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CYCLOEUDESMANOLIDES FROM *SARCANDRA GLABRA*

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Key Word Index—*Sarcandra glabra*; Chloranthaceae; cycloeudesmane; chloranthalactone A; chloranthalactone G; 4α,15α-epoxy-1,3-cyclo-7(11), 8-eudesmadien-12,8-olide.

Abstract—The aerial parts of *Sarcandra glabra* afforded, in addition to known compounds, the new cycloeudesmanolide chloranthalactone G 4α,15α-epoxy-1,3-cyclo-7(11), 8-eudesmadien-12,8-olide. The structure of chloranthalactone G was deduced from two-dimensional NMR spectroscopy and from comparison of its spectra with the known compound chloranthalactone A which was also present in the extract. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Sarcandra glabra (Thunb.) Nakai (*Chloranthus glaber* (Thunb.) Makino) is common in the woodlands of Hong Kong and is used in traditional Chinese medicine for treating various kinds of cancer [1]. Several cycloeudesmanes have been isolated previously from *C. glaber* [2–6] and a number of other cycloeudesmanes are known from the Chloranthaceae [7].

RESULTS AND DISCUSSION

Extraction of the aerial parts of *S. glabra* with dichloromethane followed by CC and HPLC yielded the novel cycloeudesmanolide **1**, named chloranthalactone G. Accurate mass spectroscopy demonstrated the elemental composition $C_{15}H_{16}O_3$ which was supported by the results of DEPT (15 carbons with 16 directly attached protons, see Table 1). Inspection of the ^{13}C spectrum revealed two double bonds (δ 149.7, 147.3, 123.0 and 119.6) as well as a carbonyl group (δ 170.9), requiring that **1** therefore contained five rings to accomodate the molecular formula. The presence of a terminal epoxide ring system was demonstrated by a characteristic AB system in the ^1H NMR spectrum (δ 2.84 *d*, $J = 4.7$ Hz; δ 2.75 *d*, $J = 4.7$ Hz) and the presence of a cyclopropane ring was indicated by a strongly upfield methylene pair (δ ^1H 0.88 and 1.07). The IR spectrum contained a strong absorbance consistent with an α,β-unsaturated butyrolactone ring (1765 cm^{-1}). The topological relationship of these three ring systems and the remaining five- and six-membered rings of **1** was established by single bond and long range CH correlation experiments (see Table 1) and ^1H–^1H COSY.

The stereochemical relationship between the rings was determined by a series of one-dimensional NOE experiments (see Table 1) which demonstrated that the epoxide ring was on the α-face as drawn (i.e. *trans* to the cyclopropane ring) and that the decalin system was *trans*-fused.

In addition to chloranthalactone G, the extract also contained the known compound chloranthalactone A (**2**) [3]. The absolute stereochemistry of **1** is derived from that of **2**, on the assumption that the two are biogeneticaly related. The identity of chloranthalactone A was confirmed by comparison of its ^1H and ^{13}C NMR spectra with those in the literature [3, 7] and complete assignments for each carbon and proton in **2** (made by means of correlation experiments in the same manner as for chloranthalactone G) supported the chemical shift assignments in **1** (see Table 2).

Compound **1** was found to be unstable on storage. After 3 months at −20° it had undergone *ca* 50% decomposition to yield a mixture of products. Although the original compound could be repurified from the mixture, no other products were characterized. Interestingly, compound **2** was also found to be unstable under the same conditions, although in this case, only 30% conversion into a single compound was observed. Repurification yielded **2** and a second crystalline substance identified as chloranthalactone B (**3**) (see Table 2 for spectral identification). It can be expected that **1** will undergo oxidation at the enolic double bond in the same manner as **2**: possibly, the presence of the extra epoxide function in the case of **1** leads to a more complex reaction profile.

In addition to the foregoing compounds, the dichloromethane extract also yielded several known dihydrochalcones with 2′-OH substitution (**4–9**), two

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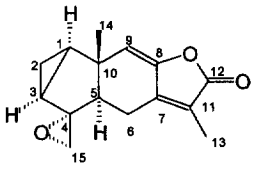
Table 1. ^{13}C and ^{1}H NMR data for **1**

Assignment	δ ^{13}C	Mult.	δ ^{1}H	Long range correlations from ^{13}C to ^{1}H at:	NOE to ^{1}H at:
1	26.5	CH	1.78	0.96	6.23; 0.88
2	15.0	CH_2	1.07		(2.84); 0.88
			0.88		1.78; 1.69; 1.07
3	22.0	CH	1.69		
4	64.8	C		2.93	
5	57.9	CH	2.93	0.96	2.40
6	19.7	CH_2	2.40		2.93; 2.11
			2.11		2.75; 2.40; 2.96
7	147.3	C		2.11; 1.86	
8	149.7	C		6.23; 2.40	
9	119.6	CH	6.23		1.78; 0.96
10	39.1	C		0.96	
11	123.0	C		1.86	
12	170.9	C		1.86	
13	8.6	CH_3	1.86		(2.40)
14	21.8	CH_3	0.96		6.23; 2.75; 2.11;1.07
15	50.0	CH_2	2.84		2.75; (1.07)
			2.75		2.84; 2.11; 0.96

NOE figures in parentheses indicate weak enhancements.



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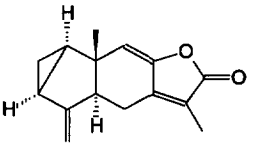

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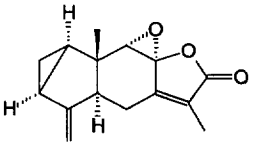

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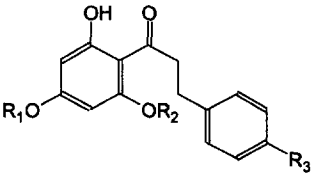


4 R_1 = H, R_2 = Me; R_3 = H

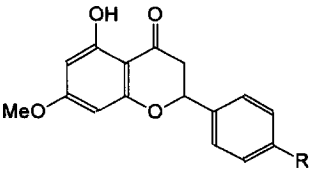
5 R_1 = H, R_2 = Me; R_3 = OMe

6 R_1 = Me, R_2 = H; R_3 = H

7 R_1 = Me, R_2 = H; R_3 = OMe

8 R_1 = Me, R_2 = Me; R_3 = H

9 R_1 = Me, R_2 = Me; R_3 = OMe



10 R=H

11 R = OMe

Table 2. ^{13}C and ^{1}H NMR data for **2** and **3**

	2			**3**		
Assignment	δ ^{13}C	Mult.	δ ^{1}H	δ ^{13}C	Mult.	δ ^{1}H
1	26.4	CH	1.66	23.9	CH	1.72
2	17.0	CH_2	0.92; 0.92	16.8	CH_2	0.93; 0.85
3	22.5	CH	1.98	23.0	CH	2.00
4	150.0	C		149.9	C	
5	62.0	CH	2.98	50.6	CH	3.40
6	21.4	CH_2	2.72; 2.28	21.3	CH_2	2.54; 2.12
7	148.1	C		152.3	C	
8	149.6	C		87.9	C	
9	119.8	CH	6.25	64.4	CH	4.18
10	40.1	C		41.1	C	
11	122.4	C		129.1	C	
12	171.1	C		170.4	C	
13	8.6	CH_3	1.91	9.0	CH_3	1.89
14	22.1	CH_3	0.79	16.9	CH_3	0.65
15	106.6	CH_2	5.06; 4.79	106.8	CH_2	5.04; 4.71

known flavanoids (**10** and **11**), coumarin, isofraxidin, scopoletin, betulinic acid and the sesquiterpenes nerolidol and spathulenol.

EXPERIMENTAL

General. Chemical shifts are expressed in ppm (δ) relative to TMS as int. standard. All NMR experiments were run on Bruker DPX 300 or DRX 500 instruments with $CDCl_3$ as solvent. Single bond and long range ^{13}C–^{1}H correlation experiments were recorded with 1024 data points in F_2 and 256 data points in F_1. MS were recorded in EI mode (70 eV) on a Finnigan-MAT 95 MS spectrometer. FTIR spectra were recorded in CH_2Cl_2 on a Shimadzu FTIR-8201 PC instrument.

Isolation of **1**. *Sarcandra glabra* (800 g) was collected in December, whilst fruiting from Pokfulam Country Park on Hong Kong Island. The sample was ground to a fine powder under liq. N_2 and immediately extracted with CH_2Cl_2 in a Soxhlet apparatus (8 hr). The organic extract was then dried and evaporated under red. pres. to yield a dark green oil (12.1 g; 1.51% w/w). **1** (11.5 mg) was isolated by CC (R_f 0.35 in 32% EtOAc–hexane; staining pink with *p*-anisaldehyde soln.) followed by HPLC (R_t 15.6 min in 32% EtOAc–hexane; flow rate 8 ml min^{-1}; column: PREP-SIL 20 mm × 25 cm).

A voucher specimen of *S. glabra* is deposited in the University of Hong Kong Herbarium (GDBROWN 95/1).

Compound **1**. Pale yellow solid, mp 134–135°. ^{1}H NMR: δ 6.23 (1H, *s*), 2.93 (1H, *dd*, J = 14.1, 3.6 Hz), 2.84 (1H, *d*, J = 4.7 Hz), 2.75 (1H, *d*, J = 4.7 Hz), 2.40 (1H, *dd*, J = 16.2, 3.6 Hz), 2.11 (1H, *dd*, J = 16.2, 14.1 Hz), 1.86 (3H, *s*), 1.78 (1H, *ddd*, J = 8.1, 8.1, 3.7 Hz), 1.69 (1H, *ddd*, J = 8.8, 8.8, 3.7 Hz), 1.07 (1H, *m*), 0.96 (3H, *s*), 0.88 (1H, *m*). IR $\nu_{max}^{CH_2Cl_2}$ cm^{-1} 3063; 2982; 2922; 1765; 1651; 1641. MS *m/z* (rel. int.): 244.1094 (53) ($[M]^+$ Δ 0.6 mmu for $C_{15}H_{16}O_3$), 229 (100); 214 (50); 213 (57); 199 (66); 185 (57); 171 (54). $[\alpha]_D^{25}$ − 58.7 (CH_2Cl_2, *c* 0.15).

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