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Artocarpol F, a phenolic compound with a novel skeleton, isolated from *Artocarpus rigida*

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Abstract—A novel phenolic compound containing an oxepine ring, artocarpol F (**1**) was isolated from the root bark of *Artocarpus rigida*. The structure including relative configuration was elucidated by spectroscopic data and computer-generated 3D drawing.

Various constituents isolated from the bark of *Artocarpus rigida* (Moraceae) have been reported by Nomura et. al.[1,2] In previous papers,[3,4] we reported five novel constituents containing an oxepane ring, artocarpols A–E, from the root bark of *A. rigida*. A further search for structurally interesting and bioactive compounds from this plant resulted in the isolation of a novel phenolic compound with an oxepine ring, artocarpol F (**1**). Here we describe the isolation and structure elucidation of **1**.

The roots of *A. rigida* were collected at Ping-Tung Hsien, Taiwan, in July 1998. The acetone extract of the root bark was chromatographed over silica gel. Elution with cyclohexane/acetone (1:0→0:1), in which a fraction eluted with cyclohexane/acetone (1:1) was purified by a silica gel column (C_6H_{12}-CH_2Cl_2-$(CH_3)_2CO$, 5:3:1.5) to afford artocarpol F.

The molecular formula, $C_{29}H_{32}O_6$, of artocarpol F {$[\alpha]_D^{25}$ −40 (*c* 0.2, acetone)}was established by HREIMS [*m*/*z* 476.2177, $[M]^+$, −2.2 mmu]. The IR absorption of **1** implied the presence of OH (3350 cm^{-1}) and aromatic ring (1622 cm^{-1}) moieties. The UV spectrum showed absorption maxima at 212 (4.51) and 297 (4.17) nm and was similar to that of artocarpols A–E,[3,4] which indicated an unconjugated aromatic system.[5] ^1H and ^{13}C NMR data (Table 1) revealed signals due to a trisubstituted and a tetrasubstituted benzene ring (B and A), a 3,3-dimethylallyl group located on an aromatic ring, as well as two sp^3 methylenes, three sp^3 methines, three tertiary Me groups, and two oxygenated quarternary carbons. The proposed structure for artocarpol F was deduced from extensive analysis of the 1D and 2D NMR data, including those from COSY, HMQC, HMBC, and NOESY experiments in $CDCl_3$ (Table 1).

The connectivity of H_2-16 to H-17 was revealed by the COSY data. In addition, the HMBC correlations between Me-19 to C-18 and C-17; H-17 to C-18 and C-16; and H-16β to C-17 established the connection between C-16 to C-19. H-16α showed HMBC correlations with C-10 and C-18, an oxygenated quarternary carbon, supported the connection of the C-ring and D-ring by the bonds of C_9–O–C_{18} and C_{10}–C_{16}.

The COSY correlations between H_2-20 to H-21; H-21 to H-22 and HMBC correlations (Table 1) established the E-ring moiety. The HMBC cross-peak of H-20 to C-18 and the NOESY cross-peak of H-17 to H-22 indicated that the D-ring and E-ring were connected by the bonds of C_{17}–O–C_{22} and C_{18}–C_{20}. The structure of the F-ring moiety also supported by the 1D and 2D NMR data (Table 1). In the EI-MS of **1** (Fig. 1), a base peak at *m*/*z* 326 $[M-b\text{-}C_5H_8+2H]^+$, and the characterized peaks at *m*/*z* 293 $[M-a+1]^+$, 225 $[293-C_5H_9+1]^+$, and 185 $[a+1]^+$ also supported the characterization of **1**.

The NOESY experiment of **1** showed cross-peaks as shown in the computer-generated 3D drawing (Fig. 2). The relative configurations at C-17, C-18, C-21, and C-22 were based on NOESY correlations of H-17/H-

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Table 1. 1D and 2D NMR data (δ in ppm, J in Hz) of **1** in acetone-d_6[a]

	δ_H	δ_C	HMBC (^{1}H)
1	6.65 (1H, s)	114.0	
1a		156.7*	1, 4
2		153.0	11
3		126.3	1, 4, 11
4	6.71 (1H, s)	107.9	
4a		140.2	1, 4
5	7.43 (1H, d, 8.4)	122.4	
6	6.82 (1H, dd, 8.4, 2.0)	113.4	
7	8.41 (1H, s, OH)	152.3**	
8	6.96 (1H, d, 2.0)	99.2	
8a		157.6*	5, 8
9		151.1**	
9a		123.2	6, 8
10		128.5	16α
11α	3.22 (1H, dd, 14.4, 6.4)	27.9	12
11β	3.33 (1H, dd, 14.4, 6.4)		12
12	5.13 (1H, t, 6.4)	125.1	11, 14, 15
13		131.5	14, 15
14	1.44 (3H, s)	18.5	12
15	1.57 (3H, s)	26.5	12
16α	1.36 (1H, m)	22.4	17
16β	1.71 (1H, m)		17
17	2.31 (1H, dd, 14.4, 2.8)	65.3	16β, 19, 22
18		82.7	16α, 17, 19, 20
19	1.34 (3H, s)	25.4	20
20	2.45 (2H, m)	48.6	19
21	3.29 (1H, dd, 12.8, 6.4)	53.8	20, 22
22	5.04 (1H, d, 2.8)	98.7	
23		80.3	22
24	1.07 (3H, s)	23.6	
25	1.26 (3H, s)	31.3	

[a] Arbitrary numbering according to Fig. 1.
*, ** Values may be interchanged.

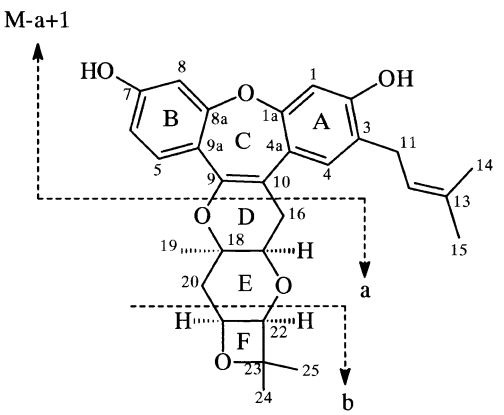

Figure 1. MS of **1** (major fragmentation).

16α, Me-19/H-17, H-20α/H-21, H-22/H-17, and H-21/H-22, while H-17, Me-19, H-21, and H-22 adopted the α-configuration. Further experiments are required to elucidate the absolute stereochemistry of **1**. From the above results, artocarpol F was characterized as **1**.

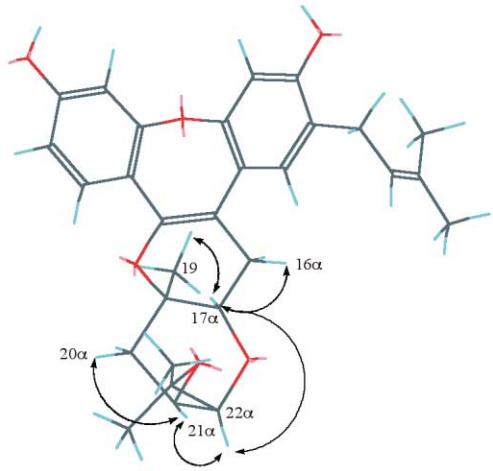

Figure 2. Selected NOESY correlations and relative stereochemistry for artocarpol F (**1**).

Based on the information from ^{1}H, COSY, and NOESY spectra, a computer-assisted 3D structure (Fig. 2) was obtained using the molecular modelling program CS CHEM 3D V3.5.1, using MM2 force field calculations for energy minimization. The calculated distances between H-16α and H-17 (2.28 Å), H-17 and Me-19 (1.11 Å), Hα-20 and H-21 (3.30 Å), H-17 and H-22 (4.00 Å), and H-21 and H-22 (3.19 Å), are all less than 4.00 Å, which were consistent with the well-defined NOESY experiments observed between each of these proton pairs. Thus, artocarpol F was characterized as 7′,7′-dimethyl-5′,7′-epoxypyrano[3′,2′:2,3]-2-(3-methyl-but-2-enyl)-dibenzo[*b*,*f*]pyrano[2,3-*d*]oxepin-3,7-diol **1**, with a configuration as shown in Fig. 2.

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