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Note

New monoterpenoids from *Dracocephalum forrestii* aerial parts

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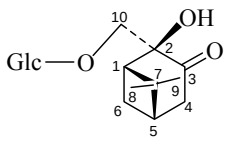
Dracocephalum forrestii (Lamiaceae) has been used as astringent, diuretic and antipyretic in traditional Tibetan medicine. Three new 2-hydroxyl substituted pinanone-type monoterpenoids, 2*β*,10-dihydroxy-3-pinanone 10-*O*-β-D-glucopyranoside **1**, 2*α*,5*α*-dihydroxypinan-3-one **2**, and 2*α*,5*α*-dihydroxy-3-pinanone 5-*O*-β-D-glucopyranoside **3**, are isolated from the whole plant of this medicine. The structures of compounds **1-3** are determined by spectroscopic methods.

Keywords: Monterpenoids, *Dracocephalum forrestii*

Dracocephalum forrestii (Lamiaceae), commonly known as qinglan, is a wild perennial plant growing in Lijiang and Diqing regions of Yunnan province, P. R. China[1]. It has been used as astringent, diuretic and antipyretic in traditional Tibetan medicine[2]. We have reported on the isolation of several known and novel pentacyclic triterpenoids from the whole plant of *Dracocephalum forrestii*[3]. As a continuation of investigation on the chemical constituents of this medicine, three new monoterpenes were isolated, namely, 2*β*,10-dihydroxy-3-pinanone 10-*O*-β-D-glucopyranoside **1**, 2*α*,5*α*-dihydroxypinan-3-one **2**, and 2*α*,5*α*-dihydroxy-3-pinanone 5-*O*-β- D-glucopyranoside **3**. The structures of compounds **1-3** were determined by spectroscopic methods.



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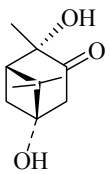

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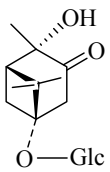

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Results and Discussion

The dried plant material of *D. forrestii* was extracted with 70% EtOH. The extract was filtered, concentrated in *vacuo* to a suitable volume, suspended in H_2O, and then successively extracted with petroleum ether, AcOEt, and *n*-BuOH. The *n*-BuOH-soluble part was purified by successive column chromatography on silica gel, RP-18 gel, and Sephadex LH-20 to afford the compounds **1-3**.

Compound **1** was obtained as a colourless oil. Its negative FAB-MS spectrum showed a quasimolecular ion peak at *m/z* 345 $[M–H]^-$. The molecular formula was determined to be $C_{16}H_{26}O_8$ by HRESI-MS (*m/z* observed 345.1557 $[M–H]^-$, calculated 345.1549), implying four degrees of unsaturation. Absorptions for hydroxyl (3424 cm^{-1}) and carbonyl (1718 cm^{-1}) groups were observed in its IR spectrum. A careful analysis of the ^1H and ^{13}CNMR spectral data of **1** revealed that **1** was a monoterpene glycoside and the aglycone portion was analogous to that of 2-hydroxy-3-pinanone[4,5]. The sugar moiety was determined to be *β*-D-glucopyranose on the basis of the large coupling constants of the anomeric proton at δ 4.26 (J = 7.8 Hz). HMBC correlations of the anomeric proton of the glucose with C-10 (δ 73.6), and H_b-10 (δ 3.47) with C-Glc-1 (δ 104.9) suggested that the sugar moiety was attached to the C-10 position. The ROESY correlations of H_b-6 (δ 1.52) with H_a-10 (δ 4.11) and H_b-4 (δ 2.52), H-8 (δ 1.36) with H_a-6 (δ 2.58) and H-1 (δ 2.39), and H-9 (δ 0.97) with H_a-4 (δ 2.68) indicated that the OH group at C-2 was *β*-oriented. Therefore, compound **1** was established as 2*β*,10-dihydroxy-3-pinanone 10-*O*-β-D-glucopyranoside.

Compound **2** was obtained as a colourless oil. Its positive ESI-MS spectrum showed a ion peak at *m/z* 207 $[M+Na]^+$. The molecular formula was determined to be $C_{10}H_{16}O_3$ by HRESI-MS (*m/z* observed 207.0989 $[M+Na]^+$, calculated 207.0997), implying three degrees of unsaturation. Absorptions for hydroxyl (3389) and carbonyl (1723) cm^{-1} groups were observed in its IR spectrum. Analysis of the ^1H and ^{13}C NMR spectra indicated that **2** was a pinanone-type monoterpene. In the HMBC spectrum, C-5 (δ 72.2) coupled to H-1 (δ 2.05), H_a-4 (δ 2.76), H_b-4 (δ 2.65), H_a-6 (δ 2.35), H_b-6 (δ 2.12), H-8 (δ 1.31), and H-9 (δ 0.89), H-10 (δ 1.38) coupled to C-1 (δ 42.8), C-2 (δ 75.0), and C-3 (δ 212.1), revealed that the OH groups were at C-2 and C-

5 positions. The ROESY correlations of H-9 with H-10 and H_a-4, H-8 with H_a-6 and H-1, and H_b-4 with H_b-6 indicated that the OH group at C-2 was α-oriented. Therefore, compound **2** was established as 2α, 5α-dihydroxypinan-3-one.

Compound **3** was obtained as a colourless oil. Its negative FAB-MS spectrum showed a quasimolecular ion peak at *m/z* 345 $[M–H]^-$. The molecular formula was determined to be $C_{16}H_{26}O_8$ by HRESI-MS (*m/z* observed 345.1560 $[M–H]^-$, calculated 345.1549), implying four degrees of unsaturation. Absorptions for hydroxyl (3379) and carbonyl (1716) cm^{-1} groups were observed in its IR spectrum. Analysis of the ^1H and ^{13}C NMR spectra revealed that **3** was a pinanone-type monoterpene glycoside and the aglycone portion was compound **2**. The sugar moiety was determined to be β-D-glucopyranose on the basis of the large coupling constants of the anomeric proton at δ 4.39 (*J* = 7.7 Hz). HMBC correlation of the anomeric proton of the glucose with C-5 (δ 78.4) and ROESY correlations of the anomeric proton with H_a-4 (δ 2.98), H_a-6 (δ 2.52), and H_b-6 (δ 2.14) were observed, which indicated the sugar moiety was attached to the C-5 position **(Figure 1)**. Therefore, compound **3** was established as 2α,5α-dihydroxy-3-pinanone 5-*O*-β-D-glucopyranoside.

Experimental Section

General. IR spectra were taken on a Nicolet AVATAR-360. Optical rotations were taken on a Perkin-Elmer-341 polarimeter. The 1D and 2D NMR spectra were recorded on a Bruker DRX-500 spectrometer. FAB-MS was performed on a VG-Autospec-3000 spectrometer. HRESI-MS was performed on a API Qstar Pulsar spectrometer. Column chromatography was carried out on silica gel (200-300 mesh, Qingdao, China), Sephadex LH-20 (Amersham Pharmacia Biotech, Uppsala, Sweden), and RP-18 (Merck, Darmstadt, Germany). TLC was carried out in silica gel (GF_{254}, Qingdao, China).

Plant material. The plant material was collected in Xianggelila county, Yunnan Province, China, in September 2002, and identified as *Dracocephalum forrestii* by Mr. A Dou (Deqing Tibetan hospital). A voucher specimen was deposited in Key Laboratory of Medicinal Chemistry for Natural Resource,

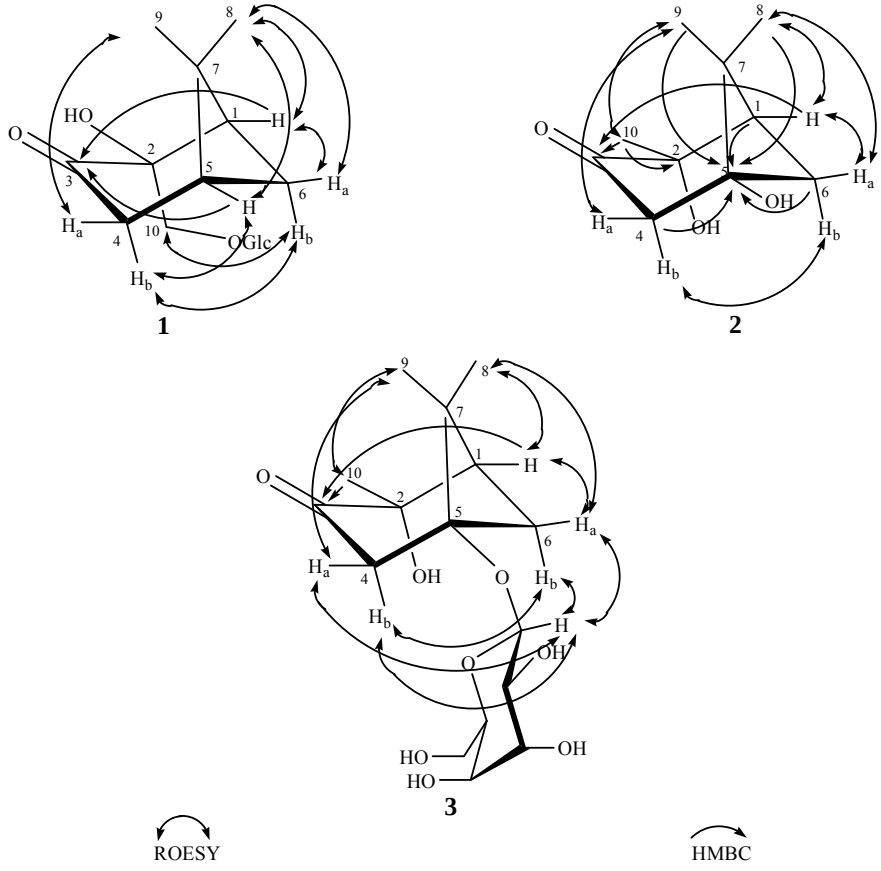

Figure 1— Selected ROESY and HMBC correlations of **1**, **2** and **3**

Table I — ^{13}C NMR spectral data of compounds **1-3** (**1**and **3** in CD_3OD, **2** in $CDCl_3$; 125 MHz; δ in ppm).

C	1	2	3
1	47.9 d	42.8 d	45.0 d
2	82.1 s	75.0 s	75.8 s
3	214.5 s	212.1 s	213.2 s
4	44.5 t	48.5 t	49.8 t
5	39.8 d	72.2 s	78.4 s
6	30.3 t	36.9 t	33.9 t
7	40.1 s	44.5 s	45.2 s
8	27.5 q	22.1 q	23.5 q
9	23.2 q	20.3 q	20.9 q
10	73.6 t	25.1 q	24.8 q
Glc-1	104.9 d		99.6 d
Glc-2	75.2 d		75.1 d
Glc-3	78.1 d		78.2 d
Glc-4	71.6 d		71.6 d
Glc-5	77.9 d		77.7 d
Glc-6	62.7 t		62.7 t

Yunnan University.

Extraction and isolation. The air-dried and powered plant (4.5 kg) was extracted with 70% EtOH (4 × 10L) at room temperature for 48 hr each time. The residue was suspended in water, and then extracted with petroleum ether, EtOAc and *n*-BuOH, successively. The *n*-BuOH extract (72 g) was chromatographed on silica gel (1.5 kg, 200-300 mesh) and eluted with $CHCl_3$ containing increasing volume of MeOH ($CHCl_3$-MeOH, 95:5-50:50). Fraction A (obtained with $CHCl_3$-MeOH 100:5) was chromatographied over RP-18 with 50% MeOH to afford four subfractions. The second subfraction was further purified by chromatography over Sephadex LH-20 with MeOH as the eluent to afford compound **1** (6 mg) and **3** (26 mg). The third subfraction was further purified by chromatography over Sephadex LH-20 with MeOH as the eluent to afford compound **2** (12 mg).

Compound **1**. colourless oil, $[\alpha]_D^{23}$ –31.1°(*c* = 0.15, MeOH); negative FAB-MS *m/z* (%): 345 $[M-H]^-$ (100), negative HRESI-MS $[M–H]^-$ (*m/z* Calcd. 345.1549, found 345.1557); IR (KBr): 3424, 2926, 1718, 1622, 1383, 1078, 633 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD,δ): 2.39 (1H, t, *J* = 6.3Hz, H-1), 2.68 (1H, dt, *J* = 3.2, 18.9Hz, H_2-4a), 2.52 (1H, dd, *J* = 2.6, 19.2Hz,, H_2-4b), 2.08 (1H, m, H-5), 2.58 (1H, m, H_2-6a), 1.52 (1H, d, *J* = 11.5Hz, H_2-6b), 1.36 (3H, s, H_3-8), 0.97 (3H, s, H_3-9), 4.11 (1H, d, *J* = 10.6Hz, H_2-10a), 3.47 (1H, d, *J* = 10.6Hz, H_2-10b), 4.26 (1H, d, *J* = 7.8Hz, Glc-H-1), 3.18 (1H, dd, *J* = 7.8, 9.2Hz, Glc-H-2), 3.34 (1H, m, Glc-H-3), 3.26 (1H, m, Glc-H-4), 3.24 (1H, m, Glc-H-5), 3.84 (1H, dd, *J* = 1.6, 12.2Hz, Glc-H_2-6a), 3.63 (1H, dd, *J* = 5.4, 12.2Hz, Glc-H_2-6b);^{13}C NMR (125 MHz, CD_3OD), **Table I**.

Compound **2**. colourless oil, $[\alpha]_D^{23}$ +5.8°(*c* = 0.12, MeOH); positive ESI-MS *m/z* (%):207 $[M+Na]^+$ (100), positive HRESI-MS $[M+Na]^+$ (*m/z* calcd. 207.0997, found 207.0989); IR (KBr): 3389, 2975, 2934, 1723, 1624, 1464, 1384, 1303, 1154, 1123, 1072, 1028, 916 cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$,δ): 2.05 (1H, d, *J* = 7.1Hz, H-1), 2.76 (1H, d, *J* = 18.8Hz, H_2-4a), 2.65 (1H, dd, *J* = 6.3, 18.8Hz, H_2-4b), 2.35 (1H, m, H_2-6a), 2.12 (1H, d, *J* = 10.7Hz, H_2-6b), 1.31 (3H, s, H_3-8), 0.89 (3H, s, H_3-9), 1.38 (3H, s, H_3-10); ^{13}CNMR (125 MHz, $CDCl_3$), **Table I**.

Compound **3**. colourless oil, $[\alpha]_D^{22}$ –12.9° (*c* = 0.35, MeOH); negative FAB-MS *m/z* (%): 345 $[M-H]^-$ (100), negative HRESI-MS $[M–H]^-$ (*m/z* calcd. 345.1549, found 345.1560); IR (KBr): 3379, 2927, 1716, 1461, 1375, 1300, 1074, 1032, 908 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD,δ): 1.98 (1H, d, *J* = 7.4Hz, H-1), 2.98 (1H, d, *J* = 18.9Hz, H_2-4a), 2.71 (1H, dd, *J* = 3.9, 18.9Hz, H_2-4b), 2.52 (1H, m, H_2-6a), 2.14 (1H, d, *J* = 10.4Hz, H_2-6b), 1.33 (3H, s, H_3-8), 0.88 (3H, s, H_3-9), 1.31 (3H, s, H_3-10), 4.39 (1H, d, *J* = 7.7Hz, Glc-H-1), 3.16 (1H, dd, *J* = 7.7, 9.1Hz, Glc-H-2), 3.33 (1H, m, Glc-H-3), 3.29 (1H, m, Glc-H-4), 3.24 (1H, m, Glc-H-5), 3.82 (1H, dd, *J* = 2.1, 12.0Hz, Glc-H_2-6a), 3.63 (1H, dd, *J* = 5.0, 12.0Hz, Glc-H_2-6b); ^{13}C NMR (125 MHz, CD_3OD), **Table I**.

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