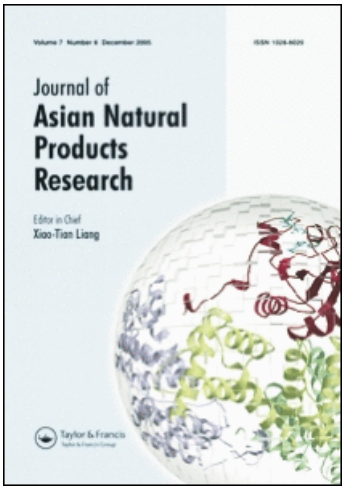

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Cyclobakuchiol C, a new bakuchiol derivative from *Psoralea coryllfolia*

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Cyclobakuchiol C, a new bakuchiol derivative from *Psoralea coryllfolia*

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A new compound, cyclobakuchiol C (**1**), together with four known bakuchiol derivatives, **2–5**, was isolated from the non-polar fraction of the seeds of *Psoralea corylifolia*, and compounds **3–5** were identified from this plant for the first time. The structure of **1** was determined by spectroscopic methods, especially 2D NMR experiments.

Keywords: *Psoralea corylifolia*; Fabaceae; Cyclobakuchiol C

1. Introduction

Psoralea corylifolia L. (Fabaceae) has a wide variety of applications in traditional Chinese medicine [1]. Bakuchiol, a meroterpene phenol, initially isolated as a major component from the same source, was reported as an important antibacterial agent [2]. In later years, its additional activities such as DNA polymerase inhibition, anti-inflammation and NO production suppression were successively discovered [3–5]. Previous research on bakuchiol derivatives from *Psoralea glandulosa* L. of this genus led to the isolation of a diasteromeric mixture of cyclobakuchiols A and B with antipyretic and anti-inflammatory effects [6], as well as some oxides of bakuchiol [7]. In the current research, we present the isolation and structure elucidation of five bakuchiol derivatives (**1–5**) from the petroleum ether soluble fraction of *P. corylifolia*. Among them, cyclobakuchiol C (**1**) is a new compound, and compounds **3–5** were identified from this plant for the first time.

2. Results and discussion

The dried seeds of *Psoralea corylifolia* were extracted with 95% EtOH to give a crude extract, which was then suspended in water to form a suspension, and was partitioned with

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petroleum ether to obtain a major oily fraction (PE). Extensive column chromatography of this fraction (PE) over silica gel gave five bakuchiol derivatives (**1–5**).

Cyclobakuchiol C (**1**), a colourless gum, showed molecular formula of $C_{18}H_{26}O_2$ as determined by HREI-MS at *m/z* 274.1925 $[M]^+$. IR absorptions exhibited the presence of hydroxyls (3525 and 3425 cm^{-1}) and aromatic ring (1616 and 1514 cm^{-1}). Analysis of ^1H NMR and ^{13}C NMR spectral data of **1** (table 1) revealed the functionalities of three methyl singlets, four methylenes (one olefinic), three methines (one olefinic), two aliphatic quarternary carbons (one oxygenated) and a typical 1,4-disubstituted benzene ring which is similar to that of bakuchiol (**2**) (figure 1), implying that compound **1** is likely a bakuchiol derivative. According to the molecular formula of **1**, six degrees of unsaturation occurred, and the benzene ring and the terminal double bond occupied five degrees of unsaturation, thus the remaining one unsaturation was only attributable to the presence of additional ring in compound **1**.

All the proton signals were assigned to their corresponding carbons by HMQC spectrum, and then the $^1H-^1H$ COSY was used to figure out some structural fragments of $-CH{=}CH_2$ and $-CH_2-CH-CH-CH_2-CH_2-$ as drawn with bold lines (figure 2). Furthermore, in the HMBC of **1** (figure 2), one methine proton at δ_H 2.58 (ddd, $J = 3.3, 11.4, 12.1$ Hz) correlated with the aromatic carbons at δ_C 139.60 (C-1) and at δ_C 130.15 (C-2/6) was assigned to the H-7 to link the benzene ring with C-7. Another methine proton at δ_H 1.71 (m) assigned to the H-12 was correlated with the C-13 (at δ_C 75.14) bearing a hydroxyl group, and the H-14 and H-15 were also correlated with C-13. The attachments of C-8, C-16 and C-18 to C-9 were made by the HMBC correlations of C-9/H-8α, C-9/H-16 and C-9/H-18, respectively. Although the HMBC correlation between H-10 and C-9 did not appear, the connection of C-9 and C-10 could be tentatively established after the other linkages were all settled, and was supported by the HMBC cross-peaks of H-18/C-10 and H-10α/C-8. Therefore, the planar structure of **1** was assigned as in figure 2.

Table 1. ^1H NMR, ^{13}C NMR data and selected HMBC correlations of **1** (in CD_3OD).

No.	δ_c	δ_H (*J, Hz*)	*HMBC (H → C)*
1	139.60		
2, 6	130.15	7.00 (1H, d, 8.4)	C-3, 4, 5, 7
		7.00 (1H, d, 8.4)	
3, 5	116.65	6.70 (1H, d, 8.4)	C-1, 2, 4, 6
		6.70 (1H, d, 8.4)	
4	157.04		
7	43.63	2.58 (1H, ddd, 3.3,11.4,12.1)	C-1, 2, 6, 8, 12
8	50.28	α 1.67 (1H, dd, 3.3, 13.4)	C-7, 9
		β 1.45 (1H, dd, 12.1, 13.4)	C-1, 16, 17
9	38.80		
10	39.10	α 1.81 (1H, m)	C-8, 11, 12
		β 1.38 (1H, m)	
11	25.55	α 1.37 (1H, m)	C-10, 12
		β 1.90 (1H, m)	C-7, 9
12	54.26	1.71 (1H, m)	C-7, 11, 13
13	75.14		
14	30.15	0.75 (3H, s)	C-12, 13, 15
15	26.64	1.00 (3H, s)	C-12, 13, 14
16	147.66	5.82 (1H, dd, 11.0, 17.8)	C-8, 9, 18
17	113.38	5.12 (1H, dd, 1.0, 11.0)	C-9, 18
		5.03 (1H, dd, 1.0, 17.8)	C-9, 16, 18
18	32.16	0.95 (3H, s)	C-8, 9, 10, 16

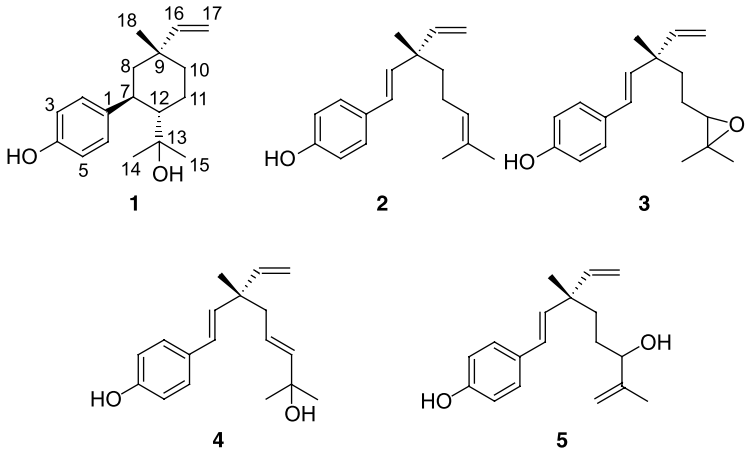

Figure 1. The structures of **1–5**.

The relative configuration and conformation of **1** were deduced by a NOESY experiment (figure 3). The H-7 correlating with H-16 at δ_H 5.82 (dd, $J = 11.0$, 17.8 Hz) and H-11α at δ_H 1.37 (m) showed that the H-7, vinyl group and H-11α occupied the *axial*-bond of C-7, C-9 and C-11, respectively, indicating that the six-membered ring took a chair conformation, and the aromatic ring at C-7 and vinyl at C-9 were in *trans*-configuration. The NOESY correlations between Me-15 (δ_H 1.00, s) and H-7 indicated that the 2-hydroxy-isopropanyl group was also in the *trans* position of the C-7 aromatic ring. The structure of cyclobakuchiol C was thus elucidated to be **1** as shown in figure 1.

For the known compounds, bakuchiol (**2**) was identified by direct comparison with authentic sample (co-TLC, ^{1}H NMR, MS); 12,13-dihydro-12,13-epoxybakuchiol (**3**), 13-hydroxyisobakuchiol (**4**) and 12-hydroxyisobakuchiol (**5**), isolated from this plant for the first time, were identified by comparison of their spectral data (^{1}H NMR, ^{13}C NMR, EI-MS) with those reported [7].

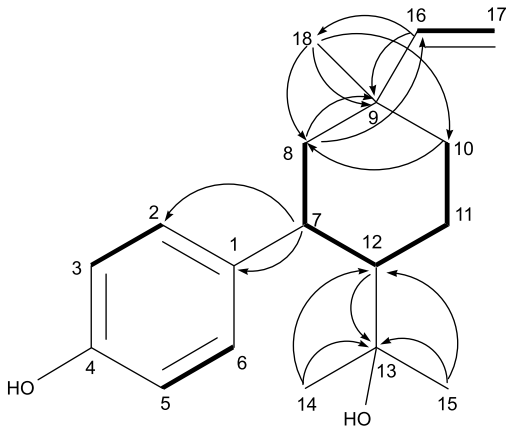

Figure 2. ^{1}H–^{1}H COSY (bold lines) of **1**; key HMBC correlations (curved lines H → C) of **1**.

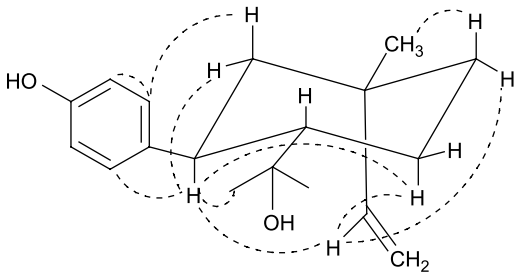

Figure 3. Selected NOESY correlations (H ··· H) of **1**.

3. Experimental

3.1 General experimental procedures

Optical rotations were recorded on a Perkin–Elmer polarimeter 341. IR spectra were measured on a Nicolet Magna 750 spectrometer with KBr disc. NMR spectra were obtained on a Bruker AM-400 MHz spectrometer. General ^{1}H NMR data were run at 400 MHz, and ^{13}C NMR data were measured at 100.6 MHz. Chemical shifts are expressed in ppm relative to TMS. EI-MS and ESI-MS were recorded on a Finnigan MAT 95 mass spectrometer.

3.2 Plant material

The seeds of *Psoralea corylifolia*, harvested in September 1999 in Anhui Province of China, were authenticated by Dr. Ying Xiang at the Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, CAS, China, where a voucher specimen is deposited (accession number Pc-1999-1Y).

3.3 Extraction and isolation

Powder of dried seeds of *P. corylifolia* (2.0 kg) was extracted with 95% EtOH three times to give 592 g crude extract. Part of the extract (392 g) was suspended in 2.5 L water and then partitioned with petroleum ether and ethyl acetate successively to give fractions petroleum ether (143 g), ethyl acetate (120 g) and water (81.5 g), respectively. The petroleum ether fraction (80 g) was subjected to column chromatography on silica gel eluted with a gradient of acetone in petroleum ether to yield fractions 1–6. Fractions 1–4 were combined to give a total of 56 g oily material, part of which (*ca*. 1 g) was separated by column chromatography to give compound **2** (100 mg). Fraction 5 (4.5 g) was re-chromatographed on a silica gel column eluted with $CHCl_3$ to give fractions 5a–5e. Fraction 5d was separated by a column of Sephadex LH-20 (ethanol) to give three major parts 5d1–5d3; each of them was further purified on a silica gel column eluted with petroleum ether/EtOAc (4:1 → 3:1) to obtain **3** (70 mg), **4** (110 mg) and **5** (37 mg), respectively. Compound **1** (11 mg) was obtained from the fraction 5c by CC on silica gel eluted with petroleum ether/EtOAc (6:1).

3.3.1 Cyclobakuchiol C (1). Colourless gum; $[\alpha]_D^{20}$ − 15.3 (*c* 0.38, MeOH); IR (KBr) ν_{max} (cm^{-1}): 3525, 3425 (OH), 2924, 2852 (C–H), 1616, 1514 (Ar-, C=C), 1452, 1379 (C–H),

1228, 1176 (C–O); ^{1}H NMR and ^{13}C NMR: see table 1. EI-MS (rel. int.): *m/z*: 274 $[M]^{+}$(22), 256 (44), 216 (33), 173 (79), 134 (94), 107 (100); HREI-MS: *m/z*: 274.1925 $[M]^{+}$ (calcd for $C_{18}H_{26}O_2$, 274.1933).

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