New Diarylheptanoids from *Amomum muricarpum* ELMER

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Two new diarylheptanoids, designated muricarpones A and B, together with three known diarylheptanoids, 1,7-di-(3′,4′-dihydroxyphenyl)-4-hepten-3-one, 1-(3′,4′-dihydroxyphenyl)-7-(4″-hydroxyphenyl)-4-hepten-3-one, and 1,7-bis(*p*-hydroxyphenyl)-4-hepten-3-one, were isolated from the rhizomes of *Amomum muricarpum* ELMER (Zingiberaceae). Their structures were determined using spectroscopic analyses.

Key words *Amomum muricarpum*; Zingiberaceae; diarylheptanoid; muricarpone

Amomum muricarpum ELMER (Zingiberaceae) is a medicinal plant 2—3 m tall which is distributed in dense forests in Guangdong and Guangxi provinces (China) at 300—1000 m above sea level.[1] The plant is also distributed in the Philippines and recently was found in Vietnam by a group of botanic taxonomists of the Vietnam Academy of Science and Technology. The lack of phytochemical reports on *A. muricarpum* prompted us to investigate the species that grows in Vietnam. We succeeded in the isolation of the two new diarylheptanoids **1** and **2** together with the three known compounds **3**—**5**, of which the isolation and structure determination are described in this paper.

The extraction of the oven-dried rhizomes of *A. muricarpum* with MeOH and sequential fractionation using solvents of increasing polarities gave *n*-hexane-, CH_2Cl_2-, EtOAc-, and 1-BuOH-soluble fractions. The isolation of compounds **1**—**5** (Fig. 1) was achieved *via* column-chromatographic separation of the CH_2Cl_2-soluble fraction on silica gel and purification of the obtained fractions by repeated preparative reversed-phase octadecyl silica (ODS) gel HPLC.

Compound **1** was isolated as a syrup, $[\alpha]_D^{25}$ −7.1°. Its molecular formula was determined to be $C_{20}H_{24}O_6$ by negative-ion high-resolution (HR)-FAB-MS. The IR spectrum showed a hydroxyl absorption band at 3305, a ketone band at 1700, and aromatic ring bands at 1606, 1522, and 1448 cm^{-1}. The ^1H-, ^{13}C-NMR (Table 1), and distortionless enhancement by polarization transfer (DEPT) spectra of **1** showed the presence of two sets of identical aromatic systems and seven carbons of a hydroxyheptanone [δ_C 211.6 (s), 77.8 (d), 48.1 (t), 46.1 (t), 36.7 (t), 31.5 (t), 29.9 (t)]. 3,4-Dihydroxy substitution patterns of two benzene rings were deduced from the ^1H-NMR [δ_H 6.43 (d, J=8.1 Hz), 6.42 (d, J=8.1 Hz); 6.37 (br s), 6.36 (br s); 6.22 (dd, J=8.1, 2.0 Hz), 6.21 (dd, J=8.1, 2.0 Hz)] and ^{13}C-NMR spectroscopic data. The presence of a methoxyl group [δ_H 3.19 (s), δ_C 57.0 (q)] in the heptanone chain was suggested from the chemical shifts of the oxygenated methine group [δ_H 3.56 (quintet, J=6.6 Hz), δ_C 77.8 (d)]. The locations of the carbonyl group at C-3 and methoxyl group at C-5 were unambiguously determined with the ^1H–^1H correlated spectroscopy (COSY) and heteronuclear multiple bond correlation (HMBC) spectra of **1** (Fig. 2). The absolute stereochemistry of the methoxyl group was determined to be 5*R* on the basis of the negative sign of the optical rotation and positive Cotton effect associated with the carbonyl $n\rightarrow\pi^*$ transition at 350 nm ($\Delta\varepsilon$ +0.57) in the circular dichroism (CD) spectrum of **1** in comparison with those of a series of analogous compounds.[2] Thus the structure of **1** was determined to be (5*R*)-5-methoxy-1,7-bis(3,4-dihydroxyphenyl)-3-heptanone, which was given the trivial name muricarpone A.

Compound **2** was obtained as a syrup. Its molecular formula was determined to be $C_{19}H_{22}O_5$ based on the results of negative-ion HR-FAB-MS. The IR spectrum exhibited a hydroxyl absorption band at 3286 and a ketone band at 1696 cm^{-1}. The ^1H-, ^{13}C-NMR (Table 1), and DEPT spectra of **2** disclosed the presence of seven carbons of the heptane chain including the isolated carbonyl group [δ_C 213.7 (s), 45.3 (t), 43.6 (t), 35.9 (t), 32.1 (t), 30.4 (t), 24.3 (t)] and two identical 3,4-dihydroxyphenyl moieties. The asymmetrical nature of the heptane chain was evident from the appearance of all seven carbons in the ^{13}C-NMR spectrum. The carbonyl group was located at C-3 by comparing the ^{13}C chemical shifts of **2** with those of yakuchinone A.[3] This assignment was further confirmed in the HMBC experiment (Fig. 3).

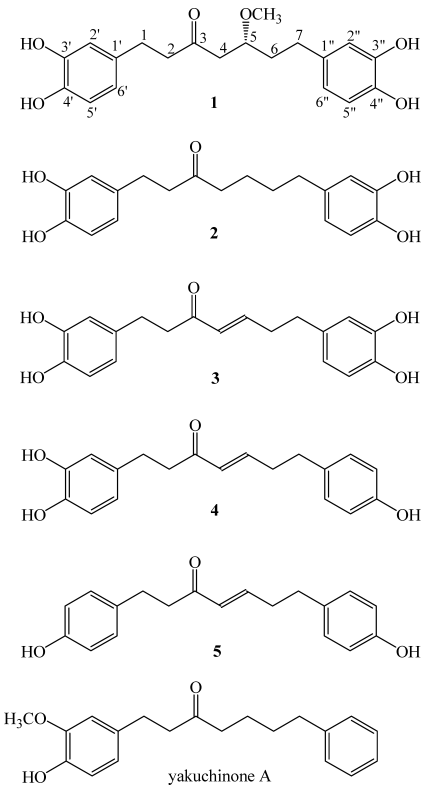

Fig. 1. Structures of Compounds **1**—**5**

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Table 1. ^{1}H- and ^{13}C-NMR Spectroscopic Data of **1** and **2** (CD_3OD)[a)]

C/H	**1**		**2**	
	C	H	C	H
1a	29.9	2.35 m	30.4	2.63 t (6.6)
b				2.66 t (6.6)
2a	46.1	2.37 m	45.3	2.62 d (16.8)
b				2.65 d (16.8)
3	211.6		213.7	
4	48.1	2.21 m	43.6	2.38 t (6.8)
5	77.8	3.56 quintet (6.6)	32.1	1.49 m
6	36.7	1.41 m	24.3	1.49 m
7	31.5	2.17 m	35.9	2.40 t (6.8)
1′	134.0		134.1	
2′	116.48	6.36 br s	116.49	6.58 d (1.9)
3′	145.92		146.0	
4′	144.0		144.1	
5′	116.2	6.43 d (8.1)	116.3	6.64 d (8.3)
6′	120.59	6.22 dd (8.1, 2.0)	120.6	6.45 dd (8.3, 1.9)
1″	134.8		135.3	
2″	116.50	6.37 br s	116.53	6.60 d (1.9)
3″	145.94		146.1	
4″	144.2		144.4	
5″	116.3	6.42 d (8.1)	116.4	6.64 d (8.3)
6″	120.64	6.21 dd (8.1, 2.0)	120.7	6.46 dd (8.3, 1.9)
5-OCH_3	57.0	3.19 s		

a) Protons and carbons were assigned on the basis of DEPT, heteronuclear single quantum correlation (HSQC), and HMBC experiments. The chemical shifts δ are in ppm, coupling constant J in Hz in parentheses.

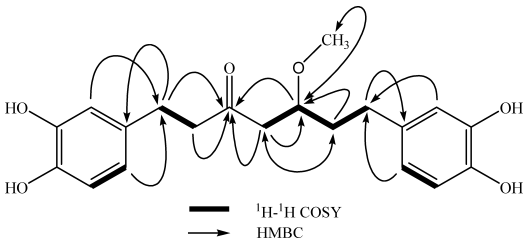

Fig. 2. ^{1}H–^{1}H COSY and Selective HMBC Correlations of **1**

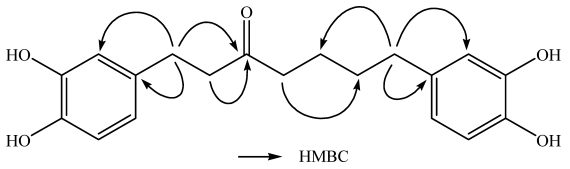

Fig. 3. Selective HMBC Correlations of **2**

Thus the structure of **2** was determined to be 1,7-bis(3,4-dihydroxyphenyl)-3-heptanone, which was given the trivial name muricarpone B.

Compound **3** was previously isolated from *Viscum cruciatum* (Viscaceae),[4] **4** from *Alnus rubra* (Betulaceae),[5] and **5** from *Alnus japonica*.[6] They showed ^{1}H- and ^{13}C-NMR spectroscopic data which agreed well with the values reported in the literature.[4—6] Very few reports on diarylheptanoids from the genus *Amomum* (Zingiberaceae) have appeared in recent years,[7,8] although they may receive renewed scrutiny as a future source of new diarylheptanoids from nature.

Experimental

General Procedure Optical rotation was measured on a Union Giken PM-101 digital polarimeter. FT-IR spectra were recorded on a Horiba FT-710 spectrophotometer. ^{1}H- (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded using a JEOL JNM-α 400 NMR spectrometer with TMS as an internal standard. Negative-ion HR-FAB-MS were measured on a JEOL SX-102 mass spectrometer with PEG-400 as a calibration matrix. HPLC was carried out with a JASCO PU-1580 pump and a UV-2075 Plus detector (set at 254 nm) on YMC ODS columns (150×4.6 mm i.d. in analytical and 150×20 mm i.d. in preparative scales) at the corresponding flow rates of 0.5 and 5 ml/min. Silica gel 60 (0.063—0.200 mm, Merck, Germany) and ODS gel (YMC, Japan) were used for open-column chromatography. TLC was carried out on Merck TLC plates (Si gel 60 F_{254}) and detected by spraying with 10% H_2SO_4 in 50% EtOH, followed by heating on a hot plate at 200 °C.

Plant Material The rhizomes of *A. muricarpum* were collected from Tam Dao, Vinh Phuc province, Vietnam, and identified by Mr. Nguyen Quoc Binh, a botanic taxonomist of the Institute of Ecology and Biological Resources, Vietnam Academy of Science and Technology, Hanoi, in October 2003. A voucher specimen (no. VN 1199) is deposited in the Herbarium of the Institute of Ecology and Biological Resources.

Extraction and Isolation of 1—5 The fresh rhizomes of *A. muricarpum* (7.3 kg) were oven-dried at 40 °C to the weight of 0.84 kg, then powdered and extracted with MeOH by percolation at room temperature (three times, for 3 d each). After filtration and concentration under reduced pressure, the MeOH extract (80 g) obtained was suspended in H_2O and fractionated successively with *n*-hexane, CH_2Cl_2, ethyl acetate, and 1-BuOH. The *n*-hexane-, CH_2Cl_2-, EtOAc-, and 1-BuOH-soluble fractions were obtained in the weights of 4.3 g, 12.5 g, 25.7 g, and 16.2 g, respectively. The CH_2Cl_2-soluble fraction was chromatographed on a silica gel open column using $CHCl_3$, $CHCl_3$–MeOH (9 : 1), and MeOH as solvent systems to give fractions I (0.5 g), II (1.5 g), III (4.5 g), IV (3.9 g), and V (0.9 g). Fraction III eluted with $CHCl_3$–MeOH (9 : 1) was subjected to open-column chromatography on silica gel using a solvent mixture of $CHCl_3$–MeOH (20 : 1). The fractions obtained were further separated and purified *via* repeated HPLC (MeOH–H_2O, 3 : 2) to afford compounds **1** (8.8 mg), **2** (302 mg), **3** (20 mg), **4** (14.8 mg), and **5** (2.6 mg).

Muricarpone A (**1**): Syrup, $[\alpha]_D^{25}$ −7.1° (c=0.88, MeOH). UV (MeOH) λ_{max} (log ε): 283 (3.73), 222 (4.00). IR ν_{max} (film) cm^{-1}: 3305, 1700, 1606, 1522, 1448, 1365, 1284, 1195, 1112, 1021, 955. CD (MeOH): $\Delta\varepsilon$ (nm): −0.91 (215), +0.75 (259), +0.57 (350) (c=2.14×10^{-5} M). ^{1}H- and ^{13}C-NMR: see Table 1. Negative-ion HR-FAB-MS: m/z 359.1475 $[M-H]^-$ (Calcd for $C_{20}H_{23}O_6$: 359.1495).

Muricarpone B (**2**): Syrup. IR ν_{max} (film) cm^{-1}: 3286, 1696, 1606, 1523, 1443, 1365, 1283, 1195, 1113, 1020, 954. ^{1}H- and ^{13}C-NMR: see Table 1. Negative-ion HR-FAB-MS: m/z 329.1362 $[M-H]^-$ (Calcd for $C_{19}H_{21}O_5$: 329.1389).

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