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J. Nat. Prod., **1994**, 57 (9), 1313-1315 • DOI:
10.1021/np50111a025 • Publication Date (Web): 01 July 2004

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DC 20036

NOVEL ANTHRAQUINONES FROM *DAMNACANTHUS INDICUS*

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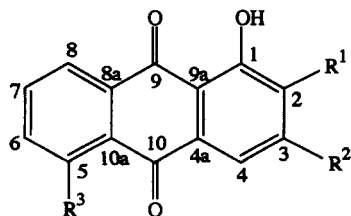
ABSTRACT.—Three new anthraquinones, 1,3-dihydroxy-2-carboethoxy-9,10-anthraquinone [1], 1,3,5-trihydroxy-2-carboethoxy-9,10-anthraquinone [2], and 1,5-dihydroxy-2-methoxy-9,10-anthraquinone [3], have been isolated from the rhizomes and roots of *Damnacanthus indicus*, and their structures were elucidated by spectroscopic methods.

Damnacanthus indicus (L.) Gaertn. f. (Rubiaceae) is an evergreen shrub that grows throughout eastern Asia and Taiwan and is widely distributed in broad-leaved forests at low to high altitudes (1). The whole plant possess anti-inflammatory, antirheumatic, and circulation-promoting properties and is used as a Chinese folk medicine (2). Previous chemical investigations of this plant have described the isolation of anthraquinones (3,4). Three minor anthraquinones, 1–3, were isolated from the rhizomes and roots of *D. indicus*. This paper describes the isolation and structural elucidation of these new anthraquinones.

The CHCl_3 residue obtained from the Me_2CO extract of the fresh rhizomes and roots of *D. indicus* afforded three new anthraquinones, compounds 1, 2, and 3, after extensive chromatography.

Compound 1, yellow needles from $\text{CHCl}_3/\text{MeOH}$, mp 189–190°, had the

molecular formula $\text{C}_{17}\text{H}_{12}\text{O}_6$ (M^+ , m/z 312.0630; calcd 312.0627) by hreims. The ir spectrum of 1 showed the presence of three carbonyl absorptions at ν max 1670, 1660, and 1625 (chelated $\text{C}=\text{O}$) cm^{-1} . The ^1H -nmr spectrum indicated a carboethoxyl group at δ 1.49 (3H, t, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$) and 4.54 (2H, q, $J=7.2$ Hz, $\text{COOCH}_2\text{CH}_3$), four aromatic protons of an AA'BB' system at δ 7.80 (2H, m, H-6, -7) and 8.30 (2H, m, H-5, -8), an aromatic proton at δ 7.38 (1H, s, H-4), and two phenolic hydroxyl protons (exchangeable with D_2O) at δ 12.73 (1H, s, OH-3) and 14.73 (1H, s, OH-1). The ^{13}C -nmr spectral data (Table 1) showed two carbonyl carbons, a carboethoxyl group, and twelve aromatic carbons. From these data, compound 1 was concluded to be a 9,10-anthraquinone derivative with tri-substitution in ring C. The C-9 carbonyl carbon signal at δ 186.86 was shifted downfield by 4.91 ppm compared to the C-10 carbonyl carbon signal at δ 181.95, supporting a strong intramolecular hydrogen bonding with the hydroxyl group at C-1 (5). The uv spectrum of 1 showed a shift from 415 nm to 480 nm upon the addition of base confirming that it is a typical 1,3-dihydroxy-9,10-anthraquinone derivative (6). The signal at δ 14.73 due to a chelated hydroxyl proton was shifted downfield from the usual location, placing another carbonyl group ortho to this hydroxyl group. Therefore, the carbo-



	R ₁	R ₂	R ₃
1	COOEt	OH	H
2	COOEt	OH	OH
3	OMe	H	OH

TABLE 1. ^{13}C -Nmr Spectral Data of Compounds **1** and **2** (ppm, in CDCl_3).^a

Carbon	Compound		Carbon	Compound	
	1	2		1	2
C-1	170.13	170.01	C-9	186.86	186.92
C-2	109.38	109.19	C-10	181.95	185.94
C-3	168.48	167.43	C-9a	105.77	105.92
C-4	109.72	109.47	C-4a	137.69	137.39
C-5	127.15	162.93	C-10a	133.65	115.90
C-6	134.47	124.55	C-8a	133.28	133.42
C-7	134.72	137.28	$\text{COOCH}_2\text{CH}_3$	170.61	170.36
C-8	127.59	119.49	$\text{COOCH}_2\text{CH}_3$	62.71	62.74
			$\text{COOCH}_2\text{CH}_3$	14.17	14.14

^aAssignments were made with the aid of DEPT experiments.

ethoxyl group was at the C-2 position, and compound **1** was established as 1,3-dihydroxy-2-carboethoxy-9,10-anthraquinone.

Compound **2**, orange-yellow needles from $\text{CHCl}_3/\text{MeOH}$, mp 198–200°, had the molecular formula $\text{C}_{17}\text{H}_{12}\text{O}_7$ (M^+ 328.0553; calcd 328.0523) by hreims. The ir spectrum of **2** showed the presence of two types of carbonyl absorptions at ν_{max} 1665 and 1630 (chelated $\text{C}=\text{O}$) cm^{-1} . The ^1H - and ^{13}C -nmr spectral data of ring C were almost identical to those of **1** except for signals from ring A. The ^1H -nmr spectrum of **2** indicated three aromatic protons for an ABC system at δ 7.30 (1H, d, $J=8.0$ Hz, H-6), 7.70 (1H, t, $J=8.0$ Hz, H-7) and 7.85 (1H, d, $J=8.0$ Hz, H-8), and a phenolic hydroxyl proton at δ 12.41 (1H, s). The uv spectrum of **2** upon the addition of base showed a λ_{max} shift from 418 nm to 465 nm, similar to norjuzunal (7). The carbonyl carbon signals at δ 186.92 (C-9) and 185.94 (C-10) revealed that both had strong intramolecular hydrogen bonding with the hydroxyl groups at C-1 and C-5. Compound **2** was confirmed as a 1,3,5-trihydroxy-9,10-anthraquinone derivative. From the signal at δ 14.76 due to a chelated hydroxyl proton, the carboethoxyl group was placed at the C-2 position, thereby establishing compound **2** as 1,3,5-trihydroxy-2-carboethoxy-9,10-anthraquinone.

Compound **3**, orange-red needles

from $\text{CHCl}_3/\text{MeOH}$, mp 192–193°, had the molecular formula $\text{C}_{15}\text{H}_{10}\text{O}_5$ (M^+ 270.0495; calcd 270.0512) by hreims. Its ^1H -nmr spectrum showed the presence of a methoxyl group at δ 4.03 (3H, s), two ortho aromatic coupled protons at δ 7.18 (1H, d, $J=8.4$ Hz, H-3) and 7.89 (1H, d, $J=8.4$ Hz, H-4), three aromatic protons of an ABC system at δ 7.31 (1H, d, $J=8.0$ Hz, H-6), 7.67 (1H, t, $J=8.0$ Hz, H-7) and 7.84 (1H, d, $J=8.0$ Hz, H-8), and two chelated hydroxyl protons (exchangeable with D_2O) at δ 12.86 and 13.09. The chemical shifts of protons in ring C were almost the same as alizalin-2-methyl ether (8), except for signals from the ring-A protons. The uv spectrum of **3** showed a λ_{max} shift from 438 nm to 512 nm after addition of base, indicating that it is a 1,5-dihydroxy-9,10-anthraquinone derivative (6,9). This was confirmed by the presence of two absorptions at 1630 and 1610 cm^{-1} due to two chelated carbonyl groups in the ir spectrum of **3**. The mass spectrum of **3** showed an $[\text{M}-\text{H}_2\text{O}]^+$ peak at m/z 252 (14) which confirmed the ortho relationship of one of the hydroxyl groups with the methoxyl group (10). Therefore, the methoxyl group was linked to the C-2 carbon. On the basis of these spectral data, compound **3** was established as 1,5-dihydroxy-2-methoxy-9,10-anthraquinone.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps

were determined on a Yanaco micro-melting point apparatus and are uncorrected. Ir spectra were measured on a Hitachi-200 spectrophotometer. Uv-vis spectra were recorded on a Hitachi UV-3200 spectrophotometer. Eims were measured on a JEOL SX-102A mass spectrometer. Hreims were measured on a JEOL JMS-HX-110 spectrometer. ¹H- and ¹³C-nmr spectra were recorded on Bruker AM-400 and AMX-400 spectrometers.

PLANT MATERIAL.—The entire fresh plants of *Damnacanthus indicus* were collected in Puli, Nantou County, Taiwan in March 1993. A voucher specimen was deposited at the Department of Biology of National Cheng-Kung University, Tainan, Taiwan.

EXTRACTION AND ISOLATION.—The fresh rhizomes and roots (6.8 kg) of *D. indicus* were extracted with Me₂CO under reflux. The concentrated extract was suspended in H₂O. The suspension was partitioned successively with CHCl₃ and *n*-BuOH. The CHCl₃ fraction (53 g) was chromatographed on a Si gel column and eluted with a *n*-hexane/EtOAc mixture of increasing polarity. Elution was monitored by tlc on Si gel PF₂₅₄ (Merck). The fractions containing anthraquinones were collected and chromatographed on a Si gel column with *n*-hexane-isopropyl ether (10:1) as eluent to give an orange residue. The substance was purified by prep. tlc on Si gel PF₂₅₄ plates, using C₂H₆-EtOAc (50:1) to give compounds **1** (3.8 mg), **2** (3.6 mg), and **3** (2.0 mg).

1,3-Dihydroxy-2-carboethoxy-9,10-anthraquinone [1].—Ir ν max (KBr) 1670, 1660, 1625, 1595, 1575, 1560, 1470, 1435, 1420, 1365, 1330, 1300, 1290, 1265, 1220, 1160, 1100, 1090, 1065, 985, 885, 830, 815, 720 cm⁻¹; uv λ max (MeOH) (log ϵ) 245 (4.46), 284 (4.34), 312 sh (3.89), 415 (3.79) nm; λ max (MeOH+NaOH) (log ϵ) 248 (4.51), 305 sh (4.35), 314 (4.43), 480 (3.97) nm. Eims m/z (75 eV) 312 (M⁺, 32), 266 (100), 238 (27), 182 (7), 154 (7), 127 (5); ¹H nmr (CDCl₃) δ 1.49 (3H, t, $J=7.2$ Hz, COOCH₂CH₃), 4.54 (2H, q, $J=7.2$ Hz, COOCH₂CH₃), 7.38 (1H, s, H-4), 7.80 (2H, m, H-6, -7), 8.30 (2H, m, H-5, -8), 12.73 (1H, s, 3-OH, exchangeable with D₂O), 14.73 (1H, s, 1-OH, exchangeable with D₂O). ¹³C nmr (CDCl₃), see Table 1.

1,3,5-Trihydroxy-2-carboethoxy-9,10-anthraquinone [2].—Ir ν max (KBr) 1665, 1630, 1595, 1575, 1480, 1460, 1420, 1370, 1310, 1240, 1185, 1100, 1010, 925, 870, 800, 770, 725 cm⁻¹; uv λ max (MeOH) (log ϵ) 232 (4.06), 248 (4.03), 285 (3.90), 294 sh (3.87), 311 (3.63), 418 (3.71), 475 sh (3.27) nm; λ max (MeOH+NaOH) (log ϵ) 244 (4.11), 308 (4.04), 465 (3.86), 485 sh (3.82) nm. Eims m/z (75 eV) 328 (M⁺, 44), 282 (100), 254 (46), 226 (7), 199 (4), 198 (11), 170 (15), 142 (11). ¹H nmr (CDCl₃) δ 1.49 (3H, t,

$J=7.2$ Hz, COOCH₂CH₃), 4.54 (2H, q, $J=7.2$ Hz, COOCH₂CH₃), 7.30 (1H, d, $J=8.0$ Hz, H-6), 7.39 (1H, s, H-4), 7.70 (1H, t, $J=8.0$ Hz, H-7), 7.85 (1H, d, $J=8.0$ Hz, H-8), 12.41 (1H, s, 5-OH, exchangeable with D₂O), 12.76 (1H, s, 3-OH, exchangeable with D₂O), 14.76 (1H, s, 1-OH, exchangeable with D₂O). ¹³C nmr (CDCl₃), see Table 1.

1,5-Dihydroxy-2-methoxy-9,10-anthraquinone [3].—Ir ν max (KBr) 1630, 1610, 1590, 1470, 1450, 1380, 1315, 1265, 1160, 1070, 1060, 1000, 935, 790 cm⁻¹. Uv λ max MeOH (log ϵ) 230 (4.23), 256 (4.15), 285 (3.85), 290 sh (3.84), 438 (3.74) nm; λ max (MeOH+NaOH) (log ϵ) 253 (4.35), 278 sh (3.73), 391 (3.33), 512 (3.77) nm. Eims m/z (75 eV) 270 (M⁺, 100), 252 (14), 242 (13), 241 (64), 224 (26), 199 (18), 171 (22), 125 (39). ¹H nmr (CDCl₃) δ 4.03 (3H, s, 2-OCH₃), 7.18 (1H, d, $J=8.4$ Hz, H-3), 7.31 (1H, d, $J=8.0$ Hz, H-6), 7.67 (1H, t, $J=8.0$ Hz, H-7), 7.84 (1H, d, $J=8.0$ Hz, H-8), 7.89 (1H, d, $J=8.4$ Hz, H-4), 12.86 (1H, s, OH, exchangeable with D₂O), 13.09 (1H, s, OH, exchangeable with D₂O).

ACKNOWLEDGMENTS

We thank the National Science Council, Republic of China, for financial support of this work (NSC 82-0208-M-041-008).

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Received 14 March 1994