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THE CONSTITUENTS OF SCHIZANDRA CHINENSIS BAILL. THE STRUCTURE OF A NEW LIGNAN, GOMISIN D

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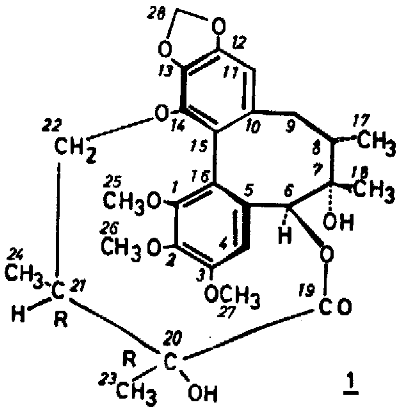
In the previous paper, we reported the structures of three new schizandrin type lignans, gomisin A,B and C, isolated from the fruits of *Schizandra chinensis* Baill.(Schizandraceae).[1)] The present paper concerns the structure of a new schizandrin type lignan, gomisin D(yield, 0.016 %), isolated from the fruits of the same plant.

Gomisin D(1): colourless prisms(from n-hexane-ether), mp 194°, $(\alpha)_D^{25}$-58.8° (c=0.265, $CHCl_3$), $C_{28}H_{34}O_{10}$(m/e, M^+, Calcd.,530.2156; Observed, 530.2144), UV λ_{max}^{EtOH}nm(log ε): 216(4.57), 256(sh, 3.94), 294(3.68), IR ν_{max}^{KBr} cm^{-1}: 3505, 3450 (OH), 1720(ester), PMR(δ in $CDCl_3$): 1.02(3H, d, J=7 Hz, H-17), 1.10(3H, d, J=7 Hz, H-24), 1.20(3H, s, H-18), 1.26(3H, s, H-23), 1.72(1H, m, H-8), 1.73(1H, s, OH), 2.0-2.6(2H, ABX octet, J_{AB}=14 Hz, J_{AX}=8 Hz, J_{BX}=1 Hz, H-9), 3.10(1H,s, OH), 3.56, 3.86, 3.92(each 3H, s, 3 x OCH_3), 3.4-4.0(2H, m, H-22), 5.71(1H, s, H-6), 5.90, 5.99(each 1H, d, J=1 Hz, $-OCH_2O-$), 6.43(1H, s, H-11) and 6.80(1H, s, H-4).

These spectral data suggested that gomisin D is a schizandrin type lignan, having a methylenedioxy group($-OCH_2O-$), a methyleneoxy group($\equiv-CH_2O-$) and three methoxyl groups attached to the aromatic ring and also has a ester linkage and two tertiary hydroxy groups.[1-3)]

Hydrolysis of 1 with 3 % ethanolic potassium hydroxide followed by methylation with diazomethane afforded a crystalline substance(2), $C_{29}H_{38}O_{11}$(m/e,

M^+-H_2O, Calcd. 544.2854; Observed, 544.2809), mp 127-128°, $(\alpha)_D^{22}$ +39.1°(c=0.307, $CHCl_3$), UV λ_{max}^{EtOH}nm(log ε): 217(4.68), 255(sh, 3.97), 278-280(sh, 3.53). IR ν_{max}^{KBr} cm^{-1}: 3430, 1730. 2 was oxidized with sodium periodide to show the presence of a 1,2-diol. The presence of a partial structural system (A) in 2 was confirmed by the double resonance experiment of PMR(in C_6D_6) and the mass spectral analysis(chart 2).



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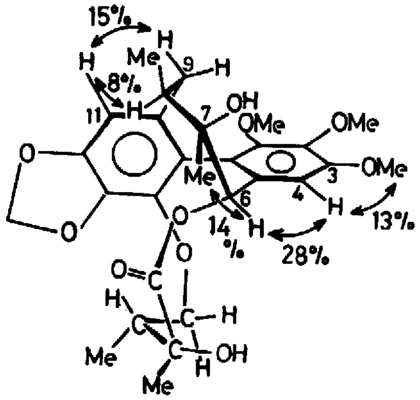
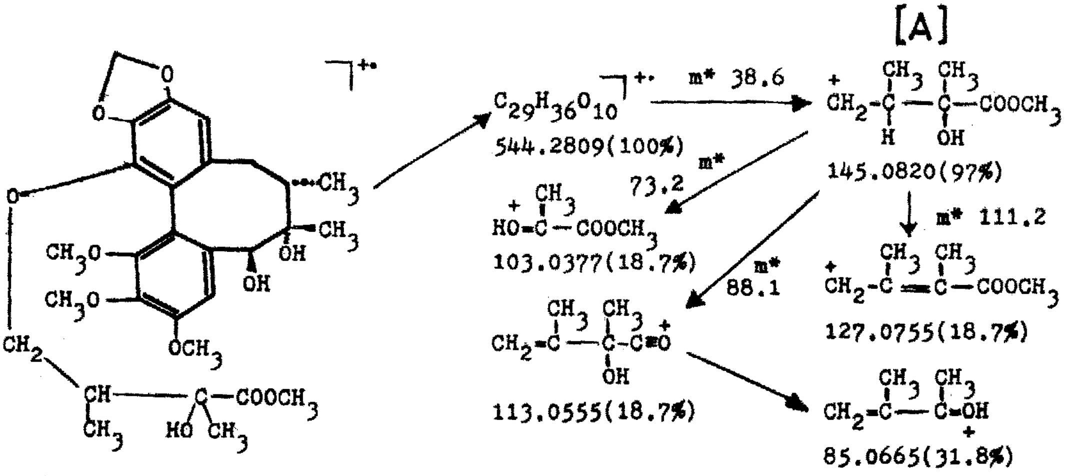


perspective view of 1

Chart 1



2, $C_{29}H_{38}O_{11}$, 562(0%)

Chart 2

These data indicate that the carboxyl terminal of (A) is linked as ester in 1. The conformational structure of 1 was thus elucidated by the measurements of NOE in 1(in $CDCl_3$).[1,2) As shown in chart 1, irradiation of a methoxyl signal(δ 3.86) and a proton(δ 5.71) caused 13 % and 28 % increase in the integrated intensity of the lower aromatic proton, respectively. On the other hand, irradiation of a tertiary methyl signal(δ 1.20) caused 14 % increase in the integrated intensity of a proton(δ 5.71), while no enhancement of the signal intensity of the both aromatic protons was observed. A higher aromatic proton (δ 6.43) was effected by irradiation of a higher field proton of methylene signal(δ 2.00, d,d, J=14/1 Hz) and a methine proton(δ 1.72, H-8), while no effect was shown by irradiation of each methoxyl signal and the doublet methyl signals. From the above results and the Dreiding model examination, the structure of gomisin D was suggested to be 1 excluding the configurations at C_{20} and C_{21}.

Finally, the structure including the absolute configuration of gomisin D was elucidated by X-ray crystallographic analysis of the 4,11-dibromo-derivative (3). Treatment of 1 with bromine in carbon tetrachloride saturated with water afforded 3 as colourless plates(from ether-petroleum ether). The crystals are orthorhombic, space group P $2_12_12_1$ with a=14.756(7), b=20.172(10), c=9.854(5) Å, U=2933.13 $Å^3$, D_m=1.54 g.cm^{-3}, D_x=1.513 g.cm^{-3}, Z=4. The density was measured by the flotation method using an aqueous potassium iodide solution.
The intensity data were measured by a Philips four-circle diffractometer using graphite monochromated Cu Kα radiation. The space group was determined by the Weissenberg photographs. Of the total 3119 independent reflections within $156° \leq 2\theta$, 3036 reflections were used for the structure determination.
Intensities of 1074 Friedel pairs were also measured on the diffractometer.
The structure was solved by the heavy atom method using three dimentional Patterson map and Fourier synthesis. Refinement was carried out by the block-diagonal least-squares method using HBLS programme[4). Final R value was 0.089 without hydrogen atoms. The absolute structure was established by using the anomalous dispersion effect of the bromine atom for Cu Kα radiation.

Of the 127 Friedel pairs for which $\left| |F_{obs}(hkl)| - |F_{obs}(h\bar{k}l)| \right|$ were estimated to be greater than $3\sigma(F_{obs}(hkl))$, 119 pairs showed the consistent F_{obs} and F_{cal} relations of the Friedel pairs and the absolute configuration was determined as shown in chart 3. The molecular structure of 3 drawn by the ORTEP programme is shown in chart 3. The bond lengths and the angles not including hydrogen atoms lie in the normal ranges. The configuration of each carbon atom is shown as 6S, 7S, 8S, 20R and 21R, respectively, and the biphenyl part is shown to be S-configuration$^{5)}$ with dihedral angle of 73°. Furthermore, the conformation of cyclooctadiene ring is shown to be twist-boat-chair form.

These data are in good agreement with the above physical data of gomisin D. Therefore, the structure of gomisin D is represented by 1.

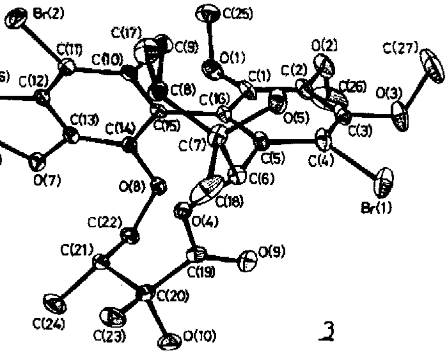


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Chart 3

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