Fitoterapia 80 (2009) 252–254

Contents lists available at ScienceDirect

Fitoterapia

journal homepage: www.elsevier.com/locate/fitote

A new proaporphine alkaloid from *Meconopsis horridula*

Haifeng Wu [a,b,d,*], Lisheng Ding [b], Jianwei Shen [a], Huajie Zhu [c], Xiaofeng Zhang [a,*]

[a] Northwest Institute of Plateau Biology, Chinese Academy of Sciences, Xining 810008, PR China
[b] Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, PR China
[c] State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650223, PR China
[d] Graduate University of Chinese Academy of Sciences, Beijing 100049, PR China

ARTICLE INFO

Article history:
Received 15 January 2009
Received in revised form 14 February 2009
Accepted 21 February 2009
Available online 3 March 2009

Keywords:
Meconopsis horridula
Papaveraceae
Proaporphine
8, 9-Dihydroprooxocryptochine

ABSTRACT

A new proaporphine alkaloid, 8, 9-dihydroprooxocryptochine (1), together with three known alkaloids, was isolated from the aerial parts of *Meconopsis horridula* Hook. f. & Thomson (Papaveraceae), a traditional Tibetan medicine. The structure of 1 was determined by spectroscopic methods.

1. Introduction

Meconopsis horridula Hook. f. & Thomson (Papaveraceae), a perennial herb growing at an altitude of 3000–5000 m in the Qinghai–Tibet plateau area, is traditionally used as Tibetan folk medicine for the treatment of headaches and fractures [1]. Among its previously investigated chemical components, isoquinoline alkaloids were noteworthy [2,3]. In continuation of our efforts to investigate bioactive components of the genus distributed in Qinghai–Tibet plateau area, a new proaporphine alkaloid, 8, 9-dihydroprooxocryptochine (1), and three known alkaloids, protopine (2) [4,5], (−)-reframoline (3) [6] and (−)-amurensinine (4) [7,8] (Fig. 1), were isolated from the ethanol extract of the aerial parts of this plant. In the present paper, we report the isolation and structure elucidation of the new proaporphine alkaloid.

2. Experimental

2.1. General

IR spectrum was recorded on a Perkin-Elmer Spectrum-One FT–IR spectrometer. NMR experiments were recorded on a Bruker AM-600 spectrometer using TMS as an internal standard. HR–ESI–MS and ESI–MS spectra were obtained using a Bruker Bio TOF Q and Finnigan LCQ^{DECA} mass spectrometers, respectively. Column chromatographies were performed on self-packed open column with silica gel (160–200, 200–300 mesh, Qingdao Marine Chemical Group Inc. China).

2.2. Plant material

The aerial parts of *M. horridula* were collected in the Yushu Tibetan Autonomy Prefecture of Qinghai Province in August 2003, and identified by Prof. Xiaofeng Zhang. A voucher specimen (M20030803) was deposited in the Herbarium of Northwest Institute of Plateau Biology, Chinese Academy of Sciences.

2.3. Extraction and isolation

Dried and powered plant material (8 kg) was extracted exhaustively with 80% EtOH at r.t. The EtOH extract was, after

* Corresponding authors. Northwest Institute of Plateau Biology, Chinese Academy of Sciences, Xining 810008, PR China. Tel.: +86 28 85223843; fax: +86 28 85222753.
E-mail addresses: wwwtony505@yahoo.com.cn (H. Wu), xfzhang@nwipb.ac.cn (X. Zhang).

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doi:10.1016/j.fitote.2009.02.007

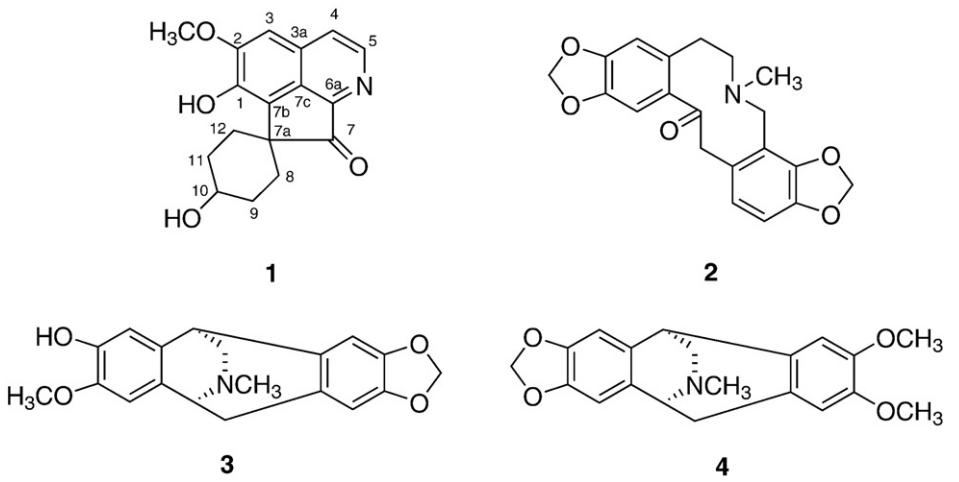

Fig. 1. The structures of compounds 1–4.

evaporation to dryness under reduced pressure, acidified with 5% HCl, filtered and extracted with EtOAc. The aqueous acid solution was made alkaline with 25% NH_4OH to pH 9. The alkaline solution was extracted exhaustively with $CHCl_3$ to give crude alkaloid mixture (5 g). The crude alkaloid mixture was subjected repeatedly to Si-gel CC eluting with petroleum ether–acetone–diethyl amine and $CHCl_3$–MeOH–diethyl amine gradient to afford compounds 1 (6 mg), 2 (20 mg), 3 (8 mg) and 4 (8 mg).

8, 9-Dihydroprooxocryptochine (1), yellow solid; IR bands (KBr): 3400, 2931, 1725, 1504, 1482, 1417, 1287, 1056 cm^{-1}; HR–ESI–MS m/z (positive mode): 322.1063 $[M+Na]^+$ (calcd. for $C_{17}H_{17}NO_4Na$: 322.1061); ESI–MS m/z: 322 $[M+Na]^+$, 300 $[M+H]^+$ and 298 $[M-H]^-$. ^1H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) data: see Table 1.

3. Results and discussion

8, 9-Dihydroprooxocryptochine (1) was obtained as an optically inactive yellow solid. Its molecular formula was determined as $C_{17}H_{17}NO_4$ by HR–ESI–MS ($[M+Na]^+$ m/z 322.1063, calcd. 322.1061). The IR absorption indicated the presence of hydroxyl (3400 cm^{-1}) and carbonyl groups (1725 cm^{-1}). The ^{13}C NMR spectrum showed 17 carbon signals including a carbonyl group (δ 206.8), nine aromatic carbons, an oxymethine (δ 69.9), a methoxyl group (δ 56.7), a quaternary carbon (δ 49.9) and four aliphatic methylenes. The ^1H NMR spectrum exhibited a pair of *ortho* aromatic protons at δ 8.64 and 7.61, an aromatic proton singlet at δ 7.05 and some aliphatic absorption. These evidences together with 2D-NMR spectra, suggested that 1 was a proaporphine alkaloid with the same skeleton as prooxocryptochine [9]. In the ^1H NMR and ^{13}C NMR spectra, the absence of olefinic signals indicated that 1 was the hydrogenation product of prooxocryptochine. The methoxyl group placed at C-2 was confirmed by the NOE correlation between OMe and H-3. H-10 was determined at be pseudo-axial by the correlations of H-10 (δ 3.83) with H-8ax (12ax) (δ 2.38) and H-9eq (11 eq) (δ 1.96) in the NOESY spectrum(Fig. 2). A full assignment of the ^1H NMR and ^{13}C NMR was established by HSQC and HMBC correlation.

Table 1
^1H and ^{13}C NMR data and key HMBC correlations for 1 in $CDCl_3$ (δ in ppm and J in Hz).

Carbon	δ_H	δ_C	HMBC (H→C)
1		141.6	
2		154.3	
3	7.05 s	100.7	C-3a, C-7c, C-1, C-4
3a		123.5	
4	7.61 d (5.7)	120.9	C-7c
5	8.64 d (5.5)	145.4	C-3a, C-6a
6a		151.2	
7		206.8	
7a		49.9	
7b		130.8	
7c		134.6	
8, 12	2.38 td (14.0, 4.0) ax	29.8	
	1.83 brd (14.0) eq		
9, 11	2.21 m ax	30.3	C-7a
	1.96 m eq		
10	3.83 m	69.9	
OMe-2	4.07 s	56.7	C-2

ax: axial; eq: equatorial.

Acknowledgements

This work was supported by grants from the Chinese Academy of Sciences (YZ-06-1) and the National Key Technology R&D Program of China (2007BAI31B02).

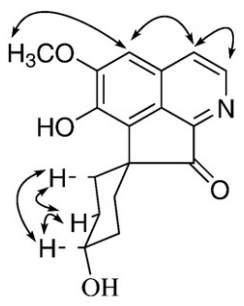

Fig. 2. Key NOESY correlations of 1.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.fitote.2009.02.007.

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