STRUCTURE OF SANGGENON O, A NATURAL DIELS-ALDER TYPE ADDUCT FROM CHINESE CRUDE DRUG "SANG-BAI-PI" (MORUS ROOT BARK)

Yoshio Hano and Taro Nomura*
Faculty of Pharmaceutical Sciences, Toho University, 2-2-1, Miyama, Funabashi-shi, Chiba 274, Japan

Abstract ——— From an acetone extract of the Chinese crude drug "Sang-Bai-Pi" (Japanese name "Sōhakuhi"), the root bark of Morus sp. (Moraceae), a new flavanone derivative was isolated and named sanggenon O, whose structure was shown to be 1 on the basis of spectral and chemical evidence. Sanggenon O (1) is a structural isomer of sanggenon C (2), and was derived from 2 by treatment of an alkaline solution. The compound (1) is regarded biogenetically as a Diels-Alder type adduct of a chalcone derivative and a dehydroprenylflavanone derivative.

Previously we reported the structure determination of a series of natural Diels-Alder type adducts, isoprenylated flavonoids, and of 2-arylbenzofuran derivatives obtained from the Chinese crude drug "Sang-Bai-Pi" (Japanese name "Sōhakuhi") imported from the People's Republic of China.[1] In this paper, the structure determination of sanggenon O (1) isolated from the crude drug, is described.

The crude drug "Sang-Bai-Pi" was extracted successively with hexane, benzene, and acetone. The acetone extract was fractionated sequentially by the silica-gel column chromatography and centrifugal thin-layer chromatography, resulting in the isolation of 1 (1.8×10^{-3} % yield from the crude drug).

Sanggenon O (1) was obtained as an amorphous powder, $[\alpha]_D^{25}$ -64° (c=0.13, MeOH), exhibiting a positive ferric chloride reaction (greenish brown), magnesium-hydrochloric acid test (orange), and sodium borohydride test (orange).[2] The compound (1) showed the following spectra: ir ν_{max}^{KBr} cm^{-1}: 3370 (br), 1640 (sh), 1625, 1600 (sh); uv λ_{max}^{EtOH} nm (log ε): 222 (sh 4.68), 284 (4.48), 287 (sh 4.47), 305 (sh 4.39); $\lambda_{max}^{EtOH+AlCl_3}$: 287 (4.46), 318 (4.45), 360 (sh 3.80). The uv spectra were similar to those of sanggenons C (2)[1c] and D (3).[1d] The FD-MS of 1 showed the molecular

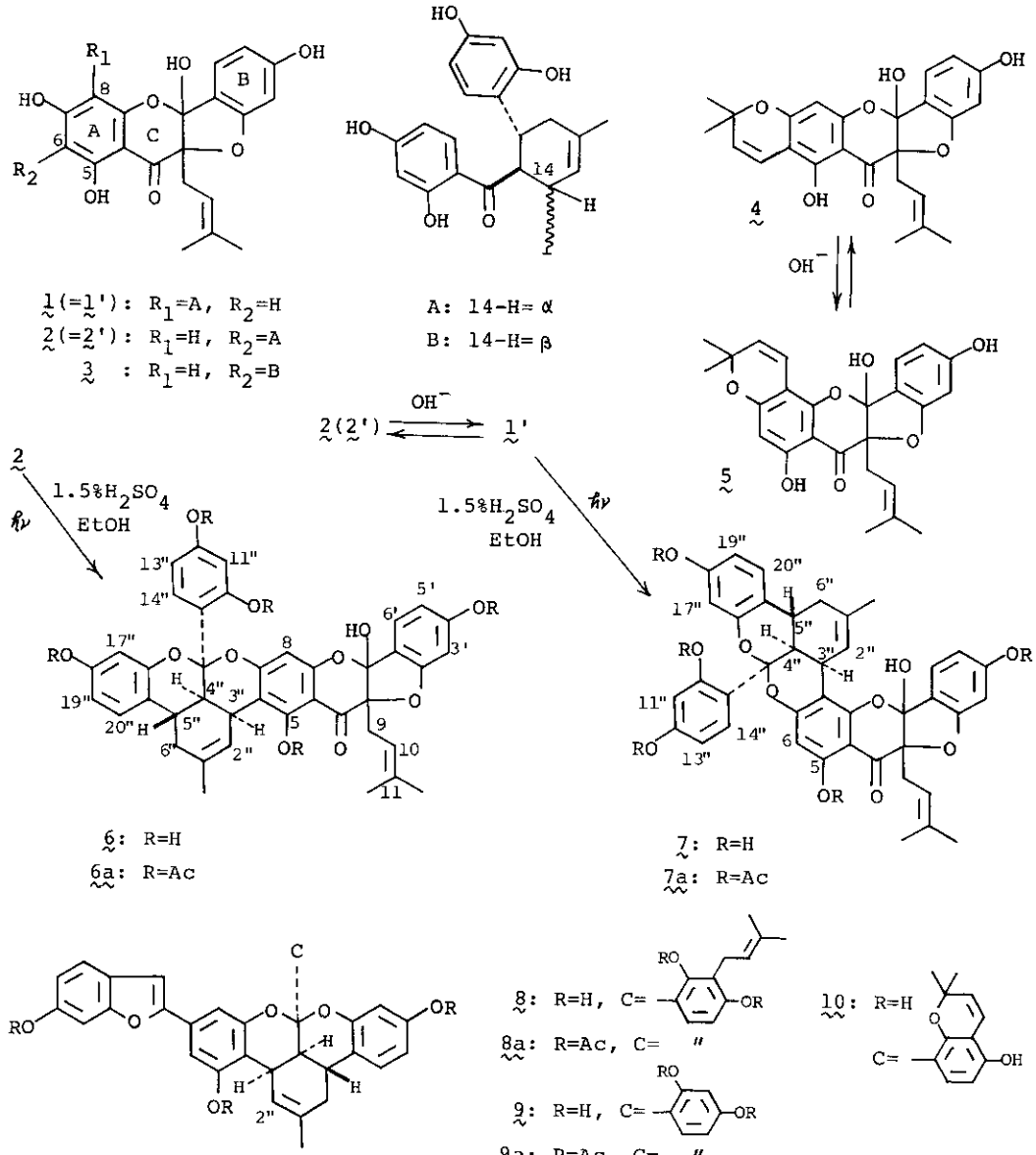

Fig. 1

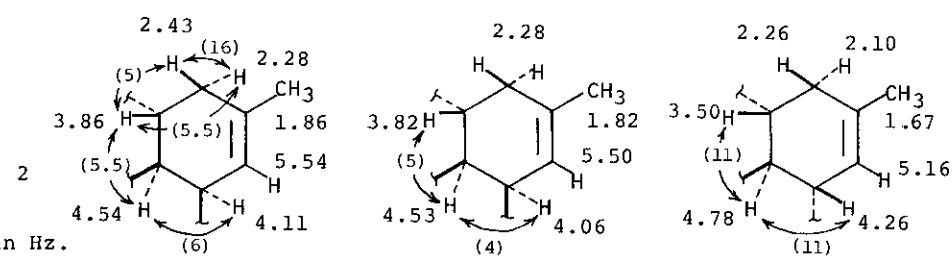

Fig. 2
( ): J in Hz.

1 (acetone-d_6) 2 (acetone-d_6) 3 (DMSO-d_6, 120°C)

ion peak at m/z 708. These results suggest that 1 is a structural isomer of 2 or 3. This suggestion was supported through a comparative examination of ^{1}H nmr of 1, 2, and 3. The ^{1}H nmr spectrum of 1 (400 MHz, acetone-d_6) showed the signals of three 2,4-dioxygenated phenyl moieties as follows: δ 6.47 (1H, d, J=2), 6.50 (1H, dd, J=2 and 8), 7.36 (1H, d, J=8); δ 6.36 (1H, dd, J=2 and 8), 6.38 (1H, d, J=2), 8.34 (1H, d, J=8); δ 6.19 (1H, d, J=2), 6.27 (1H, dd, J=2 and 8), 6.93 (1H, d, J=8). The spectrum also showed the signals of a 3,3-dimethylallyl group as follows: δ 1.22, 1.53 (each 3H, s), 2.68 (1H, dd, J=6 and 14), 3.08 (1H, dd, J=9 and 14), 5.08 (1H, dd, J=6 and 9), and showed an aromatic proton signal [δ 5.72 (1H, s)] and two hydrogen-bonded hydroxyl group signals [δ 12.05 (1H, s), 12.45 (1H, s)]. Fig. 2 depicts the chemical shifts and coupling constants of protons of the relevant methylcyclohexene rings of 1, 2,[1c] and 3.[1d] In respect to the chemical shifts and coupling constants of the relevant methylcyclohexene ring, 1 was more similar to 2 than to 3. These results suggest that sanggenons O (1) and C (2) have the same relative configuration. All these results indicated that the structure of sanggenon O is possibly represented by 1.

In the previous paper,[1h] our group reported that sanggenon A (4)[1a] was easily isomerized in an alkaline solution to give a 2 : 5 equilibrium mixture of sanggenons A (4) and M (5). To confirm the structure of 1, the same alkaline treatment was carried out. Sanggenon C (2, 100 mg) was dissolved in 5 % sodium carbonate solution, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was purified by prepararive TLC to give 1' (43 mg) and 2' (55 mg). The ir, nmr, and uv spectra of 1' and 2' were identified with those of sanggenons O (1) and C (2), respectively.[3] The compound (1') was easily isomerized in an alkaline solution to give the same equilibrium mixture of 1' and 2'. From this result, it was confirmed that sanggenons O (1) and C (2) have the hemiketal partial structure such as sanggenon A (4). The location of the methylcyclohexene ring on the A ring of 1 was confirmed by considering the following acetylation shifts of the olefinic protons of the methylcyclohexene ring moieties of the ketal compounds (6 and 7). The ketal compound (6) was derived from 2 as follows: a solution of 2 (100 mg) in ethanol containing 1.5 % sulfuric acid was irradiated in a glass vessel with 100 W high-pressure mercury lamp, and the reaction product was purified by preparative TLC to give 6 (20 mg).[4] The same intramolecular ketalization in the acidic solution were reported in the case of mulberrofurans F (8),[5] G (9),[5] and K (10).[1i] Work up of 6 with acetic anhydride in pyridine gave the pentaacetate

(6a)[6] which was negative to the ferric chloride reaction.

On the other hand, the compound (7)[7] was derived from 1' by the intramolecular ketalization reaction in the acidic solution. The pentaacetate (7a)[8] was obtained by the acetylation of 7. Comparison of the ^{1}H nmr spectra of 6 and 6a indicates that the acetylation of the phenolic hydroxyl groups caused a higher field shift of the olefinic proton in the methylcyclohexene ring (Table 1). On the other hand, in the case of 7, the acetylation of the phenolic hydroxyl groups of 7 caused little shift of the olefinic proton in the methylcyclohexene ring of 7a (Table 1). The difference of these acetylation shifts seems to be arised from the acetylation of the hydroxyl group at C-5 position. The similar shifts were observed in the case of mulberrofurans F (8) and G (9) (Table 1).[5] From these results, the location of the methylcyclohexene ring on the A ring was confirmed to be at C-8 position. So we propose the formula (1) as the structure of sanggenon O.

Table 1. Acetylation shifts for C-2"-H of 6, 7, 8 and 9

6 6.36	7 6.31	8 6.47	9 6.46
6a 6.04	7a 6.36	8a 6.00	9a 6.00
Δ +0.32	Δ −0.05	Δ +0.47	Δ +0.46

(ppm) measured in acetone-d_6

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3. Optical rotation values of 1' (+11.4°, c=0.175, MeOH) and 2' (+241°, c=0.208, MeOH) were different from those of 1 (-64°, c=0.13, MeOH) and 2[1c] (+304°, c=0.180, MeOH), respectively. More detailed study for the alkaline treatment of 2 are now in progress. The similar results were observed in the case of sanggenons A (4) and M (5).[1h]

4. The compound (6) showed the following color reaction and spectral data: $FeCl_3$ (brown); FD-MS

m/z: 690 (M^+); uv λ_{max}^{EtOH} nm (log ε): 225 (4.43), 284 (4.15), 288 (infl. 4.14), 310 (4.26), 360 (sh 3.42); $\lambda_{max}^{EtOH+AlCl_3}$: the spectrum showed no change in the absorption maxima; ^{1}H nmr (200 MHz, acetone-d_6): δ 1.46, 1.56 (each 3H, s, C-11-CH_3), 1.77 (3H, s, C-1"-CH_3), 2.08 (1H, m, C-6"-H), 2.75 (2H, m, C-6"-H and C-9-H), 2.86 (1H, td, J=5 and 11, C-5"-H), 3.17 (1H, dd, J=9 and 15, C-9-H), 3.32 (1H, m, C-3"-H), 3.44 (1H, dd, J=5 and 11, C-4"-H), 5.25 (1H, br, C-10-H), 6.00 (1H, s, C-8-H), 6.22 (1H, dd, J=2 and 8, C-13"-H), 6.36 (1H, br d, J=5, C-2"-H), 6.39 (1H, d, J=2, C-17"-H), 6.46 (2H, d, J=2, C-3'-H and C-11"-H), 6.54 (1H, dd, J=2 and 8, C-5'-H), 6.57 (1H, dd, J=2 and 8, C-19"-H), 7.02 (1H, d, J=8, C-14"-H), 7.17 (1H, d, J=8, C-20"-H), 7.44 (1H, d, J=8, C-6'-H), 12.35 (1H, s, C-5-OH).

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6. The compound (6a) showed the following spectral data: FD-MS m/z: 900 (M^+); ^{1}H nmr (200 MHz, acetone-d_6): δ 1.47, 1.57 (each 3H, s, C-11-CH_3), 1.79 (3H, s, C-1"-CH_3), 1.92 (3H, s, $COCH_3$), 2.10-2.20 (1H, m, C-6"-H, overlapping with solvent), 2.24, 2.25, 2.26, 2.34 (each 3H, s, $COCH_3$), 2.79 (1H, dd, J=8 and 15, C-9-H), 2.80-3.00 (3H, m, C-4", 5", and 6"-H), 3.15 (1H, m, C-3"-H), 3.27 (1H, dd, J=9 and 15, C-9-H), 5.22 (1H, m, C-10-H), 6.04 (1H, br, C-2"-H), 6.48 (1H, s, C-8-H), 6.65 (1H, d, J=2, C-17"-H), 6.84 (1H, dd, J=2 and 8, C-5'-H), 6.87 (1H, dd, J=2 and 8, C-19"-H), 6.89 (1H, d, J=2, C-3'-H), 7.02 (1H, dd, J=2 and 8, C-13"-H), 7.09 (1H, d, J=2, C-11"-H), 7.28 (1H, d, J=8, C-14"-H), 7.46 (1H, d, J=8, C-20"-H), 7.67 (1H, d, J=8, C-6'-H).
7. The compound (7) showed the color reaction and spectral data as follows: $FeCl_3$ test (brown); FD-MS m/z: 690 (M^+); uv λ_{max}^{EtOH} nm (log ε): 224 (4.79), 285 (4.37), 288 (infl. 4.35), 310 (4.43), 348 (sh 3.71); $\lambda_{max}^{EtOH+AlCl_3}$: 224 (4.80), 285 (4.38), 300 (infl. 4.35), 312 (4.46), 356 (infl. 3.81); ^{1}H nmr (400 MHz, acetone-d_6): δ 1.50, 1.72 (each 3H, s, C-11-CH_3), 1.75 (3H, s, C-1"-CH_3), 2.00 (1H, dd, J=10 and 16, C-6"-H), 2.68 (1H, dd, J=6 and 16, C-6"-H), 2.78 (1H, dd, J=6 and 14, C-9-H), 2.80 (1H, ddd, J=6, 10 and 11, C-5"-H), 3.20 (1H, dd, J=9 and 14, C-9-H), 3.30 (1H, br t, J=5, C-3"-H), 3.38 (1H, dd, J=5 and 11, C-4"-H), 5.22 (1H, m, C-10-H), 5.95 (1H, s, C-6-H), 6.29 (1H, dd, J=2.5 and 9, C-13"-H), 6.31 (1H, br, C-2"-H), 6.35 (1H, d, J=2.5, C-11"-H), 6.38 (1H, d, J=2, C-17"-H), 6.47 (1H, d, J=2, C-3'-H), 6.49 (1H, dd, J=2 and 8, C-19"-H), 6.52 (1H, dd, J=2 and 8, C-5'-H), 7.08 (1H, d, J=9, C-14"-H), 7.09 (1H, d, J=8, C-20"-H), 7.37 (1H, d, J=8, C-6'-H), 12.28 (1H, s, C-5-OH).
8. The compound (7a) showed the color reaction and spectral data as follows: $FeCl_3$ test (negative); FD-MS m/z: 900 (M^+); ^{1}H nmr (400 MHz, acetone-d_6): δ 1.35, 1.70 (each 3H, s, C-11-CH_3), 1.71 (3H, s, C-1"-CH_3), 1.96 (3H, s, $COCH_3$), ~2.10 (1H, m, C-6"-H, overlapping with solvent), 2.23 (6H, s, $COCH_3$ x 2), 2.24, 2.27 (3H, s, $COCH_3$), ~2.8 (1H, m, C-9-H), 2.92 (2H, m, C-6" and 5"-H), 3.02 (1H, dd, J=6 and 11, C-4"-H), 3.12 (1H, m, C-9-H), 3.25 (1H, m, C-3"-H), 5.25 (1H, m, C-10-H), 6.36 (1H, br, C-2"-H), 6.52 (1H, s, C-6-H), 6.60 (1H, d, J=2, C-17"-H), 6.75 (1H, d, J=2, C-3'-H), 6.80 (1H, dd, J=2 and 8, C-5'-H), 6.82 (1H, dd, J=2 and 8, C-19"-H), 7.05 (1H, dd, J=2 and 8, C-13"-H), 7.11 (1H, d, J=2, C-11"-H), 7.26 (1H, d, J=8, C-14"-H), 7.39 (1H, d, J=8, C-20"-H), 7.46 (1H, d, J=8, C-6'-H).

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