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A GUAIANE-TYPE SESQUITERPENE, VALERACETATE FROM *VALERIANA OFFICINALIS*

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Key Word Index—*Valeriana officinalis*; Valerianaceae; valeracetate; guaiane-type sesquiterpene; α-kessyl acetate; kessyl glycol diacetate; kessyl glycol 8-acetate.

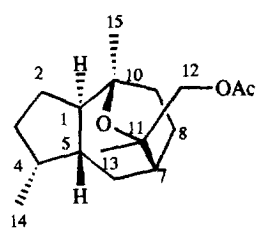
Abstract—Valeracetate, a new guaiane-type sesquiterpene, and three previously known sesquiterpenes have been isolated from *Valeriana officinalis* and their structures were determined by spectroscopic techniques.

INTRODUCTION

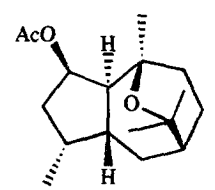
Valeriana plants have been used for sedative and antispasmodic purposes [1–13]. In a continuation of our investigation of biologically active substances, we collected *V. officinalis* in Tokushima prefecture and investigated the chemical constituents of the ethyl acetate extract of this plant. We now report the isolation and structure determination of a new guaiane-type sesquiterpene, valeracetate (**1**), and the previously known compounds, α-kessyl acetate (**2**), kessyl glycol diacetate (**3**) and kessyl glycol 8-acetate (**4**) [12].

RESULTS AND DISCUSSION

The ethyl acetate extract was separated by a combination of silica gel and Sephadex LH-20 CC. Valeracetate (**1**) had a molecular formula $C_{17}H_{29}O_3$ which was revealed by CIHRMS (CH_4). The ^{1}H NMR and IR spectra showed the presence of an acetyl group (1740 cm^{-1}; δ2.08 (*s*)), which was supported by the ^{13}C NMR spectrum (δ171.0). The INEPT experiments indicated the presence of four methyl groups, six methylene groups, four methine groups and three quaternary carbon atoms (Table 1). Two of the oxygen atoms were accounted for by an acetoxyl group and the remaining oxygen atom must be assigned to an ether, which was verified by the presence of three low-field carbon atoms bearing oxygen functions (δ70.6, 74.5, 75.5). The degree of unsaturation of valeracetate is 4 and therefore compound **1** is tricyclic. The COSY spectrum indicated little information due to the overlapping nature of the proton signals. However, the HMBC and HMQC spectra showed three partial structures as shown in Fig. 1. The two lowest resonating protons appeared as an AB quartet and were independent in the proton network. The acetoxymethyl group was attached to the quaternary carbon (δ75.5) bearing an oxygen and a methyl group (δ1.29). The proton resonating at δ1.72 as a triplet of doublets (H-1) had several correlation peaks including CH at δ41.6 (C-5), which was next to the carbon bearing a secondary methyl group. Thus, these three partial structures were connected to each other to make a guaiane-type skeleton (Table 2). The stereochemistry was revealed by a NOESY spectrum. The methyl group at C-11 had a correlation peak



1



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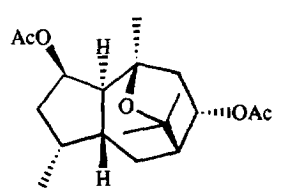

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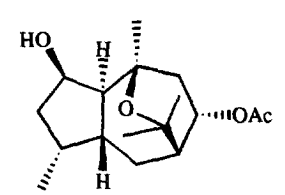

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*Author to whom correspondence should be addressed.

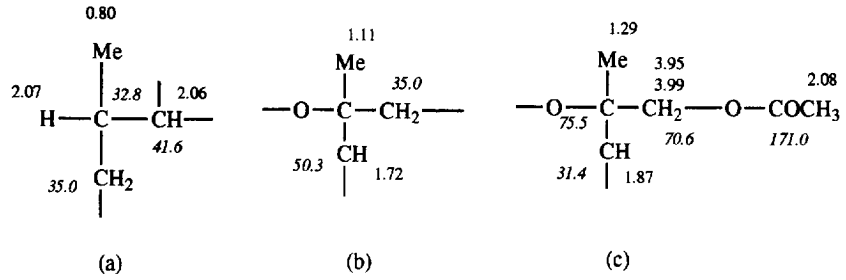

Fig. 1. Three partial structures for valeracetate (1).

Table 1. ^{1}H NMR (600 MHz) and ^{13}C NMR (100 MHz) data for valeracetate (1)

C	^{1}H	^{13}C
1	1.72 *td* (12, 6.2)	50.3
2	1.41 *m* (α)	28.2
	1.54 *m* (β)	
3	1.07 *m* (α)	32.0
	2.00 *m* (β)	
4	2.07 *m*	32.8
5	2.06 *m*	41.6
6	1.37 *m* (α)	33.0
	1.99 *m* (β)	
7	1.87 *dd* (7.8, 7.1)	31.4
8	2.03 *m* (α)	23.7
	1.57 *m* (β)	
9	1.62 *t* (10, 8) (α)	35.0
	1.82 *m* (β)	
10	—	74.5
11	—	75.5
12	3.99 *d* (10.8)	70.6
	3.95 *d* (10.8)	
13	1.29 *s*	23.4
14	0.80 *d* (6.8)	18.4
15	1.11 *s*	27.9
Ac	2.08 *s*	21.0
		171.0

Table 2. HMBC correlations for valeracetate (1)

C	Correlated protons
1	9β
3	14
4	14
5	1α, 7α, 14
7	12, 13
8	7α
9	1α, 7α, 15
10	9β, 15
11	12, 13
12	13
13	12

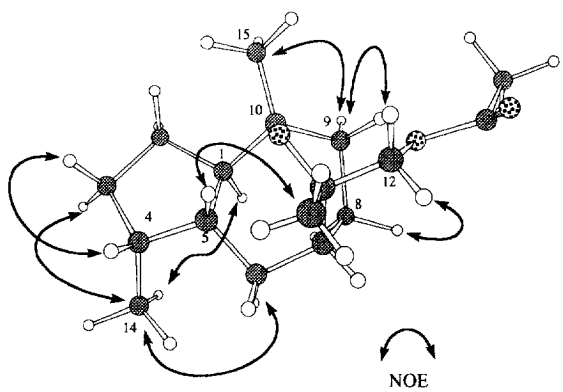

Fig. 2. The NOEs detected for valeracetate (1).

with the proton at C-5 and the protons at δ 3.99 and 3.95 were correlated with H-9β. Therefore the acetoxymethyl group must be at C-12 and the methyl group at C-13. Since the secondary methyl group at C-4 had correlation peaks with H-3α, H-1 and H-6α, H-14 must be α-oriented, while H-5 should be β-oriented. Therefore the structure of valeracetate was established as depicted in structure **1**.

Valeracetate (**1**) is the first compound whose methyl group is oxygenated in guaiane-type sesquiterpenoids, to the best of our knowledge.

EXPERIMENTAL

^{1}H NMR: 400 or 600 MHz, ^{13}C NMR: 100 MHz (in $CDCl_3$ soln, TMS as int. standard). CC: Silica gel 60 (70–230 mesh, Merck) and Sephadex LH-20 (Pharmacia). TLC: silica gel 60 F_{254} plates (Merck).

Isolation of valeracetate. Valeriana officinalis L. var. *latifolia* Miq. was collected in Tokushima Prefecture in June, 1986. The voucher specimen was deposited in the herbarium of Tokushima Bunri University and was identified by Y. Asakawa. The half-dried root (216 g) was extracted with EtOAc to afford a reisdue (13.1 g). The extract was subjected to Sephadex LH-20 ($CHCl_3$–MeOH, 9:1) followed by silica gel column chromatography (C_6H_6–EtOAc, gradient) several times to give sitosterol (57 mg), α-kessyl acetate (**2**) (74 mg), kessyl glycol

diacetate (**3**) (558 mg), kessyl glycol 8-acetate (**4**) (97 mg) and valeracetate (**1**) (58 mg).

Valeracetate (**1**). $[\alpha]_D^{24}$ + 1.0 ($CHCl_3$, *c* 1.4); CIHRMS (CH_4) *m/z* 281.2122, $C_{17}H_{29}O_3$ requires 281.2117. CIMS (CH_4) *m/z* 281 $[M + 1]^+$, 263, 221, 207, 203 (base), 189, 163, 124, 95 and 81; nmax (cm^{-1}): 1740; ^1H and ^{13}C NMR see Table 1.

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REFERENCES

1. Itô, S., Kodama, M. and Nozoe, T. (1963) *Tetrahedron* **19**, 1787.
2. Hikino, Y., Hikino, H., Takeshita, Y., Shirata, K., Ono, M. and Takemoto, T. (1967) *Chem. Pharm. Bull.* **15**, 324.
3. Hikino, H., Takeshita, Y., Hikino, Y., Takemoto, T. and Itô, S. (1967) *Chem. Pharm. Bull.* **15**, 485.
4. Itô, S., Kodama, M. and Nozoe, T. (1967) *Tetrahedron* **23**, 553.
5. Hikino, H., Hikino, Y., Kato, H., Takeshita, Y. and Takemoto, T. (1969) *Yakugaku Zasshi* **89**, 118.
6. Hikino, H., Hikino, Y., Takeshita, Y., Isuguri, Y. and Takemoto, T. (1971) *Yakugaku Zasshi* **91**, 650.
7. Hikino, H., Ono, M. and Takemoto, T. (1972) *Yakugaku Zasshi* **92**, 479.
8. Takamura, K., Nabata, H. and Kawaguchi, M. (1975) *Yakugaku Zasshi* **95**, 1205.
9. Hendricks, H., Bos, R., Allersma, D. P., Malingré, T. M., Koster, A. S. (1981) *Planta Medica* **42**, 62.
10. Hendricks, H., Bos, R., Woerdenbag, H. J., Koster, A. S. (1985) *Planta Medica* **46**, 28.
11. Oshima, Y., Hikino, Y. and Hikino, H. (1986) *Tetrahedron Letters* **27**, 1829.
12. Nishiya, K., Kimura, T., Takeya, K. and Itokawa, H. (1992) *Phytochemistry* **31**, 3511.
13. Oshima, Y., Matsuoka, S., Ohizumi, Y. (1995) *Phytochemistry* **43**, 169.