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SESQUITERPENOIDS FROM *VALERIANA FAURIEI*

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Key Word Index— *Valeriana fauriei*; Valerianaceae; sesquiterpenoids; patchouli alcohol; 8-acetoxyl-patchouli alcohol; 8-hydroxyl-patchouli alcohol.

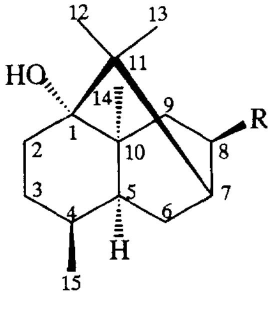
Abstract— Two new patchoulane sesquiterpenoids together with patchouli alcohol, patrinoside and kanokoside A, have been isolated from the rhizomes and roots of *Valeriana fauriei* purchased on a market in China. The structures of these new compounds were determined by various spectroscopic methods in this paper.

INTRODUCTION

The crude drug Japanese Valerian, prepared from the rhizomes and roots of *Valeriana fauriei* or allied plants, has been used for sedative and antispasmodic purposes. *V. fauriei* cultivated in Hokkaido, 'Hokkai-kisso', is characterized by containing sesquiterpenoids of the kessane skeleton, in particular, kessyl glycol diacetate in a large quantity and iridoid glycosides [1–7]. In the present work, we studied the constituents, bisabolane sesquiterpenoids from *V. fauriei* cultivated in Korea [8]. In this paper we report the isolation and structural determination of constituents **1**–**3** and two known iridoid glycosides, patrinoside (**4**) and kanokoside A (**5**) from *V. fauriei* purchased from a market in China.

RESULTS AND DISCUSSION

The methanolic extract of the rhizomes and roots of *V. fauriei* was partitioned between *n*-hexane and water. The aqueous layer was further partitioned between ethyl acetate and water, and between *n*-butanol and water, successively. Compounds **1-3** were isolated from the hexane fraction and **4** and **5** from the butanol fraction.



1 : R = H

2 : R = OAc

3 : R = OH

Compound **1** was obtained as solid, $[M]^+$ at *m/z* 222, and showed a hydroxyl group (3480 cm^{-1}) in its IR spectrum. The ^1H NMR spectrum showed a secondary methyl signal (δ0.79), and three tertiary methyl signals (δ0.84, 1.07 and 1.08).

Compound **2** was isolated as needles, and its CI-mass spectrum showed a peak due to $[M - 1]^+$ at *m/z* 279. The IR spectrum showed a hydroxyl group (3520 cm^{-1}) and an acetoxyl group (1722 and 1275 cm^{-1}). The ^1H NMR spectrum showed a secondary methyl signal (δ0.80), three tertiary methyl signals (δ0.89, 1.10 and 1.15), an acetoxylmethyl signal (δ2.01) and a methine proton of acetoxylmethyl group (δ4.79).

Compound **3** was obtained as needles, $[M]^+$ at *m/z* 238, and showed hydroxyl groups (3410 and 3370 cm^{-1}) in its IR spectrum. The ^1H NMR spectrum showed a secondary methyl signal (δ0.81), three tertiary methyl signals (δ0.88, 1.09 and 1.18) and a methine proton of hydroxylmethyl group (δ3.88).

On the basis of a comparison of the IR, ^1H and ^{13}C NMR spectral data among those of **1**–**3**, they were deduced to have same type of tricyclic skeleton. The presence of partial structure $-CH_2-CH_2-CH(Me)-CH-CH_2-CH(OAc)-CH_2-$ was revealed by ^1H NMR double resonance and $^1H-^{13}C$ correlation spectroscopy (COSY) experiments of **2**. The relative sterochemistry of **2** was confirmed by a difference NOE experiment. Irradiation at the methyl proton signal at δ1.15 enhanced the signal intensity of the acetoxylmethyl signal at δ2.01. This experiment demonstrated that the acetoxyl group is close to H_3-13. From these spectral data, **1** was characterized as patchouli alcohol [9], and **2** and **3** were identified as 8-acetoxyl-pathchouli alcohol and 8-hydroxyl-pathouli alcohol, respectively (Table 1).

Compound **3** was derived from hydroxylation of patchouli alcohol by fermentation with a fungus [10]. To the

Table 1. ^{13}C NMR chemical shifts for **1**–**3** in $CDCl_3$

C	**1***	**1**	**2**	**3**
1	75.1	75.6	75.0	76.4
2	33.0	32.8	32.7	33.0
3	29.0	28.7	28.6	29.7
4	28.4	28.2	27.7	29.0
5	44.0	43.8	42.5	44.2
6	24.7	24.4	23.5	25.2
7	39.6	39.2	43.4	47.7
8	24.9	24.6	74.6	73.1
9	29.1	28.9	36.0	39.9
10	37.8	37.7	39.2	40.2
11	40.4	40.2	40.1	41.7
12	27.2	26.8	25.1	26.0
13	24.4	24.3	27.8	29.0
14	20.7	20.6	20.0	21.0
15	18.7	18.6	18.8	19.3
–OAc			21.6	
			170.8	

*In C_6D_6 [9].

best of our knowledge, however, **2** and **3** as natural constituents have not been reported previously. We also draw attention to patchouli alcohol as one of the chemotaxonomic constituents of *Valeriana* species (e.g. *V. officinalis* and *V. celtica*) [11, 12].

We also isolated two known iridoid glycosides'(**4**, **5**) as hygroscopic amorphous substances and amorphous powders by preparative ODS HPLC. They were identified by comparison of their ^{1}H and ^{13}C NMR spectra with those of the known iridoid compounds, contained in *V. fauriei*, irrespective of the different sources [7, 8]..

EXPERIMENTAL

^{1}H NMR: 400 MHz, $CDCl_3$, TMS as int. standard; ^{13}C NMR: 100 MHz.

Plant material. The dried rhizomes and roots of a commercial strain of *V. fauriei* were purchased from a market in China in 1992, and a morphological and microscopic comparison was made with an authentic original specimen by Dr Daitoku, M. (Department of Pharmacognosy, Tokyo College of Pharmacy). The voucher specimen is kept in the laboratory of one of the authors (K.N.).

Extraction and isolation. The dried rhizomes and roots of a commercial strain of *V. fauriei* purchased on a market in China (2.0 kg) were extracted with MeOH (3 x). The MeOH extract (259 g) was partitioned between *n*-hexane and H_2O to give the hexane fr. (30.1 g). The aq. layer was further partitioned between EtOAc and H_2O to give the EtOAc fr. (28.2 g), and between *n*-BuOH and H_2O to give the BuOH fr. (47.7 g), successively. The hexane fr. was subjected to silica gel CC using the solvent systems *n*-hexane–EtOAc (4:1 and 7:3) and EtOAc. The hexane–EtOAc eluted frs were further purified by silica gel CC. and prep. ODS HPLC (Inertsil PREP-ODS (250 mm × i.d. 20 mm, GL Sciences Inc., Tokyo, Japan), detected by refractive index) eluting with MeOH–H_2O (9:1) to give **1** (0.028% from the rhizomes and roots), and eluting with MeOH–H_2O (4:1) to give **2** (0.046%). Compound **3** (0.0052%) was obtained as needles from the hexane–EtOAc eluted frs by recrystallization from *n*-hexane–EtOAc. The BuOH fraction was subjected to Diaion HP-20 (Mitsubishi Chem. Ind. Co.) CC using the solvent systems H_2O, MeOH–H_2O (2:3) and MeOH. The MeOH–H_2O (2:3) eluted frs were further purified by prep. ODS HPLC eluting with MeOH–H_2O (2:3) to give **4** (0.012%) and **5** (0.018%).

Compound **1**. Solid, mp. 55–56°. EI-MS *m/z*: 222 $[M]^+$; $[\alpha]_D - 118.1°$ ($CHCl_3$; *c* 1.88); IR ν_{max}^{liquid} cm^{-1}: 3480, 2940, 1468, 1387, 1041, 999; ^{1}H NMR ($CDCl_3$): δ0.79 (3H, *d*, J = 6.7 Hz), 0.84, 1.07, 1.08 (each 3H, each *s*); ^{13}C NMR: Table 1.

Compound **2**. Needles, mp 85–86°. EI-MS *m/z*: 262 $[M - 18]^+$, 220 $[M - 60]^+$; CI-MS *m/z*: 279 $[M - 1]^+$; $[\alpha]_D - 114.8°$ ($CHCl_3$; *c* 3.30); IRν_{max}^{KBr} cm^{-1}: 3520, 2935, 1722, 1369, 1275, 1034; ^{1}H NMR ($CDCl_3$): δ0.80 (3H, *d*, J = 6.7 Hz), 0.89, 1.10, 1.15, 2.01 (each 3H, each *s*), 4.79 (1H, *ddd*, J = 1.6, 9.0, 9.0 Hz, 8-H); ^{13}C NMR: Table 1.

Compound **3**. Needles, mp 133–135°. EI-MS *m/z*: 238 $[M]^+$; 220 $[M - 18]^+$; $[\alpha]_D - 115.8°$ (MeOH; *c* 0.41); IR ν_{max}^{KBr} cm^{-1}: 3410, 3370, 2990, 1464, 1379, 1057, 1049; ^{1}H NMR ($CDCl_3$): δ0.81 (3H, *d*, J = 6.7 Hz), 0.88, 1.09, 1.18 (each 3H, each *s*), 3.88 (1H, *ddd*, J = 0.9, 8.5, 8.5 Hz, 8-H); ^{13}C NMR: Table 1.

REFERENCES

1. Hikino, H., Hikino, Y., Takeshita, Y., Isurugi, Y. and Takemoto, T. (1971) *Yakugaku Zasshi* **91**, 650.
2. Hikino, H., Hikino, Y., Kobinata, H., Aizawa, A., Konno, C. and Oh'izumi, Y. (1980) *Shoyakugaku Zasshi* **34**, 19.
3. Oshima, Y., Hikino, Y. and Hikino, H. (1986) *Tetrahedron Letters* **27**, 1829.
4. Taguchi, H. and Endo, T. (1974) *Chem. Pharm. Bull. (Tokyo)* **22**, 1935.
5. Endo, T. and Taguchi, H. (1977) *Chem. Pharm. Bull. (Tokyo)* **25**, 2140.
6. Taguchi, H., Endo, T., Yosioka, I. and Iitaka, Y. (1979) *Chem. Pharm. Bull. (Tokyo)* **27**, 1275.
7. Nishiya, K., Kimura, T., Takeya, K. and Itokawa, H. (1992) *Phytochemistry* **31**, 3511.
8. Nishiya, K., Kimura, T., Takeya, K. and Itokawa, H. (1994) *Phytochemistry*, **36**, 1547.
9. Neszmelyi, A. and Lukacs, G. (1981) *J. Chem. Soc., Chem. Commun.* 999.
10. Becher, E. *et al.* (1978) *Ger. Offen* **27**, 39 449.
11. Rücker, G. and Tautges, J. (1976) *Phytochemistry* **15**, 824.
12. Bicchi, C., Sandra, P., Schelfaut, M. and Verzele, M. (1983) *HRC CC, J. High Resolut. Chromatogr, Chromatogr. Commun.* **6**, 213.