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Structural Elucidation of a Coumarin with New Skeleton from *Artemisia ordosica*

Wugedunqiqige Bao, Qinghu Wang * and Junsheng Hao

College of Traditional Mongolian Medicine, Inner Mongolia University for Nationalities, Tongliao, Inner Mongolia 028000, P. R. China

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Abstract: A new coumarin, named as arteordocoumarin A (**1**), together with eight known compounds (**2-9**) were isolated from the $CHCl_3$ extract of *Artemisia ordosica* (*A. ordosica*). The structures of **1** was elucidated by spectroscopic methods, including UV, IR, HR-ESI-MS and extensive 1D and 2D NMR techniques.

Keywords: Arteordocoumarin A; *Artemisia ordosica*; NMR.

1. Introduction

A. ordosica, Asteraceae family, is one of the main arido-active shrubs growing in the arid and semi-arid areas of the north China including Inner Mongolia, Ningxia, Gansu and Shanxi [1, 2]. The aerial parts of A. ordosica is utilized as a folk medicine for expelling rheumatism, clearing heat, and dispelling swelling [3]. Sterols [4], coumarins [5], terpenoids [6], flavonoids [7, 8] and acetylenes [3] were isolated previously from this plant. However, the secondary metabolites from *Artemisia ordosica* often differ when grown in different ecological environments. In order to continue our research on the bioactive secondary metabolites from *Artemisia ordosica* collected in Tongliao of Inner Mongolia, China, we now describe the isolation and structure elucidation of a new coumarin compound, together with eight known ones.

2. Materials and Methods

2.1. Instrumentation and Reagents

A Shimadzu UV-2201 spectrometer (Shimadzu, Japan) was used to record the he UV spectra. The IR spectra were recorded in KBr discs on a Thermo Nicolet 200 double beam spectrophotometer (Shimadzu, Japan). A Waters Xevo G2-S QT (Waters, USA) was used to measure the HR-ESI-MS spectra. NMR spectra were measured on a Bruker AV–500 spectrometer (Bruker, Germany) with tetramethylsilane (TMS) as the internal reference, and chemical shifts are expressed in δ (ppm). Column

* Corresponding author: E-Mail: wqh196812@163.com; Phone:086-0475-8314242 Fax:086-0475-8314242

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chromatography was performed by using silica gel (200-300 mesh, Marine Chemical Factory, Qingdao, China).

2.2. Plant Materials

The aerial parts of *A. ordosica* were collected in Tongliao, Inner Mongolia of China, in June 2017, and identified by Prof. Buhebateer (Inner Mongolia University for Nationalities). A voucher (ref. no. 20170612) has been deposited at the Herbarium of college of Traditional Mongolian Medicine of Inner Mongolia University for Nationalities.

2.3. Extraction

Ground-dried aerial parts of *A. ordosica* (2.0 kg) were extracted with $CHCl_3$ (25 L) under reflux after extraction with 10 L petroleum ether. Evaporation of the solvent under reduced pressure delivered the $CHCl_3$ extract (150.0 g). The $CHCl_3$ extract was fractionated by column chromatography on silica gel and gradiently eluted with petroleum ether-CH_3COCH_3 (60:1 to 20:1) to give 3 fractions (Fr. 1-3). Fr. 1 (320 mg) was separated by TLC (cyclohexane-ethyl acetate, 10:1) yielding **1** (17 mg), **2** (11 mg) and **3** (15 mg); Fr. 2 (400.0 mg) was further eluted on a Sephadex LH-20 column with MeOH:$CHCl_3$ (*v*:*v*, 1:1) and then separated by TLC (cyclohexane-ethyl acetate, 7:1) yielding **4** (13 mg), **5** (9 mg), **6** (15 mg) and **7** (18 mg). Fr. 3 (330 mg) was separated by TLC (cyclohexane-ethyl acetate, 3:1) yielding **8** (16 mg) and **9** (21 mg).

*Arteordocoumarin A (**1**):* White needle; ^{1}H-NMR (500MHz, DMSO-d_6) and ^{13}C-NMR (125MHz, DMSO-d_6) spectral data see Table 1; HR-ESI-MS at *m/z* 209.0467 $[M-H]^-$ (calcd for $C_{10}H_9O_5$, 209.0450).

*6,7-dimethoxycoumarin (**2**)* [9]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 6.31 (1H, d, *J* = 9.5 Hz, H-3), 7.65 (1H, d, *J* = 9.5 Hz, H-4), 6.86 (1H, s, H-5), 6.88 (1H, s, H-8), 3.94 (3H, s, 6-OCH_3), 3.97 (3H, s, 7-OCH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 161.5 (C-2), 113.6 (C-3), 143.3 (C-4), 107.9 (C-5), 146.3 (C-6), 152.8 (C-7), 100.0 (C-8), 150.0 (C-9), 111.4 (C-10), 56.4 (6-OCH_3), 56.3 (7-OCH_3).

*6,7,8-trimethoxycoumarin (**3**)* [10]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 6.06 (1H, d, *J* = 9.0 Hz, H-3), 7.52 (1H, d, *J* = 9.0 Hz, H-4), 7.30 (1H, s, H-5), 3.88 (3H, s, 6-OCH_3), 3.86 (3H, s, 8-OCH_3), 3.82 (3H, s, 7-OCH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 165.4 (C-2), 115.5 (C-3), 140.3 (C-4), 114.9 (C-5), 145.0 (C-6), 125.1 (C-7), 133.5 (C-8), 134.4 (C-9), 120.7 (C-10), 56.4 (6-OCH_3), 56.1 (8-OCH_3), 55.8 (7-OCH_3).

*6-hydroxy-7-methoxycoumarin (**4**)* [9]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 6.31 (1H, d, *J* = 9.5 Hz, H-3), 7.64 (1H, d, *J* = 9.5 Hz, H-4), 6.93 (1H, s, H-5), 6.85 (1H, s, H-8), 3.91 (3H, s, 7-OCH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 161.6 (C-2), 113.5 (C-3), 143.5 (C-4), 108.3 (C-5), 147.3 (C-6), 152.0 (C-7), 103.0 (C-8), 153.0 (C-9), 113.4 (C-10), 56.5 (7-OCH_3).

*4-hydroxylacetophenone (**5**)* [11]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 7.93 (2H, d, *J* = 8.5 Hz, H-2,6), 6.91 (2H, d, *J* = 8.5 Hz, H-3,5), 2.58 (3H, s, -CH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 130.4 (C-1), 131.0 (C-2), 115.3 (C-3), 160.1 (C-4), 115.3 (C-5), 131.0 (C-6), 197.9 (C=O), 26.3 (-CH_3).

*4-hydroxy-5-methoxylacetophenone (**6**)* [11]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 7.59 (1H, d, *J* = 2.0 Hz, H-2), 6.98 (1H, d, *J* = 8.0 Hz, H-5), 7.62 (1H, d, *J* = 8.0, 2.0 Hz, H-6), 3.90 (3H, s, -OCH_3), 2.51 (3H, s, -CH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 129.9 (C-1), 111.1 (C-2), 147.0 (C-3), 146.8 (C-4), 114.4 (C-5), 126.9 (C-6), 190.3 (C=O), 56.8 (-OCH_3), 26.3 (-CH_3).

*4-hydroxybenzaldehyde (**7**)* [12]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 7.82 (2H, d, *J* = 8.5 Hz, H-2,6), 7.02 (2H, d, *J* = 8.5 Hz, H-3,5), 9.85 (1H, s, -CHO); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 139.3 (C-1), 132.5 (C-2), 116.0 (C-3), 162.0 (C-4), 116.0 (C-5), 132.5 (C-6), 191.3 (-CHO).

*4-hydroxy-5-methoxybenzaldehyde (**8**)* [13]: White needle; ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 7.43 (1H, brs, H-2), 7.05 (1H, d, J = 8.5 Hz, H-5), 7.45 (1H, brd, J = 8.5 Hz, H-6), 9.83 (1H, s, -CHO), 3.99 (3H, s, -OCH_3); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 129.9 (C-1), 108.8 (C-2), 151.7 (C-3), 147.2 (C-4), 114.4 (C-5), 127.6 (C-6), 191.0 (C=O), 56.1 (-OCH_3).

*4,5-dihydroxybenzaldehyde (**9**)* [13]: ^{1}H-NMR (500MHz, $CDCl_3$) δ_H: 7.44 (1H, d, J = 2.0 Hz, H-2), 6.96 (1H, d, J = 8.0 Hz, H-5), 7.46 (1H, brd, J = 8.0, 2.0 Hz, H-6), 9.85 (1H, s, -CHO); ^{13}C-NMR (125MHz, $CDCl_3$) δ_C: 129.8 (C-1), 108.9 (C-2), 146.8 (C-3), 146.2 (C-4), 114.3 (C-5), 127.7 (C-6), 191.0 (C=O).

3. Results and Discussion

From the $CDCl_3$ of *A. ordosica*, six compounds were obtained using chromatographic methods (CC and TLC). On the basis of ^{1}H, ^{13}C NMR, COSY, HSQC, HMBC and HR-ESI-MS spectra, and modified Mosher's method as well as by comparison with previous reports [9-13], compounds **1** was identified as a coumarin with new skeleton while the remaining eight compounds were found to be the known compounds, 6,7-dimethoxycoumarin (**2**), 6,7,8-trimethoxycoumarin (**3**), 6-hydroxy-7-methoxycoumarin (**4**), 4-hydroxylacetophenone (**5**), 4-hydroxy-5-methoxylacetophenone (**6**), 4-hydroxybenzaldehyde (**7**), 4-hydroxy-5-methoxybenzaldehyde (**8**) and 4,5-dihydroxybenzaldehyde (**9**) (Figure 1).

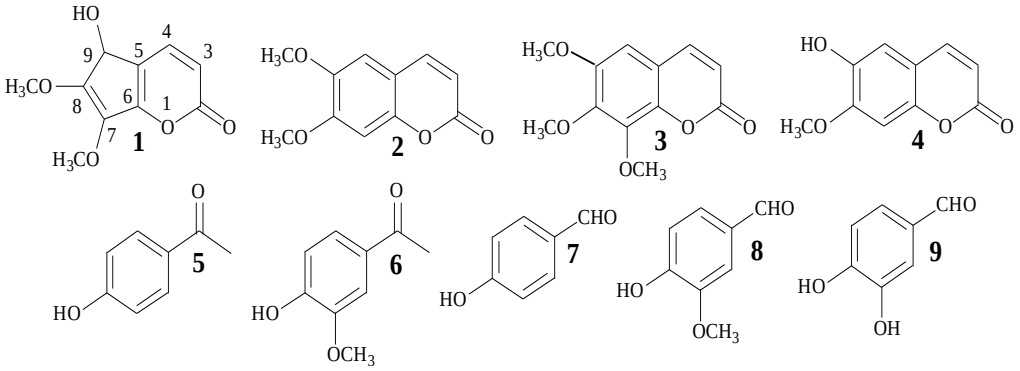

Figure 1. Structures of compounds **1**-**9**

Compound **1** was obtained as a white needle, mp 137-139 °C; IR (KBr) ν_{max} (cm^{-1}): 3312, 1683, 1643 and 1320 cm^{-1}. The molecular formula was determined to be $C_{10}H_{10}O_5$ by HR-ESI-MS exhibiting a pseudomolecular ion peak at *m/z* 209.0467 $[M-H]^-$ (calcd for $C_{10}H_9O_5$, 209.0450). In the ^{1}H NMR spectrum (Table 1), two characteristic resonances for H-3 and H-4 of a coumarin at δ_H 6.03 (1H, d, J = 10.0 Hz, H-3) and 8.06 (1H, d, J = 10.0 Hz, H-4). In addition, the signals at δ_H 3.64 (3H, s) and 3.82 (3H, s) indicated the presence of two methoxy groups. The remaining signal at δ_H 6.39 (1H, s) was assigned to H-9 compared with the data of H-25 (δ_H 6.21) in fasciospongides **A** [14], which was confirmed by the HMBC correlations (Figure 2) from δ_H 6.39 (1H, s, H-9) to C-5 (δ_C 104.8), C-6 (δ_C 152.3) and C-7 (δ_C 133.5).

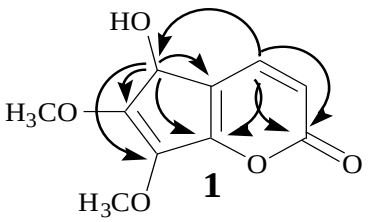

Figure 2. Selected HMBC correlations for **1**

Table 1. ^{1}H (500 MHz) and ^{13}C-NMR (125MHz) data of compound **1** in DMSO-d_6

Position	δ_H (ppm), *J* (Hz)	δ_c (ppm)
2	—	161.5
3	6.03 d (10.0)	109.1
4	8.09 d (10.0)	141.1
5	—	104.8
6	—	152.3
7	—	133.5
8	—	157.0
9	6.39 s	89.7
7-OCH_3	3.64 s	60.6
8-OCH_3	3.82 s	56.5

The ^{13} C NMR spectrum of **1** showed 10 carbon signals, of which 8 were assigned to the coumarin skeleton part and 2 to the two methoxy groups. In coumarin skeleton part, there were only 8 carbon signals (δ_C 161.5, 109.1, 141.8, 104.8, 152.3, 133.5, 157.0, 89.7), which was different from the 9 carbon signals of an usual coumarin skeleton [9, 10]. The benzene in an usual coumarin skeleton was substituted by the 1,3-diene cyclopentane in the new coumarin skeleton, in which the HMBC correlations from H-4 to C-2 (δc 161.5), C-6 (δc 152.3) and C-9 (δc 89.7), and H-3 to C-2 (δc 161.5) and C-5 (δc 104.8), H-9 to C-5 (δ_C 104.8), C-6 (δ_C 152.3) and C-7 (δ_C 133.5) were show. In addition, the HMBC correlationsδ_H 3.64 (-OCH_3) to δc 133.5 (C-7) and 3.82 (-OCH_3) to δc 157.0 (C-8) revealed that the two methoxy groups were linked to the C-7 and C-8, respectively. The modified Mosher's method was used to produce (*R*)- and (*S*)-MTPA esters (**1a**, **1b**), and signals corresponding to H-3, H-4 and 8-OCH_3 were relatively deshielded in **1a** compared to **1b**, indicating that the absolute configuration of C-9 is *S* (Figure 3). Thus, the structure of compound **1** was elucidated and named as arteordocoumarin A.

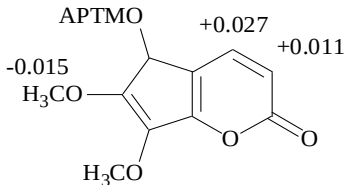

Figure 3. Results with the modified Mosher's method ($\Delta = \delta_S - \delta_R$) for compound **1**

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Supporting Information

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ORCID
Wugedunqiqige Bao: 0000-0003-0744-8361
Qinghu Wang: 0000-0002-6272-6398
Junsheng Hao: 0000-0002-7733-133X

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