SANGGENON A, A NEW FLAVANONE DERIVATIVE FROM CHINESE CRUDE DRUG "SĀNG-BÁI-PÍ" (MORUS ROOT BARK)

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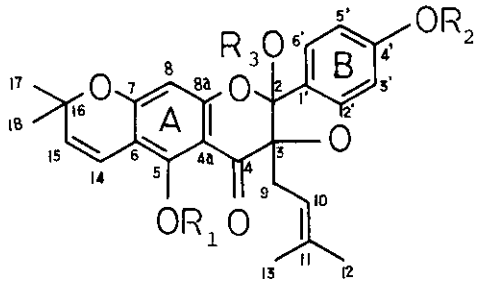
From the benzene extract of the Chinese crude drug "Sāng-Bái-Pí" (Japanese name Sōhakuhi), the root bark of Morus sp. (Moraceae), a novel isoprene substituted flavanone, sanggenon A, was isolated whose structure was shown to be I on the basis of spectral data.

"Sāng-Bái-Pí" (Japanese name "Sōhakuhi) is a crude drug in Chinese medicine having antipyretic, antitussive, expectorant, diuretic and laxative effects, and is prepared from the root bark of certain species of Morus (Moraceae).[1] In recent years a series of isoprene substituted flavonoids have been isolated from the root bark of Morus species.[3-5] We report here the isolation and structure determination of a new isoprene substituted flavanone derivative sanggenone A (I).

The crude drug "Sāng-Bái-Pí" (8.0 Kg) imported from the People's Republic of China was cut, and extracted with n-hexane and then with benzene. The benzene extract was fractionated sequentially by column and preparative thin-layer chromatography over silica gel, resulting in the isolation of a new flavanone derivative sanggenon A in 0.006% yield.

Sanggenon A (I), $C_{25}H_{24}O_7$,[6] amorphous powder,[7] uv[λ_{max}^{MeOH} nm(log ε): 208(4.41), 228(4.19), 235(infl. 4.16), 270(sh 4.46), 279(4.50), 315(4.08), 377(3.37); $\lambda_{max}^{MeOH+AlCl_3}$: 209(4.51), 225(sh 4.29), 278.5(4.49), 332(4.10), 380(infl. 3.44); $\lambda_{max}^{MeOH+NaOMe}$: 248(4.28), 287(4.41), 395(3.67)], $[\alpha]_D^{20}$ = + 14°(c=0.3 in chloroform), which gave an olive-green color with methanolic ferric chloride and was both positive to magnesium-hydrochloric acid test (red) and the sodium-borohydride test[8]

(reddish violet). The treatment of I with acetic anhydride in pyridine at room temperature for three min yielded a monoacetate (Ia),[7] $C_{27}H_{26}O_8$(M^+ 478), amorphous powder, uv[λ_{max}^{MeOH} nm(log ε): 279(4.54), 318(4.31), 374(3.32); $\lambda_{max}^{MeOH+AlCl_3}$: 279(4.53), 337(4.30), 442(4.31)], ir(ν_{max}^{Nujol} cm^{-1}: 3400, 1765), pmr($CDCl_3$, δ 2.27), which gave an olive-green color with methanolic ferric chloride test. The treatment of Ia with the same reagent at room temperature for one hr yielded a diacetate (Ib), $C_{29}H_{28}O_9$(M^+ 520), amorphous powder,[7] uv[λ_{max}^{MeOH} nm(log ε): 256(4.73), 290(infl. 3.94), 346(3.54); $\lambda_{max}^{MeOH+AlCl_3}$: 256(4.73), 290(infl. 3.94), 346(3.60)], ir(ν_{max}^{Nujol} cm^{-1}: 3400, 1775), pmr($CDCl_3$, δ 2.31, 2.47), which was negative to ferric chloride test. The treatment of Ib with the same reagent at room temperature for 30 hr yielded a triacetate (Ic),[7] $C_{31}H_{30}O_{10}$(M^+ 562), amorphous powder, uv [λ_{max}^{MeOH} nm(log ε): 258(4.27), 270(sh 4.24), 300(infl. 3.87), 343(3.51)], ir(ν_{max}^{Nujol} cm^{-1}: 1775, no absorption in the hydroxyl region), pmr($CDCl_3$, δ 2.21, 2.33, 2.14). These results suggest that I has two phenolic hydroxyl groups and one tertiary hydroxyl group. Considering the molecular formula, the seventh oxygen atom seems to be in the ether linkage. Sanggenon A (I) showed the singlet at δ 12.06 in the pmr spectrum (acetone-d_6, C_5-OH). These findings suggest that I is a flavanone derivative having a hydroxyl group at C_5. The pmr spectrum of I lacks the characteristic signals of C_2- and C_3-H of flavanone skeleton and indicates the presence of 2,2-dimethylchromene ring [δ 1.42, 1.43(each 3H,s,C_{16}-CH_3), 5.63 (1H,d,J=10 Hz,C_{15}-H),[9] 6.56(1H,d,J=10 Hz,C_{14}-H)[9]] and γ,γ-dimethylallyl group [δ 1.52, 1.63(each 3H,s,C_{11}-CH_3), 2.72(1H,dd,J=7 and 14 Hz,C_9-H),[9] 3.13(1H,dd, J=10 and 14 Hz,C_9-H),[9] 5.05-5.32(1H,m,C_{10}-H)]. The methylene group protons (δ 2.72 and 3.13) appear to be nonequivalent and suggest that the γ,γ-dimethyl-allyl group was located at the asymmetric center.[10] The arrangements of substituents in the A ring and the B ring are assumed by the pmr spectrum as follows: a singlet signal at δ 5.77(C_8-H) indicate that the A ring was unsubstituted at the 6- or 8-position[11] and a doublet signal at δ 6.41(1H,J=2 Hz,C_3,-H), double doublet at δ 6.63(1H,J=2 and 8 Hz,C_5,-H), and doublet at δ 7.35(1H,J=8 Hz, C_6,-H) indicate that the B ring of I was substituted in the 2'- and the 4'-position.[4] The presence of 2,2-dimethylchromene ring system in the A ring was supported by the mass spectrum fragmentation as follows: the mass spectrum[12] of I gave the fragments at m/e 421($C_{24}H_{21}O_7$, M^+ - CH_3),[4a] 219($C_{12}H_{11}O_4$, II, base peak),[13] 203($C_{11}H_7O_4$, III, from the ion at 421 by a retro Diels-Alder reaction).[4a] The later two fragments are from the ring A. The linear structure (I) for



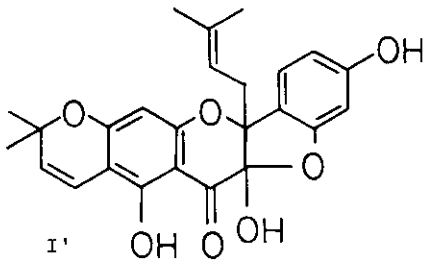
I :R_1=R_2=R_3=H

Ia :R_1=R_3=H, R_2=$COCH_3$

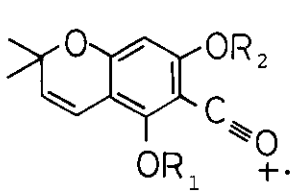
Ib :R_1=R_2=$COCH_3$, R_3=H

Ic :R_1=R_2=R_3=$COCH_3$

Id :R_1=R_2=$COCH_3$, R_3=$COCH_2CH_3$



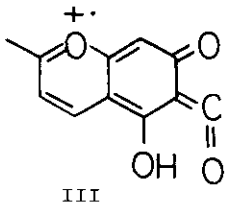
I'



II :R_1=R_2=H

IV :R_1=R_2=$COCH_3$

V :R_1=$COCH_3$, R_2=$COCH_2CH_3$



III

Chart 1

sanggenon A is supported by the changes in the chemical shift of chromene olefinic protons in its monoacetate (Ia) compared with the diacetate (Ib) (Table 1). These changes are of the same sign and in the same order of magnitude as those observed by many investigators for similar compounds, in which the hydroxyl group is peri to C_{14}-H.[14] From these results, sanggenon A is represented as I or I'.

Table 1. Chemical Shift (ppm) for C_{14}-H and C_{15}-H in Ia and Ib[a]

compound	C_{14}	C_{15}
Ia	6.63	5.50
Ib	6.39	5.63
Δ	+ 0.24	- 0.13

a) measured in $CDCl_3$

Although there is no unequivocal evidence for the discrimination between I and I', I is suggested to be more probable than I' by the biogenetic analogy to other prenylflavonoids isolated from Moraceae,[3-5] as well as by the biogenetic pathway of 3-prenylated flavone derivatives postulated by Rama Rao et al[15] (Chart 2). The following pmr and mass spectrum data can be accounted for on the basis of the structure (I). Comparison between pmr spectra of Ib and Ic indicates that the

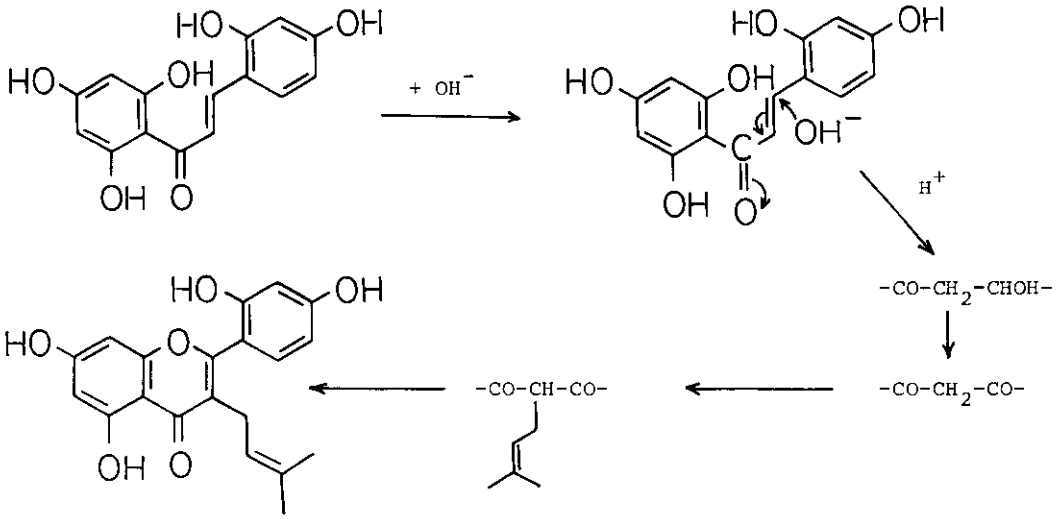


Chart 2

acetylation of the tertiary hydroxyl group at C_2 in Ib caused a higher applied magnetic field shift of the $C_{6'}$-H ($CDCl_3$, Ib, δ 7.42; Ic, δ 7.16). The similar result was reported in the case of kuwanon D.[4c,16] The mass spectrum of Ic and Id[7,17] gave the fragments at m/e 303(IV, 40%)[12] and 317(V, 42%), respectively. These fragments are assumed to be formed by the acyl migration of the C_2-O-acyl group.

In order to corroborate the structure of I, the cmr spectrum was analysed as follows: δ in $CDCl_3$, 18.03(q,C_{13}), 25.78(q,C_{12}), 28.41(q,intense,C_{17} and C_{18}), 31.18(t,C_9), 78.85(s,C_{16}), 90.85(s,C_2 or C_3), 96.42(d,C_8), 99.45(d,$C_{3'}$), 101.03 (s,intense,C_2 or C_3 ,and C_{4a}), 102.75(s,C_6), 109.39(d,$C_{5'}$), 115.06(d,C_{14}), 116.98 (d,C_{10}), 121.13(s,$C_{1'}$), 124.94(d,$C_{6'}$), 126.38(d,C_{15}), 136.84(s,C_{11}), 158.65 (s,intense,C_2, and C_5), 160.23(s,$C_{4'}$), 162.39(s,C_7), 164.25(s,C_{8a}), 186.36(s,C_4). Assignments of the carbon atoms in I were performed by comparison of the cmr spectrum of the model compounds.[4c,f,18]

From these results, we tentatively propose the formula (I) for the structure of sanggenon A. To the authors knowledge, sanggenon A is the first example of a flavanone derivative which has a hydroxyl group at C_2-position as well as a ether linkage between C_3- and $C_{2'}$-position.

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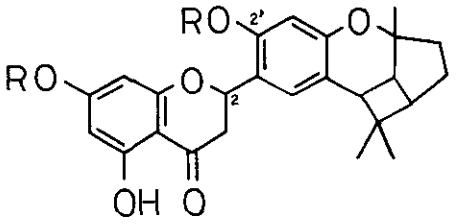
16 Comparison between pmr spectra of kuwanon D (VI) and kuwanon D diacetate (VIa) indicates that the acetylation of the $C_{2'}$-hydroxyl group in VI caused a higher applied magnetic field shift of the C_2-H(pyridine-d_5, VI, δ 6.23; VIa, δ 5.85).



VI :R=H

VIa:R=$COCH_3$

17 This compound (Id) was obtained by the treatment of Ib with propionic anhydride in pyridine at room temperature for 48 hr.

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