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The Constituents of *Schizandra chinensis* Baill. I. The Structures of Gomisin A, B and C

Three new schizandrin type lignans, gomisin A, B and C, were isolated from the fruits of *Schizandra chinensis* Baill. (Schizandraceae) and their structures were elucidated to be I, II and III, respectively.

The fruits of *Schizandra chinensis* Baill. (Schizandraceae) are used as an antitussive and tonic under the name of Kita-gomisi. Schizandrin, deoxyschizandrin, schizandrol and γ-schizandrin have been isolated from the unhydrolyzed fraction of the seed oil of this plant by Kochetkov, *et al.*[1]

In this communication, we wish to report the structures of three new schizandrin type lignans, named gomisin A (I, yield 0.14%), B (II, 0.022%) and C (III, 0.004%), isolated from the fruits of the same plant. Their physical data are shown below.

Gomisin A (I) $C_{23}H_{28}O_7$ (M^+ 416.1868, Calcd. 416.1839), mp 88—89°, $[\alpha]_D$ +67.9°, ultraviolet (UV) λ_{max}^{EtOH} nm (log ε): 218 (4.88), 253 (4.30), 281 (sh 3.70) and 290 (sh 3.57), infrared (IR) ν_{max}^{KBr} cm^{-1}: 3500 (OH), nuclear magnetic resonance (NMR), δ in $CDCl_3$: 0.80 (3H, d, J=7 Hz, $>CH{-}C\underline{H}_3$), 1.25 (3H, s, $HO{-}\overset{|}{\underset{|}{C}}{-}C\underline{H}_3$), 1.80 (1H, m, $-\overset{|}{\underset{|}{C}}H$), 1.85 (1H, s, OH), 2.44 (center) (2H, $\underline{AB}$X octet, J_{AB}=14 Hz, J_{AX}=2 Hz, J_{BX}=6 Hz, $-\overset{|}{C}H{-}C\underline{H}_2{-}$), 2.50 (center) (2H, AB q, J_{AB}=13.5 Hz, $-CH_2-$), 3.50 (3H, s), 3.80 (3H, s), 3.90 (6H, s) (4×OCH_3), 5.96 (2H, s, $-OCH_2O-$), 6.49 (1H, s, arom. H) and 6.62 (1H, s, arom. H).

Gomisin B (II), $C_{28}H_{34}O_9$ (M^+ 514), mp 95—97°, $[\alpha]_D$ −26.6°, UV λ_{max}^{EtOH} nm (log ε): 218 (4.98), 257 (sh 4.24) and 292 (sh 3.65), IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1715 (C=O), NMR, δ in $CDCl_3$: 1.13 (3H, d, J=7 Hz, $-\overset{|}{C}H{-}C\underline{H}_3$), 1.33 (3H, s, $HO{-}\overset{|}{\underset{|}{C}}{-}C\underline{H}_3$), 1.40 (3H, q, J=1.5 Hz, $CH_3CH{=}C(C\underline{H}_3){-}$), 1.60 (1H, s, OH), 1.86 (3H, d.q, J=7/1.5 Hz, $C\underline{H}_3CH{=}C(CH_3){-}$), 1.90 (1H, m, $-\overset{|}{\underset{|}{C}}H$), 2.0—2.45 (2H, m, $-CH_2-$), 3.57, 3.75, 3.85, 3.93 (each 3H, s, 4×OCH_3), 5.70 (1H, s, $-\overset{|}{C}\underline{H}{-}OCOR$), 5.90 (2H, s, $-OCH_2O-$), 6.00 (1H, q,q, J=7/1.5 Hz, $={\overset{|}{C}}H$), 6.48 (1H, s, arom. H) and 6.83 (1H, s, arom. H).

Gomisin C (III), $C_{30}H_{32}O_9$ (M^+ 536), mp 115—116°, $[\alpha]_D$ −186° UV λ_{max}^{EtOH} nm (log ε): 222 (4.91), 255 (sh 4.11) and 292 (sh 3.48), IR ν_{max}^{KBr} cm^{-1}: 3340 (OH), 1720 (C=O), 715 (arom. ring), NMR, δ in $CDCl_3$: 1.16 (3H, d, J=7 Hz, $-\overset{|}{C}H{-}C\underline{H}_3$), 1.36 (3H, s, $HO{-}\overset{|}{\underset{|}{C}}{-}C\underline{H}_3$), 1.65 (1H, s, OH), 1.65 (1H, m, $-\overset{|}{\underset{|}{C}}H$), 2.0—2.50 (2H, m, $-CH_2-$), 3.32 (3H, s), 3.60 (3H, s), 3.93 (6H, s)

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[1] *a)* N.K. Kochetkov, A. Khorlin, and O.S. Chizhov, *Zh. Obshch. Khim.*, **31**, 3454 (1961); *b)* N.K. Kochetkov, A. Khorlin, O.S. Chizhov, and V.I. Sheichenko, *Tetrahedron Letters*, **1961**, 730; *c)* N.K. Kochetkov, A. Khorlin, and O.S. Chizhov, *Tetrahedron Letters*, **1962**, 361; *d)* N.K. Kochetkov, A. Khorlin, and O.S. Chizhov, *Izv. Akad. Nauk S.S.S.R., Ser. Khim.*, **1964**, 1036.

($4\times OCH_3$), 5.75 (2H, q, $-OCH_2O-$), 5.90 (1H, s, $-\dot{C}\underline{H}-OCOR$), 6.60 (1H, s, arom. H), 6.89 (1H, s, arom. H) and 7.3—7.7 (5H, m, arom. H; δ 7.30 5H, br s in D_6-acetone).

From these spectral data, three compounds can be regarded as schizandrin type lignans,[1,2] having a methylenedioxy group and four methoxyl groups attached to the aromatic ring and also have a tertiary OH group.

Treatment of I with bromine in carbon tetrachloride afforded 4,11-dibromide (Ia), $C_{23}H_{26}O_7Br_2$ (M^+ 576).[3] The NMR spectrum of Ia shows the lack of two aromatic protons observed in that of I. Furthermore, two benzylic methylene groups observed at δ 2.25—2.70 in I shifted to δ 2.60—3.20 in Ia. This shift to lower field is observed in the case of schizandrin dibromide. These facts suggest the aromatic protons and the methylene groups are present in sterically close position in I. On the other hand, the presence of a partial structure of $-CH_2-\dot{C}H-CH_3$ was confirmed by the double resonance experiment of I. On irradiation at δ 1.80, a doublet at δ 0.80 was found to change into singlet and a octet at δ 2.44 to change into quartet.

Finally, the structure including the position of each functional group and conformation of I were elucidated by measurements of intramolecular nuclear Overhauser effects (NOE).[2] The results is shown in Chart 2. The mass spectrum of gomisin A (I) shows good agreement with the structure I (Chart 3).

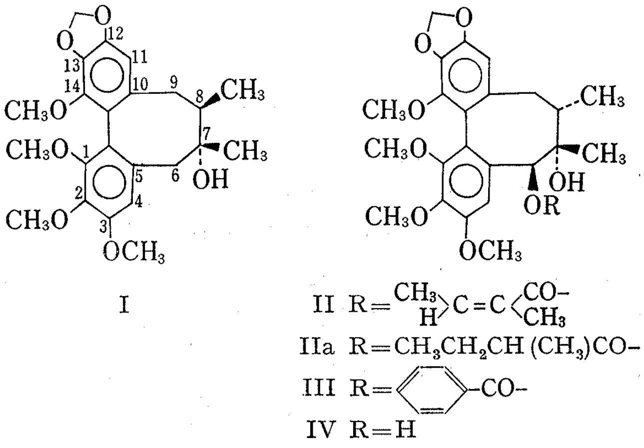

Chart 1

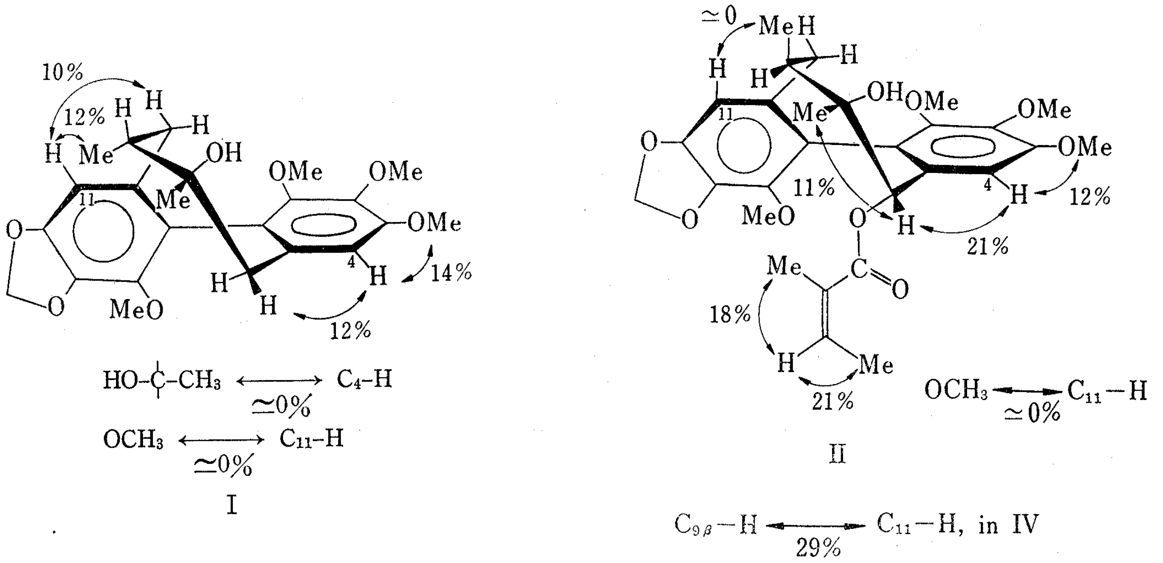

Chart 2. NOE observed in I II and IV

II and III show the presence of an ester linkage in their IR spectra. Their NMR and mass spectra indicate that II has an angeloyl group (*m/e* 431 ($M^+-CH_3CH{=}C(CH_3)CO$), 414 ($M^+-CH_3CH{=}C(CH_3)COOH$), 83 ($CH_3CH{=}C(CH_3)CO$)) and III has benzoyl group (*m/e* 414

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[2] Y.-P.-Chen, R. Liu, H.-Y. Hsu, S. Yamamura, Y. Shizuri, and Y. Hirata, *Tetrahedron Letters*, **1973**, 4257.

[3] R.M. Keefer, J.H. Blake, III, and L.J. Andrews, *J. Am. Chem. Soc.*, **76**, 3062 (1954).

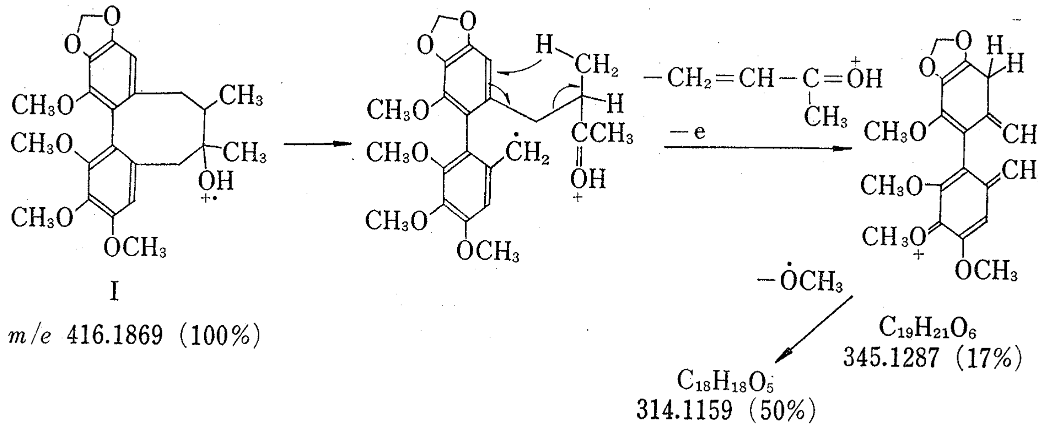

Chart 3

($M^+-C_6H_5COOH$), 105 (C_6H_5CO), 77 (C_6H_5)). Catalytic hydrogenation of II with platinum oxide in acetic acid afforded a dihydroderivative (IIa), $C_{28}H_{36}O_9$ (m/e 516 (M^+), 414 (M^+-102)).

Hydrolysis of II and III with 3% ethanolic potassium hydroxide afforded a crystalline substance (IV), $C_{23}H_{28}O_8$ (M^+ 432), mp 209—210°, $[\alpha]_D$ −91.8°, NMR, δ in $CDCl_3$: 1.11 (3H, d, $-\overset{|}{C}H-C\underline{H}_3$), 1.40 (3H, s, $HO-\overset{|}{C}-C\underline{H}_3$), 1.56 (2H, s, 2×OH), 1.85 (1H, m, $-\overset{|}{C}H$), 2.0—2.45 (2H, $\underline{AB}$X octet $J_{AB}=12$ Hz, $J_{AX}=8.5$ Hz, $J_{BX}=1$ Hz, $-C\underline{H}_2\underset{|}{C}H-$), 3.61 (3H, s), 3.90 (3H, s), 3.93 (6H, s) (4×OCH_3), 4.59 (1H, s, $-\overset{|}{C}\underline{H}OH$), 5.95 (2H, s, $-OCH_2O-$), 6.51 (1H, s, arom. H) and 6.62 (1H, s, arom. H), and corresponding acids.

IV was oxidized with potassium periodate, showing the presence of a 1,2-glycol. The presence of a partial structure $-CH_2-\underset{|}{C}H-CH_3$ in IV was confirmed by the double resonance experiment.

Finally, the structure of II and III were also established by measurements of NOE in II and IV.2) In the case of II, irradiation at δ 3.93 and 5.70 caused in 12% and 21% increases in integrated intensity of the aromatic proton signal at δ 6.83 (C_4–H), respectively, whereas any enhancement of the signal intensity of the aromatic proton at δ 6.48 (C_{11}–H) was not detected by irradiation of each methoxyl group. On the other hand, irradiation at δ 1.33 corresponding to tertiary methyl group caused 11% increase in integrated intensity of C_6 proton at δ 5.70, whereas any enhancement of the signal intensity of the aromatic proton at δ 6.83 was not detected. These facts indicate that the methylenedioxy group must be located at the position adjacent to C_{11}–H and a tertiary methyl group be placed in such a space as shown in Chart 2. Furthermore, the interaction between methylene protons and C_{11} proton was detected in NOE measurements in IV. From the above data, gomisin B and C can be formulated as II and III, respectively. These facts agree with J value between C_8 proton and C_9 methylene protons in the NMR spectrum of IV ($J_{8,9\alpha}=8.5$ Hz, $\phi_{8,9\alpha}\fallingdotseq 150°$; $J_{8,9\beta}=1$ Hz, $\phi_{8,9\beta}\fallingdotseq 90°$).

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