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Chemical constituents from the bark of *Cerbera manghas*

Xiao-Po Zhang^{ab}, Ming-Sheng Liu^{bc}, Jun-Qing Zhang^{bc}, Sheng-Li Kang^{bc} and Yue-Hu Pei^{a*}

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Two new compounds, 1,3-bis(*m*-carboxylphenyl)-propan-2-one (**1**) and 2-(*m*-carboxylphenyl)-3-(*m*-carboxylbenzyl) succinic acid (**2**), were isolated from the barks of *Cerbera manghas*, and their structures were established on the basis of spectroscopic methods.

Keywords: Apocynaceae; *Cerbera manghas* L.; 2-(*m*-carboxylphenyl)-3-(*m*-carboxylbenzyl) succinic acid; 1,3-bis(*m*-carboxylphenyl)-propan-2-one

1. Introduction

Cerbera manghas L. (Apocynaceae) belongs to mangrove plant and is widely distributed in the coastal areas of Southeast Asia, tropical Australia, Polynesia, and Indian Ocean [1]. Extracts of *C. manghas* have shown analgesic, anticonvulsant, cardiotoxic, and hypotensive activities [2]. Previous phytochemical investigations resulted in the isolation of many secondary metabolites, including cardenolides [3,4], lignans [5–8], and iridoid monoterpenes [9]. During the course of our investigation, two new compounds were isolated from the bark of *C. manghas*. This paper reports the isolation and structural elucidation of these compounds (**1**, **2**).

2. Results and discussion

Compound **1** was obtained as colorless needles. Its molecular formula was determined as C₁₇H₁₄O₅ by HR-ESI-MS at *m/z* 297.0792 [M–H][–]. The IR spectrum of **1** indicated the presence of hydroxyl

(3440 cm^{–1}), carbonyl (1715 cm^{–1}), conjugated carbonyl (1684 cm^{–1}) groups, and benzene ring (1590, 1456 cm^{–1}) moiety. The ¹H and ¹³C NMR spectra indicated the existence of two methylenes at δ_H 3.98 (4H, s, H-1, 3) and δ_C 48.1, two carboxyl groups at δ_H 12.70 (2H, brs) and δ_C 167.4, two 1,3-disubstituted benzene rings at δ_H 7.76 (2H, brs, H-2', 2''), 7.79 (2H, d, *J* = 7.8 Hz, H-4', 4''), 7.42 (2H, t, *J* = 7.8 Hz, H-5', 5''), 7.40 (2H, d, *J* = 7.8 Hz, H-6', 6''), and δ_C 135.2 (C-1', 1''), 130.9 (C-2', 2''), 130.9 (C-3', 3''), 127.6 (C-4', 4''), 128.5 (C-5', 5''), 134.3 (C-6', 6''), and one carbonyl moiety at δ_C 205.2 as shown in Table 1. In the HMBC experiment, long-range correlations between H-1, H-3 at δ 3.98 and C-1', C-1'' at δ 135.2, C-2', C-2'' at δ 130.9, C-6', C-6'' at δ 134.3 revealed that the methylene groups of C-1 and C-3 were attached to the benzene rings of C-1' and C-1'', respectively. HMBC correlations between H-1, H-3 at δ 3.98 and C-2 at δ 205.2 indicated that both the two methylene groups were linked with carbonyl group, and

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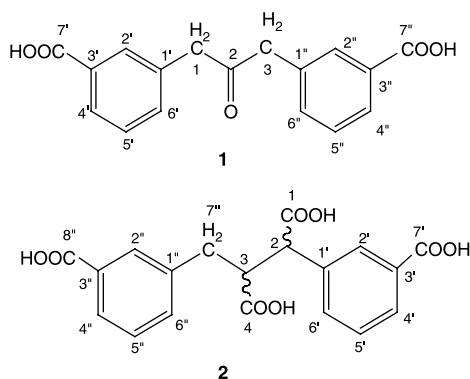
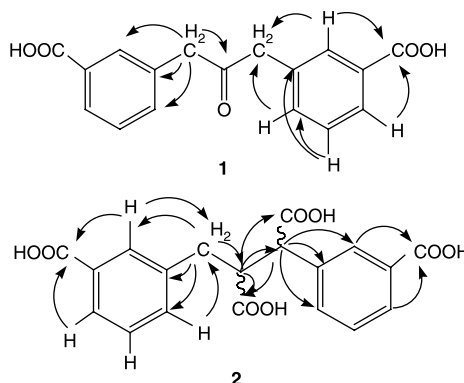
Table 1. ^1H and ^{13}C NMR spectral data for compounds **1** and **2** in $\text{DMSO-}d_6$.

No.	1		2	
	^1H (J, Hz)	^{13}C	^1H (J, Hz)	^{13}C
1	3.98 s	48.1	–	173.0
2	–	205.2	3.77 d (10.8)	53.8
3	3.98 s	48.1	3.27 dt (3.6, 10.8)	50.9
4	–	–	–	173.2
1'	–	135.2	–	139.1
2'	7.76 s	130.9	7.90 s	129.1
3'	–	130.9	–	130.9
4'	7.79 d (7.8)	127.6	7.82 brd (7.8)	128.6
5'	7.42 t (7.8)	128.5	7.45 t (7.8)	128.8
6'	7.40 d (7.8)	134.3	7.56 brd (7.8)	133.0
7'	–	167.4	–	167.3
1''	–	135.2	–	137.5
2''	7.76 s	130.9	7.76 brs	129.6
3''	–	130.9	–	130.9
4''	7.79 d (7.8)	127.6	7.78 brd (8.0)	127.6
5''	7.42 t (7.8)	128.5	7.42 t (8.0)	128.5
6''	7.40 d (7.8)	134.3	7.43 brd (8.0)	133.3
7''	–	167.4	2.90 t (10.8)	37.0
8''	–	–	2.97 brd (10.8)	–
OH	12.70 brs	–	12.82 brs	–

the correlations between H-2', H-2'' at δ 7.76, H-4', H-4'' at δ 7.79, and C-7', C-7'' at δ 167.4 showed that the two carboxyl groups of C-7' and C-7'' were attached to C-3' and C-3'' of the aromatic rings, respectively. Therefore, compound **1** was elucidated as a new compound and assigned to be 1,3-bis(*m*-carboxylphenyl)-propan-2-one (Figures 1 and 2).

Compound **2** was obtained as white amorphous powder. The HR-ESI-MS gave

a molecular ion $[\text{M}-\text{H}]^-$ at m/z 371.0775, consistent with a molecular formula of $\text{C}_{19}\text{H}_{16}\text{O}_8$. Comparison of its ^1H and ^{13}C NMR spectra with those of **1** showed that they shared many spectral features in common. The differences of their NMR spectra could be accounting for the presence of two carboxyl groups and two methine groups and the disappearance of the carbonyl group. Based on these and further analysis

Figure 1. Structures of **1** and **2**.Figure 2. Main HMBC correlations of **1** and **2**.

of 1D- and 2D-NMR spectral data, including DEPT, HSQC, and HMBC experiments, three partial substructures were established, which were fragments **A** (*m*-carboxylphenyl), **B** (*m*-carboxylbenzyl), and **C** (succinic acid) as shown in Figure 3. In the HMBC experiment, cross-peaks between H-3 at δ 3.27 and C-1'' at δ 137.5, H-7'' at δ 2.90, 2.97 and C-3 at δ 50.9, C-4 at δ 173.2 indicated that fragments **B** and **C** were connected between C-7'' at δ 37.0 and C-3 at δ 50.9, and cross-peaks between H-2 at δ 3.77 and C-1' at δ 139.1, C-2' at δ 129.1, C-6' at δ 133.0 revealed that fragments **A** and **C** were linked between C-2 at δ 53.8 and C-1' at δ 139.1. Finally, the planar structure of **2** was established as shown in Figure 1. The coupling constant of H-2 and H-3 (10.8 Hz) indicated a trans relationship of them, whereas the absolute stereostructure of **2** was undetermined. Thus, compound **2** was characterized as a new compound and assigned to be 2-(*m*-carboxylphenyl)-3-(*m*-carboxylbenzyl) succinic acid.

3. Experimental

3.1 General experimental procedures

Melting points were determined on an XT-5 melting point apparatus and are uncorrected. Optical rotation was measured on a WZZ-1 spectrometer. IR spectra were obtained on a JASCO-FT-IR-4100 infrared spectrophotometer. UV spectra were taken on a UV-9100 spectrophotometer. The NMR data were recorded on a Bruker AV-600 spectrometer (600 MHz for ^1H and 150 MHz for ^{13}C) in $\text{DMSO}-d_6$ with TMS as internal standard. Chromatography was performed on silica gel column (200–300 mesh, Qingdao Haiyang Chemical Co. Ltd, Qingdao, China)

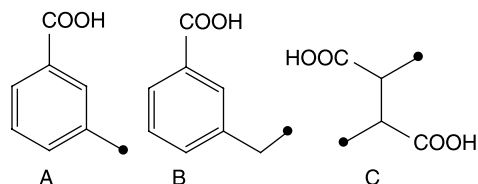


Figure 3. Structures of fragments **A**, **B**, and **C**.

and Sephadex LH-20 column (Pharmacia Biotech, Uppsala, Sweden).

3.2 Plant material

The bark of *C. manghas* L. was collected from Hainan Island, China, in August 2006. A voucher specimen (No. CML-0608) was identified by Prof. Wei-Ping Chen, which is deposited in Department of Pharmacy, Hainan Medical College.

3.3 Extraction and isolation

The air-dried bark was exhaustively extracted with 95% ethanol after grounding into powder (10 kg). The solvent was removed under reduced pressure to afford an extract (1.5 kg). Then the extract was successively partitioned with petroleum ether, chloroform, ethyl acetate, and *n*-butanol. The chloroform extract (100 g) was subjected to a silica gel chromatography, eluting with a gradient of CHCl_3 –MeOH (1:0–0:1, v/v), to give eight fractions (1–8). Fraction 3 (600 mg) was applied to silica gel column chromatography, eluting with CHCl_3 –MeOH (85:15, v/v), to furnish five fractions (A–E). Fraction D (50 mg) was separated by a column of Sephadex LH-20 eluted with CHCl_3 –MeOH (1:1) to afford compound **1** (15 mg). Fraction 6 (1.0 g) was subjected to silica gel column, eluting with CHCl_3 –MeOH (75:25, v/v) to give five fractions (I–V). Fraction IV (100 mg) was purified by Sephadex LH-20 column chromatography eluted with MeOH, to furnish compound **2** (25 mg).

3.3.1 1,3-Bis(*m*-carboxylphenyl)-propan-2-one (**1**)

Colorless needles, mp: 281.0–284.2°C; UV (MeOH) λ_{max} (log ϵ) 242 (3.80) nm; IR (KBr) ν_{max} 3440, 2920, 1715, 1684, 1590, 1456, 1424, 1020, 775 cm^{-1} ; ^1H and ^{13}C NMR spectral data [^1H (600 MHz) and ^{13}C (150 MHz) in $\text{DMSO}-d_6$], see Table 1; Main HMBC correlations, see Figure 2; negative ion ESI-MS m/z : 297 [$\text{M}-\text{H}$] $^-$, negative ion

HR-ESI-MS m/z : 297.0792 $[M-H]^-$ (calcd for $C_{17}H_{13}O_5$, 297.0763).

3.3.2 2-(m-carboxylphenyl)-3-(m-carboxylbenzyl) succinic acid (2)

White amorphous powder, $[\alpha]_D = +18$ ($c = 0.01$, MeOH); UV (MeOH) λ_{max} ($\log \epsilon$) 240 (3.50) nm; IR (KBr) ν_{max} 3400, 2920, 1695, 1590, 1421, 1020, 931, 771 cm^{-1} ; 1H and ^{13}C NMR spectral data [1H (600 MHz) and ^{13}C (150 MHz) in DMSO- d_6], see Table 1; main HMBC correlations, see Figure 2; negative ion ESI-MS m/z : 371 $[M-H]^-$, negative ion HR-ESI-MS m/z : 371.0755 $[M-H]^-$ (calcd for $C_{19}H_{15}O_8$, 371.0767).

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