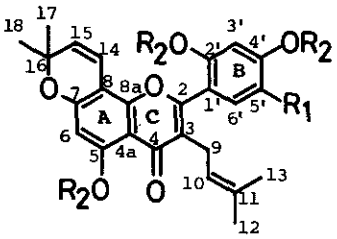
ARTONINS E AND F, TWO NEW PRENYLFLAVONES FROM THE BARK OF ARTOCARPUS COMMUNIS FORST.[1]

Yoshio Hano, Yukiko Yamagami, Miki Kobayashi, Ryoko Isohata, and Taro Nomura*
Faculty of Pharmaceutical Sciences, Toho University, 2-2-1, Miyama, Funabashi-shi, Chiba 274, Japan

Abstract —— Two new prenylflavones, artonins E (1) and F (2), were isolated from the bark of Artocarpus communis Forst. (Moraceae), along with a known compound, cycloartobiloxanthone (3). The structures of artonins E and F were shown to be 1 and 2, respectively, on the basis of spectroscopic data.

In the previous papers, we reported the structure determination of the isoprenoid-substituted phenolic compounds isolated from the Indonesian moraceous plants, Artocarpus heterophyllus Lamk.[2,3] and Antiaris toxicaria Lesch.[4] Artocarpus communis Forst. is also Indonesian moraceous plant, and its leaves are used for hepatomegalis and febris, and its flowers are used against parulis and adontalgia.[5] Furthermore the dried flower of the plant has been used as a mosquito repellent.[6] On the constituents of the flower, Fujimoto et al. reported the five new isoprenoid-substituted phenols; two flavanones and three dihydrochalcones, all of which exhibited the inhibitory effect on 5-lipoxygenase.[6] This paper describes the characterization of two new prenylflavones isolated from the bark of A. communis Forst.

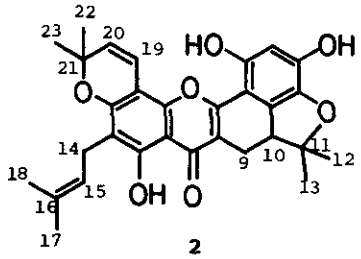
The dried bark of A. communis, collected in Indonesia, was extracted successively with n-hexane, benzene and acetone. Artonins E (1), F (2), and cycloartobiloxanthone (3)[7] were isolated from the benzene extract as described in "EXPERIMENTAL". Artonin E (1) is yellow needles, mp 244-248 °C, exhibited positive ferric chloride reaction and magnesium-hydrochloric acid test, while negative Gibbs test. The molecular formula of 1 was determined by HR-ms to be $C_{25}H_{24}O_7$. Treatment of 1 with acetic anhydride in pyridine gave the tetraacetate (1a). The uv spectrum exhibited maxima at 211, 266, 300 (sh), and 349 nm, and was similar to that of



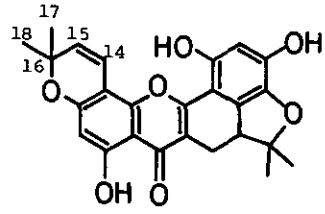
1 : R_1=OH, R_2=H

1a : R_1=OAc, R_2=Ac

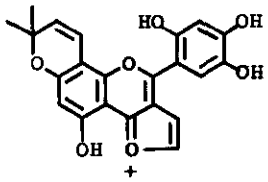
4 : R_1=R_2=H



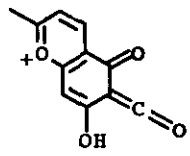
2



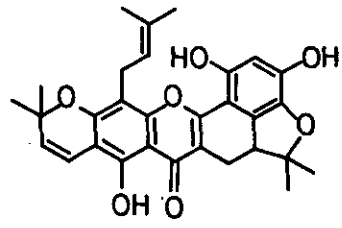
3



5



6



7

Table 1 ^{1}H Nmr chemical shifts (ppm) of C-14-H and C-15-H in **1** and **1a**

	C-14-H	C-15-H
1	6.54	5.70
1a	6.53	5.87
Δ	+0.01	-0.17

Table 2 ^{13}C Nmr chemical shifts (ppm) of **1**, **2**, **3**, **4** and **7**

	1*	**1****	**4***	**2****	**7****	**3**#**		**1***	**1****	**4***	**2****	**7****	**3**#**
C-2	161.6	162.2	162.0	161.4	161.6	161.5	C-9	23.6	24.7	23.7	20.5	20.5	20.3
C-3	119.9	121.7	120.0	112.6	112.6	112.7	C-10	121.4	122.5	121.6	47.6	47.6	47.5
C-4	181.8	183.3	181.8	181.5	181.7	181.4	C-11	131.2	132.3	131.3	93.7	93.7	93.7
C-4a	104.2	105.6	104.4	105.0	105.0	104.9	C-12	25.4	25.8	25.4	28.2	28.4	28.4
C-5	160.9	162.8	161.1	159.6	154.5	162.6	C-13	17.3	17.7	17.3	22.9	22.9	22.8
C-6	98.7	99.7	98.9	112.6	105.9	99.9	C-14	114.1	115.5	114.3	21.9	116.4	116.0
C-7	158.4	160.0	158.6	158.0	157.0	159.5	C-15	127.5	128.0	127.6	123.2	128.9	127.8
C-8	100.4	101.6	100.5	101.6	108.3	101.9	C-16	78.0	78.8	78.0	131.5	78.4	78.7
C-8a	151.7	153.3	151.9	157.1	155.3	152.0	C-17	27.6	28.3	27.7	25.9	28.4	28.3
C-1'	109.3	111.6	110.9	105.0	105.3	105.4	C-18	27.6	28.3	27.7	18.0	28.4	28.3
C-2'	148.7	149.8	156.7	151.5	151.5	151.5	C-19				116.3	22.0	
C-3'	103.9	104.8	103.0	105.5	105.4	105.5	C-20				127.7	123.7	
C-4'	148.5	149.5	160.7	147.0	147.0	147.0	C-21				78.6	131.7	
C-5'	138.0	139.1	107.0	137.9	138.0	137.9	C-22				28.4	25.9	
C-6'	116.1	117.1	131.3	133.7	133.7	133.6	C-23				28.3	18.2	

Solvent: *; DMSO-d_6 **; acetone-d_6 # our data

morusin (**4**).[8] The uv spectrum of **1** showed a remarkable bathochromic shift upon addition of aluminum chloride. The ^{1}H nmr spectrum showed the signals of the following protons; 1) protons in a 3,3-dimethylallyl (prenyl) group and a 2,2-dimethylpyran ring, δ 1.42 (9H, s, one of the methyl signals in a prenyl group and two methyl signals in a 2,2-dimethylpyran ring), 1.57 (3H, br s), 3.06 (2H, br d, J=7.0 Hz), 5.06 (1H, m), 5.70 (1H, d, J=10.0 Hz), 6.54 (1H, dd, J=0.5 and 10.0 Hz); 2) three aromatic protons, δ 6.22 (1H, d, J=0.5 Hz), 6.48, 6.70 (each 1H, s), and 3) a proton in a hydrogen-bonded hydroxyl group, δ 13.21 (1H, s). A ^5J long-range coupling was observed between the olefinic proton at δ 6.54 and the aromatic proton at δ 6.22 (J=0.5 Hz). The EI-ms spectrum of **1** showed the following significant fragment ions; m/z 393 ($M^+-C_3H_7$, 5)[9] and m/z 203 (**6**).[8] This result suggests that a 2,2-dimethylpyran ring is located in the A ring,[8] and a prenyl group at the C-3 position.[9] The angular structure for the pyran ring was confirmed by the acetylation shift values of the olefinic protons in a pyran ring. The changes in chemical shift values of the tetraacetate (**1a**) and **1** indicate the angular structure to be preferable to the linear one (Table 1).[10] In the ^{13}C nmr spectrum of **1**, the chemical shift values of all the carbon atoms except the carbon atoms at the C-2', -4', -5', and -6' positions were similar to those of the relevant carbon atoms of **4** (Table 2). The angular structure for the pyran ring and the location of the prenyl group were further confirmed on the following evidences. In the ^{13}C nmr spectrum of **1** (in acetone-d_6 at room temperature, gated decoupling with NOE), the C-6 signal at δ 99.7 was observed as a doublet of doublet (^1J=163.6 Hz, ^3J=7.3 Hz), and the C-4 signal at δ 183.3 as a triplet (^3J=4.4 Hz). When a proton signal at δ 13.25 (C-5-OH) was irradiated, the signal at δ 99.7 changed to doublet (^1J=163.6 Hz). When the proton signal at δ 3.16 (C-9-H x 2) was irradiated, the signal at δ 183.3 changed to a singlet. From above results, the formula **1** was confirmed as the structure of artonin E.

Artonin F (**2**) is yellow needles, mp 248 °C, $[\alpha]_D$ 0°, exhibited positive ferric chloride reaction and magnesium-hydrochloric acid test. The molecular formula of **2** was determined by HR-ms to be $C_{30}H_{30}O_7$. The uv spectrum exhibited maxima at 204, 229, 257, 278, 335, and 390 nm, and was similar to that of cycloartobiloxanthone (**3**).[7] The ^{1}H nmr spectrum showed the signals of the following protons; 1) protons in a 3,3-dimethylallyl group, δ 1.66, 1.80 (each 3H, br s), 3.31 (2H, br d, J=7.0 Hz), 5.23 (1H, m); 2) protons in a 2,2-dimethylpyran ring, δ 1.46, 1.49 (each 3H, s), 5.68, 6.95 (each 1H, d, J=10.0 Hz); 3) an aromatic proton, δ 6.41 (1H, s);

4) protons of two methyl groups, δ 1.33, 1.66 (each 3H, s); 5) ABX type protons, δ 2.36 (1H, t, J=15.1 Hz), 3.22, 3.41 (each 1H, dd, J=7.1 and 15.1 Hz); and 6) a proton in a hydrogen-bonded hydroxyl group, δ 13.70 (1H, s). In the ^{1}H nmr spectrum of **2**, the chemical shift values of an aromatic proton, the two methyl groups' protons (δ 1.33 and 1.66), and ABX type protons were similar to those of the relevant protons of artonin A (**7**).[2] In the ^{13}C nmr spectrum of **2**, the chemical shift values of all the carbon atoms except the values of C-5, C-6, C-8, and C-8a were similar to those of **3**[7] and **7**[2] (Table 2). From the above results, compound **2** was suggested to be a structural isomer of **7**, and the formula **2** was proposed for the structure of artonin F.

EXPERIMENTAL

Abbreviations: s=singlet, d=doublet, dd=double doublet, t=triplet, m=multiplet, br=broad, sh=shoulder. The general procedures followed as described in our previous papers.[3,11] The instruments used are described in our previous paper.[3]

Plant Materials

The bark of *Artocarpus communis* Forst. (Moraceae) was collected in Botanical Garden of Bogor, Indonesia in February 1988, and identified by the members of the botanical garden. The sample was deposited in the Herbarium of Toho University.

Isolation of Artonins E (1) and F (2) from the Bark of A. communis Forst.

The dried bark of *A. communis* Forst. (1 Kg) was extracted with *n*-hexane (8 l) at room temperature for 3 days and such was repeated two more times. The residue was extracted successively with benzene (8 l x 3) and acetone (8 l x 3) as described above. Evaporation of the *n*-hexane, benzene, and acetone solutions to dryness yielded 15 g, 7 g, and 45 g of the residue, respectively. The benzene extract (7 g) was chromatographed on silica gel (200 g) with *n*-hexane containing increasing amount of acetone as an eluent, each fraction being monitored by tlc. A part of the fraction eluted with *n*-hexane containing 25% acetone was evaporated to give a residue (200 mg), which was purified by recrystallization from benzene-acetone to give yellow needles, artonin E (**1**, 80 mg). Another part of the fraction eluted with *n*-hexane containing 25% acetone was evaporated to give a residue (1 g), which was rechromatographed on silica gel (50 g) with chloroform as an eluent, each fraction (eluted volume 50 ml) being monitored by tlc. The fractions 2-4 (0.1 g of residue) were purified by preparative tlc (solvent system, benzene:ethyl acetate=3:1, silica gel), followed by recrystallization from benzene-acetone to give yellow needles, artonin F (**2**, 10 mg). The fractions 5-12 (0.05 g) were purified by recrystallization from benzene-acetone to give yellow needles, mp 294-296 °C, cycloartobiloxanthone (**3**, 35 mg). The physical data of **3** were identified with the published data.

Artonin E (1)

Compound **1** was obtained as yellow needles, mp 244-248 °C. $FeCl_3$ test: positive (green). Mg-HCl test: positive (orange). Gibbs test: negative. Uv λ_{max}^{EtOH} nm (log ε): 211 (4.21), 266 (4.34), 300 (sh 3.63), 349 (3.51). Uv $\lambda_{max}^{EtOH+AlCl_3}$ nm (log ε): 226 (4.17), 277 (4.38), 410 (3.55). Ir ν_{max}^{KBr} cm^{-1} :3440, 3390, 1662, 1650 (sh), 1645, 1605, 1585, 1560, 1525, 1483, 1462. EI-Ms: m/z 436 [M^+], 421 (base peak), 393 (**5**), 203 (**6**). High-resolution Ms (HR-Ms): m/z 436.1530 ($C_{25}H_{24}O_7$ requires:

436.1522), 421.1274 ($C_{24}H_{21}O_7$ requires: 421.1288), 393.0983 ($C_{22}H_{17}O_7$ requires: 393.0974), 203.0388 ($C_{11}H_7O_4$ requires: 203.0344). ^{1}H Nmr (DMSO-d_6): δ 1.42 (9H, s, C-16-CH_3 x 2 and C-11-CH_3), 1.57 (3H, br s, C-11-CH_3), 3.06 (2H, br d, J=7.0 Hz, C-9-H x 2), 5.06 (1H, m, C-10-H), 5.70 (1H, d, J= 10.0 Hz, C-15-H), 6.22 (1H, d, J=0.5 Hz, C-6-H), 6.48 (1H, s, C-3'-H), 6.54 (1H, dd, J=0.5 and 10.0 Hz, C-14-H), 6.70 (1H, s, C-6'-H), 13.21 (1H, s, C-5-OH); (acetone-d_6): δ 1.44 (6H, s, C-16-CH_3 x 2), 1.47, 1.58 (each 3H, br s, C-11-CH_3), 3.16 (2H, br d, J=7.0 Hz, C-9-H x 2), 5.14 (1H, m, C-10-H), 5.66 (1H, d, J=10.1 Hz, C-15-H), 6.15 (1H, d, J=0.7 Hz, C-6-H), 6.60 (1H, s, C-3'-H), 6.61 (1H, dd, J=0.7 and 10.1 Hz, C-14-H), 6.88 (1H, s, C-6'-H), 13.25 (1H, s, C-5-OH).

Artonin E Tetraacetate (1a)

A mixture of 1 (9.5 mg), acetic anhydride (0.3 ml), and pyridine (0.1 ml) was kept at room temperature for 3 days and treated as usual. Artonin E tetraacetate (1a) was crystallized from n-hexane-ether to give colorless needles, mp 185-188 °C. EI-Ms: m/z 604 [M^+], 562, 547, 519, 505, 503. ^{1}H Nmr (DMSO-d_6): δ 1.28 (3H, br s, C-11-CH_3), 1.45 (6H, s, C-16-CH_3 x 2), 1.53 (3H, br s, C-11-CH_3), 2.10 (3H, s, $COCH_3$), 2.32 (6H, s, $COCH_3$ x 2), 2.33 (3H, s, $COCH_3$), 3.32 (2H, br, overlapping with H_2O signal, C-9-H x 2), 4.92 (1H, m, C-10-H), 5.87 (1H, d, J=10.0 Hz, C-15-H), 6.53 (1H, dd, J=0.6 and 10.0 Hz, C-14-H), 6.65 (1H, d, J=0.6 Hz, C-6-H), 7.45 (1H, s, C-3'-H), 7.61 (1H, s, C-6'-H).

Artonin F (2)

Compound 2 was obtained as yellow needles, mp 248 °C, $[\alpha]_D$ 0°. $FeCl_3$ test: positive (green). Mg-HCl test: positive (orange). Uv λ_{max}^{EtOH} nm (log ε): 204 (4.62), 229 (4.45), 257 (4.38), 278 (4.40), 335 (3.95), 390 (4.04). Uv $\lambda_{max}^{EtOH+AlCl_3}$ nm (log ε): 233 (4.44), 250 (sh 4.38), 287 (4.41), 322 (4.10), 354 (3.99), 428 (4.01). Ir ν_{max}^{KBr} cm^{-1} : 3400 (br), 1650, 1550, 1470. EI-Ms: m/z 502 [M^+], 487 (base peak), 459, 447. HR-Ms: m/z 502.1982 ($C_{30}H_{30}O_7$ requires 502.1992), 487.1726 ($C_{29}H_{27}O_7$ requires 487.1757), 459.1422 ($C_{27}H_{23}O_7$ requires 459.1444), 447.1455 ($C_{26}H_{23}O_7$ requires 447.1444). ^{1}H Nmr (acetone-d_6): δ 1.33 (3H, s, C-11-CH_3), 1.46, 1.49 (each 3H, s, C-21-CH_3), 1.66 (3H, s, C-11-CH_3), 1.66 (3H, br s, C-16-CH_3), 1.80 (3H, br s, C-16-CH_3), 2.36 (1H, t, J=15.1 Hz, C-9-H), 3.22 (1H, dd, J=7.1 and 15.1 Hz, C-10-H), 3.31 (2H, br d, J=7.0 Hz, C-14-H x 2), 3.41 (1H, dd, J=7.1 and 15.1 Hz, C-9-H), 5.23 (1H, m, C-15-H), 5.68 (1H, d, J=10.0 Hz, C-20-H), 6.41 (1H, s, C-3'-H), 6.95 (1H, d, J=10.0 Hz, C-19-H), 13.70 (1H, s, C-5-OH).

ACKNOWLEDGEMENT

We are grateful to Eisai Co., Ltd., and to P.T. Eisai Indonesia Co., Ltd., for their kind supply with the plant material. Authors' thanks are due to the members of Botanical Garden of Bogor, Indonesia, for their identification of plant materials.

REFERENCES AND NOTES

1. Part 8 in the series "Constituents of the Moraceae Plants". For part 7 see Y. Hano, Y. Matsumoto, K. Shinohara, J.-Y. Sun, and T. Nomura, Planta Med., submitted.
2. Y. Hano, M. Aida, M. Shiina, T. Nomura, T. Kawai, H. Ohe, and K. Kagei, Heterocycles, 1989, **29**, 1447.
3. Y. Hano, M. Aida, and T. Nomura, J. Nat. Prod., in press.
4. Y. Hano, P. Mitsui, and T. Nomura, Heterocycles, 1990, **30**, 1023.

5. S. Kasahara and S. Hemmi, "Medicinal Herb Index in Indonesia", P.T. Eisai Indonesia, Jakarta, 1986, p. 184.
6. a) Y. Fujimoto, J. Uzawa, S. Suhanda, A. Soemartono, M. Sumatra, and Y. Koshihara, 29th Symposium on the Chemistry of Natural Products, Symposium Paper, p. 721, Aug. 1987, Sapporo, Japan; b) Y. Koshihara, Y. Fujimoto, and H. Inoue, Biochem. Pharmacol., 1988, **37**, 2161; c) J. Nakano, K. Uchida, and Y. Fujimoto, Heterocycles, 1989, **29**, 427.
7. M. U. S. Sultanbawa and S. Surendrakumar, Phytochemistry, 1989, **28**, 599.
8. T. Nomura, T. Fukai, S. Yamada, and M. Katayanagi, Chem. Pharm. Bull., 1978, **26**, 1394.
9. M. Takayama, T. Fukai, and T. Nomura, Mass Spectrosco. (Japan), 1989, **37**, 129.
10. a) B. Jackson, P.J. Owen, and F. Sheinmann, J. Chem. Soc. (C), 1971, 3389; b) A. Arnone, G. Cardillo, L. Merlini, and R. Mondelli, Tetrahedron Lett., 1967, 4201.
11. T. Fukai and T. Nomura, Phytochemistry, 1989, **27**, 259.

Received, 19th February, 1990