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Sesquiterpene alkaloids from *Tripterygium hypoglaucum*

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Abstract

A novel sesquiterpene pyridine alkaloid was isolated from the roots of *Tripterygium hypoglaucum* (Levl.) Hutch, together with other known alkaloids, wilfordine, wilfortrine, wilformine and wilfornine. Its structure was elucidated mainly by 2D NMR spectroscopy.

Keywords: *Tripterygium hypoglaucum*; Celastraceae; Sesquiterpene pyridine; Alkaloids; Hypoglaunine

1. Introduction

The roots of *Tripterygium hypoglaucum* Hook. f. (Celastraceae) are used in Chinese folk medicine for the treatment of various diseases. In the last 30 years, many sesquiterpenoids, diterpenoids, triterpenoids and alkaloids (Kupchan, Court, Dailey, Gilmore, & Bryan, 1972; Zhang, Zhang, & An, 1990; Duan, Kawazoe, & Takaishi, 1997) have been isolated from this plant. In order to elucidate its active principles, a thorough phytochemical investigation is being undertaken. From the roots of this plant, a new alkaloid, named hypoglaunine (**1**), and four known compounds, wilfordine (**2**) (Wu, 1986; Li, Strunz, & Calhoun, 1990), wilfortrine (**3**) (Deng, Cao, Xia, Lin, & Wang, 1987a; He, Li, Fang, & Hong, 1989), wilformine (**4**) (He, Li, Fang, & Hong, 1987) and wilfornine (**5**) (Deng, Cao, Xia, Lin, & Wang, 1987b) were isolated. In this paper, we deal with the structural elucidation of the new alkaloid.

2. Results and discussion

Hypoglaunine (**1**) was isolated as an amorphous powder. The IR spectrum showed bands for hydroxyl, ester carbonyl and pyridine groups at 3421, 1747 and 1653 cm^{-1}, respectively. The absorptions at 239 and 264 nm observed in the UV spectrum were also consistent with the presence of the pyridine moiety. The ^1H NMR spectrum of **1** contained five signals for acetyl (Ac) groups (δ_H 2.22, 2.12, 1.88, 1.86, 1.73), one furanoyl (Fu) group [δ_H 6.96 (d, $J=0.8$ Hz), 7.48 (s), 8.50 (d, $J=0.8$ Hz)], and two tertiary methyl groups [δ_H 1.63 and 1.58 (s)]. In addition, two sets of methylene protons [δ_H 4.20, 5.18 (each 1H, d, $J=11.2$ Hz), 4.98, 5.03 (each 1H, d, $J=13.2$ Hz)] and seven methine protons (δ_H 2.44, 4.69, 5.29, 5.31, 5.48, 5.62 and 6.81) were observed. Resonances at δ_H 7.83, 8.66 and 8.95, along with one secondary methyl doublet at δ_H 1.17 (3H, d, $J=6.4$ Hz) and one tertiary methyl at δ_H 1.32 (s), led to a structure for the dibasic acid moiety that was an isomeric with 8-hydroxy evoninic acid. The ^{13}C NMR and DEPT spectra of **1** indicated the presence of nine methyl carbons, two oxygenated methylene carbons, eight methine carbons, eight ester carbonyl carbons, five quaternary carbons, one furanoyl group [δ_C 110.1 (d), 119.0 (s), 143.9 (d) and 149.1 (d)] and an isomeric with 8-hydroxy evoninic acid moiety [δ_C 17.0 (q), 24.0 (q), 41.7 (d), 76.7 (s), 123.4 (d), 127.5 (s), 150.9 (s), 151.8 (d), 152.2 (d), 169.5 (s, –COO–) and 174.7 (s, –COO–)]. The characteristic ion peak at 250 in EI mass spectrum also supported the presence of an isomeric with 8-hydroxy evoninic acid moiety (He et al., 1989). These data agreed with a molecular formula of **1** as $C_{41}H_{47}O_{20}N$, which was supported by the EI and FAB mass spectral data. Thus, compound **1** was concluded to be a sesquiterpene pyridine alkaloid derived from the dihydroagrofuran polyol ester found in the Celastraeae (Wu, 1986; Deng et al., 1987a; He et al., 1987; Deng et al., 1987b; He et al., 1989; Li et al., 1990; Duan et al., 1997). The NMR spectroscopic properties of **1** (Table 1) suggested that it was a hydroxy substituted isomerine-type sesquiterpene alkaloid (Li, Strunz, & Calhoun, 1991; Klass, Tinto, Reynolds, & Mclean, 1993; Calzada &

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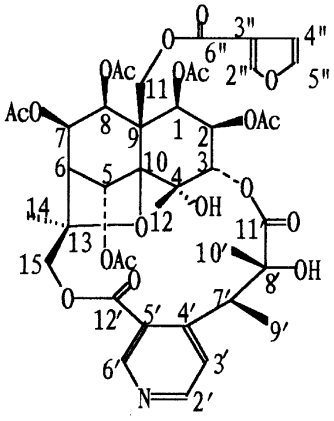

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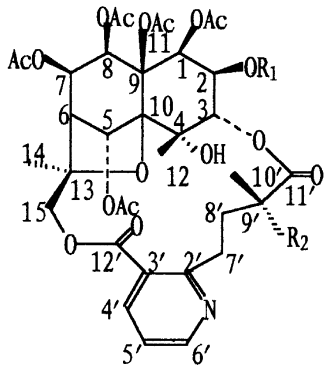

	R_1	R_2
2	C_6H_5CO	OH
3	$(C_4H_3O)CO$	OH
4	CH_3CO	H
5	$(C_5H_5N)CO$	H

Mata, 1995; Duan et al., 1997), having five acetyl groups and one furanoyl group. By comparison of the NMR spectral data of **1** with those of hyponine B (Duan et al., 1997) and peritassines A (Klass et al., 1993), the spectral data of the sesquiterpenoid structure pattern of **1** was similar to those of hyponine B, which indicated the position of five acetates and one furanzoate on the dihydroagrofuran nucleus of **1** as those of hyponine B; on the other hand, the spectral data of the diester moiety of **1** was similar to those of peritassines A, except H-8′ of peritassines A instead of hydroxy group in **1**, which indicated that the diester moiety of **1** (isomeric with hydroxy evoninic acid moiety) contained a 4,5-substituted nicotinic acid group other than a 2,3-substituted one.

To confirm its structure, 2D NMR spectra including ^1H–^1H COSY, HETCOR and COLOC were recorded. The ^1H–^1H COSY and the couplings among the six methine protons [δ_H 5.62 (1-H), 5.31 (2-H), 4.69 (3-H), 2.44 (6-H), 5.48 (7-H) and 5.29 (8-H)] revealed their connections in the dihydroagrofuran core; the remaining methine at δ_H 6.81 (5-H) correlated with the carbon signal at δ_C 83.5 (C-13), which also correlated with the signal at δ_H 1.58 (14-H_3) in the COLOC spectrum. The 2D NMR spectra of **1** allowed the assignments of all proton and carbon signals (Table 1). The relative stereochemistry around the dihydroagrofuran nucleus was determined from the coupling constants to be the same as other alkaloids from this plant. Lastly, cross-peaks of proton signals with the ester groups in the COLOC spectrum of **1** were not clear, and ester group placement on the molecule was determined by comparison with known compounds as described earlier.

3. Experimental

^1H and ^{13}C NMR spectra were recorded on an AC-P 300 instrument, 2D NMR spectra were recorded on an INOVA-400 instrument, respectively. IR spectra were obtained using a Nicolet MX-1 spectrophotometer and UV spectra employed a PE 260 spectrophotometer. Optical rotations were measured on a PE-241 Polarimeter, and EIMS and FABMS were recorded on a ZAB-Spec mass spectrometer.

3.1. Plant material

The roots of *Tripterygium hypoglaucum* were collected in May, 1994 in Xichang, Sichuan Province, and identified by Professor Xiaohong Hu. A voucher specimen is deposited in the Chengdu Institute of Biology, Chinese Academy of Sciences.

3.2. Extraction and isolation

Dried and finely powdered roots (13.0 kg) were soaked with EtOH at room temperature. The EtOH extracts were concentrated under reduced pressure and fractionated by a series of solvent partitions into a $CHCl_3$-soluble fraction. The residue (37.1 g) of this fraction was subjected

Table 1
NMR spectral data of compound **1** ($CDCl_3$)

1	H	C
1	5.62 (d, 3.6)	73.3 d
2	5.31 (dd, 3.6, 2.8)	69.0 d
3	4.69 (d, 2.8)	76.6 d
4		70.4 d
5	6.81 (s)	74.6 d
6	2.44 (d, 3.6)	50.7 d
7	5.48 (dd, 3.6, 6.0)	68.3 d
8	5.29 (d, 6.0)	70.6 d
9		52.7 s
10		93.1 s
11	4.98 (d, 13.2); 5.03 (d, 13.2)	60.0 t
12	1.63 (s)	23.4 q
13		83.5 d
14	1.58 (s)	17.9 q
15	4.20 (d, 11.2); 5.18 (d, 11.2)	70.1 t
2′	8.66 (brs)	151.8 d
3′	7.83 (brs)	123.4 d
4′		150.9 s
5′		127.5 s
6′	8.95 (s)	152.2 d
7′	4.22 (q, 6.4)	41.7 d
8′		76.7 s
9′	1.17 (d, 6.4)	17.0 q
10′	1.33 (s)	24.0 q
11′		174.7 s
12′		169.5 s
2″	7.48 (s)	149.1 d
3″		119.0 s
4″	6.96 (d, 0.8)	110.1 d
5″	8.50 (d, 0.8)	143.9 d
6″		162.1 s
OH-8′	3.45 (s)	
OH-4	5.02 (s)	
1-Ac	1.86 (s)	20.4 q, 169.4 s
2-Ac	2.12 (s)	21.0 q, 168.6 s
5-Ac	1.73 (s)	20.2 q, 170.2 s
7-Ac	2.22 (s)	21.7 q, 169.6 s
8-Ac	1.88 (s)	20.3 q, 168.9 s

to CC over silica gel; the column was eluted with a chloroform–methanol gradient (10: 0–10:3) to yield 19 frs. Fr. 4 (2.5 g) was rechromatographed on silica gel with cyclohexane–acetone (2: 1) as eluting solvent to give **2** (5 mg) and **3** (312 mg); Fr. 10 (5.0 g) was rechromatographed on silica gel with petroleum ether–EtOAc (3: 2) to give **1** (100 mg); Fr. 14 (3.4 g) was rechromatographed on silica gel with chloroform–acetone (9: 1) to yield **4** (212 mg) and **5** (194 mg).

Hypoglaunine (**1**), amorphous powder, $[\alpha]^{10}_{D}$ +41.2° ($CHCl_3$, $c=0.12$). UV ($CHCl_3$, nm): 239, 264. EI-MS m/z (rel. int.): 873 $[M]^+$ (100), 858 $[M–CH_3]^+$ (15), 840 $[M–CH_3CO]^+$ (4), 814 (32), 748 (25), 710 (10), 250 (7), 222 (15), 194 (20), 176 (41), 150 (61), 95 (50). FAB-MS m/z: 874 $[M+1]^+$. IR (KBr, cm^{-1}): 3421, 2924, 2800, 1747, 1652, 1610, 1373, 1308, 1231, 1159, 1118, 1034, 770, 620. ^1H NMR and ^{13}C NMR spectral data of **1** see Table 1.

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