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CONFIRMATION OF THE STRUCTURES OF KUWANONS G AND H (ALBANINS F AND G) BY PARTIAL SYNTHESIS[1]

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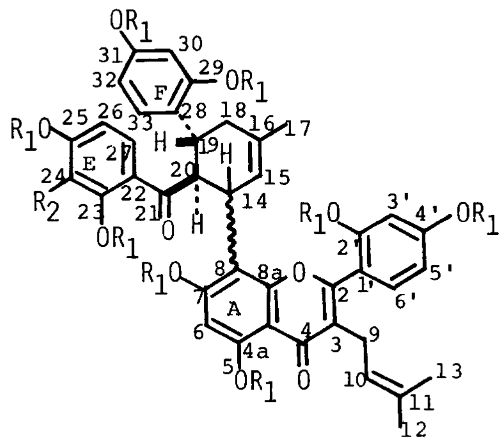
Conclusive evidence is presented supporting structures **1** and **2** for two natural Diels-Alder adducts isolated from mulberry and designated as kuwanon G (albanin F, moracenin B) and Kuwanon H (albanin G, Moracenin A).

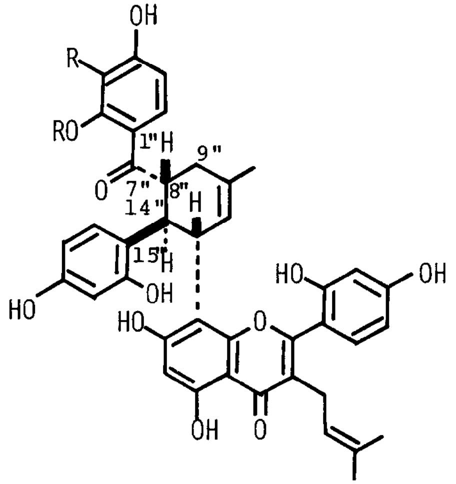
In 1980 our two groups and Oshima's group reported independently the isolation and structure elucidation of two natural products regarded as Diels-Alder adducts with two chalcones and a dehydroprenylflavone. One (Nomura)[2] of our groups designated two hypotensive principles (**1** and **2**), isolated from root barks of mulberry (Morus alba Linné), as kuwanons G and H, while the other (Takasugi)[3] named two antifungal components (**1** and **2**), isolated from shoot epidermis of the plant, albanins F and G. On the other hand, Oshima and co-workers[4] designated two hypotensive compounds (**2** and **1**), obtained from crude drug prepared from root barks of certain species of Morus plants, as moracenins A and B. While kuwanons G and H have been established to be identical with albanins F and G (TLC, IR, and ^{1}H NMR)[3] and with moracenins B and A (TLC, IR, and ^{1}H and ^{13}C NMR),[5] respectively, two formulas differing only in the manner of cycloaddition have been proposed for the respective compounds; namely, we assigned formulas **1** and **2** to the two compounds (**1** and **2**),[2,3] whereas Oshima and collaborators proposed those **1**' and **2**' for the compounds.[4,6] We now wish to report additional data confirming our proposed structures.

We previously obtained trans-2,2',4,4'-tetramethoxychalcone (**3**) and dehydrokuwanon C tetramethyl ether (**4**) by pyrolysis of octamethyl ether (**1a**) of **1**[3] and also tetramethylmorachalcone A (**5**) and **4** by that of octamethyl ether (**2a**) of **2**,[3] respectively. The former fragmentation compounds (**3**) and (**4**), when heated in toluene in the presence of 2,6-di-*t*-butyl-*p*-cresol at 160 °C (bath temp) for 81 h in a sealed tube, gave two cycloadducts (**6**) and (**7**), each amorphous, after chromatography in 35% [39% based on the recovered diene (**4**)] and 32% (35%) yields, respectively: **6**, m/e 804.3549 (M^+, $C_{48}H_{52}O_{11}$); λ_{max} (EtOH) 310 nm (ε 15300), 298 (15900), 261 (32100), 228 (49300), and 207 (84200); ν_{max} ($CHCl_3$) 1650 and 1603 cm^{-1}; δ ($CDCl_3$) 1.38 (3H, s), 1.58 (6H, s), 1.7 ∿ 2.2 (2H, m), 3.06 (2H, br s), 3.41 and 3.61 (each 3H, s), 3.66, 3.68, 3.80, and 3.82 (total 18H, each s), 3.7 (1H, m), 4.28 (1H, br d, J = 11 Hz), 4.75 (1H, t, J = 11), 5.12 (1H, br s), 5.16 (1H, br t, J = 7), 5.86 (1H, s), 5.90 (1H, d, J = 2), 6.1 ∿ 6.3 (3H, m), 6.46 (1H, d, J = 2), 6.52 (1H, dd, J = 8 and 2), 6.87, 7.11, and 7.23 (each 1H, d, J = 8): **7**, m/e 804.3468 (M^+, $C_{48}H_{52}O_{11}$); λ_{max} (EtOH) 298 nm (ε 16900), 261 (33000), 228 (47800), and 206 (90900); ν_{max} ($CHCl_3$) 1650 and 1603 cm^{-1}; δ ($CDCl_3$) 1.38 (3H, s), 1.58 (6H, s), 1.7 ∿ 2.2 (2H, m), 2.93 (2H, br d, J = 7 Hz), 3.62, 3.70, 3.75, 3.84, and 3.91 (total 24H, each s), 4.1 (1H, m), 4.54 ∿ 4.60 (2H, m), 5.13 (1H, br t, J = 7), 5.32 (1H, br s), 6.1 ∿ 6.3 (4H, m), 6.43 (1H, d, J = 2), 6.48 (1H, dd, J = 8 and 2), 6.89 and 7.18 (each 2H, d, J = 8). The same treatment of the latter compounds (**5**) and (**4**) (170 °C, 81 h) afforded two cycloadducts (**8**) and (**9**), each amorphous, after chromatography, in 24% (27%) and 24% (27%) yields, respectively (the spectral data will be described in a full paper). It is emphasized that no other cycloadducts were detected in the respective reaction mixtures. In view of the stereospecificity and regioselectivity due to substituents[7] of the Diels-Alder reaction, structures **6** and **7**, diastereoisomeric each other, were reasonably assigned to the former adducts, and those **8** and **9** to the latter adducts, respectively. As expected two (**6**) and (**8**) of the adducts were identified as the octamethyl ethers (**1a**) and (**2a**) of (±)-kuwanons G and H [(±)-albanins F and G], respectively, by direct comparison with the natural samples (TLC, UV, IR, and ^{1}H NMR). In order to ascertain the regioselectivity of the reactions, we prepared two model compounds (**10**), mp 184-186 °C (46%), and (**11**), mp 144-146 °C (25%), by cycloaddition of (unsubstituted) *trans*-chalcone and 3-methyl-1-phenyl-1,3-butadiene[8] (250 °C, 5 h), and elucidated their stereostructures by the X-ray crystallography (Figs. **1** and **2**; the details will by described in a full paper).[9] The result indicates that the synthetic products (**6** ∿ **9**) are formulated by the assigned structures and hence the natural products are represented most favorably by formulas **1** and **2**, respectively.

Oshima and co-workers[4] proposed their formulas (**1**' and **2**') only on the basis of the presence of $^{13}C-^{1}H$ spin couplings between the 21-carbonyl carbon atom (C-21) (C-7" according to their numbering) (δ 209.8 in CD_3CN) and two methylene hydrogens at C-18 (18-H) (9"-H) (1.92) and between C-22 (C-1") (115.5) and 19-H (8"-H) (3.66) as well as the absence of that between C-28 (C-15") and 20-H (14"-H). We examined carefully the presence of these couplings by the

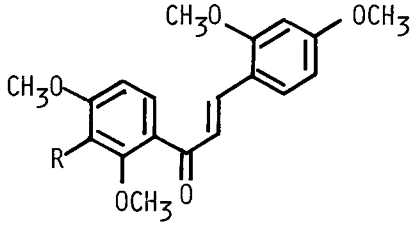


1		14β-H, $R_1=R_2=H$
1a	(=6)	14β-H, $R_1=CH_3$, $R_2=H$
2		14β-H, $R_1=H$, R_2=prenyl
2a	(=8)	14β-H, $R_1=CH_3$, R_2=prenyl
7		14α-H, $R_1=CH_3$, $R_2=H$
9		14α-H, $R_1=CH_3$, R_2=prenyl



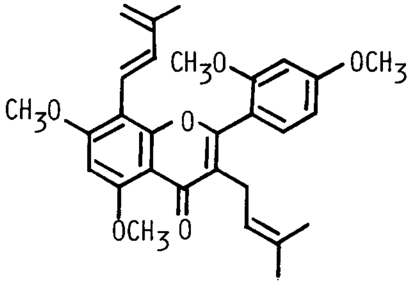
1' R=H

2' R=prenyl



3 R=H

5 R=prenyl



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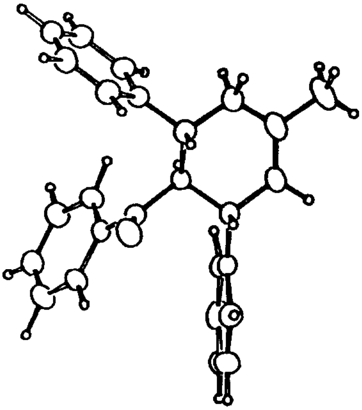

Fig. 1 X-ray structure of 10

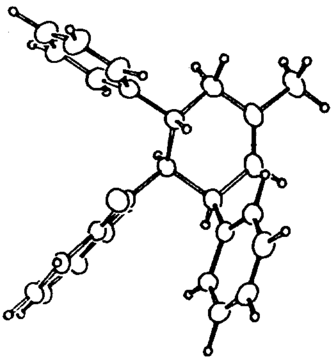

Fig. 2 X-ray structure of 11

long range selective decoupling (LSPD) technique.[10] Contrary to their observation, the signal at δ 208.1 (in DMSO-d_6) due to C-21 remained essentially unchanged on irradiation at δ 1.80 (18-H), 1.90 (18-H), and 3.60 (19-H) under different conditions, while the relevant signal increased by 30% in area on weak irradiation at δ 4.30 (both 14-H and 20-H). The result reveals that formulas **1**' and **2**' proposed for moracenins B and A are improbable.

In conclusion, the present results establish that kuwanons G and H (albanins F and G) are represented by formulas **1** and **2** with the indicated (relative) configuration.

References and Notes

1) Presented orally at the 23rd Symposium on the Chemistry of Natural Products held in Nagoya, Japan, on October 25th, 1980.

2) a) T. Nomura and T. Fukai, *Chem. Pharm. Bull.*, **28**, 2548 (1980). b) T. Nomura, T. Fukai, and T. Narita, *Heterocycles*, **14**, 1943 (1980).

3) M. Takasugi, S. Ishikawa, S. Nagao, T. Masamune, A. Shirata, and K. Takahashi, *Chem. Lett.*, **1980**, 1577.

4) a). Y. Oshima, C. Konno, H. Hikino, and K. Matsushita, *Tetrahedron Lett.*, **21**, 3381 (1980). b) Y. Oshima, C. Konno, H. Hikino, and K. Matsushita, *Heterocycles*, **14**, 1287 (1980).

5) The ^{13}C NMR spectra (in CD_3CN) of Kuwanons G and H were completely identical with the reported data of moracenins B[4a] and A,[4b] respectively (the details will be described in a full paper). Dr. Oshima, Tohoku University, also informed us that kuwanons G and H were identified as moracenins B and A, respectively, by direct comparison of the samples (TLC, IR, and ^{1}H NMR).

6) Presented orally at the 87th Annual Meeting of Tohoku Branch of Pharmaceutical Society of Japan held in Sendai, Japan, on December 20th, 1980.

7) J. Saure, *Angew. Chem. Internat. Edit.*, **6**, 16 (1967).

8) A. Klages, *Ber.*, **35**, 2649 (1902).

9) Crystallographic data have been deposited with the Cambridge Crystallographic Data Center.

10) *Cf.*, J. Uzawa and S. Takeuchi, *Org. Magn. Reson.*, **11**, 502 (1978); J. Uzawa and M. Uramoto, *ibid.*, **12**, 612 (1979).

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