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A NEW 9,10-DIHYDROPHENANTHRENEDIONE FROM *Cannabis sativa*

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The structure of a new 9,10-dihydrophenanthrenedione, which was isolated from the leaves and branches of Cannabis sativa *L., was elucidated as 9,10-dihydro-2,3,5,6-tetramethoxyphenanthrene-1,4-dione (**1**) on the basis of MS, ^{1}H NMR, and ^{13}C NMR methods, especially 2D NMR techniques (HMBC and NOESY).*

Keywords: *Cannabis sativa* L., hemp, 9,10-dihydrophenanthrenedione.

Cannabis sativa L., a member of the Cannabinaceae family, is widespread in the world. It contains mainly cannabinoids and flavonoids, steroids, terpenes, noncannabinoid phenols, nitrogenous compounds, and so on [1]. The fruits of *Cannabis sativa* L. have been used in folk medicine (Chinese traditional medicine) for the treatment of cancer of the stomach, constipation due to dryness of the bowels, arthralgia caused by wind dampness, dysentery, irregular menstruation, and constipation due to deficiency of blood and consumption of body fluids [2]. Modern pharmaceutical investigations have revealed cannabinoids that might be of therapeutic value as an analgesic, muscle relaxant, immunosuppressant, anti-inflammatory, anti-allergic, anti-emetic, bronchodilator, neuroprotector, antineoplastic, sedative, mood enhancer, and appetite stimulant, and for its ability to lower intraocular pressure [3]. However, tetrahydrocannabinol (THC), a main constituent of hemp, is psychoactive, so the cannabis drug is only available for human use as an investigational drug. Now, scientists have cultivated some new varieties, named industrial hemp, with the content of THC below 0.3% [4, 5]. In continuation of our phytochemical study on the subject, herein we report the isolation and structure elucidation of a new 9,10-dihydrophenanthrenedione derivative, 9,10-dihydro-2,3,5,6-tetramethoxyphenanthrene-1,4-dione (**1**), which was isolated from a new hemp variety (Yunma series).

The branches and leaves of *Cannabis sativa* L. were collected in Yunnan Province, P. R. China in July 2006 and identified by Prof. HongYan Guo, Yunnan Academy of Agricultural Sciences, Yunnan Province, P. R. China. A voucher specimen has been deposited in the Yunnan Academy of Agricutural Sciences, Yunnan Province, P. R. China. The air-dried branches and leaves were extracted with absolute methanol three times at ambient temperature.The solution was concentrated and partitioned sequentially with petroleum ether, ethyl acetate, and *n*-butanol, yielding 131, 27, and 33 g of extracts, respectively. Part of the petroleum ether extract (88 g) was chromatographed on a silica gel (200~300 mesh) column using petroleum ether–$CHCl_3$ and petroleum ether–EtOAc as elutents and further pruified by Sephadex LH-20 (eluted with MeOH) chromatography and semipreparative liquid chromatography (MeOH–H_2O as the mobile phase). After the reported 14 known compounds [6], an additional compound (compound **1**) was isolated from the petroleum ether–$CHCl_3$ elution part, and its structure was established by UV, IR, mass, and NMR spectra, especially 2D NMR techniques (HMBC and NOESY).

Compound **1** was isolated as an orange powder, mp 113–115°C. Its molecular formula was established as $C_{18}H_{18}O_6$ by HR-ESI-MS: *m/z* 353.1007 $[M + Na]^+$ (calcd 353.1001) and ESI-MS: *m/z* 353 $[M + Na]^+$, 683 $[2M + Na]^+$, implying ten degrees of unsaturation. Its UV spectrum (MeOH, λ_{max}, nm): 428, 330, 254, 218 and IR spectrum (KBr, ν, cm^{-1}): 1666, 1651, 1636, 1568, 1480 showed the presence of aromatic rings and carbonyl groups. It had a neat ^{1}H NMR spectrum with two doublets at δ 6.92 (1H, d, J = 8.4 Hz) and 6.90 (1H, d, J = 8.4 Hz), four singlets integrated as 3H at δ 4.07 (3H, s), 4.04 (3H, s), 3.91 (3H, s), and 3.87 (3H, s), and two broad singlets integrated as 2H at δ 2.64 (2H, br.s) and 2.55 (2H, br.s).

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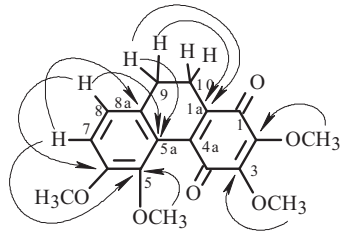
TABLE 1. The ^{1}H, ^{13}C NMR Data and Correlations from HMBC and NOESY of **1** ($CDCl_3$, δ, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC (H to C)	NOESY (H to H)
1		182.4		
2		143.3		
3		146.1		
4		182.3		
5		147.0		
6		151.8		
7	6.90 (d, J = 8.4)	122.1	5, 8a	H-14, H-8
8	6.92 (d, J = 8.4)	114.3	6, 5a	H-7, H-9
9	2.64	27.8	1a, 4a, 5a	H-8, H-10
10	2.55	20.5		H-9
1a		139.9		
4a		132.0		
5a		123.0		
8a		132.3		
11	4.04	60.6	2	
12	4.07	61.1	3	
13	3.91	61.0	5	
14	3.87	56.0	6	

The downfield signals in the ^{1}H NMR spectrum implied a tetra-substituted benzene structure. The four singlet signals between δ 3.87–4.07 suggested that compound **1** contains four methoxyl groups. Consistent with the molecular formula of **1**, a total of 18 signals was observed in the ^{13}C NMR and DEPT spectra, comprising ten quaternary, two tertiary, and two secondary carbon atoms, as well as four methoxyl groups. Among them, two carbonyl carbons at δ 182.4 (C-1) and 182.3 (C-4) were observed. The ten downfield signals at δ 151.8 (C-6), 147.0 (C-5), 146.1 (C-3), 143.3 (C-2), 139.9 (C-1a), 132.3 (C-8a), 132.0 (C-4a), 123.0 (C-5a), 122.1 (C-7), and 114.3 (C-8) were due to ten olefinic carbons, some of which were characteristic of aromatic carbons. In addition, two secondary carbons at 27.8 (C-9) and 20.5 (C-10) were observed in the high field. Two out of the ten degrees of unsaturation belonged to two carbonyl groups, and the remaining eight degrees of unsaturation were accounted for by two rings, one of which was cyclohexadiene and the other a benzene ring. These data pointed to a 9,10-dihydrophenanthrenedione structure.

Analysis of the HMBC spectrum and the correlations of H-C(11)/C(2), H-C(12)/C(3), H-C(13)/C(5), and H-C(14)/C(6) showed that the four methoxyl groups were directly connected to olefinic carbons individually. The presence of the 9,10-dihydro-5,6-dimethoxyphenanthrenedione structure was further confirmed by the HMBC correlations of H-C(9)/C(1a), H-C(9)/C(5a), H-C(7)/C(5), H-C(7)/C(8a), and H-C(8)/C(6), and the NOESY correlations of H-C(9)/ H-C(8), H-C(7)/H-C(14), H-C(9)/H-C(10), and H-C(7)/H-C(8). Figure 1 shows the main correlations in **1**. Complete ^{1}H NMR and ^{13}C NMR assignments were achieved through a combination of HMBC and NOESY experiments (see Table 1). All these data show the structure of compound **1** to be 9,10-dihydro-2,3,5,6-tetramethoxyphenanthrene-1,4-dione.



1

Fig. 1. Main HMBC correlations of **1**.

EXPERIMENTAL

9,10-Dihydro-2,3,5,6-tetramethoxyphenanthrene-1,4-dione. $C_{18}H_{18}O_{6,}$, orange powder; mp 113–115°C; UV (MeOH, λ_{max}, nm): 428, 330, 254, 218; IR (KBr, ν, cm^{-1}): 1666, 1651 (C=O), 1568, 1480 (Ar); ^1H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): see Table 1; ^{13}C NMR (150 MHz, $CDCl_3$): see Table 1; ESI-MS: *m/z*: 353 $[M + Na]^+$, 683 $[2M + Na]^+$, HR-ESI-MS: *m/z* 353.1007 $[M + Na]^+$ (calcd for $C_{18}H_{18}O_6$ 353.1001).

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