

(-)-Popisabahnine, a bisbenzyltetrahydroisoquinoline alkaloid from *Popowia pisocarpa* (Annonaceae)

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Abstract: The bark of *P. pisocarpa* (Annonaceae) yielded (-)-popisabahnine, a new alkaloid containing two benzyltetrahydroisoquinoline moieties that are linked through an ether linkage between the *m*- and *p*-positions of their benzyl groups. The structure of bisbenzyltetrahydroisoquinoline was established by spectroscopic method.

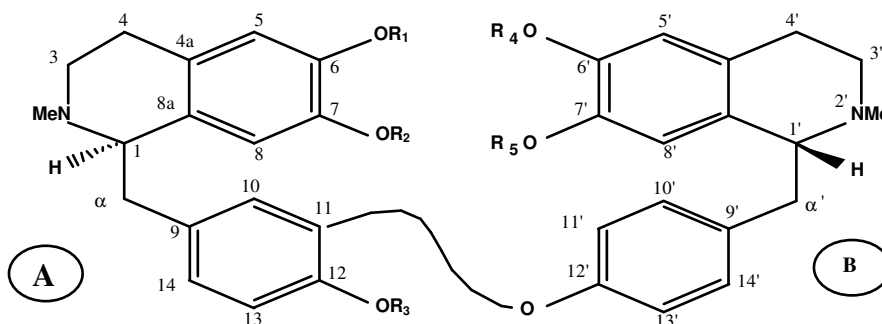
Abstrak: Kulit *P. pisocarpa* (Annonaceae) menghasilkan (-)-popisabahnina, satu alkaloid baru yang mengandungi dua unit benziltetrahidroisoquinolina yang di sambung melalui eter pada lokasi *m* and *p* pada kumpulan benzil. Struktur bisbenziltetrahidroisoquinolina di tentukan secara kaedah spektroskopi.

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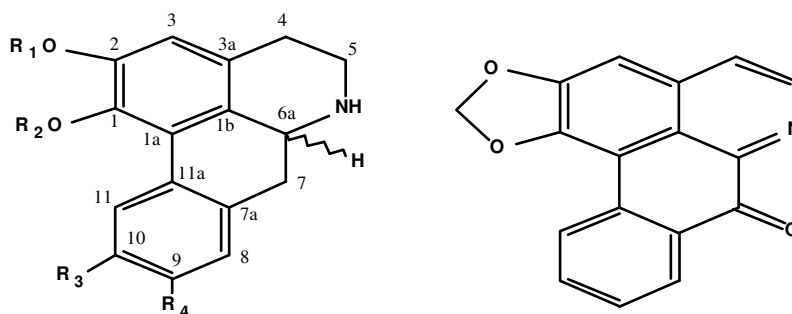
Introduction

Popowia pisocarpa of the Annonaceae family is a common shrub or small tree that grows to about 6 m tall. It can be found in lowland and hill forests throughout Peninsular Malaysia, Thailand, Indo-China, Sumatra and Borneo. Our previous studies [1, 2] on the phytochemistry of *P. pisocarpa*

collected in the hill forests of Sabah, Malaysia have suggested similarities in the alkaloids of this species to those of the Indonesian variety [3]. The bark and leaves of *P. pisocarpa* afforded *O*-methylauricine, popisopine, popisine, popisonine, popidine, popisidine, wilsonirine, asimilobine and liriodenine.



- 1 $R_1 = R_3 = R_4 = \text{Me}, R_2 = R_5 = \text{H}$
- 2 $R_1 = R_2 = R_3 = R_4 = R_5 = \text{Me}$
- 3 $R_1 = R_5 = \text{H}, R_2 = R_3 = R_4 = \text{Me}$
- 4 $R_1 = R_2 = R_3 = R_4 = \text{Me}, R_5 = \text{H}$
- 5 $R_1 = R_4 = \text{H}, R_2 = R_3 = R_5 = \text{Me}$
- 6 $R_1 = \text{H}, R_3 = R_4 = R_5 = \text{Me}$
- 7 $R_1 = R_2 = R_3 = \text{Me}, R_4 = \text{Me}, R_5 = \text{H}$
- 11 $R_1 = R_4 = \text{Me}, R_2 = R_3 = R_5 = \text{H}$



- 8 $R_1 = \text{H}, R_2 = \text{Me}, R_3 = R_4 = \text{H}, \text{H-6a} (\beta)$
- 9 $R_1 = \text{Me}, R_2 = \text{H}, R_3 = R_4 = \text{OMe}, \text{H-6a} (\alpha)$

10

Experimental

The bark and leaves of *P. pisocarpa* were collected from the Danum Valley, Sabah, East Malaysia. A voucher specimen (No. JTP 188) was at the herbarium of the Forest Research Centre, Sepilok, Sabah.

Dried ground bark was extracted with 95% EtOH at room temperature. The EtOH extracts were concentrated *in vacuo* and acidified with 5% HCl. Filtration to remove non-alkaloidal material followed by basification with 25% NH₄OH to pH 10 to release the alkaloidal mixture which was then partitioned and extracted with CHCl₃ to yield the crude alkaloids. The crude alkaloids were fractionated by using silica gel (MERCK 9385) column chromatography to afford a partial separation of the alkaloids, and further fractionations by a Chromatotron and preparative TLC resulted in the isolation of pure alkaloids **1** - **10**. The leaves were similarly extracted and chromatographed. The distribution of the alkaloids isolated from the bark and from the leaves is listed in Table 1.

Table 1: Alkaloidal yields from *P. pisocarpa*

Alkaloid	bark ^a	leaves ^a
(-)-popisabahnine (1)	7.4 (2.5%)	18.2 (4.2%)
(-)- <i>O</i> -methyldauricine (2)	97.5 (29.5%)	
(-)-popisopine (3)	18.5 (5.6%)	
(-)-popisine (4)	5.9 (1.8%)	325.0 (73.7%)
(-)-popisonine (5)	93.8 (28.4%)	
(-)-popidine (6) and (-)-popisidine (7)	49.0 (14.8%) ^b	
(-)-asimilobine (8)	6.6 (2.0%)	55.7 (12.8%)
(+)-wilsonirine (9)	48.0 (14.5%)	
liriodenine (10)	3.4 (1.0%)	36.0 (8.3%)

^a weight in mg (% of total alkaloids), 0.8 kg and 1.8 kg of dried bark and leaves respectively were extracted.

^b (-)-popidine (**6**) and (-)-popisidine (**7**) were isolated as a mixture and the ratio of **6** to **7** was approximately 2:1 based on the ¹HNMR data.

Results and Discussion

The bark of *P. pisocarpa* yielded a new bisbenzyltetrahydroisoquinoline, (-)-popisabahnine (**1**), as well as *O*-methyldauricine (**2**), popisopine (**3**), popisine (**4**), popisonine (**5**), popidine (**6**), popisidine (**7**), asimilobine (**8**), wilsonirine (**9**) and liriodenine (**10**). Compounds **8** and **9** are aporphines whereas compound **10** is an oxoaporphine. (-)-Popisabahnine (**1**) is an *O*-methyl derivative of *N,N'*-dimethylindoldhamine [4] (**11**), which is also known as (-)-guattegaumerine [5-7].

The molecular ion of **1** was recorded on LCMS (API100) which showed the [M+H]⁺ peak at 611.20, and confirmed by high resolution EIMS (VG Prospec) that showed the M⁺ peak at 610.3039 which corresponds to the molecular formula C₃₇H₄₂O₆N₂. The EIMS spectrum showed a base

peak of 192, which corresponds to the 7-hydroxy - 2 - methyl - 6 - methoxytetrahydro - isoquinoline (C₁₁H₁₄NO₂) fragment. The cleavage pattern of **1** to give the m/z 192 fragment as well as C₁₉H₂₂NO₃ and C₁₈H₂₀NO₂ fragments is typical of a dauricine-type dimers that incorporates a tail-to-tail coupling through a diaryl ether bridge [5, 8].

The ¹HNMR (270MHz, CDCl₃) spectrum of **1** displayed two *N*-methyl (δ 2.47s, 2.43s) and three methoxyl [δ 3.84s (3H), 3.83s (3H), 3.83s (3H)] signals. The downfield shift of the methoxy signals at 3.84, 3.83 and 3.83 of **1** compared to those of popisopine, as well as the absence of a methoxy signal at δ3.50 with the corresponding presence of protons H-8 (δ 6.35s), H-8' (δ 6.29s), H-5 (δ 6.48s), H-5' (δ 6.53s), argued in favor of phenolic functions [5] at C7 and C7'. H-1 (δ 3.60t) and H-1' (δ 3.7t) protons were both triplet of J = 6.3 Hz.

The H-10' (δ 7.01d), H-11' (δ 6.80d), H-13'(δ

6.80d), and H-14' (δ 7.01d) protons were two doublets, each of which represented by two protons with coupling constant J = 8.3 Hz. The absorption signal for proton H-10 appeared as a broad singlet at δ 6.68 whereas H-13 and H-14 protons were recorded as multiplet at δ 6.78 - 6.88. Complete ¹³CNMR assignments of **1** (Table 2) were made based on 1D and 2DNMR spectral data. The proton-attached carbons were assigned directly from the HETCOR spectrum. The signals of quaternary carbons were assigned based on DEPT spectrum.

The ¹HNMR data of **1** displayed similarity to those previously reported for (+)-thaligrisine⁶ which had 1*R*, 1'*S* configuration. However, the specific rotation of **1** is [α]_D -91.0 (c = 0.134, CHCl₃), having an opposite sign to that of (+)-thaligrisine, suggesting that **1** to have 1*R*, 1'*R* configuration [7].

Table 2: ^{13}C NMR data for Compounds 1, 3 and 4

Carbon	1		3		4	
	A	B	A	B	A	B
C-1	64.6	64.3	64.7	64.6	64.6	64.5
C-3	46.5	47.2	46.9	46.9	46.9	46.3
C-4	24.8	25.2	25.0	25.0	24.6	25.3
C-4a	125.2	124.9	126.5	125.1	125.5	125.1
C-5	110.5	110.5	114.4	110.3	111.2	110.5
C-6	145.4	145.2	144.1	145.4	147.2	145.6
C-7	143.3	143.4	145.4	143.5	146.3	143.4
C-8	114.1	113.8	110.6	114.1	110.9	114.2
C-8a	129.4	129.6	127.8	129.6	129.7	128.8
C- α	40.5	40.6	40.5	40.3	40.8	40.6
C-9	132.5	133.8	132.7	133.9	132.8	134.1
C-10	117.7	130.5	117.5	130.9	117.4	130.6
C-11	145.1	112.2	144.5	112.2	145.3	112.2
C-12	149.1	155.8	149.3	155.9	149.3	155.8
C-13	117.7	121.2	117.5	121.7	117.4	121.3
C-14	125.0	130.5	125.5	130.9	125.3	130.6
N-methyl	42.3		42.4		42.5	
	42.3		42.3		42.1	
O-methyl	56.0		55.6		56.1	
	55.8		55.8		55.7	
	55.7		56.1		55.7	
					55.5	

In addition, the magnitude and sign of specific rotation **1** was similar to that of bisbenzyltetrahydroisoquinoline alkaloids (**2-7**) reported earlier [3, 9], thus confirming **1** to have the *1R*, *1'R* configuration^{6-8, 13-14}.

The alkaloids **2 - 10** were identified based on comparison of their spectral properties with those reported in the literature [3-15]. The ^{13}C NMR data for compounds **3** and **4** (Table 2) were reported for the first time. The ^{13}C NMR data of **8** are 147.4 (C-9), 146.9 (C10), 146.0 (C-2), 140.8 (C-1), 128.6 (C-1b), 128.2 (C-7a), 124.9 (C-3a), 119.2 (C-1a), 112.2 (C-11), 110.7 (C-8), 109.2 (C-3), 55.7 (MeO at C-9), 55.7 (MeO at C-10), 55.6 (MeO at C-2), 53.6 (C-6a), 43.2 (C-5), 36.8 (C-7) and 28.4 (C-4) were consistent to those reported [15].

The alkaloidal distributions in the bark and leaves were markedly different, the bark provided ten alkaloids whereas in the leaves only four were detected. The major alkaloids in the bark were **2** and **5** whereas the major alkaloid in leaves was **4** (Table 1).

In the previous report [3, 9] of alkaloids from the Indonesian *P. pisocarpa*, the occurrence of derivatives of wilsonirine such as 4-hydroxywilsonirine and its bisaporphine dimers, bipowine and bipowinone, seems prominent but these derivatives were not detected in the present study. The Indonesian *P. pisocarpa*, had yielded bisbenzyltetrahydroisoquinolines of both dauricine-type and pisopowine-type of alkaloids. The pisopowine-type dimers are linked by a tail-to-tail, carbon-carbon biphenyl bond without any diaryl ether coupling as compared to dauricine-type

dimers. The present studies showed, among the alkaloids isolated, none were of pisopowine-type that were previously reported [3,9] to be predominant. The present study showed that species of different geographical regions may be taxonomically identified to be similar yet chemotaxonomically different.

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