

Two new rearranged abietane diterpenoids from tropical *Isodon coetsa*

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(Received 20 January 2005; revised 23 May 2005; in final form 31 May 2005)

Two new rearranged abietane diterpenoids, sincoetsin A (**1**) and sincoetsin B (**2**), were isolated from the
aerial part of *Isodon coetsa* (Buth-Ham ex D.Don) Hara collected in Singapore, and their structures were
determined by spectroscopic methods, especially 2D NMR techniques.

Keywords: *Isodon coetsa*; Sincoetsin A; Sincoetsin B; Abietane diterpenoids

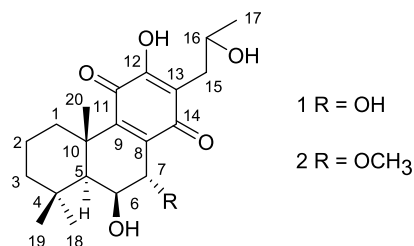
1. Introduction

Many plants of the genus *Isodon* have been used in traditional Chinese folk medicine as anti-bacterial, anti-inflammatory and anti-tumour reagents, and have become an abundant resource of naturally occurring bioactive *ent*-kauranoid [1]. *Isodon coetsa* (Buth-Ham ex D.Don) Hara, native to different areas of the Chinese mainland, has been reported to contain *ent*-kauranoids [2–7], but no chemical constituents have been reported on tropical species up to now. Our investigation on this plant collected in Singapore led to the isolation of two rearranged abietane derivatives, sincoetsin A (**1**) and sincoetsin B (**2**), which was the first time abietane diterpenoids from *I. coetsa* have been isolated. Herein, we present the isolation and structural determination of these two new abietane diterpenoids.

2. Results and discussion

Sincoetsin A (**1**) (figure 1) was obtained as a yellow powder. Its molecular formula $C_{20}H_{28}O_6$ was deduced from quasimolecular ion peak $[M + Na]^+$ at m/z 387 in positive

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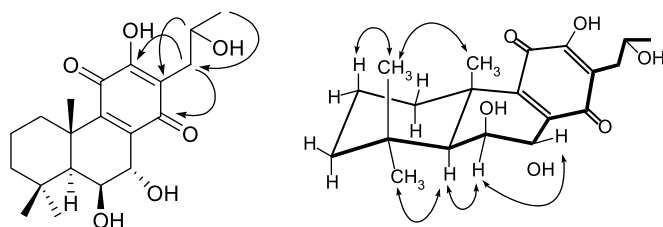
Figure 1. Structures of compounds **1** and **2**.

ESI-MS and NMR data (see table 1), which was consistent with a quasimolecular ion peak $[M + Na]^+ 387.1790$ (calcd for $C_{20}H_{28}O_6Na$, 387.1783) in HRESI-MS (positive). UV spectrum analysis showed the maximum absorptions at 207, 219 and 275 nm. IR spectra demonstrated absorptions at 3442, 2964, 2927 1631, and 1376 cm^{-1} , revealed the presence of carbonyl groups and hydroxyl groups. ^1H NMR data showed four methyls at δ_{H} 0.98, 0.92, 1.16 and 1.50. The ^{13}C NMR spectrum exhibited 20 carbon signals, including four methyls (δ_{C} 23.3, 33.5, 23.7 and 21.4), four methylenes, four methines and eight quaternary carbons. Characteristic signals at δ_{C} 183.5 and 187.3 indicated an 8,12-dien-11,14-dione abietane skeleton [8]. The NMR data of **1** showed close similarity with the known compound lophanthoidin E [8] except for those of the side chain, which implied that **1** contained a different side chain at the C-13 position relative to lophanthoidin E. A 2-hydroxyl propyl group linked to the C-13 position was elucidated

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

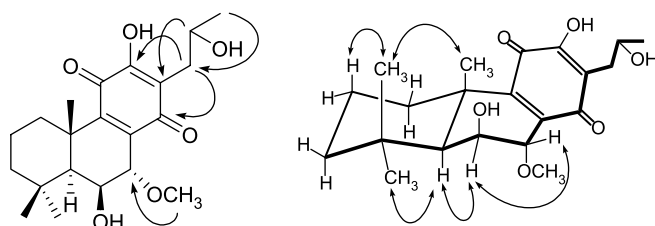
No.	<i>1</i>		<i>2</i>	
	δ_{H} (mult, J)	δ_{C} (mult.)	δ_{H} (mult, J)	δ_{C} (mult.)
1	1.06 (m), 2.49 (m)	37.7 (t)	1.04 (m), 2.50 (m)	38.1 (t)
2	1.45 (m), 1.75 (m)	18.8 (t)	1.43 (m), 1.75 (m)	18.9 (t)
3	1.35 (m), 1.12 (m)	42.1 (t)	1.41 (m), 1.17 (m) ^a	42.0 (t)
4		33.3 (s)		33.3 (s)
5	1.43 (s)	47.7 (d)	1.48 (s)	48.9 (d)
6	4.05 (br s)	68.2 (d)	4.42 (d, 1.9 Hz)	65.4 (d)
7	4.36 (d, 4.1 Hz)	65.7 (d)	4.09 (d, 1.9 Hz)	75.7 (d)
8		140.3 (s)		138.8 (s)
9		146.8 (s)		148.6 (s)
10		38.3 (s)		38.6 (s)
11		183.5 (s)		182.9 (s)
12		154.1 (s)		152.8 (s)
13		117.1 (s)		117.1 (s)
14		187.3 (s)		188.1 (s)
15	2.43 (dd, 6.5, 12.5 Hz) 2.36 (dd, 5.6, 12.5 Hz)	32.5 (t)	2.61 (dd, 6.5, 12.5 Hz) 2.52 (dd, 5.6, 12.5 Hz)	32.4 (t)
16	3.76 (m)	65.2 (d)	3.96 (m)	67.4 (t)
17	0.98 (d, 6.1 Hz)	23.3 (q)	1.23 (d, 4.0 Hz)	23.4 (q)
18	0.92 (s)	33.5 (q)	0.98 (s)	33.6 (q)
19	1.16 (s)	23.7 (q)	1.17 (s) ^a	24.1 (q)
20	1.50 (s)	21.4 (q)	1.53 (s)	21.6 (q)
OMe			3.49 (s)	58.4 (q)

^aOverlapped signals.

Figure 2. The key HMBC and ROESY correlations of **1**.

from key HMBC correlations of Me-17 (δ_{H} 0.98) with C-15 (δ_{C} 32.5), H-16 (δ_{H} 3.76) with C-13 (δ_{C} 117.1), H-15a (δ_{H} 2.43) and H-15b (δ_{H} 2.36) with C-12 (δ_{C} 154.1) and C-13 (figure 2). Biogenetically, the relative configuration of Me-19 and Me-20 of abietane diterpenoid takes a β orientation, while Me-18 and H-5 have an α orientation. From ROESY spectra, the correlations of H-6 with H-5 suggested that H-6 was an α configuration, while H-7 was a β orientation due to the small coupling constant and the ROESY correlation between H-7 and H-6 (figure 2). Therefore, compound **1** was identified as a rearranged abietane derivative, 17(15 \rightarrow 16)-abeo-6 β ,7 α ,11,16-tetrahydroxy-8,12-abietadiene-11,14-dione, and was named *sincoetsin A*.

Sincoetsin B (**2**) (figure 1) was obtained as a yellow powder, and has a molecular formula of $\text{C}_{21}\text{H}_{30}\text{O}_6$ determined by analysis of ^1H NMR, ^{13}C NMR and DEPT data (see table 1), which was verified by positive HRESI-MS ($[\text{M} + \text{Na}]^+ m/z$ 401.1911 (calcd for $\text{C}_{21}\text{H}_{30}\text{O}_6\text{Na}$, 401.1940). UV spectra showed maximum absorptions at 205 and 275 nm. IR spectra demonstrated absorptions at 3427, 2928, 1638, 1360, 1323 cm^{-1} , and revealed the presence of carbonyl groups and hydroxyl groups. ^1H NMR spectra displayed four methyl signals at δ_{H} 1.23, 0.98, 1.17, 1.53 and a methoxyl at δ_{H} 3.49. ^{13}C NMR and DEPT spectra of **2** exhibited signals for 21 carbons, including one methoxyl, four methyls, four methylenes, four methines and eight quaternary carbons. Detailed comparison of ^1H NMR and ^{13}C NMR data of **2** with those of **1** displayed extremely close analogy except for an additional methoxyl and downfield shift of C-7 in **2**, which suggested that the C-7 position of **2** was possibly substituted by a methoxyl instead of a hydroxyl group in **1**. HMBC correlations of the methoxyl signal at δ_{H} 3.49 (s) with C-7 (δ_{C} 75.7) further confirmed the above deductions (figure 3). The ROESY spectrum of **2** established the same relative configurations with those of **1** (figure 3). Thus, the structure of **2** was determined to be 17(15 \rightarrow 16)-abeo-6 β ,11,16-trihydroxy-7 α -methoxyl-8,12-abietadiene-11,14-dione, and was named *sincoetsin B*.

Figure 3. The key HMBC and ROESY correlations of **2**.

3. Experimental

3.1 General experimental procedures

Melting points were measured on an XRC-1 micromelting apparatus and are uncorrected. IR and UV spectra were obtained on a Bio-Rad FTS-135 infrared spectrometer with KBr pellets and a Shimadzu double-beam 210A spectrometer, respectively. MS spectra were performed on a VG Autospec-3000 spectrometer. ^1H , NMR ^{13}C NMR and 2D NMR were recorded on a Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. The silica gel for TLC and column chromatography was obtained from Qingdao Marine Chemical Inc., China.

3.2 Plant material

The leaves of *Isodon coetsa* were collected in Singapore in May 2004 and identified by Professor Xi-Wen Li, Kunming Institute of Botany, Chinese Academy of Sciences. The voucher specimen is deposited in the Natural Science and Science Education Department, Nanyang Technological University of Singapore.

3.3 Extraction and isolation

The air-dried and powdered leaves of *I. coetsa* (1.8 kg) were extracted with 70% acetone for three times and filtered. The combined filtrate was concentrated *in vacuo* and partitioned with petroleum ether and EtOAc. The EtOAc extract was evaporated to afford residue (11.2 g), which was applied to the silica gel column (200–300 m) eluting with CHCl_3 and an acetone gradient system (1:0, 9:1, 8:2 and 7:3) to give fractions I–IV. Fraction III was repeatedly chromatographed over a silica gel column eluting with petroleum/isopropyl (9:1) to obtain compounds **1** (78 mg) and **2** (33 mg).

3.3.1 Sincoetsin A (1). Yellow powder, $\text{C}_{20}\text{H}_{28}\text{O}_6$; $[\alpha]_D^{14} - 11.56$ (*c* 0.5, MeOH); UV (MeOH): λ_{max} (log ϵ) = 207 nm (4.18), 219 nm (4.19), 275 nm (3.96); IR (KBr) ν_{max} (cm^{-1}): 3442, 2964, 2927, 1631, 1376; ^1H NMR (DMSO, 500 MHz) and ^{13}C NMR (DMSO, 100 MHz): see table 1; ESI-MS (positive) m/z : 387 $[\text{M} + \text{Na}]^+$; HRESI-MS (positive) m/z : 387.1790 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{20}\text{H}_{28}\text{O}_6\text{Na}$, 387.1783).

3.3.2 Sincoetsin B (2). Yellow powder, $\text{C}_{21}\text{H}_{30}\text{O}_6$; $[\alpha]_D^{14} + 0.00^\circ$ (*c* 0.5, CHCl_3); UV (MeOH): λ_{max} (log ϵ) = 205 nm (4.81), 275 nm (3.94); IR (KBr) ν_{max} (cm^{-1}): 3427, 2928, 1638, 1360, 1323; ^1H NMR (MeOH, 500 MHz) and ^{13}C NMR (DMSO, 100 MHz): see table 1; ESI-MS (positive) m/z : 401 $[\text{M} + \text{Na}]^+$; HRESI-MS (positive) m/z : 401.1911 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{21}\text{H}_{30}\text{O}_6\text{Na}$, 401.1940).

Acknowledgements

This project was supported by a grant (P-04-12) from the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany. The author is also grateful to Professor Chang-xiang Chen of Kunming Institute of Botany, Chinese Academy of Sciences.

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