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A New Alkaloid from *Sinomenium acutum*

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Abstract: *Sinomenium acutum* is widely used in East and South Asia for the treatment of many diseases, especially rheumatoid arthritis (RA). The chemical research on *Sinomenium acutum* led to the isolation of a new alkaloid compound (**1)**. On the basis of chemical evidences and spectral analysis, **1** was identified as N-(1, 7-dimethoxylphenanthren-2-yl)acetamide.

Keywords: *Sinomenium acutum*, alkaloid, N-(1, 7-dimethoxylphenanthren-2-yl)acetamide.

The whole plant of *Sinomenium acutum* has been used as a traditional Chinese medicine (TCM) for the treatment of rheumatoid arthritis, arrhythmia, and pain *etc*.[1-4]. Sinomenine, the main effective alkaloid isolated from *S. acutum*, was reported to possess a variety of pharmacological effects, such as immunosuppression, conscious-sedation, anti-arrhythmia, analgesia, organs-protection from the damage caused by shock, Ca-antagonist *etc*. [5-9].

Though the chemical research about *S. acutum* started early in the middle of last century, and several other alkaloids were also obtained[10], there was not a systematic research on the structure-bioactivity relationships of the chemical constituents. In order to investigate the relationships, firstly, a systematic chemical research on the 70% ethanol extract of *S. acutum* was carried out and a new alkaloid was obtained. The present paper describes the isolation and the structural elucidation of **1** (see **Figure 1**).

The isolation and purification of **1** from *S. acutum* was performed by chromatographic separation on silica gel column (chloroform:methanol 3:7 as mobile phase), repeated ODS column and preparative HPLC (Xterra RP18 column, 20×250 mm, mobile phase methanol:water=54:46, 256 nm).

1, obtained as yellowish green needle crystal, was positive to Dragendorff's reagent, revealing it was an alkaloid compound. It exhibited maximal absorptions at 256, 282 and 310nm in the ultraviolet (UV) spectrum, similar to phenanthrene derivatives[11]. The positive ESI-MS showed two quasi-molecular ion peaks at *m/z* 296 ($[M+H]^+$), and 313 ($[M+NH_4]^+$), and the MS-MS gave three fragment ions at *m/z* 254 ($[M+H\text{-}COCH_3]^+$), 223 ($[M+H\text{-}COCH_3\text{-}OCH_3]^+$) and 194($[M+H\text{-}COCH_3\text{-}OCH_3\text{-}OCH_3]^+$). The high-resolution ESI-MS showed the quasi-molecular ion $[M+H]^+$ at *m/z* 296.3214 (calcd. 296.

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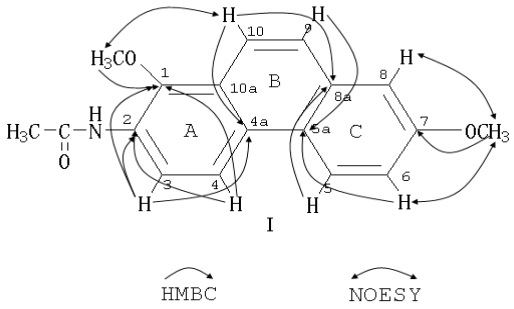
Figure 1 The structures of **1**



3218), corresponding to the molecular formula $C_{18}H_{17}NO_3$, which was further supported by the ^{1}H-NMR and ^{13}C-NMR spectral data. The ^{1}H-NMR and ^{1}H-^{1}H COSY spectrum (600MHz, $CDCl_3$) displayed tow pairs of *ortho*-coupled aromatic protons at δ 7.74 (d, 1H, *J*=8.6Hz) and 7.30 (d, 1H, *J*=8.6Hz), and δ 7.51 (d, 1H, *J*=8.7Hz) and 7.62 (d, 1H, *J*=8.7Hz), and a ABX system at δ 9.01 (d, 1H, *J*=9.2Hz), 7.20 (dd, 1H, *J*=9.2, 1.9Hz) and 7.23 (d, 1H, *J*=1.9Hz), and other signals at δ 3.97 (s, 3H, OC**H$_3$**), 3.95 (s, 3H, OC**H$_3$**) and 2.54 (s, 3H, -CO-C**H$_3$**), among which the two pairs of *ortho*-coupled aromatic protons and the ABX system aromatic protons must be located in different aromatic rings because no correlative peaks were observed between each other. The ^{13}C-NMR spectrum exhibited eighteen carbon signals including one carbonyl, three methyl, seven methyne and seven quarternary carbons.

In the HMBC spectrum, correlations from H-5 (δ 9.01) to C-7 (δ 158.0) and C-8a (δ 135.2), H-6 (δ 7.20) to C-5a (δ 122.9), C-7 (δ 158.0) and C-8 (δ 109.2), H-8 (δ 7.23) to C-5a (δ 122.9), C-6 (δ 116.2) and C-7 (δ 158.0) indicated that aromatic ring C was 1, 2, 4-substituted. The correlative peaks from δ 3.95 (OC**H$_3$**) to H-6 (δ 7.20) and H-8 (δ 7.23) in the NOESY spectrum demonstrated the methoxyl group at δ 3.95 was linked to C-7. The correlations from H-9 (δ 7.51) to C-5a (δ 122.9) and C-10a (δ 127.3), H-10 (δ 7.62) to C-4a (δ 124.3) and C-8a (δ 135.2) indicated the existence of aromatic ring B. The correlations from H-6 (δ 7.20) and H-9 (δ 7.51) to C-5a (δ 122.9), H-5 (δ 9.01) and H-10 (δ 7.62) to C-8a (δ 135.2) in the HMBC spectrum suggested that C-5a and C-8a were the two bridge carbons connecting the two aromatic rings B and C. The correlations from H-3 (δ 7.74) to C-1 (δ 149.9), C-2 (δ 136.3) and C-4a (δ 124.3), H-4 (δ 7.30) to C-1 (δ 149.9), C-2 (δ 136.3) and C-10a (δ 127.3) indicated the existence of aromatic ring A with C-4a and C-10a as the bridge carbons of A and B. Furthermore, the correlative peak was observed from δ 3.97(OC**H$_3$**) to H-10 (δ 7.62) in the NOESY spectrum, and the correlative peak from δ 3.97(OC**H$_3$**) to C-1 (δ 149.9) in the HMBC spectrum indicated that the methoxyl group at δ 3.97 must be linked to C-1. The correlative peak from -C**H$_3$** (δ 2.54) to -CO-(δ 168.8) proved the existence of acetyl group. Therefore, the remaining -NH should be located in C-2 and form an acetamide with the acetyl group (detailed information of HMBC see **Table 1**). Thus, **1** was identified as N-(1, 7-dimethoxylphenanthren-2-yl)acetamide. The protons and carbons of **1** were fully assigned on the basis of 2D-NMR techniques, including HMQC, ^{1}H-^{1}H COSY, HMBC and NOESY (detailed information see **Table 1**).

Table 1 The ^{13}C-NMR (150MHz) and ^{1}H-NMR (600MHz), ^{1}H-^{1}H COSY, HMBC data of **1** (in $CDCl_3$, δ ppm)

No.	Carbon	Proton	2D-NMR	
	δ (ppm)	δ (ppm)	^{1}H-^{1}H COSY *J*(Hz)	HMBC
1	149.9	--	--	--
1-O**C**H$_3$	56.6	3.97	--	C-1
2	136.3	--	--	--
N-**C**O	168.8	--	--	--
N-CO**C**H$_3$	21.3	2.54	--	N-**C**O
3	127.1	7.74	H3-H4 *J*=8.6 Hz	C-1, 2, 4a
4	111.5	7.30		C-1, 2, 10a
4a	124.3	--	--	--
5	128.1	9.01	H5-H6 *J*=9.2 Hz	C4a, 7, 8a
5a	122.9	--	--	--
6	116.2	7.20	H6-H5 *J*=9.2 Hz H6-H8 *J*=1.9 Hz	C-5a, 7, 8
7	158.0	--	--	--
7-O**C**H$_3$	55.3	3.95	--	C-7
8	109.2	7.23	H8-H6 *J*=1.9Hz	C-4a, 5a, 6, 7
8a	135.2	--	--	--
9	125.3	7.51	H9-H10 *J*=8.7Hz	C-5a, 8, 8a, 10a
10	127.4	7.62		C-4a, 8a, 10a
10a	127.3	--	--	--

Notes: a) Recorded on BRUKER ARX 600.
b) The carbon and proton signals were assigned unambiguously on ^{1}H-NMR, ^{13}C-NMR, ^{1}H-^{1}HCOSY, NOESY, HMQC, HMBC.

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