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NEW ANTHRAQUINONES FROM ELEUTHERINE AMERICANA

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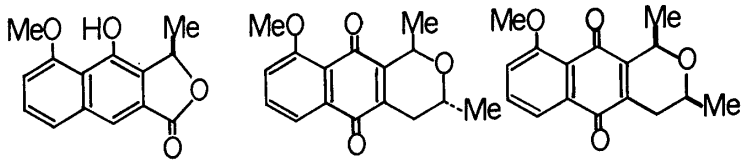
Three minor new anthraquinones were isolated from the bulb of Eleutherine americana Merr. et Heyne. Their structures were elucidated as methyl ethers of 3,4,8-trihydroxy-1-methyl-anthra-9,10-quinone-2-carboxylic acid methyl ester 4-6 by spectral analyses including long-range selective proton decoupling (LSPD) experiments in ^{13}C-NMR.

KEYWORDS——Eleutherine americana; pigment; 3,4,8-trihydroxy-1-methyl-anthra-9,10-quinone-2-carboxylic acid methyl ester; long-range selective proton decoupling (LSPD)

Eleutherine americana Merr. et Heyne (Iridaceae) is widely cultivated in Hainan Island, China, as an ornamental and medicinal plant. The red bulb is used to treat cardiac diseases, especially coronary disorders. We have reported three aromatic compounds, eleutherol, eleutherin, and isoeleutherin, 1-3, as vasodepressants in isolated guinea pig heart.[1] In addition to these naphthalenic compounds, we have isolated three new minor anthraquinone pigments from the same ethanol extract, and have determined the structure to be methyl ethers of 3,4,8-trihydroxy-1-methyl-anthra-9,10-quinone-2-carboxylic acid methyl ester, 4-6, as follows.



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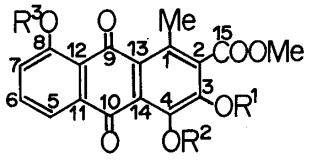


	R^1	R^2	R^3
4	Me	H	H
5	H	Me	H
6	Me	Me	H
7	Me	Me	Me

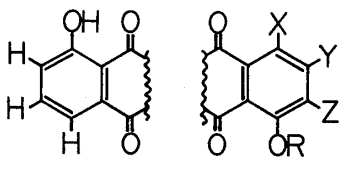
Upon concentration, an ethanol extract of dried and powdered bulb afforded a crude crystalline mixture, which was chromatographed on SiO_2(pet. ether-CH_2Cl_2) to give crystalline

TABLE 1. ^{1}H-NMR and IR Data of Compounds 4-7

Compd	^{1}H-NMR (in $CDCl_3$)									IR ν(C=O) cm^{-1}			
	1-Me	OMe	OH	5-H(dd)	6-H(t)	7-H(dd)	$J_{5,6}$	$J_{5,7}$	$J_{6,7}$	Ester free	Ester H-bond	Quinone free	Quinone H-bond
4	2.57	4.08 3.97	13.60 12.80	7.70	7.56	7.24	7.6	1.7	7.6	1732			1628
5	2.74	2.00 3.98	12.69	7.65	7.58	7.24	7.3	2.3	7.3		1724	1670	1634
6	2.68	4.03 3.99 3.97	12.53	7.66	7.57	7.22	7.1	2.7	7.1	1730		1675	1623
7	2.60	4.00 4.00 3.98 3.98		7.72	7.66	7.26	7.6	2.2	7.6	1739		1678	

compound 4, $C_{18}H_{14}O_7$, mp 138°C(EtOH), MS(EI), 282(33%, M-60), 295(48%, M-Me-MeOH), 327(39%, M-Me) and 342(100%, M^+, obs., 342.0738), UV(MeOH), λ_{max} 229nm(ε 16,600), 254(11,300), 285 (sh, 5,100), 290(5,100), 426(sh, 5,000) and 442(5,400); acetate, mp 213-215°C(EtOH). From the mother liquid of the crude crystalline mixture, compounds 5 and 6 were isolated after chromatography on SiO_2(CH_2Cl_2-MeOH); 5, $C_{18}H_{14}O_7$, mp 148°C(EtOH), MS(EI), 282(100%, M-60), 310(32%, M-MeOH) and 342(48%, M^+, obs., 342.0722), UV(MeOH), λ_{max} 223nm(ε 20,500), 247(sh, 11,000), 268(15,800), 286(sh, 12,500) and 409(5,600); 6, $C_{19}H_{16}O_7$, mp 224°C(acetone), MS(EI), 281(29%, M-60-Me), 296(26%, M-60), 309(39%, M-Me-MeOH) and 356(100%, M^+, obs., 356.0912), UV(MeOH), λ_{max} 224nm(ε 18,000), 259(14,800), 286(sh, 6,000) and 400(4,400). Upon methylation (Me_2SO_4/K_2CO_3 in refluxing acetone), 4-6 gave the identical permethyl derivative 7 (quantitatively), $C_{20}H_{18}O_7$, MS(EI), 323(28%, M-Me-MeOH), 355(60%, M-Me) and 370(100%, M^+, obs., 370.1084), UV(MeOH), λ_{max} 220nm(ε 24,500), 257(20,300) and 373(4,900).

In their ^{1}H-NMR (Table 1), only three aromatic protons were observed other than aromatic methyl, methoxy, and hydrogen-bonded phenolic protons; thus a substructure A was established unambiguously from these three aromatic protons. The substitution pattern of another ring has been determined as B based on the rule of elimination as follows. The number of methoxy and hydroxyl groups proved 4 and 5 to be monoethers, and 6 to be diether. In their IR spectra (Table 1), $\nu_{C=O}$(ester) suggested the presence of H-bonded ester in 5, i.e., the free hydroxyl group should be on a carbon adjacent to the ester position. The quinone absorptions ($\nu_{C=O}$) showed that two of the quinones in 4 were H-bonded but only one of them in 5 and 6 suggesting that the quinone functions were flanked with OH and/or OMe groups. Therefore, the following five substructures B-F are proposed as candidates. Considering the



A

R=H,Me

	X	Y	Z
B	Me	COOMe	OR
C	Me	OR	COOMe
D	COOMe	OR	Me
E	OR	COOMe	Me
F	OR	Me	COOMe

biosynthesis of the anthraquinones from polyketide precursor,[2] the methyl and carboxylic functions should be next to each other; therefore **C** and **D** were discarded. If the substructures **E** or **F** had been correct, H-bonded ester IR absorption in **5** should not have been observable, because the OH group adjacent to carboxylic ester would be flanked with the quinone function which is a stronger H-bond acceptor. Therefore **E** and **F** are unlikely for the substructure; only **B** is possible for the skeleton of **4**-**6**.

The combination of the two substructures **A** and **B** gave two possible structures, one with parallel and the other with antiparallel hydroxyl groups flanking the quinones. The former structure was discarded because each of the quinone carbonyls should be flanked with OH's, leaving the latter as the only possible structure. The structure **4** was confirmed by long-range selective proton decoupling (LSPD) experiments[3] in ^{13}C-NMR as follows. Selective irradiation of aromatic methyl protons(1-Me) at 2.57 ppm sharpened C-9(broad singlet, $^{4}J_{CH}$= 1.5 Hz, others $J_{CH}\leqslant 0.7$), while C-10 was left unchanged. In contrast, irradiation of H-5 at 7.70 ppm changed C-10(broad doublet, $^{3}J_{CH}$=4.4 Hz, others $J_{CH}\leqslant 0.7$) to a broad singlet, while C-9 showed no changes. Moreover, C-9 and C-10 were independently sharpened by irradiation with 8-OH(12.80 ppm) and 4-OH(13.60 ppm), respectively.

TABLE 2. ^{13}C-NMR Assignments of the Carbons (in $CDCl_3$)*

Carbons	4	5	6	7	Carbons	4	5	6	7
C-1	137.4	138.6	137.0	136.6	C-11	132.3	133.8	134.2	133.7
C-2	132.3	133.8	136.1	133.7	C-12	116.8	116.7	116.5	123.4
C-3	150.2	153.4	152.1	150.8	C-13	125.2	124.8	128.1	131.5
C-4	155.1	146.3	155.4	153.8	C-14	117.9	128.1	129.8	128.9
C-5	118.7	118.5	118.5	118.7	C-15	166.7	167.4	166.8	167.1
C-6	135.9	135.9	136.1	134.2	1-Me	19.6	20.8	20.1	18.8
C-7	125.4	124.0	123.6	117.1	15-OMe	52.7	53.0	52.9	52.6
C-8	162.5	161.9	161.8	158.8	OMe	61.5	62.3	61.9	61.9
C-9	188.9	189.6	189.7	184.6				61.5	61.7
C-10	188.7	182.4	182.4	183.6					56.5

*Assignments were obtained by LSPD technique and/or from their signal multiplicities.

Consequently, the structures of the quinones were determined as **4**-**7**, and the assignments of carbons are summarized in Table 2. The oxidation pattern of these quinones is the same as that of naphthalene derivatives **1**-**3** isolated from the same extract, and it is quite similar to that of aloesaponarins[4] obtained from Aloe saponaria Haw. Pharmacological studies, especially on vasodilator activity of these three newly isolated quinones are in progress.

REFERENCES AND NOTES

1) Z.X. Chen, H.Z. Huang, C.G. Wang, Y.H. Li, and J.M. Ding, Zhongcaoyao, 12, 484(1981).

2) Biosynthesis of eleutherin **2**, whose oxidation pattern is the same as that of newly isolated anthraquinones, followed the acetate pathway, see: U. Weiss and J.M. Edwards, in "The Biosynthesis of Aromatic Compounds", John Wiley and Sons, New York(1980). Therefore, it is more likely that these two series of compounds, **1**-**3** and **4**-**6** share the same polyketide precursor.

3) For conditions, see: H. Komura, K. Mizukawa, and H. Minakata, Bull. Chem. Soc. Jpn., 55, 3053(1982).

4) A. Yagi, K. Makino, and I. Nishioka, Chem. Pharm. Bull., 22, 1159(1974).

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