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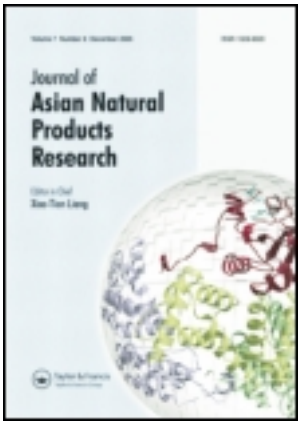

Journal of Asian Natural Products Research

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ganp20

Terpenoids from Incarvillea arguta

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Published online: 11 Dec 2012.

To cite this article: Yong-Ming Yan , Min Hu , Mei Yang , Xiao-Ping Dong & Yong-Xian Cheng (2013) Terpenoids from Incarvillea arguta, Journal of Asian Natural Products Research, 15:1, 9-14, DOI: 10.1080/10286020.2012.739617

To link to this article: http://dx.doi.org/10.1080/10286020.2012.739617

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Journal of Asian Natural Products Research, 2013
Vol. 15, No. 1, 9–14, http://dx.doi.org/10.1080/10286020.2012.739617

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Terpenoids from Incarvillea arguta

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(*Received 21 June 2012; final version received 10 October 2012*)

One new monoterpenoid, (+)-argutoid A (**1**), three new iridoids, (−)-incarvoid A (**2**), (+)-incarvoid B (**3**), and incarvoid C (**4**), and five known compounds were isolated from *Incarvillea arguta*. Their structures were characterized by means of spectroscopic methods.

Keywords: *Incarvillea arguta*; Bignoniaceae; monoterpenoid; iridoid

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1. Introduction

Incarvillea arguta (Bignoniaceae) is a well-known ethnobotanical herb in China. It has been used to treat hepatitis, nephritis, and cancer in the Yi-nationality and Miao-nationality regions [1,2], and this has aroused great interest in the past [3]. Our previous work on the whole plants of *I. arguta* led to the isolation of eremophilane sesquiterpenes and their dimers [4]. In a continuing study on this plant, we isolated four new terpenoids and five known compounds (Figure 1).

2. Results and discussion

Compound **1** had the molecular formula of $C_{10}H_{14}O$ from its HR-EI-MS at *m/z* 150.1050 $[M]^+$, ^{13}C NMR, and DEPT spectra, indicating four degrees of unsaturation. The ^{13}C NMR and DEPT spectra showed 10 carbons attributed to 1 methyl, 5 methylene including 2 oxygenated carbons and 1 olefinic carbon, 1 methine, and 3 olefinic quaternary carbons. In addition to two double bonds, there should be two rings in the structure. The COSY spectrum showed a spin system of H-9/H-5/H-6/H-7. The architecture of **1** was assembled by HMBC correlations, which were H_3-9/C-4, H-8/C-3a, and H-7/C-3a (Figure 2). C-1 and C-3 are linked via an ether bond evidenced from HMBC correlations of H-1/C-3 and their characteristic carbon chemical shifts. The configuration determination at C-5 is challengeable. In this study, we did not assign its absolute configuration yet. Accordingly, the structure of **1** was assigned as shown in Figure 1, named (+)-argutoid A.

The molecular formula of compound **2** was established as $C_{10}H_{14}O$ from its HR-EI-MS at *m/z* 150.1042 $[M]^+$, ^{13}C NMR, and DEPT spectra, indicative of four degrees of unsaturation. The ^1H and ^{13}C NMR spectral data of **2** (Table 2) were similar to those of **5** which is a seco-iridoid. However, compared to **5**, **2** had two more degrees of unsaturation, in addition to one more double bond present

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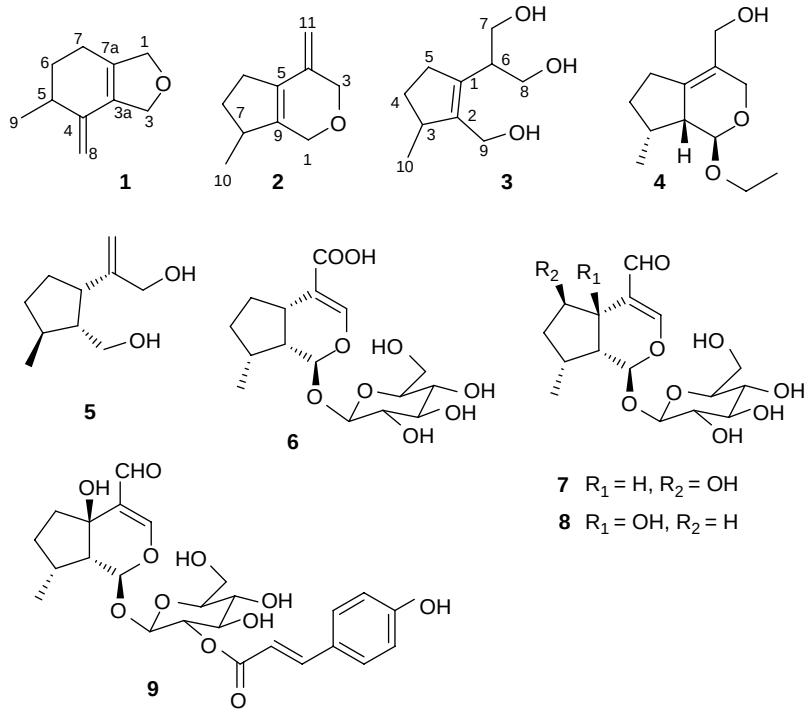

Figure 1. The structures of compounds **1**–**9**.

in **2**, the rest one degree of unsaturation required that a ring was formed in **2**. This conclusion was supported by the HMBC correlation of H-3/C-1. The $^{1}H-^{1}H$ COSY correlation of H-6/H-7/H-8/H_3-10, together with HMBC correlations of H-6/C-5 (δ 138.1) and H_3-10/C-9 (δ 143.6) (Figure 2), suggested a double bond between C-5 and C-9. The stereochemistry at C-8 of **2** remained still unsolved. Thus, the structure of **2** was assigned as shown in Figure 1 and named (−)-incarvoid A.

The molecular formula of compound **3** was deduced as $C_{10}H_{18}O_3$ by its HR-EI-MS at *m/z* 186.1264 $[M]^+$, ^{13}C NMR, and DEPT spectra, requiring two degrees of unsaturation. The IR spectrum showed the presence of hydroxy group (3396 cm^{-1}). The ^{13}C NMR and DEPT spectra showed 10 carbons attributive to 1 methyl, 5 methylene, 2 methine, and 2 olefinic quaternary carbons. In addition to one double bond, there should be one ring in the molecule. The position of the double

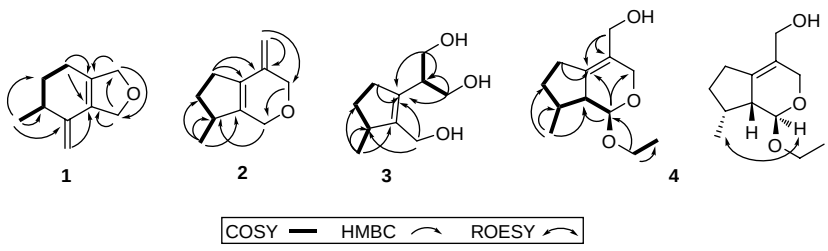

Figure 2. COSY and HMBC correlations of **1**–**4**.

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bond between C-1 and C-2 was evidenced from the HMBC correlations of H-5, H-7, H-8/C-1, and H_3-10, H-9/C-2 (Figure 2). In contrast to **5**, an olefinic CH_2 (C-7) in **5** was replaced by a hydroxymethyl group in **3**. The $^1H-^1H$ COSY correlation of H-7/H-6/H-8 and the featured carbon chemical shift of C-7 confirmed the above conclusion. Likewise, the configuration at C-3 remained unknown. Thus, the structure of **3** was assigned as shown in Figure 1 and named (+)-incarvoid B.

Compound **4** had the molecular formula of $C_{12}H_{20}O_3$ from its HR-EI-MS at *m/z* 212.1409 $[M]^+$, ^{13}C NMR, and DEPT spectra, indicating three degrees of unsaturation. The ^{13}C NMR and DEPT spectra showed 12 carbons, in addition to a typical ethoxy group, 10 of which were attributed to 1 methyl, 4 methylene including 2 oxygenated ones, 3 methine, and 2 olefinic quaternary carbons. Except for one double bond, the molecule should have two rings. The $^1H-^1H$ COSY spectrum showed spin systems of H-1/H-9/H-8/H-7/H-6 and H-8/H_3-10. The structure of **4** was constructed mainly by HMBC correlations. The HMBC correlations of H-6, H-11, H-1/C-5, H-11/C-4, and H-1/C-3 suggested that compound **4** is a typical iridoidal derivative as shown. The position of ethyl group was assigned due to the HMBC correlation of H-1′ at δ 3.86 and 3.51 with C-1. ROESY correlations of H-1/H_3-10 suggested that H-1 and H_3-10 are spacially vicinal (Figure 2). The $J_{H\text{-}1,H\text{-}9}$ value (7.2 Hz) indicated that H-1 and H-9 have a *trans*-relationship. Accordingly, the structure of **4** was assigned as shown, named incarvoid C.

The known compounds were identified as (2-((1*S*,2*R*,3*S*)-2-(hydroxymethyl)-3-methylcyclopentyl)prop-2-en-1-ol (**5**) [5], methylation of 8-epideoxyloganic acid (**6**) [6], 6β-hydroxyboschnalosid (**7**) [7], plantarenaloside (**8**) [8], and 2′-*O*-coumaroyl-plantarenaloside (**9**) [9], respectively, by comparing their spectroscopic data with literature data.

3. Experimental

3.1 General experimental procedures

Optical rotations were recorded on a Horiba SEPA-300 polarimeter (Horiba, Kyoto, Japan). UV spectra were recorded on a Shimadzu double-beam 210A spectrometer (Shimadzu, Kyoto, Japan). IR spectra were recorded on a Tensor 27 spectrometer (Bruker Optics, Germany) with KBr pellets. NMR spectra were determined on a Bruker AV-400, or a DRX-500 (Bruker, Switzerland), or an Avance III 600 spectrometer (Bruker, Switzerland), with TMS as an internal standard. Mass spectra were obtained on a VG Auto Spec-3000 mass spectrometer (VG, Manchester, England). Column chromatography (CC) was performed on silica gel (200–300 mesh, Qingdao Marine Chemical, Inc., Qingdao, China), RP-18 (40–60 μm, Daiso Co., Japan), MCI gel CHP 20P (75–150 μm, Tokyo, Japan), and Sephadex LH-20 (Amersham Biosciences, Sweden). Semi-preparative HPLC was carried out using an Agilent 1200 liquid chromatograph, the column used was a 250 mm × 4.6 mm i.d., 5 μm, Zorbax SB-C_{18}.

3.2 Plant material

Whole plants of *I. arguta* were collected in July 2008 from Dongchuan County, Yunnan Province, China, and were identified by Mr Bin Qiu of Yunnan Institute of Materia Medica. A voucher specimen (CHYX-0474) is deposited at the Kunming Institute of Botany, Chinese Academy of Sciences.

3.3 Extraction and isolation

Dried whole plant powders of *I. arguta* (20 kg) were extracted three times with 95% EtOH (each 25 liters, 48 h) at room temperature to give an extract (3 kg), which was suspended in H_2O and partitioned with petroleum ether, EtOAc, and *n*-BuOH (each 4 × 8 liters). The EtOAc

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extract (75 g) was subjected to silica gel CC ($CHCl_3$/MeOH, 1:0 to 0:1) to produce fractions A–F. Fraction B (7.3 g) was separated into fractions B1–B6 by MCI gel CHP 20P with gradient aqueous MeOH (40–100%) as the eluent. Fraction B3 (1.2 g) was gel filtered over Sephadex LH-20 (MeOH), followed by RP-18 column (aqueous MeOH, 40–70%), to give B3.3 (160 mg), which was further purified by using preparative TLC eluted with $CHCl_3$/MeOH (20:1) and semi-preparative HPLC (aqueous acetonitrile, 40%, 2 ml/min, detection at 210 nm) to give compound **4** (0.6 mg, $R_t = 19.4$ min). Fraction C (11.4 g) was separated into fractions C1–C6 by MCI gel CHP 20P with aqueous MeOH (20–100%) as the eluent. Fraction C3 (1.9 g) was gel filtered over RP-18 column (aqueous MeOH, 20–40%) to give C3.6 (100 mg), which was further purified by using preparative TLC eluted with $CHCl_3$/MeOH (15:1) to give compound **2** (14 mg). Fraction C3.8 (110 mg) was gel filtered over Sephadex LH-20 (MeOH), followed by preparative TLC eluting with petroleum ether/^{i}PrOH (7:1) and finally purified via semi-preparative HPLC (aqueous acetonitrile, 30%, 2 ml/min, detection at 210 nm) to afford **5** (9.5 mg, $R_t = 20.3$ min) and **1** (8 mg, $R_t = 21.4$ min). Fraction D (31.6 g) was divided into D1–D6 by MCI gel CHP 20P eluted with aqueous MeOH (10–60%), of which fraction D2 (1.5 g) was gel filtered over Sephadex LH-20 (MeOH) followed by silica gel CC ($CHCl_3$/Me_2CO, 3:1) and finally purified by preparative TLC eluting with $CHCl_3$/MeOH (7:1) to give **7** (11 mg) and **3** (7.5 mg). Fraction E (12.5 g) was divided into D1–D5 by MCI gel CHP 20P eluted with aqueous MeOH (10–60%). Among them, fraction E2 (1.4 g) was submitted to Sephadex LH-20 CC (MeOH) and further purified by RP-18 column (aqueous MeOH, 10–40%) and silica gel CC ($CHCl_3$/Me_2CO, 3:1) to give **6** (35 mg), **8** (23 mg), and **9** (25 mg).

Table 1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectral data of **1** (δ in ppm, J in Hz).

	1[a]	
No.	δ_H	δ_C
1	4.43 (d, 12.0) 4.34 (d, 12.0)	61.7 (CH_2)
3	4.24 (s)	62.8 (CH_2)
3a		139.9 (qC)
4		154.3 (qC)
5	2.42 (m)	40.8 (CH)
6	1.91 (m) 1.17 (m)	32.8 (CH_2)
7	2.50 (ddd, 16.5, 8.8, 3.0) 2.34 (m)	28.8 (CH_2)
7a		135.3 (qC)
8	5.24 (s) 5.00 (s)	109.1 (CH_2)
9	1.06 (d, 6.6)	15.3 (CH_3)

[a] Acetone-d_6.

3.3.1 (+)-Argutoid A (*1*)

Colorless gums; $[\alpha]_D^{23} + 11.8$ (c 0.26, MeOH). UV (MeOH) λ_{max} (log ε) 241 (2.69), 206 (2.87) nm. IR (KBr) ν_{max}: 2955, 2933, 2870, 1631, 1454, 1384, 1049, and 582 cm^{-1}. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectral data (see Table 1). EI-MS: *m/z* 150 $[M]^+$. HR-EI-MS: *m/z* 150.1050 $[M]^+$ (calcd for $C_{10}H_{14}O$, 150.1045).

3.3.2 (−)-Incarvoid A (*2*)

Colorless gums; $[\alpha]_D^{23} -7.5$ (c 0.28, MeOH). UV (MeOH) λ_{max} (log ε) 205 (2.93) nm. IR (KBr) ν_{max}: 2954, 2928, 2871, 1630, 1454, 1382, 1116, 1047, and 583 cm^{-1}. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectral data (see Table 2). EI-MS: *m/z* 150 $[M]^+$. HR-EI-MS: *m/z* 150.1042 $[M]^+$ (calcd for $C_{10}H_{14}O$, 150.1045).

3.3.3 (+)-Incarvoid B (*3*)

Colorless gums; $[\alpha]_D^{23} + 22.4$ (c 0.32, MeOH). UV (MeOH) λ_{max} (log ε) 206 (3.09) nm. IR (KBr) ν_{max}: 3396, 2951,

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Table 2. ^{1}H and ^{13}C NMR spectral data of **2–4** (δ in ppm, J in Hz).

	2[a]		**3**[b]		**4**[c]	
No.	δ_H[d]	δ_C[d]	δ_H[d]	δ_C[d]	δ_H[e]	δ_C[e]
1a	4.28 (d, 12.0)	57.4 (CH_2)		139.4 (qC)	4.32 (d, 7.2)	102.0 (CH)
1b	4.08 (d, 12.0)					
2				144.3 (qC)		
3a	4.21 (d, 13.0)	65.4 (CH_2)	2.85 (m)	42.0 (CH)	4.29 (d, 15.5)	66.7 (CH_2)
3b	4.16 (d, 13.0)				4.16 (d, 15.5)	
4a		145.2 (qC)	2.05 (m)	32.3 (CH_2)		129.7 (qC)
4b			1.36 (m)			
5a		138.1 (qC)	2.32 (m)	31.3 (CH_2)		135.2 (qC)
5b			2.26 (m)			
6a	2.44 (t, 7.2)	34.7 (CH_2)	2.89 (m)	45.2 (CH)	2.39 (m)	25.7 (CH_2)
6b					2.28 (m)	
7a	2.09 (m)	31.3 (CH_2)	3.65 (dd, 11.1, 6.4)	62.8 (CH_2)	1.73 (m)	32.2 (CH_2)
7b	1.39 (m)		3.63 (dd, 11.1, 6.4)		1.42 (ddd, 12.2, 8.3, 1.3)	
8a	2.91 (m)	41.8 (CH)	3.51 (dd, 15.3, 7.7)	62.7 (CH_2)	2.29 (m)	34.5 (CH)
8b			3.49 (dd, 15.3, 7.7)			
9a		143.6 (qC)	4.21 (d, 12.0)	56.7 (CH_2)	2.31 (m)	49.1 (CH)
9b			4.05 (d, 12.0)			
10	1.09 (d, 6.9)	19.4 (CH_3)	1.07 (d, 6.9)	19.7 (CH_3)	0.72 (d, 6.8)	14.6 (CH_3)
11a	5.18 (s)	114.6 (qC)			4.05 (s)	60.0 (CH_2)
11b	4.90 (s)					
1′a					3.86 (dq, 9.6, 7.1)	64.0 (CH_2)
1′b					3.51 (dq, 9.6, 7.1)	
2′					1.17 (d, 7.1)	15.7 (CH_3)

[a] $CDCl_3$.
[b] CD_3OD.
[c] Acetone-d_6.
[d] ^{1}H (400 MHz) and ^{13}C (100 MHz).
[e] ^{1}H (600 MHz) and ^{13}C (150 MHz).

2870, 1631, 1454, 1372, 1044, 981, and 583 cm^{-1}. ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectral data (see Table 2). EI-MS: *m/z* 186 $[M]^+$. HR-EI-MS: *m/z* 186.1264 $[M]^+$ (calcd for $C_{10}H_{18}O_3$, 186.1256).

*3.3.4 Incarvoid C (**4**)*

Colorless gums; $[\alpha]_D^{23}$ −77.2 (*c* 0.04, MeOH). UV (MeOH) λ_{max} (log ε) 206 (3.01) nm. IR (KBr) ν_{max}: 3441, 2958, 2926, 2855, 1630, 1452, 1384, 1069, and 568 cm^{-1}. ^1H (600 MHz) and ^{13}C NMR (150 MHz) spectral data, see Table 2. EI-MS: *m/z* 212 $[M]^+$. HR-EI-MS: *m/z* 212.1409 $[M]^+$ (calcd for $C_{12}H_{20}O_3$, 212.1412).

Acknowledgments

This work was financially supported by the Open Research Fund of State Key Laboratory Breeding Base of Systematic Research, Development and Utilization of Chinese Medicine Resources, Project of Natural Compound Library Construction from Chinese Academy of Sciences (KSCX2-EW-R-15), and National Natural Science Foundation of China (no. 81060361).

Note

1. These authors contributed equally to this paper.

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