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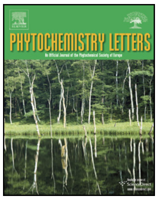

Two new hopane-type triterpenes from the aerial part of *Chelidonium majus*

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ABSTRACT

Two new hopane-type triterpenes, 1-oxo-3α-hydroxy-22(30)-hopen-29-oic acid (**1**) and 3α-hydroxy-22(30)-hopen-29-oic acid (**2**), and the known compounds dihydrosanguinarine (**3**), *dl*-stylopine (**4**), dihydrochelirubine (**5**), dihydromacarpine (**6**), dihydrochelerythrine (**7**), dihydrochelilutine (**8**), and norsanguinarine (**9**) were isolated from the aerial part of *Chelidonium majus*. The structures of the new compounds were elucidated based on extensive spectroscopic evidence, especially from 1D and 2D NMR and HRESIMS experiments. The shared structure features of the hopane-type triterpenes are the presence of a mono-hydroxyl substitution at the 3-position and an acrylic acid-2-yl moiety, as a manifestation of the isopropyl group connected to C-21 of the hopane skeleton. Phytotaxonomically, the hopane-type triterpenes might be another important chemical marker in addition to the benzophenanthridine alkaloids of *C. majus*.

1. Introduction

Chelidonium majus L. is a slightly toxic species from the Papaveraceae family that grows in many regions of China. The whole *C. majus* plant has traditionally been applied for the treatment of certain skin diseases and inflammations. Several extracts and purified compounds obtained from *C. majus* have been reported to exhibit potent pharmacological properties, such as anticancer, antibacterial, anti-inflammatory, and antispasmodic activities (Wei et al., 2009; Niu and He, 1994; Vavrečková et al., 1996; Hiller et al., 1998). Previous phytochemical studies on this plant have mainly led to the isolation of alkaloids, including benzophenanthridines, protopines, protoberberines, and aporphines (Zhou et al., 1989; Rosa and Vincenzo, 1992; Kadan et al., 1992). Recently, a further investigation on the chemical constituents of *C. majus* was conducted in our laboratory, and two new triterpenes, 1-oxo-3α-hydroxy-22(30)-hopen-29-oic acid (**1**) and 3α-hydroxy-22(30)-hopen-29-oic acid (**2**) (Fig. 1), along with six known benzophenanthridine alkaloids and one known protoberberine alkaloid, were isolated from the aerial part of *C. majus*. Here, we report the isolation and structure elucidation of these compounds and their possible taxonomic sense.

2. Results and discussion

The $CHCl_3$-soluble portion of the 80% ethanol extract from the aerial part of *C. majus* was subjected to various methods of CC, affording two new triterpenes (**1** and **2**) and several known benzophenanthridine and protoberberine alkaloids (**3–9**). The new compounds were identified as triterpenoids possessing 30 carbon atoms each, according to both their molecular formulas obtained from the HRESIMS measurements and their ^{13}C NMR spectra. The basic skeleton of the triterpenes was classified as hopane-type based on the common features in their NMR spectroscopic data (see Table 1 and the Experimental section). Six tertiary methyl groups were detected in the higher field region as singlets in each ^{1}H NMR spectrum, showing the general characteristics of Me-23, 24, 25, 26, 27, and 28 of the skeleton of hopane-type triterpenoids (Grammes et al., 1994; Liu et al., 2015). Both compounds were also indicated to possess an acrylic acid-2-yl moiety by the two signals of an olefinic methylene, all as broad singlets in each ^{1}H NMR spectrum, and by the signals of a carboxycarbonyl carbon, an olefinic methylene carbon, and an olefinic quaternary carbon collectively detected in the ^{13}C and DEPT NMR spectra of each compound, which are the manifestation of the isopropyl group connected to C-21 of the hopane core (Table 1). All of these features were confirmed by HSQC and other 2D NMR experiments.

Compound **1** was obtained as a white amorphous powder. The molecular formula was determined to be $C_{30}H_{46}O_4$ with a

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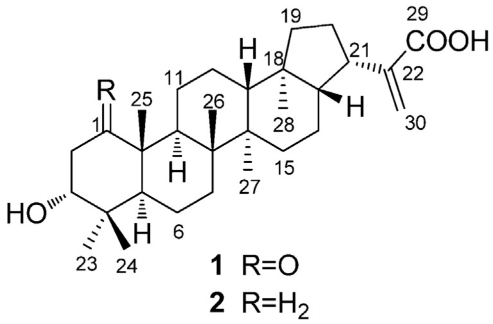

Fig. 1. Chemical structures of compounds **1** and **2**.

Table 1
^{1}H and ^{13}C NMR spectroscopic data of **1** and **2**.

No.	**1** (in $CDCl_3$)		**2** (in C_5D_5N)	
	δ_H (mult., *J* in Hz)	δ_C (DEPT)	δ_H (mult., *J* in Hz)	δ_C (DEPT)
1		214.9 s	1.79[a]	33.9 t
2	α 2.16 dd (13.2, 4.2) β 3.37 dd (13.2, 3.6)	42.8 t	1.76 ov, 1.99 ov	26.57 t
3	3.85 dd (4.2, 3.6)	80.6 d	3.63 br s	75.3 d
4		38.2 s		38.1 s
5	1.51 dd (12.6, 1.2)	51.8 d	1.62 ov	49.1 d
7	1.20 ov, 1.43 ov	32.7 t	1.46[a]	33.6 t[b]
8		41.8 s		42.2 s[c]
9	2.03 dd (12.0, 3.0)	41.4 d	1.43 ov	50.4 d
10		52.8 s		37.6 s
13	1.38 ov	49.8 d	1.37 ov	49.5 d
14		42.5 s		42.1 s[c]
15	1.19 ov, 1.38 ov	33.3 t	1.10[a]	33.5 t[b]
17	1.43 ov	54.5 d	1.47 ov	54.8 d
18		45.4 s		45.6 s
19	1.07 ov, 1.67 ov	41.7 t	1.07 ov, 1.67 ov	42.0 t
20	1.94 ov	26.4 t	1.76 ov, 1.99 ov	26.65 t
21	3.35 m	39.3 d	3.81 m	40.0 d
22		142.9 s		145.9 s
23	0.98 s	27.3 q	1.22 s	29.3 q
24	1.07 s	22.1 q	0.91 s	22.6 q
25	1.23 s	15.0 q	0.90 s	16.1 q
26	1.01 s	17.1 q	0.98 s[d]	16.9 q[e]
27	0.95 s	17.0 q	0.79 s[d]	16.8 q[e]
28	0.70 s	15.7 q	0.72 s	15.9 q
29		173.0 s		171.6 s
30	5.67 br s, 6.27 br s	124.8 t	5.74 br s, 6.60 br s	121.7 t

[a~e] Data with superscripts of the same letters in the same column may interchange.

deprotonated ion at *m*/*z* 469.3332 in the HRESIMS experiment in the negative ion mode, indicating eight indices of hydrogen deficiency. The IR spectrum showed absorption bands for hydroxy (3434 cm^{-1}), carboxy (2643, 1692 cm^{-1}), and olefinic (1621 cm^{-1}) functionalities. In addition to the aforementioned diagnostic signals of hopane-type triterpene in the ^{1}H NMR spectrum that resonated at δ_H 1.23 (3H, s, Me-25), 1.07 (3H, s, Me-24), 1.01 (3H, s, Me-26), 0.98 (3H, s, Me-23), 0.95 (3H, s, Me-27), 0.70 (3H, s, Me-28), 6.27 (1H, br s, H-30$_a$), and 5.67 (1H, br s, H-30$_b$), the signal of one methineoxy proton was also evident at δ_H 3.85 (1H, dd, *J* = 4.2, 3.6 Hz, H-3) (Table 1). The DEPT NMR experiment classified the 30 carbons into six methyl carbons, ten methylene carbons including one olefinic methylene carbon at δ_C 124.8 (C-30), six methine carbons including one methineoxy carbon at δ_C 80.6 (C-3), six quaternary carbons including one quaternary olefinic carbon at δ_C 142.9 (C-22), and two carbonyl carbons at δ_C 214.9 (C-1) and 173.0 (C-29), with the olefinic and oxygenated carbons, including carbonyl carbons, being categorized unequivocally by chemical shifts (Table 1). These ^{1}H, ^{13}C, and DEPT NMR data for compound **1** closely resembled the data for 1-oxo-2,22(30)-hopdien-29-oic acid, a known hopane-type triterpene previously isolated and identified by our group from *Macleaya microcarpa* of the Papaveraceae family (Liu et al., 2015). In the ^{1}H NMR spectrum, the main difference was that the set of resonances of the 1,2-bissubstituted ethenylene group of the conjugated olefinic ketone moiety at δ_H 6.26 (1H, d, *J* = 10.0 Hz, H-3) and 5.64 (1H, d, *J* = 10.0 Hz, H-2) in the known compound was replaced by a set of resonances of an oxygenated ethylene moiety at δ_H 2.16 (1H, dd, *J* = 13.2, 4.2 Hz, H-2α), 3.37 (1H, dd, *J* = 13.2, 3.6 Hz, H-2β), and 3.85 (1H, dd, *J* = 4.2, 3.6 Hz, H-3) in compound **1**, with the chemical shifts of the methylene at the 2-position being commensurable with the carbonylated C-1. In the ^{13}C and DEPT NMR spectra, the main differences lay in the replacement of the signals for two olefinic methine carbons at δ_C 124.4 (C-2) and 154.3 (C-3) in the known compound by the signals of a methylene carbon at δ_C 42.8 (C-2) and a methineoxy carbon at δ_C 80.6 (C-3) in **1**, with downfield shifts of Δ_δ +7.5, +1.9, and +4.9 from C-1, 4, and 10 in **1**, respectively, compared with the previously observed values (Table 1) (Liu et al., 2015). Along with the HSQC experiment, these assignments were confirmed by the correlations from both Me-23 and Me-24 to C-3, 4 and 5, from H-3 to C-1 and 5, and from H_2-2 to C-4 and 10 in the HMBC spectrum and by the mutual homonuclear coupling correlations among H-2α, H-2β, and H-3 in the ^{1}H–^{1}H COSY spectrum. The HMBC experiment also unequivocally elucidated the 2D structure of compound **1** as 2-(9-hydroxy-5a,5b,8,8,11a,13b-hexamethyl-11-oxoicosahydro-1*H*-cyclopenta[*a*]chrysen-3-yl)acrylic acid based on the correlations from Me-25 to C-1, 5, 9, and 10, from Me-26 to C-7, 8, 9, and 14, from Me-27 to C-8, 13, 14, and 15, from Me-28 to C-13, 17, 18, and 19, from H-21 to C-18, 29, and 30, and from H_2-30 to C-21, 22, and 29, among others (Fig. 2 for key MHBC correlations). The NOE difference experiment, along with the coupling constants, established the relative configuration of **1** (Fig. 3). The NOE correlations of Me-25/H-2β, Me-25/Me-24, Me-25/Me-26, Me-27/H-9, Me-27/Me-28, and Me-28/H-30, along with the lack of NOE correlations of Me-25/H-5, Me-27/H-13, and Me-28/H-17 according to the numbering system of hopane-type triterpenoids, showed that H-13, H-17, H-21, Me-25, and Me-26 were all in the β orientation, while H-5, H-9, Me-27, and Me-28 were all in the α orientation, typical stereochemistry for hopane-type triterpenes. The coupling constants of 4.2 Hz between H-2α and H-3 and of 3.6 Hz between H-2β and H-3 clearly indicated an equatorial and β-oriented H-3. Thus, the structure of compound **1** was established as 1-oxo-3α-hydroxy-22(30)-hopen-29-oic acid.

Compound **2** was obtained as a white amorphous powder. The molecular formula was determined to be $C_{30}H_{48}O_3$ with a deprotonated ion at *m*/*z* 455.3540 in the HRESIMS experiment in the negative ion mode, indicating seven indices of hydrogen deficiency. The IR spectrum showed absorption bands for hydroxy (3477 cm^{-1}), carboxy (2629, 1702 cm^{-1}), and olefinic (1623 cm^{-1}) functionalities. The diagnostic signals of hopane-type triterpene in the ^{1}H NMR spectrum resonated at δ_H 1.22 (3H, s, Me-23), 0.98 (3H, s, Me-26), 0.91 (3H, s, Me-24), 0.90 (3H, s, Me-25), 0.79 (3H, s, Me-27), 0.72 (3H, s, Me-28), 6.60 (1H, br s, H-30$_a$), and 5.74 (1H, br s, H-30$_b$). A well-resolved methineoxy signal was also evident at δ_H 3.63 (1H, br s, H-3) (Table 1). The DEPT NMR experiment classified the

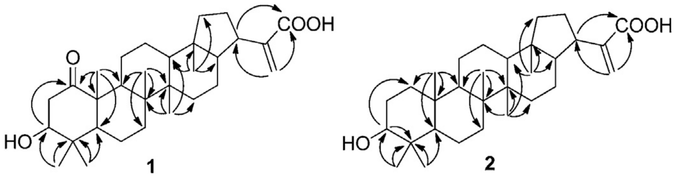

Fig. 2. Key HMBC (H → C) correlations of **1** and **2**.