

A DITERPENOID WITH A NEW CARBON SKELETON FROM *PYGMAEOPREMNA HERBACEA*

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Key Word Index—*Pygmaeopremna herbacea*, Verbenaceae; diterpenoid, pygmaeocine E

Abstract—Pygmaeocine E, a diterpenoid with a new carbon skeleton, was isolated from roots of *Pygmaeopremna herbacea*. Its structure was established by spectroscopic methods and verified by X-ray crystallography.

INTRODUCTION

Pygmaeopremna herbacea (Roxb.) Moldenke is used as a folk remedy in the Yunnan province of China to reduce inflammation and to cure malaria. To date, there is no published work on the chemistry of *Pygmaeopremna* species. From the diethyl ether extract of roots of *P. herbacea*, seven crystalline compounds were isolated. One of them, named pygmaeocine E, is reported in this paper. Its structure was determined by spectroscopic methods and verified by X-ray diffraction as a diterpenoid with a new carbon skeleton.

RESULTS AND DISCUSSION

Pygmaeocine E (1), $C_{20}H_{20}O_4$ (MS and elemental analysis), was obtained as brownish red prisms. Its structure was originally deduced from 1H NMR, ^{13}C NMR, and IR data as 1,1,10-trimethyl-7-isopropyl-3-hydroxyanthran-2,5,6-trione, but in view of its novelty it was confirmed by X-ray crystallography. The X-ray analysis procedure is given in the Experimental section. Fig. 1 is a stereoscopic view of the molecule.

The main spectroscopic grounds for establishing structure 1 were as follows. The 1H NMR data showed the presence of three methyl groups [δ 2.72 (s, 3H) and 1.56 (s, 6H)] and an isopropyl group [δ 1.17 (d, 6H, J = 7 Hz) and 3.02 (sept, 1H, J = 7 Hz)]. IR bands at 3380.0 and 1216.8 cm^{-1} and an 1H NMR signal at δ 6.48 (s, 1H, disappeared on deuteration) established the presence of a hydroxyl group. The IR spectrum also revealed the presence of a benzene ring (1580.6 and 1460 cm^{-1}). Three carbonyl groups were shown by signals at δ 198.2, 182.2 and 181.3 in the ^{13}C NMR spectrum (Table 1). The last two signals are characteristic of an *ortho*-quinone system and this was confirmed by three weak IR absorptions at 1679.5, 1650.5 (buried beneath the strong absorption of a ketonic carbonyl), and 1614.5 cm^{-1} , because generally an *ortho*-quinone system affords three rather weak IR absorptions in the 1680–1610 cm^{-1} region [1–3]. The

signal at δ 198.2 was attributed to an α,β -unsaturated ketonic carbonyl, the strong IR absorption of which was at a rather low frequency (1650.5 cm^{-1}) and suggested that the conjugated system of the α,β -unsaturated ketonic carbonyl extended to the benzene ring and the hydroxyl attached to its α -position [4]. In view of the high degree of unsaturation and the presence of seven quaternary sp^2 -carbons in 1, it could be deduced that the benzene ring was fused to the *ortho*-quinone system. The DEPT sequence indicated only one aliphatic quaternary carbon at a rather low field (δ 48.1) which led us to the conclusion that it was flanked both by the benzene ring and the ketonic carbonyl. One *ortho*-quinone carbonyl (C-10) of 1 gave a ^{13}C NMR signal at δ 182.2, i.e. 1.3 ppm downfield from that of C-2 of β -naphthoquinone. This suggested that there was an alkyl (isopropyl) group in the α -position to this carbonyl [5]. Furthermore, the 13-methyl group of 1 gave a 1H NMR signal at a relatively low field (δ 2.72) which indicated that it need to be located *peri* to an *ortho*-quinone carbonyl group in order to be deshielded by the carbonyl group.

All the above data support structure 1 for pygmaeo-

Table 1 ^{13}C NMR spectral data of pygmaeocine E (50.3 MHz, pyridine- d_5)*

C	δ	C	δ
1	112.4 d	11	181.3 s
2	149.8 s	12	141.2 s
3	198.2 s	13	127.9 s
4	48.1 s	14	147.9 s
5	134.2 s	15	27.4 q
6	125.8 d	16	27.4 q
7	145.0 s	17	15.8 q
8	139.9 d	18	26.8 d
9	131.4 s	19	21.1 q
10	182.2 s	20	21.1 q

* Multiplicities assigned by DEPT sequence

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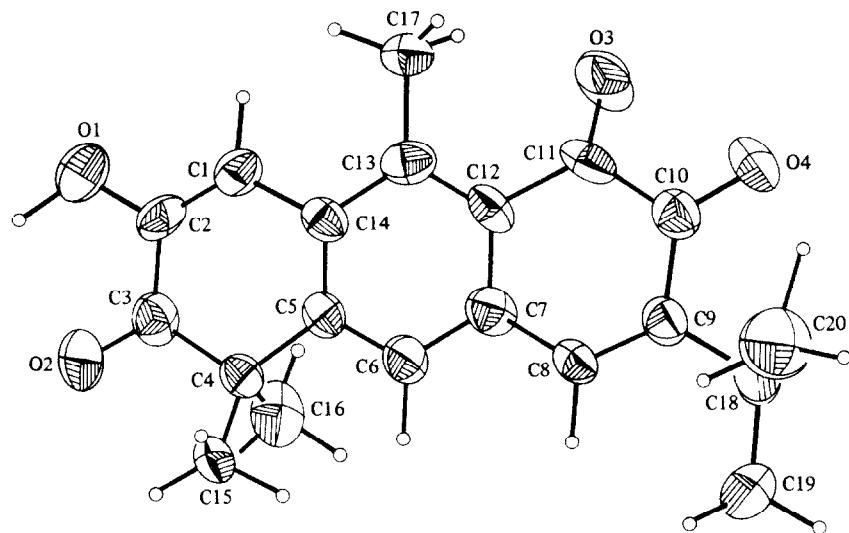
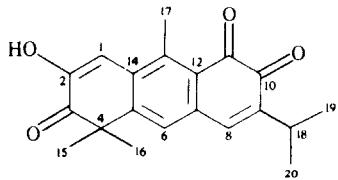


Fig. 1



1

cine E, as did the calculations of the predicted substituent effects on the ^{13}C NMR chemical shifts of benzene carbons [5]. To our knowledge, pygmaeocine E is a diterpenoid with a new carbon skeleton. We propose to name the skeleton pygmaeocane E.

EXPERIMENTAL

General Mps uncorr, ^1H NMR 200 MHz, TMS as internal standard, ^{13}C NMR 50.3 MHz, TMS as internal standard, IR KBr, MS 70 eV, UV MeOH

Isolation and separation of pygmaeocine E Roots of *Pygmaeopremna herbacea* (Roxb.) Moldenke (18 kg), collected in Shuangjiang County, Yunnan Province of China, were extracted ($\times 3$) with Et_2O at room temp. The crude extract was concd (682 g), mixed with the same amount of kieselguhr and extracted in turn with petrol (60–90°), C_6H_6 and Et_2O in a Soxhlet apparatus, respectively. The petrol extract (130 g) was chromatographed over 1500 g silica gel packed in petrol, 500 ml fractions being collected as follows 1–20 (petrol), 21–70 (petrol– Et_2O , gradient elution), 71–95 (petrol– Et_2O –MeOH, gradient elution). Fractions 47–50 afforded compound 1 (135 mg) which was recrystallized from CHCl_3 –MeOH (1:1).

Pygmaeocine E (1) Brownish-red prisms, mp 192–193°, $\text{C}_{20}\text{H}_{20}\text{O}_4$ (Calc. C4.04, H6.21, Found, C74.68, H6.32) UV $\lambda_{\text{max}}^{\text{MeOH}}$ (nm) 219.2(s), 267.2(s), 284.0(s), 335.2(s), 482.0(w, br), IR $\nu_{\text{max}}^{\text{KBr}}$ (cm^{-1}) 3380.0, 2962.5, 2928.4, 1679.5, 1650.5, 1614.5, 1580.6, 1460.0, 1420.2, 1395.4, 1377.0, 1258.6, 1216.8, ^1H NMR (200 MHz, CDCl_3) δ 7.25 (s, 1H), 7.09 (s, 1H), 6.48 (s, 1H, disappeared on deuteration), 3.02 (sept, 1H, $J = 7$ Hz), 2.72 (s,

3H), 1.56 (s, 6H), 1.17 (d, 6H, $J = 7$ Hz) ^{13}C NMR Table 1, MS m/z (rel. int.) 324 [M] $^+$ (16), 296 (64), 281 (8), 254 (100), 239 (39), 225 (8), 210 (3), 195 (4), 43 (19)

X-ray analysis Single crystals were grown by slow crystallization from CHCl_3 –MeOH. Crystal data are monoclinic, space group $P_{2_{1},a}$, $a = 10.603$ (4), $b = 14.680$ (7), $c = 11.169$ (7) \AA , $\beta = 105.71$ (4)°, $V = 1673$ \AA^3 , $Z = 4$, and $\mu(\text{MoK}\alpha) = 0.83$ cm^{-1} . The size of the crystal used for collection was $\text{c}a$ $0.1 \times 0.4 \times 0.6$ mm^3 . The determination of the unit cell parameters and the collection of intensities were performed on a computer controlled Nicolet P3/F four-circle diffractometer with graphite monochromatized $\text{MoK}\alpha$ radiation. Cell dimensions were calculated on the basis of 25 reflections in the range $20 < 2\theta < 45$ ° and refined by least squares. 2145 independent reflections were collected in the interval $0 < 2\theta < 45$ ° by the $\omega/2\theta$ scan technique using a variable scan rate of 4.0–29.3°/min determined by a fast pre-scan. The intensity data were corrected for Lorentz–polarization effects. Semi-empirical absorption corrections were made on the basis of scan data with six different 2θ values reflections. Only 1160 reflections were considered as observed [$I \geq 2.5\sigma(I)$] and used for structure solving and refinement. The structure was solved using the direct-method. All the non-hydrogen atoms could be recovered from the E-map. The refinement was performed by least-square method using a block-diagonal matrix. All the hydrogen atoms were located in a difference map and refined isotropically. The last difference Fourier map was essentially featureless with no peaks greater than ± 0.2 e\AA^{-3} . The final discrepancy index was $R = 0.053$.

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