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Two new epimeric isopavine N-oxides from *Meconopsis horridula* var. *racemosa*

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Abstract

Two new epimeric isopavine N-oxides, amuresinine N-oxide A (**1**) and B (**2**), were isolated from *Meconopsis horridula* var. *racemosa*. Their structures were elucidated by spectroscopic methods.

Keywords: Meconopsis horridula var. *racemosa*; Amuresinine N-oxides

1. Introduction

Meconopsis, a relatively large genus in the family Papaveraceae, is mainly distributed discontinuously in both East Asia and West Europe. There are some species in the north-west Yunnan Province in China. *Meconopsis* are an important and traditional Tibetan plant medicine and have long been used by Tibetan people. Many isoquinoline alkaloids were isolated from plants of this genus and some of them have shown bioactivities such as anti-inflammatory and analgesic activity [1–3]. We describe here two new epimeric isopavine N-oxides from *Meconopsis horridula* var. *racemosa* (Maxim.) Prain.

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2. Experimental

2.1. Plant material

M. horridula var. *racemosa* whole plants were collected on mountains, at altitudes between 3350 and 4800 m, in Li jiang county and Di qin Tibetan Autonomy Prefecture, north-west Yunnan Province, China, from August to September 1998. A voucher specimen has been deposited in the Department of Ethnobotany, Kunming Institute of Botany, Chinese Academy of Sciences.

2.2. Extraction and isolation

Air-dried, powdered plant (1 kg) was extracted by hot 95% EtOH. The extract was evaporated, 5% HCl was added to pH 3–4, and CH_3Cl extraction (I) was performed. The aqueous layer was added with 5% Na_2CO_3 to pH 11–12 and then extracted with CH_3Cl (II). The residue of the latter (400 mg) was Si-gel CC eluting with $CHCl_3/CH_3OH$ gradient (from 20:1 to 8:1) to afford a mixture which was separated by HPLC (Bondapack C18) eluting with 1 ml/min CH_3OH–$(NH_4)_2CO_3$(0.01 M) 45:55 to afford **1** (5 mg) and **2** (7 mg).

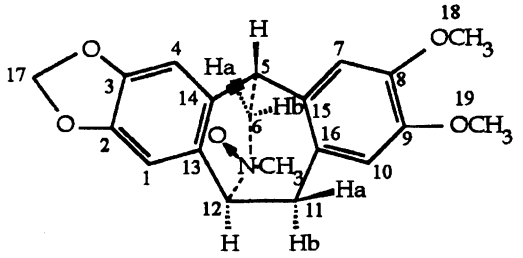
Compound **1**. $[\alpha]_D^{27}$ −101.03° ($CHCl_3$, *c* 0.30); FAB-MS *m/z*: 356[M + H]$^+$(100), 340(24), 295(22), 188(3); HR-FABMS *m/z*: 356.1547[M + H]$^+$ (calc. for $C_{20}H_{21}NO_5$ + H: 356.1498); EI-MS *m/z*: 355[M]$^+$(2), 353[M-2]$^+$(8), 339[M-16]$^+$(39), 296(54), 295(58), 188(100); IR bands (KBr): 3012, 2927, 2853, 1609, 1518, 1486, 1457, 1376, 1352, 1252, 1235, 1201, 1117, 1037, 928, 871 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.92 (1H, *s*, H-1), 6.76 (1H, *s*, H-4), 3.75 (1H, *d, J* 5.38 Hz, H-5), 4.15 (1H, *dd, J* 12.67 and 5.38 Hz, H-6_a), 4.24 (1H, *d, J* 12.67 Hz, H-6_b), 6.61 (1H, *s*, H-7), 6.50 (1H, *s*, H-10), 3.15 (1H, *dd, J* 19.07 and 3.20 Hz, H-11_a), 3.65 (1H, *dd, J* 19.07 and 4.22 Hz, H-11_b), 4.68 (1H, *dd, J* 4.22 and 3.20 Hz, H-12), 5.93 (1H, *d, J* 1.41 Hz, H-17), 5.92 (1H, *d, J* 1.41 Hz, H-17), 3.86 (3H, *s*, H-18), 3.80 (3H, *s*, H-19), 3.52 (3H, *s*, NCH_3); ^{13}C-NMR (125 MHz, $CDCl_3$): 108.86 (C-1), 147.11 (C-2), 147.84 (C-3), 106.39 (C-4), 44.19 (C-5), 78.33 (C-6), 110.81 (C-7), 147.67 (C-8), 148.65 (C-9), 113.55 (C-10), 34.89 (C-11), 78.47 (C-12), 127.22 (C-13), 131.22 (C-14), 132.58 (C-15), 122.55 (C-16), 101.16 (C-17), 56.00 (C-18), 55.95 (C-19), 59.77 (NCH_3).

Compound **2**. $[\alpha]_D^{27}$ −88.98° (CH_3Cl, *c* 0.38); HR-FABMS *m/z*: 356.1489[M + H]$^+$ (calc. for $C_{20}H_{21}NO_5$ + H: 356.1498); EI-MS *m/z*: 355[M]$^+$(2), 353[M-2]$^+$(7), 339[M-16]$^+$(19), 296(47), 295(100), 188(36); IR bands (KBr): 3010, 2923, 2853, 1609, 1517, 1485, 1486, 1457, 1374, 1353, 1253, 1233, 1210, 1118, 1036, 933, 870 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.81 (1H, *s*, H-1), 6.75 (1H, *s*, H-4), 3.66 (1H, *d, J* 5.38 Hz, H-5), 3.98 (1H, *dd, J* 12.67 and 5.38 Hz, H-6_a), 4.22 (1H, *d, J* 12.67 Hz, H-6_b), 6.56 (1H, *s*, H-7), 6.58 (1H, *s*, H-10), 2.91 (1H, *dd, J* 19.07 and 3.20 Hz, H-11_a), 4.73 (1H, *dd J* 19.07 and 4.22 Hz, H-11_b), 4.34 (1H, *dd, J* 4.22 and 3.20 Hz, H-12), 5.98 (1H, *d, J* 1.41 Hz, H-17), 5.91 (1H, *d, J* 1.41 Hz, H-17), 3.85 (3H, *s*, H-18), 3.78 (3H, *s*, H-19), 3.12 (3H, *s*, NCH_3); ^{13}C-NMR (125 MHz, $CDCl_3$): 108.14(C-1), 146.83(C-2), 147.34(C-3), 106.54(C-4), 45.00(C-5), 75.94(C-6), 110.14(C-

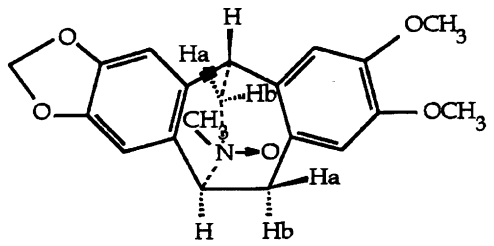
7), 146.19(C-8), 147.13(C-9), 113.83(C-10), 31.43(C-11), 78.48(C-12), 126.40(C-13), 132.21(C-14), 133.77(C-15), 125.14(C-16), 101.37(C-17), 56.03(C-18), 55.98(C-19), 62.38(NCH_3).

3. Results and discussion

The two bases were isolated from the ethanol extract on silica column chromatography and preparative HPLC.



1



2

Compound **1** showed the quasi-molecular ion peak at m/z 356$[M + H]^+$ in FABMS. In combination with ^{13}C and DEPT spectra, its molecular formula was deduced by HR-FABMS showing the molecular ion peak at m/z 356.1547(calc. for $C_{20}H_{21}NO_5$ + H: 356.1498). ^{13}C and ^1H-NMR spectra showed signals characteristic of two 1,2,4,5 tetra-substituted aromatic rings, two aromatic methoxy groups and one double-oxygenated methene. In addition, a deshielded NCH_3 group at δ 3.52 was present. EI-MS showed a fragment pattern similar to amurensinine [4,5], which contains 16 m.u. less in its molecular weight. Compound **1** was therefore assigned the structure of amurensinine N-oxide. In fact, its EI-MS showed peaks at m/z 339$[M-16]^+$, 353$[M-2]^+$, and 355$[M]^+$ similarly to (−)-argemonine N-oxide [6], as

expected for N-oxides [7]. In addition, compared with refractamine [8], the signals for NCH_3, H-6 and H-12 are deshielded by 0.7–1.3 p.p.m. and, compared with isothalisopavine [9], the signals for carbons NCH_3, C-6 and C-12 are deshielded by 14–20 p.p.m.

NOESY, showing that the proton signal of NCH_3 was correlated with H-11_b and H-12, suggested the relative configuration of NCH_3. The large negative optical rotation, typical of all isopavines so far isolated, suggested the assigned absolute configuration [9]. Though amurensinine has been isolated from other plants of the same genus (*M. horridula*, *M. napaulensis* and *M. sinuata*) [2,3], compound **1** is a new natural product, named amurensinine N-oxide A.

Compound **2** showed IR, EI-MS, ^1H and ^{13}C-NMR spectra similar to compound **1**. Compared to **1**, the signals for protons H-12, H-11_a, NCH_3 and H-6_a were upfielded by 0.17–0.40 p.p.m. and H-11_b was deshielded to 4.73 p.p.m. Meanwhile, the signals for carbons C-6 and C-11 were upfielded by 2.28 and 3.46 p.p.m., but NCH_3 and C-16 were deshielded by 2.61 and 2.59 p.p.m., respectively. All the above evidence suggests compound **2** to be the epimer N-oxide of **1**. This was confirmed by NOESY which showed a correlation between NCH_3 and H-12. Compound **2** was named amurensinine N-oxide B.

Acknowledgements

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