

Jasonone, a Nor-sesquiterpene from *Jasonia montana*

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A new natural nor-sesquiterpene was isolated from the leaves of *Jasonia montana*, in addition to another rare nor-sesquiterpene. Their structures were established by spectroscopic methods, including ^1H , ^{13}C , DEPT, ^1H - ^1H COSY, HMQC, HMBC, NOESY, IR and HR-MS.

Key words: *Jasonia montana*, Asteraceae, Nor-sesquiterpenes

Introduction

The genus *Jasonia* (Asteraceae, Inuleae, subtribe Inulinae) is a small genus with about five species mainly distributed in the Mediterranean region [1]. Some species of the genus *Jasonia* have held a place of importance from ancient times, due to their medicinal properties [2]. They are rich in sesquiterpenes, especially germacranes [3], guaianolides and pseudoguaianolides [4] and highly oxygenated eudesmane alcohols [5–10]. Most of the species of this genus exhibited a number of biological activities like anti-inflammatory [11], antidiabetic [12] and antimicrobial activity [14]. Five methoxylated flavonoids and thirteen flavonoid aglycons were isolated from the aerial parts of *Jasonia montana* [13, 14]. The essential oils of *Jasonia candicans* and *J. montana* showed antibacterial activity against *Bacillus subtilis* and also a marked antifungal activity against *Trichophyton mentagrophytes*, *Cryptococcus neoformans* and *Candida albicans* [15].

Results and Discussion

The methylene chloride extract of the air-dried leaves of *J. montana* was chromatographed on silica gel and Sephadex LH-20 columns to give a new natural nor-sesquiterpene **1**, for which the name jasonone was chosen, together with another rare nor-sesquiterpene **2**. Compound **1** was isolated as a yellowish oil, $[\alpha]_{\text{D}}^{25} = -8$ ($c = 0.23$, CHCl_3), and its IR spectrum showed absorption bands at 3450 cm^{-1} (OH) and 1706 cm^{-1} (C=O). The low resolution EIMS showed the molecular ion peak $[\text{M}]^+$ at $m/z = 196$. The high resolu-

tion mass spectrum exhibited the molecular ion peak $[\text{M}]^+$ at $m/z = 196.1464$ (calcd. 196.1459), in accord with a molecular formula of $\text{C}_{12}\text{H}_{20}\text{O}_2$. The structure of jasonone (**1**) was determined from careful investigation of the 1D and 2D NMR data. The ^1H NMR spectrum showed a triplet at $\delta = 3.60$ ($J = 9\text{ Hz}$, H-4) which showed clear correlation in the ^1H - ^1H COSY spectrum with the multiplets at $\delta = 1.44$ (H-3 β) and 2.05 (H-3 α). Moreover, the examination of the connectivities in the ^1H - ^1H COSY spectrum of compound **1** indicated strong correlations between the multiplet at $\delta = 1.26$ (H-1) with the multiplets at $\delta = 1.61$ (H-10), 1.30 (H-2 β) and 1.72 (H-2 α). Furthermore, the ^1H NMR spectrum revealed the presence of the methyl groups as a singlet at $\delta = 0.63$ (H-11) and a doublet at $\delta = 0.97$ ($J = 5.0\text{ Hz}$, H-12). Long range coupling was clearly observed from the ^1H - ^1H COSY spectrum between the multiplet at $\delta = 1.26$ (H-1) and the doublets at $\delta = 2.45$ (H-9 α) and 0.97 (H-12).

The ^{13}C NMR data (Table 1) revealed the presence of 12 carbon atoms and their multiplicities (by DEPT analysis) confirmed the number of hydrogen atoms of the formula given above. The carbon atoms were assigned as two methyl carbons at $\delta = 9.51$ and 21.42 (C-11 and C-12), five methylene carbons at $\delta = 24.95$, 29.37, 31.64, 40.51, and 52.66 (C-2, C-3, C-6, C-7, and C-9), three methine carbons at $\delta = 55.79$, 80.74 and 32.33 (C-1, C-4, and C-10) and two quaternary carbons at $\delta = 45.78$ and 214.0 (C-5 and C-8), respectively. Moreover, all proton and carbon signals were determined by ^1H - ^1H COSY, HMQC and HMBC (Tables 1, 2). Confirmation of the structure of **1** was given by the results of the 2D long range heteronuclear corre-

	1		2	
Position	δ_H	δ_C	δ_H	δ_C
H-1 α	1.26 (1H, m)	55.79 d	1.66 (1H, m)	40.60 t
H-1 β			1.37 (1H, ddd, $J = 15, 5, 2$)	
H-2 α	1.72 (1H, m)	24.95 t	1.70 (2H, m)	19.46 t
H-2 β	1.30 (1H, m)			
H-3 α	2.05 (1H, m)	29.37 t	1.98 (1H, m)	42.26 t
H-3 β	1.44 (1H, m)		1.57 (1H, ddd, $J = 12, 5.5, 5$)	
H-4 α	3.60 (1H, t, $J = 9$)	80.74 d		72.40 s
H-5		45.78 s		174.90 s
H-6 α	1.55 (1H, dd, $J = 9.5, 9.5$)	31.64 t	6.35 (1H, s)	122.50 d
H-6 β	1.99 (1H, ddd, $J = 16, 9.5, 9.5$)			
H-7	2.49 (2H, dd, $J = 9.5, 9.5$)	40.51 t		200.39 s
H-8 α		214.0 s	1.76 (1H, dd, $J = 5, 2$)	40.83 t
H-8 β			1.94 (1H, ddd, $J = 15, 5, 2$)	
H-9 α	2.45 (1H, d, $J = 11$)	52.66 t	2.56 (1H, dd, $J = 5.5, 5$)	33.39 t
H-9 β	2.35 (1H, dd, $J = 11, 1.8$)		2.40 (1H, m)	
H-10 β	1.61 (1H, m)	32.33 d		36.17 s
H-11	0.63 (3H, s)	9.51 q	1.32 (3H, s)	29.63 q
H-12 α	0.97 (3H, d, $J = 5.0$)	21.42 q	1.44 (3H, s)	24.50 q

Table 1. ^1H NMR and ^{13}C NMR data of compounds **1** and **2** (500 MHz, 125 MHz, CDCl_3 , TMS as internal standard).

lation (HMBC) analysis (Table 2). The most important correlations were observed between H-1 ($\delta = 1.26$, m) and C-2 ($\delta = 24.95$), C-5 ($\delta = 45.78$), C-9 ($\delta = 52.66$), C-10 ($\delta = 32.33$), C-12 ($\delta = 21.42$); H-2 ($\delta = 1.30$, m, 1.72, m) and C-1 ($\delta = 55.79$), C-3 ($\delta = 29.37$), C-4 ($\delta = 80.74$), C-10 ($\delta = 32.33$); H-4 ($\delta = 3.60$, t) and C-2 ($\delta = 24.95$), C-3 ($\delta = 29.37$), C-5 ($\delta = 45.78$), C-6 ($\delta = 31.64$), C-11 ($\delta = 9.51$); H-6 ($\delta = 1.99$ ddd, 1.55 dd) and C-4 ($\delta = 80.74$), C-5 ($\delta = 45.78$), C-7 ($\delta = 40.51$), C-8 ($\delta = 214.0$), C-11 ($\delta = 9.51$); H-9 ($\delta = 2.45$ d, 2.35 dd) and C-1 ($\delta = 55.79$), C-7 ($\delta = 40.51$), C-8 ($\delta = 214.0$), C-10 ($\delta = 32.33$), C-12 ($\delta = 21.42$), and H-10 ($\delta = 1.61$, m) and C-8 ($\delta = 214.0$). The stereochemistry of compound **1** was deduced from the chemical shifts and the values of the coupling constants and confirmed by the NOESY spectrum with inspection of Dreding models. The NOESY spectrum indicated clear effects between H-11 ($\delta = 0.63$, s), H-8 β ($\delta = 1.99$, ddd), and H-10 β ($\delta = 1.61$, m) as well as between H-12 ($\delta = 0.97$, d), H-1 α ($\delta = 1.26$, m), and H-2 α ($\delta = 1.72$, m). Further correlations of the HMBC and NOESY experiments are listed in Table 2. To our knowledge, compound **1** is a new natural compound. It may be an interesting intermediate on the way to Confertin which has attracted considerable attention because of its cytotoxic and antitumor activity [16–19].

Compound **2** was obtained as yellowish oil, $[\alpha]_D^{25} = +31$ ($c = 0.13$, CHCl_3). The structure of **2** was assigned to be a nor-sesquiterpene, teuhetenone A [21], on the basis of the following considerations: Its EI mass spectrum showed the molecular ion peak at $m/z = 194$, in accord with the molecular formula $\text{C}_{12}\text{H}_{18}\text{O}_{32}$.

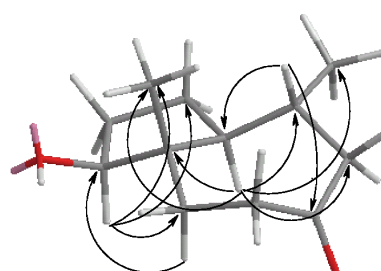
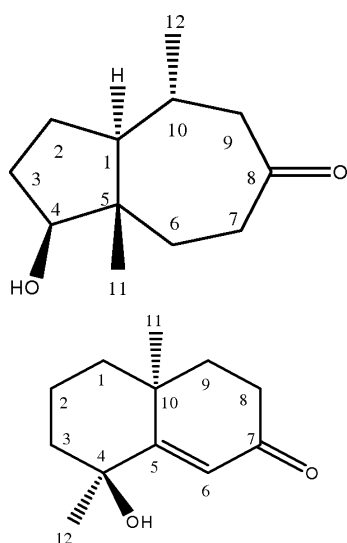
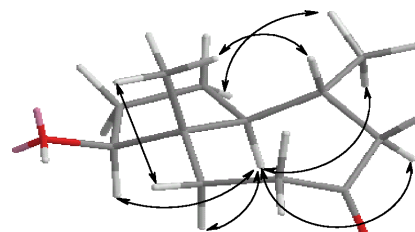
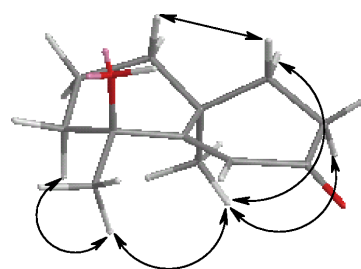
Its IR spectrum showed absorbances of hydroxyl and carbonyl groups. The ^1H NMR spectrum revealed the presence of the angular methyl groups as two singlets at $\delta = 1.32$ (H-11) and 1.44 (H-12). Additionally, a multiplet at $\delta = 1.66$ (H-1 α) was observed which showed correlations in ^1H - ^1H COSY with the multiplets at $\delta = 1.37$ (H-1 β) and 1.70 (H-2). The latter proton showed clear correlation in ^1H - ^1H COSY with a pair of doublet of doublets at 1.57 and 1.98 (H-3). Furthermore, it revealed the olefinic proton as a singlet at $\delta = 6.35$. The ^{13}C NMR spectrum (DEPT) indicated the presence of twelve carbon atoms in the molecule (Table 1) classified as two methyl, five methylene, three quaternary, one olefinic protonated and one carbonyl carbon. On the basis of these results, the structure of compound **2** was assigned to the nor-sesquiterpene teuhetenone A [20], detected in a mixture before but was not isolated before. Its stereochemistry was determined now by the NOESY spectrum, where H-11 and H-12 correlated with each other, indicating the α -orientation of these protons. Other correlations accrued between H-11 α ($\delta = 1.32$) and H-1 α ($\delta = 1.66$) and H-9 α ($\delta = 2.56$), as well as between H-12 α ($\delta = 1.44$) and H-8 α ($\delta = 1.76$).

Experimental Section

General

NMR spectra were measured with a Bruker AMX-400 spectrometer, with TMS as an internal standard. The IR spectra [oily film, CHCl_3] were taken on a Perkin Elmer FT-IR spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter operating at

Proton No.	HMBC with C	NOESY with H
H-1 α	C-2, C-5, C-9, C-10, C-11, C-12	H-6 α , H-9 α , H-12 α
H-2 α	C-1, C-3, C-4, C-5	H-12 α
H-2 β	C-1, C-3, C-4, C-10	H-10 β , H-11 β
H-3 α	C-1, C-2, C-4, C-5	
H-3 β	C-1, C-4	H-11 β
H-4 α	C-2, C-3, C-5, C-6, C-11	H-1 α
H-6 α	C-4, C-7, C-8, C-11	H-1 α , H-3 α , H-9 α
H-6 β	C-4, C-7, C-8, C-11	H-11 β
H-7	C-5, C-6, C-9	
H-9 α	C-1, C-7, C-8, C-10, C-12	H-1 α
H-9 β	C-1, C-7, C-8, C-10, C-12	
H-10 β	C-1, C-8, C-9, C-12	H-11 β
H-11 β	C-1, C-4, C-5, C-6	H-3 β , H-6 β
H-12 α	C-1, C-9, C-10	H-1 α , H-2 α

Table 2. HMBC and NOESY data for compound **1**.Selected HMBC of **1**.NOESY observed in **1**.NOESY observed in **2**.

the sodium D line. CC: Silica gel (Merck, 60–120 mesh) and Sephadex LH-20 (Pharmacia). TLC and preparative TLC: Silica gel 60 GF₂₅₄ (Merck). The compounds were visualized either by spraying with vanillin or under an UV lamp.

Plant material

Jasonia montana (vahl) botsch. was collected in 2001 from the North of Sinai, Egypt. A voucher specimen of the collection was identified by Prof. Mohamed Jaber and was deposited in the Department of Botany, Aswan Faculty of Science, Egypt.

Extraction and isolation

Air dried and powdered leaves (500 g) of *Jasonia montana* were extracted with CH₂Cl₂ at r. t. for 24 h. The extract was concentrated *in vacuo* to give a residue (15 g), which was chromatographed by using flash column chromatography

on a silica gel eluted with an *n*-hexane-CH₂Cl₂ step-gradient. The *n*-hexane-CH₂Cl₂ fraction (75%) was carefully chromatographed on a Sephadex LH-20 column eluted with *n*-hexane-CH₂Cl₂-MeOH (7 : 4 : 0.5) by increasing the polarity to give the new nor-sesquiterpene **1** (15 mg) and compound **2** (10 mg).

Jasonone; 4-hydroxy-5,10-dimethyl-octahydro-azulen-8-one (**1**)

C₁₂H₂₀O₂; yellowish oil, $[\alpha]_D^{25} = -8$ ($c = 0.23$, CHCl₃). – IR (KBr): $\nu = 3450$ (OH), 1706 cm^{-1} (C=O). – ¹H NMR: The ¹H assignments were achieved by ¹H-¹H correlation spectroscopy (COSY), see Table 1. – ¹³C NMR: The ¹³C assignments were achieved by HMQC and HMBC, see Ta-

bles 1 and 2. – MS (EI, 70 eV): m/z (%) = 196 (21) [M⁺], 178 (80) [M⁺-H₂O], 150 (55) [M⁺-CO]; calcd. 196.1459; found 196.1464.

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