Pergamon

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TWO 7,7′-BISDEHYDROAPORPHINE ALKALOIDS FROM *POLYALTHIA BULLATA*

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Key Word Index—*Polyalthia bullata*; Annonaceae; stem bark; 7,7′-bisdehydroaporphine alkaloids; 7,7′-bisdehydro-*O*-methylisopiline; 7-dehydronornuciferinyl-7′-dehydro-*O*-methylisopiline.

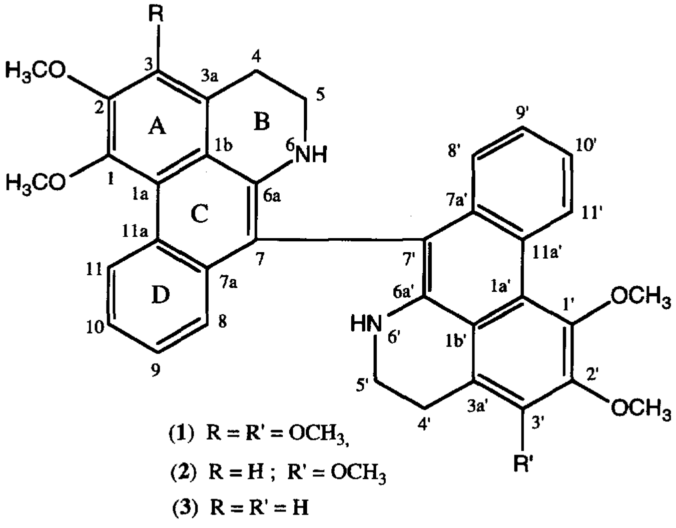
Abstract—Two new 7,7′-bisdehydroaporphine alkaloids, 7,7′-bisdehydro-*O*-methylisopiline and 7-dehydronornuciferine-7′-dehydro-*O*-methylisopiline, and the known bisdehydroaporphine alkaloid, urabaine, have been isolated from the stem bark of *Polyalthia bullata*. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

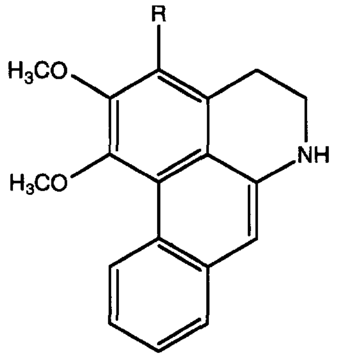
The genus *Polyalthia* comprises 120 species of shrubs and trees, which are distributed in tropical and subtropical regions [1]. Several *bis*aporphine alkaloids have been isolated from *P. beccarii* [2] and *P. cauliflora* [3]. *P. bullata* is a small tree which grows widely in the Indian subcontinent and Malay peninsula. The plant is one of the species used in Malaysia as the aphrodisiac 'tonquat ali' (the other species is *Eurycoma longifolia*). We have studied the constituents of the bark of *P. bullata*. and the present paper deals with the determination of the structures of two new *bis*aporphine alkaloids, 7,7′-bisdehydro-*O*-methylisopiline (**1**) and 7-dehydronornuciferinyl-7′-dehydro-*O*-methylisopiline (**2**), isolated from the ethyl acetate extract of the stem bark. The new compounds represent further additions to the small group of 7,7′-bisdehydroaporphine alkaloids. The known bisaporphinoid, urabaine (**3**) [4], was also obtained.

RESULTS AND DISCUSSION

7,7′-Bisdehydro-*O*-methylisopiline (**1**), 7-dehydronornuciferinyl-7′-dehydro-*O*-methylisopiline (**2**) and urabaine (**3**) were isolated from the ethyl acetate extract of the stem bark of *P. bullata* by a combination of column chromatography over silica gel and preparative TLC. 7,7′-Bisdehydro-*O*-methylisopiline (**1**) was obtained as yellowish brown microcrystals, mp 268–270°. The IR spectrum exhibited bands at 3390 (NH) and 3020, 1600, 1560, 930 (aromatic) cm^{-1}. The mass



(**1**) R = R′ = OCH_3,
(**2**) R = H ; R′ = OCH_3
(**3**) R = R′ = H



(**4**) R = OCH_3

(**5**) R = H

spectrum showed a $[M]^+$ at *m/z* 616 and an $[M/2+H]^+$ peak at *m/z* 309 and HREI-mass spectrometry confirmed the molecular formula as $C_{38}H_{36}N_2O_6$ for $[M]^+$ and $C_{19}H_{19}NO_3$ for $[M/2+H]^+$, which is equivalent to the $[M+1]^+$ peak for dehydro-*O*-methylisopiline (**4**) [5]. The absence of any fragmentation in the region *m/z* 309–616 indicated a dimeric structure for **1**. The UV spectrum had maxima at λ_{max} 213 (log ε 4.53), 265 (log ε 4.62) and 323 (log ε 4.02) nm, characteristic of a dehydroaporphine system with substitution at the C-7 position [6]. It was apparent from the ^{1}H NMR spectrum of **1** that it was closely related to urabaine (**3**) [4]. Thus, its monomeric unit had a strongly deshielded proton [δ_H 9.60 (*dd*, $J = 8.6$, 0.6 Hz, H-11, H-11′)] [4, 7], which formed part of a four-spin aromatic system [δ_H 7.15 (*dd*, $J = 8.2$, 1.5 Hz, H-8, H-8′), 7.23 (*dt*, $J = 8.2$, 1.4 Hz, H-9, H-9′), 7.37 (*dt*, $J = 8.4$, 1.4 Hz, H-10, H-10′)]. The lack of any further aromatic protons and the appearance of three methoxyl signals [δ_H 4.14 (*s*), 4.06 (*s*) and 4.00 (*s*)] indicated that ring A was fully substituted. The aliphatic methylene resonances appeared as a complex multiplet between δ_H 3.15 and 3.37. The fact that no signal appeared near δ_H 6.60, as would be expected for protons at C-7 or C-7′, revealed that **1** was a symmetrical dimer of two dehydro-*O*-methylisopiline (**4**) [4, 8] units.

The ^{13}C NMR spectrum of **1** (Table 1) showed the expected features of a 7,7′-bisdehydroaporphine with ring A fully substituted. Thus, the monomeric unit had four aromatic methines (δ_C 123.1, 123.8, 126.8 and 127.2), two methylene (δ_C 23.8 and 40.5) and three methoxyl carbons (δ_C 60.4, 60.9 and 61.3], in addition to ten aromatic quaternary carbons. The chemical shifts of the methoxyl-bearing carbons indicated the lack of neighbouring protons. The carbons of the monomeric units were assigned by comparison with the monomeric unit of urabaine [4] for the carbons of the C and D rings and with dehydro-*O*-methylisopiline [9] for the carbons of rings A and B. This is the first report of the isolation of **1**.

7-Dehydronornuciferinyl-7′-dehydro-*O*-methylisopiline (**2**) was obtained as yellowish brown microcrystals, mp > 310° and its IR showed bands for NH (3391 cm^{-1}) and aromatic (3020, 1602, 1560 and 932 cm^{-1}) absorption. The mass spectrum showed an $[M]^+$ at *m/z* 586 ($C_{37}H_{37}N_2O_5$), with major fragments at *m/z* 309 ($C_{19}H_{19}NO_3$) and 279 ($C_{18}H_{17}NO_2$), suggesting an asymmetric structure for **2**, resulting from a C-7-C-7′ bond between a dehydronornuciferine unit (**5**) [8] and a dehydro-*O*-methylisopiline unit (**4**) [10]. The UV and HREI-mass spectra confirmed this suggestion.

The ^{1}H NMR spectrum of **2** showed two highly deshielded protons at δ_H 9.65 (*br*, *d*, $J = 8.5$ Hz, H-11) and 9.58 (*br*, *d*, $J = 8.1$ Hz, H-11′), an aromatic proton singlet at δ_H 7.12 (H-3), six other aromatic protons between δ_H 7.10 and 7.14 (*m*), five methoxyl groups

Table 1. ^{13}C NMR chemical shifts of compounds **1** and **2**

C	(1)	(2)	C	(1)	(2)
1	148.5 (*s*)	145.7 (*s*)	7	120.1 (*s*)	120.2 (*s*)
1′	148.5 (*s*)	148.7 (*s*)	7a	132.5 (*s*)	133.3 (*s*)
1a	125.6 (*s*)	125.8 (*s*)	7′a	132.5 (*s*)	132.4 (*s*)
1′a	125.6 (*s*)	125.6 (*s*)	8	127.2 (*d*)	128.0 (*d*)
1b	121.8 (*s*)	118.1 (*s*)	8′	127.2 (*d*)	127.3 (*d*)
1′b	121.8 (*s*)	121.7 (*s*)	9	126.8 (*d*)	127.4 (*d*)
2	146.7 (*s*)	151.6 (*s*)	9′	126.8 (*d*)	126.9 (*d*)
2′	146.7 (*s*)	146.8 (*s*)	10	123.8 (*d*)	123.6 (*d*)
3	151.1 (*s*)	111.8 (*d*)	10′	123.8 (*d*)	124.0 (*d*)
3′	151.1 (*s*)	151.1 (*s*)	11	123.1 (*d*)	123.0 (*d*)
3a	121.8 (*s*)	130.0 (*s*)	11′	123.1 (*d*)	123.5 (*d*)
3′a	121.8 (*s*)	121.7 (*s*)	11a	122.5 (*s*)	125.8 (*s*)
4	23.8 (*t*)	30.7 (*t*)	11′a	122.5 (*s*)	122.4 (*s*)
4′	23.8 (*t*)	23.6 (*t*)	MeO-1	60.4 (*q*)	59.9 (*q*)
5	40.5 (*t*)	41.1 (*t*)	MeO-1′	60.4 (*q*)	60.4 (*q*)
5′	40.5 (*t*)	40.7 (*t*)	MeO-2	60.9 (*q*)	56.5 (*q*)
6a	139.5 (*s*)	139.3 (*s*)	MeO-2′	60.9 (*q*)	60.9 (*q*)
6′a	139.5 (*s*)	140.0 (*s*)	MeO-3	61.3 (*q*)	—
7	120.1 (*s*)	118.1 (*s*)	MeO-3′	61.3 (*q*)	61.3 (*q*)

[δ_H 4.13 (*s*), 4.06 (*s*), 4.05 (*s*), 3.99 (×2) (*s*)] and eight aliphatic protons between δ_H 3.15 and 3.43 (*m*). These data readily led us to the conclusion that the two monomeric units are dehydronornuciferine (**5**) and dehydro-*O*-methylisopiline (**4**). The ^{13}C NMR (Table 1) also confirmed an asymmetric structure for **2**. The assignments of the ^{1}H and ^{13}C resonances were made by comparison with published data for the appropriate monomers [4, 11, 12] and are listed in the Experimental and in Table 1. Structure **2** is a new natural product.

Urabaine (**3**) was obtained as green crystalline powder, mp >282°, and was readily identified by spectroscopic analysis and comparison with literature data [4, 11]. The first natural bis-7,7′-dehydroaporphines were isolated from *Popowia pisocarpa* [12], another member of Annonaceae.

EXPERIMENTAL

General. Mp are uncorr. UV were recorded in MeOH and IR in $CHCl_3$. ^{1}H NMR were run at 200 MHz and ^{13}C NMR at 50 MHz in $CDCl_3$ soln relative to $CHCl_3$ at 7.25 ppm and $CDCl_3$ at 77.0 ppm.

Plant material. Stem bark of *P. bullata* was collected in Malaysia in September 1992. A voucher specimen is deposited in the Herbarium of the Malaysian Forest Research Institute, Kepong.

Extraction and isolation. Dried ground stem bark (400 g) was extracted in a Soxhlet apparatus with EtOAc. The EtOAc extract (3.6 g) was concd *in vacuo* and fractionated by CC over silica gel eluting with petrol, increasing amounts of EtOAc in petrol and finally with MeOH. Multiple prep. TLC, using petrol–EtOAc [(4:1), (22:13) and (17:3)] of the stem bark fractions gave the following: (fr. 15 gave (**3**) (17 mg), fr. 8 (**1**) (55 mg) and fr. 10 (**3**) (21 mg).

7,7′-Bisdehydro-O-methylisopiline (**1**). Yellowish brown microcrystals (MeOH), mp 268–270° UV λ_{max}: 213 (log ε 4.53), 265 (log ε 4.62), 323 (log ε 4.02) nm. IR ν_{max}: 3390 (NH), 3020, 2936, 2856, 1600, 1560, 1420, 1020, 930 cm^{-1}. EIMS *m*/*z* (rel. int.): 616 $[M]^+$ (100), 309 $[M/2+H]^+$ (35), 294 $[309-CH_3]^+$ (9), 278 $[309-CH_3O]^+$ (10), 263 (13). ^{1}H NMR: δ 9.60 (*dd*, $J=8.6$, 0.6 Hz, H-11, H-11′), 7.37 (*dt*, $J=8.4$, 1.8 Hz, H-10, H-10′), 7.23 (*dt*, $J=8.2$, 1.4 Hz, H-9, H-9′), 7.15 (*dd*, $J=8.2$, 1.5 Hz, H-8, H-8′), 3.15–3.37 (*m*, 2H-4, 2H-4′, 2H-5, 2H-5′), 4.0, 4.06, 4.14 (CH_3O-1, 1′, 2, 2′, 3, 3′). ^{13}C NMR: see Table 1. HREIMS: found $[M]^+$ 616.2510; $C_{38}H_{36}N_2O_6$ requires 616.2502; found $[M/2+H]^+$ 309.1345; $C_{19}H_{19}NO_3$ requires 309.1330.

7-Dehydronornuciferinyl-7′-dehydro-O-methylisopiline (**2**). Yellowish brown microcrystals (MeOH), mp >310°. UV λ_{max}: 210 (log ε 3.82), 255 (log ε 4.26), 261 (log ε 4.38), 327 (log ε 3.76) nm [IR. ν_{max}: 3391 (NH), 3020, 2937, 2853, 1602, 1560, 1522, 1456, 1020, 932 cm^{-1}. EIMS /*z* (rel. int.); 586 $[M]^+$ (100), 309 $[M-278+H]^+$ (22), 279 $[M-308+H]^+$ (30). ^{1}H NMR: δ 9.65 (*br d*, $J=8.5$ Hz, H-11), 9.58 (*br d*, $J=8.1$ Hz, H-11′), 7.12 (*s*, H-3), 7.10–7.40 (*m*, H-8, H-8′, H-9, H-9′, H-10, H-10′, H-11, H-11′), 3.15–3.43 (*m*, 2H-4, 2H-4′, 2H-5, 2H-5′), 3.99 (*s*, CH_3O-1, CH_3O-1′), 4.06, 4.05, 4.13 (CH_3O-2, 2′, 3′). ^{13}C NMR: see Table 1. HREIMS: found $[M]^+$ 586.2468; $C_{37}H_{34}N_2O_5$ requires 586.2474.

Urabaine (**3**). Green crystalline powder (MeOH), mp >282°. IR ν_{max}: 3404 (NH), 3020, 2940, 2840, 1523, 1420, 1020, 930 cm^{-1}. Identified by UV, ^{1}H NMR, ^{13}C NMR and MS comparison with published data [4, 11].

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