Pergamon

Tetrahedron Letters, Vol. 38, No. 29, pp. 5205-5208, 1997
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0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01112-X

The Structures of Three Novel Sesquiterpenoids from *Valeriana Jatamansi Jones*

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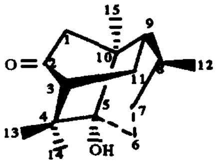
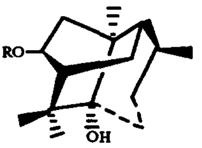
Abstract : Three new sesquiterpenoids valeriananoids A (1) , B (2) and C (3) , possessing an unprecedented sesquiterpene skeleton, have been isolated from the roots and rhizomes of *Valeriana jatamansi Jones* . The structures were elucidated by chemical and spectroscopic means and, in the case of **1**, confirmed by X-ray crystallography. © 1997 Elsevier Science Ltd.

Valeriana jatamansi Jones, distributed widely in southwestern areas of China, has been used as a traditional Chinese medicine due to its hypnotic, tranquilizing and antiviral activities . In our previous paper [1] 40 chemical constituents of essentials oils from four Valeriana species have been reported. Described herein is the structure elucidation of three new sesquiterpenoids valeriananoids A-C (**1**-**3**) obtained from an EtOAc extract of the roots and rhizomes of *Valeriana jatamansi Jones*. Compounds **1**-**3** possess a unique carbon skeleton which has not been found in the sesquiterpenoids before. Valeriananoids B exhibited moderate in vitro antirotavirus activities .



1



2 R=H
3 R=OAc

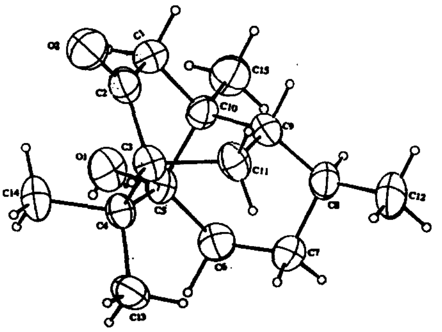
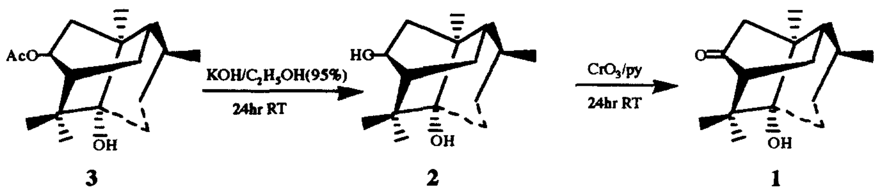


Figure 1. X-ray structure of 1

Compound **1** is a colorless crystal (Me_2CO), m.p. 122-124 ^{0}C , $[\alpha]_D^{28}$-34.6 (c = 0.231, $CHCl_3$). The molecular formula was established as $C_{15}H_{24}O_2$ by EIMS [2] and elemental analysis. IR absorptions at 3440 and 1710 cm^{-1} implied that **1** possessed both hydroxyl and carbonyl groups. Analyses of the ^1H NMR, ^{13}C NMR (Table 1) and DEPT data of **1** revealed the existence of one carbonyl, four methyls, four methylenes, three methines and three quaternary (one of them bearing an oxygen atom) carbons. One out of the four unsaturations was thus characterized, and compound **1** was therefore inferred to contain three rings. H-1a (δ 1.77, d J=19.3) and H-1b (δ 2.63, d J=19.3) formed an AB system in the ^1H NMR spectrum of compound **1**. The assignments of protons and carbons were obtained by the analysis of its 2D NMR spectra. The structure of compound **1** was confirmed by single crystal X- ray analysis. The compound **1** crystallized in the orthorhombic space group $P_1\,2_1\,2_1$ with one molecule of composition $C_{15}H_{24}O_2$ (Z=4) forming the asymmetric unit. Accurate cell constants of a =10.133(2)Å, b =11.566(3)Å, c =11.600(3)Å, v =1359.62(8)$Å^3$ were determined by a least-squares fit of fifteen moderate 2θ-angle values. All unique diffraction maxima with 2θ<114 were collected on a Nicolet R3M/E using graphite monochromated CuKα radiation (1.54178Å) and variable speed ω scans. After correction for Lorentz, polarization and background effects , 1036 of the 1082 independent reflections were judged observed [I>3σ(I)]. The structure was solved by SAPI programs and MAC science crystanG. Hydrogen atoms were located in a difference electron density synthesis after full least - squares refinement of the non-hydrogenatoms. The final conventional crystallographic residual is R =0.087 for 1036 observed reflections. The final X-ray model is shown in figure 1. The final atomic parameters, bond lengths and angles will be deposited at the Cambridge Crystallographic Data Center. An unequivocal assignment of the absolute configuration was not achieved by X- ray diffraction . However, compound **1** showed positive Cotton effect at 300 nm (Δ ε +0.21) in its CD spectrum. This band could be assigned to the $n \rightarrow \pi^*$ transition of the twisted cyclohexanone carbonyl group of **1** . Application of the octant rules for twisted bridged-ring ketones [5] suggested for this compound the absolute configuration shown in the structure **1** .

Compound **2** , colorless needles, m.p. 200-202 ^{0}C, $[\alpha]_D^{28}$ -57.87 (c=0.197, $CHCl_3$) , was determined to have the molecular formula $C_{15}H_{26}O_2$ by EIMS [3] and elemental analysis . IR absorptions[3] at 3420, 3380 cm^{-1} suggested the presence of hydroxy. ^1H,^{13}C NMR data (Table 1) and DEPT spectra of **2** revealed 15 signals: four methyls, four methylenes, four methines (including an oxymethine), three quaternary (one of them bearing an oxygen atom) carbons. Comparison of spectroscopic data of the compound **1** with those of compound **2** showed that the carbonyl group of **1** was replaced in **2** by a hydroxyl group. Compound **3** was also obtained as colorless needles (Me_2CO) , m.p. 79-80 ^{0}C, $[\alpha]_D^{28}$ -56.88 (c=0.160 $CHCl_3$). Its IR spectrum[4] contained absorptions for hydroxyl(3505 cm^{-1}) and ester(1715cm^{-1}) functional groups and some structural features found in **1** and **2**. The identification of 17 carbons in the ^{13}C NMR (Table 1) and DEPT experiment , and the EIMS[4] indicated a molecular formula of $C_{17}H_{28}O_3$. Compound **1** and **3** showed very similar NMR spectra except for that the signals of one acetyl group were present only in the spectra of **3**. Moreover, hydrolysis (KOH/95%C_2H_5OH) of **3** afforded **2** and oxidation (CrO_3/py) of **2** gave **1** (scheme 1). Both **2** and **1** thus obtained were identified by comparison of their R_f's, mp's, IR and MS. Thus the structures of valerianananoids B and C were concluded to be **2** and **3**, respectively.



Scheme 1. Transformation of **3** into **2** and **1**.

Table 1. NMR data for **1**, **2** and **3**.

Compound	1		2		3	
Position	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1a	2.63d(19.3)		2.00dd(13.6,6.6)		1.95dd(14.1, 7.6)	36
1b	1.77d(19.3)	46.5	1.57dd(13.6,7.8)	39.5	1.63dd(14.1,10.4)	
2		215.9	3.84ddd(7.8,6.6,1.4)	72.6	4.78ddd(10.4,7.6,1.8)	74.6
3	1.84dd(5.0,5.6)	57.7	1.44t(7.5)	46.8	1.46t(6.4)	43.4
4		40.5		39.5		39.1
5		74.3		77.2		75.0
6 a	1.72m	33.1	1.50m	32.6	1.51m	32.7
6 b	1.88m		1.70m		1.74m	
7 a	1.41m	28.3	1.31m	28.6	1.34m	28.6
7 b	1.58m		1.52m		1.53m	
8	2.04m	27.9	1.93m	27.7	1.94m	27.7
9	1.53m	43.6	1.37m	42.5	1.41m	42.5
10		42.4		40.9		40.1
11 a	1.43m	20.7	1.35m	24.1	1.37m	23.5
11 b	1.61m		1.53m		1.54m	
12-Me	0.84d(6.7)	16.7	0.77d(6.7)	16.9	0.80d(6.7)	18.7
13-Me	1.17s	23.0	1.20s	25.4	1.14s	25.0
14-Me	1.01s	27.7	1.05s	28.1	1.10s	27.8
15-Me	0.97	19.4	0.84s	20.2	0.89s	20.0
16						170.8
17					2.01s	21.5

* Spectra were recorded at 500MHz for ^{1}H and 125MHz for ^{13}C (CDCl$_3$), with chemical shifts (δ) in ppm and coupling constants in Hz put in ( ).

The ^{1}H-^{1}H and ^{1}H-^{13}C COSY NMR spectra (500MHz,$CDCl_3$) of **3** established the relationships between the signals at δ 0.80(Me-12) and 1.94(H-8); δ 1.95, 1.63(H-1) and 4.78(H-2) ; δ 1.51, 1.74 (H-6) and 1.34, 1.53 (H-7); δ1.94 (H-8) and 1.41(H-9); δ1.46(H-3) and 1.37, 1.54(H-11), which allowed the unambiguous assignment of the upfield protons such as H-1a and H-8, H-6 and H-7, and revealed connectivities of C-1 to C-2, C-6 to C-7, C-8 to C-9, C-9 to C-11, and C-11 to C-3. Of interest was the absence of coupling between H-2 and H-3, which suggested a torsion angle of nearly 90° (it can be observed in Dreiding models). The w type long-range coupling between H-2 and H-11 was observed in the ^{1}H NMR spectrum, along with the couplings between H-2 and H-1a as well as H-1b. The results indicated a β-oriented acetoxy group at C-2 since only αH would produce w type long- range coupling with H-11. The assignments of protons and carbons of **3** were summarized in Table 1.

Acknowlegements. This work was supported by the foundation of Chinese Medical Board. We thank Dr. Jixian Guo for identifying *V. jatamansi*.

References and Notes

1. Ming, Dongsheng; Guo, Jixian. *Chinese Traditional Patent Medicine*, **1994**, *16* (1) , 41.
2. Spectroscopic data for valeriananoids A(**1**): EIMS m/z (rel. intensity) $[M^+]$ 236 (33), 201(5), 153(33), 135(33), 125(95), 109(25), 107 (20), 96(15), 83(100), 69(40), 55(42), 42(66). IR (cm^{-1}): 3440, 1720, 1470, 1390, 1340, 1220, 1100, 1070, 1050 1000, 890, 590.
3. Spectroscopic data for valeriananoids B (**2**): EIMS m/z (rel. intensity) $[M^+]$ 238(0.4), 220(5), 205(5), 159(4), 15(3), 125(100), 107(12), 96(45), 81(13), 55(15), 42(20). IR(cm^{-1}): 3420, 3380, 1470, 1380, 1340, 1170, 1110, 1050, 1010, 920, 620.
4. Spectroscopic data for valeriananoids C (**3**): EIMS m/z (rel. intensity) $[M^+ - AcOH]$ 220(12), 205(13), 203(10), 177(12), 125(100), 109(9), 107(18), 96(80), 81(13), 69(5), 55(9), 42(40). IR (cm^{-1}): 3500, 1720, 1470, 1400, 1370, 1270, 1210, 1160, 1030, 1010, 980, 900, 560.
5. Kirk, D.N. *Tetrahedron*, **1986**, *42* (3), 777.

(*Received in China* 15 *January* 1997; *revised* 26 *February* 1997; *accepted* 23 *May* 1997)