reagent, and showed the signal at δ 3.30 assignable to 3α-H. By mass spectrum of (Ia), the fragment ion peaks were observed at *m/e* 474 (M^+), 456 (M^+-H_2O), 207, 189 and 135 which had been characterized as the hopane skeleton.[3] On the other hand, the nature of three other oxygen atoms, was presumed to be an ozonide functional group, since no proton neighbouring to those oxygen atoms was observed by PMR and characteristic signals appeared at δ 112.4 ppm and 111.8 ppm on ^{13}C-nuclear magnetic resonance (^{13}C–NMR) spectrum.

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[1] Y. Kamano, Y. Tachi, T. Otake, J. Sawada, and I. Tanaka *Yakugaku Zasshi*, **96**, 1202 (1976).
[2] Y. Tachi, Y. Kamano, J. Sawada, I. Tanaka, and H. Itokawa, *Yakugaku ZAsshi*, **96**, 1213 (1976).
[3] G.R. Waller, "Biochemical Applications of Mass Spectrometry," Wiley-Interscience, 1972.