STRUCTURE OF ISORUGOSIN B, AND THE ORIENTATION OF VALONEOYL GROUP IN THE RELATED MONOMERIC, DIMERIC AND TRIMERIC HYDROLYZABLE TANNINS

Tsutomu Hatano, Reiko Kira, Taeko Yasuhara, and Takuo Okuda*
Faculty of Pharmaceutical Sciences, Okayama University, Tsushima, Okayama 700, Japan

Abstract —— A new hydrolyzable tannin, named isorugosin B (1), was isolated from Liquidambar formosana, and the structure in which the orientation of valoneoyl group at O-4 ~ O-6 of the glucose core is the reverse of that in rugosin B (2) and in rugosin A (3), was determined. The orientation of valoneoyl group in rugosin A (3) was established by the long range ^{1}H-^{13}C correlation nmr spectroscopy. The structures of rugosins D (6), E (7) and G (8), coriariins C (9), D (10), E (11) and F (12), cornusiin A (13), camptothins A (15) and B (16), were fully established on the basis of chemical correlations with 1 or 3.

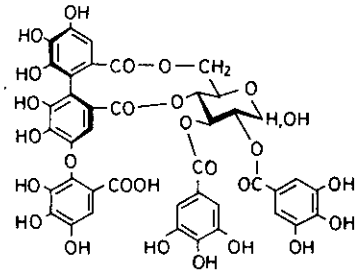
In the continuation of the study of tannins of the leaves of Liquidambar formosana,[1] we have isolated a new tannin, named isorugosin B (1), in which only the orientation of the valoneoyl group at O-4 ~ O-6 is different from that in rugosin B (2).[2] Comparison of several hydrolyzable tannins with 1 and 2 [or a related tannin, rugosin A (3)[2]] provided evidence of the orientation of valoneoyl group in these tannins. This paper deals with the structure elucidation of isorugosin B, and the orientation of valoneoyl group in the related hydrolyzable tannins.

Isorugosin B (1), $[\alpha]_D$ +28° (c=1, methanol), FAB-MS m/z 977 ($[M+Na]^+$), was obtained as a light brown amorphous powder. The ^{1}H nmr spectrum (400 MHz, in acetone-d_6) of 1 indicates that this tannin, forming an anomer mixture

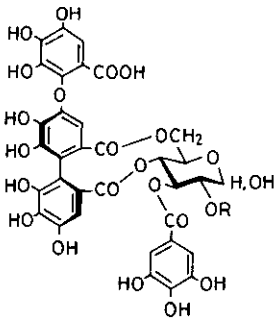
(α : β =4:3), possesses two galloyl groups [δ 7.05 (β-anomer), 7.04 (α-anomer) (each s, 2H in total); 6.90 (α), 6.88 (β) (each s, 2H in total)], a valoneoyl group [δ7.28 (β), 7.27 (α) (each s, 1H in total); 6.66 (β), 6.65 (α) (each s, 1H in total); 6.31 (α), 6.25 (β) (each s, 1H in total)] and a glucopyranose core [δ 5.54 (t, J=3.5 Hz, H-1), 5.10 (dd, J=3.5, 10 Hz, H-2), 5.69 (t, J=10 Hz, H-3), 5.03 (t, J=10 Hz, H-4), 4.57 (ddd, J=1, 7, 10 Hz, H-5), 5.28 (dd, J=7, 13 Hz, H-6), 3.75 (dd, J=1, 13 Hz, H-6) (α-anomer); 5.05 (d, J=8 Hz, H-1), 5.22 (dd, J=8, 10 Hz, H-2), 5.39 (t, J=10 Hz, H-3), 5.02 (t, J=10 Hz, H-4), 4.20 (ddd, J=1, 7, 10 Hz, H-5), 5.29 (dd, J=7, 13 Hz, H-6), 3.82 (dd, J=1, 13 Hz, H-6) (β-anomer)]. The coupling constants of the glucose protons show that the glucose core adopts the $^4C_1$ conformation, and the chemical shifts of H-4 and two H-6 protons of both anomers indicate that the biphenyl part of the valoneoyl group locates at O-4 ~ O-6 of the glucose core.[3] Therefore, two galloyl groups should be at O-2 and O-3, since the hydroxyl group at the anomeric center is not acylated. These locations of the acyl groups were confirmed by the production of 2,3-di-O-galloyl-D-glucose (**4**)[4] and valoneic acid dilactone (**5**) upon the treatment of aqueous solution of **1** in boiling water-bath for 18 hours. A positive Cotton effect in the short wavelength region ($[\theta]_{222}$ +9.0 x 10^4) of the CD spectrum of **1** indicates the S-configuration[3] of the biphenyl part of the valoneoyl group. Therefore, isorugosin B is 2,3-di-O-galloyl-4,6-O-(S)-valoneoyl-D-glucopyranose, and the structural difference between **1** and **2** should be in the orientation of the valoneoyl group.

The orientation of the valoneoyl group in **2** was confirmed to be identical with that in rugosin A (**3**), by partial hydrolysis of **3**, which afforded **2**.[2] Although the orientation of valoneoyl group at O-4 ~ O-6 of the glucose core in **3** has not yet been determined,[5] the orientation of this group in rugosins D (**6**),[6] E (**7**)[6] and G (**8**),[6] and coriariins C (**9**),[3] D (**10**),[3] E (**11**)[3] and F (**12**)[3] has been proved to be identical with that in rugosin A (**3**), by chemical correlation with **3**.[3,6]

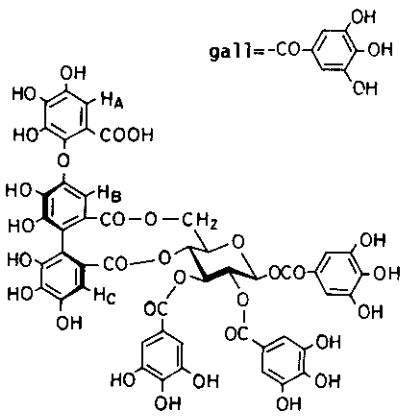
Rugosin A (**3**) showed the valoneoyl protons at δ 7.14, 6.51 and 6.32 in the ^{1}H nmr spectrum (90 MHz, in acetone-d_6 + D_2O). The signal at δ7.14 is apparently of the H_A proton in formula **3**. Addition of pyridine-d_5 to the solution of **3** in acetone-d_6 - D_2O caused a large downfield shift of the proton at δ6.32 (to δ 6.58), while only small downfield shifts were observed for the signals at δ 7.14 (to δ7.24) and at δ6.51 (to δ6.61). The large downfield shift of the signal at δ6.32 is regarded as an effect of the pyridine(-d_5) molecule which is



1

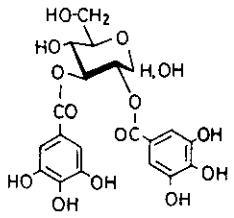


2: R=gall
12: R=H

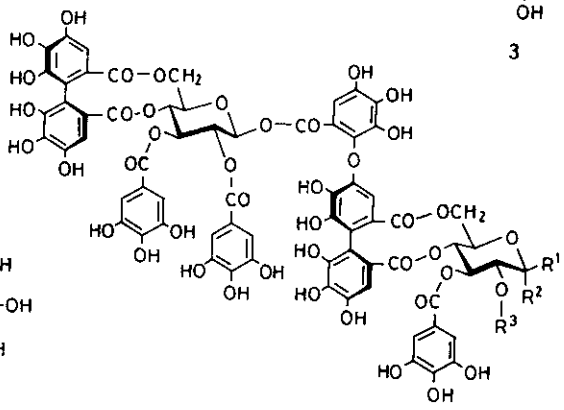


gall=-CO-

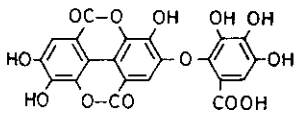
3



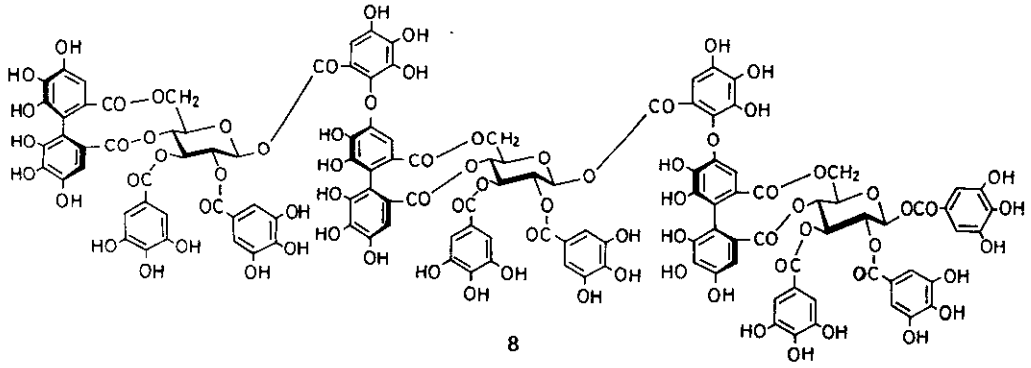
4



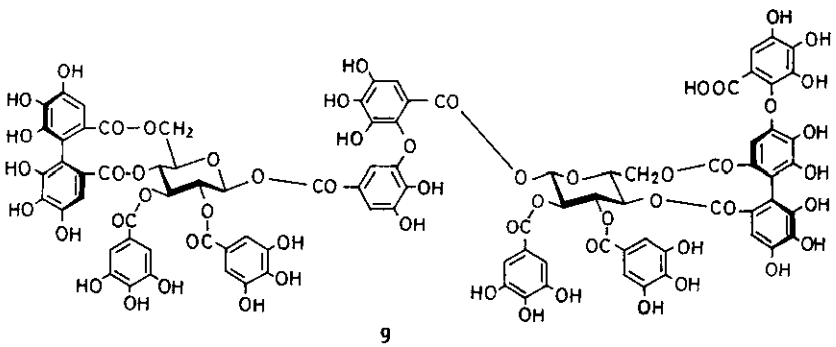
6: R^1=O-gall
R^2=H
R^3=gall
7: R^1, R^2=H, OH
R^3=gall
11: R^1, R^2=H, OH
R^3=H



5



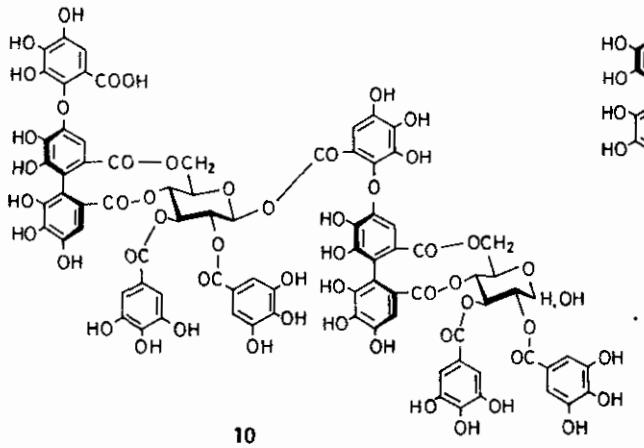
8



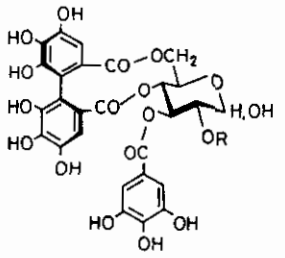
9

located nearby the H_B proton, by approaching the carboxyl group of the valoneoyl group. The signal at δ 6.51 therefore is that of the H_C proton. The long range ^1H-^{13}C correlation spectrum[7] (in acetone-d_6) of **3** showed a cross peak for one of the H-6 protons (δ 3.79) of the glucose core and an ester carbonyl carbon at δ 167.8, and another cross peak for the H_B proton and the same ester carbonyl carbon. The spectrum also showed a cross peak for the H-4 proton (δ 5.16) of the glucose core and an ester carbonyl carbon at δ 167.6, and another cross peak for the H_C proton and this ester carbonyl carbon. These cross peaks indicate that the orientation of the valoneoyl group in rugosin A is as in structure **3**. Therefore, rugosins B, D, E and G, and coriariins C, D, E and F, and isorugosin B, should be formulated as **2**, **6**, **7**, **8**, **9**, **10**, **11**, **12** and **1**, respectively.

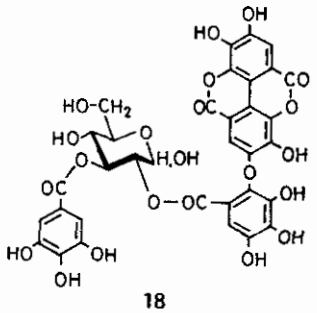
Cornusiin A (**13**), the main tannin in the fruits of Cornus officinalis,[4] was reported to have a dimeric structure,[4] which could be biogenetically produced



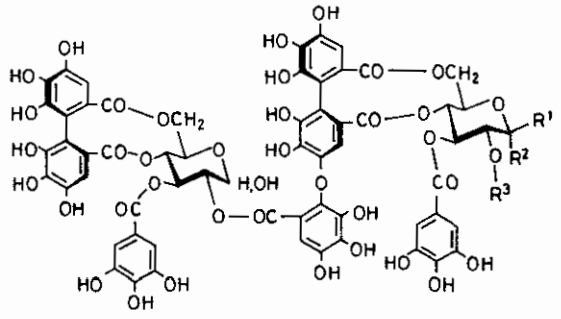
10



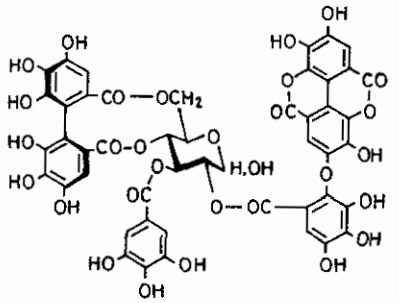
14: R=gall
17: R=H



18



13: R^1, R^2=H,OH, R^3=gall
15: R^1, R^2=H,OH, R^3=H
16: R^1=O-gall, R^2=H, R^3=gall



19

from two molecules of tellimagrandin I (**14**), although the orientation of the valoneoyl group in **13** has not yet been determined. However, the orientation of the valoneoyl group in camptothins A (**15**)[8] and B (**16**)[8] is identical with that in **13**, since **15** and **16** were chemically correlated with **13**.[8] Now treatment of **13** in water at 50 °C for 7 days afforded isorugosin B (**1**) and gemin D (**17**),[4] along with **4**, oenothein C (**18**)[4] and cornusiin B (**19**).[4] Therefore, cornusiin A should be formulated as structure **13**, in which the orientation of the valoneoyl group is identical with that in **1**. The orientation of this group in camptothins A and B also should be formulated as in structures **15** and **16**.

ACKNOWLEDGEMENTS

We thank Prof. T. Shingu, Faculty of Pharmaceutical Sciences, Kobe Gakuin University for the measurement of the 400 MHz nmr spectra. We are also indebted Prof. T. Fujita, Faculty of Pharmaceutical Sciences, Kyoto University, and Assoc. Prof. Y. Takeda and Mrs. Y. Yoshioka, Faculty of Pharmaceutical Sciences, Tokushima University, for measuring the FAB mass spectra.

REFERENCES AND NOTES

1. T. Hatano, R. Kira, M. Yoshizaki, and T. Okuda, Phytochemistry, 1986, **25**, 2787; T. Okuda, T. Hatano, T. Kaneda, M. Yoshizaki, and T. Shingu, Phytochemistry, 1987, **26**, 2053.
2. T. Okuda, T. Hatano, K. Yazaki, and N. Ogawa, Chem. Pharm. Bull., 1982, **30**, 4230.
3. T. Hatano, S. Hattori, and T. Okuda, Chem. Pharm. Bull., 1986, **34**, 4533.
4. T. Okuda, T. Hatano, N. Ogawa, R. Kira, and M. Matsuda, Chem. Pharm. Bull., 1984, **32**, 4662.
5. Although the orientation of valoneoyl group in rugosin C was determined on the basis of the chemical correlation of rugosin C with praecoxin C, the orientation for rugosin A in ref. 2 was assumed on the basis of its co-occurrence with rugosin C in Rosa rugosa. See T. Okuda, T. Hatano, and K. Yazaki, Chem. Pharm. Bull., 1983, **31**, 333.
6. T. Okuda, T. Hatano, and N. Ogawa, Chem. Pharm. Bull., 1982, **30**, 4234.
7. Measured on a Varian VXR-500 instrument in the SC-NMR Laboratory of Okayama University.
8. T. Hatano, Y. Ikegami, T. Shingu, and T. Okuda, Chem. Pharm. Bull., accepted.

Received, 23rd May, 1988