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Triterpenoids from Flower Buds of *Tussilago farfara* L.

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A new triterpenoid, bauer-7-ene-3β,16α-diol, and two known triterpenoids, bauerenol and isobauerenol, were isolated from dried flower buds of *Tussilago farfara* L. (Compositae). The structure of the new compound was elucidated by the spectroscopic data.

Keywords : *Tussilago farfara*; flower bud; Compositae; triterpenoid

The flower buds of *Tussilago farfara* L. (Compositae) have been widely used for treatment of cough, bronchitis and asthmatic disorders in China. [1] In previous papers, we reported the isolation and structural elucidation of the essential oil components [2] and sesquiterpenoids [3] from the plant. In the present paper, we report the isolation and structural elucidation of a new triterpenoid, bauer-7-ene-3β,16α-diol (**1**). Two known compounds, bauerenol (**2**)[4] and isobauerenol (**3**)[5] were also isolated, and identified by its spectral data. This is the first report of isolation of **2** and **3** from the flower buds of *T. farfara*. Extraction and isolation were carried out as described in the experimental section.

Compound **1** was shown to have the molecular formula $C_{30}H_{50}O_2$ by high-resolution (HR)-MS data. The IR spectrum showed the presence of hydroxyl groups (3329 cm^{-1}), and the electron ionization (EI)-MS gave significant fragment ion peaks at *m/z* 424 (M^+-H_2O), 406 (M^+-2H_2O), 273 (a), 255 (a$-H_2O$), 247 (b), 229 (b$-H_2O$), 221 (c) and 203 (c$-H_2O$) (Fig. 1). These fragment ions suggested that **1** was a bauerane or multiflorane derivative with hydroxyl groups in the rings A/B and rings D/E of the molecule.[6] The ^{1}H-NMR spectrum of **1** indicated the presence of six tertiary methyl groups, two secondary methyl groups, two hydroxy methine groups and one trisubstituted olefinic proton. The ^{1}H-detected heteronuclear multiple bond connectivity (HMBC) analysis showed correlations between H_3-24 and C-3, C-4 and C-5; H_3-25 and C-1, C-5, C-9 and C-10; H_3-26 and C-8, C-13 and C-14; H_3-28 and C-16, C-17, C-18 and C-22; H_3-29 and C-18, C-19 and C-20; and H_3-30 and C-19, C-20 and C-21, suggesting that **1** was a bauerane-type triterpenoid (Fig. 2). The HMBC spectrum determined the position of the trisubstituted double bond hydrogen to be at C-7, by showing correlations between H-7 and C-5 and C-9; and H_3-26 and C-8, and the positions of the hydroxyl groups to be at C-3 and C-16, by the correlations between H_3-24 and C-3; H-15 and C-16; and H_3-28 and C-16 (Fig. 2). From the above data, the planar structure of **1** was determined to be bauer-7-ene-3,16-diol. The stereostructure was ascertained by the nuclear Overhauser effect (NOE) interactions observed in the nuclear Overhauser enhancement spectroscopy (NOESY) spectrum (Fig. 3). These NOEs implied *trans*-junctions of the rings A/B and the rings C/D, and *cis*-junction of the rings D/E, and that the rings A and D had chair conformation, the ring B half chair conformation and the rings C and E boat conformation. The configuration of the hydroxyl groups at C-3 and C-16 were determined by ^{1}H-NMR and NOESY spectra. In the ^{1}H-NMR spectrum, the coupling patterns and constants for H-3 [δ_H 3.21 (dd, *J*=11.0, 4.8Hz)] and H-16 [δ_H 3.62 (dd, *J*=12.8, 4.8Hz)] suggested that the hydroxyl groups at C-3 and C-16 had β and α configurations, respectively. The same conclusion was derived from the NOESY cross-peaks observed between H-3 α and H_3-23; and H-16 β and H_3-26 (Fig. 3). Accordingly, the structure of **1**

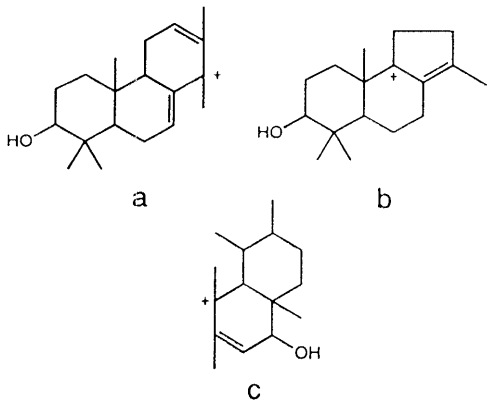


Fig. 1

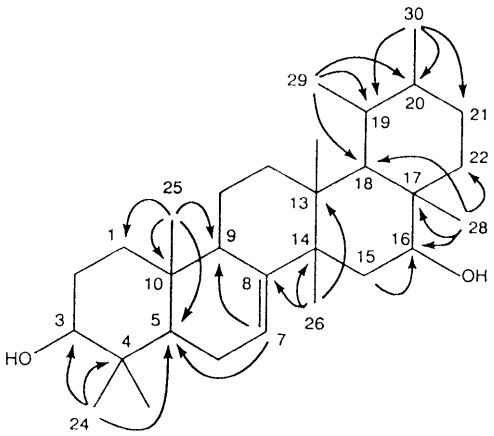


Fig. 2

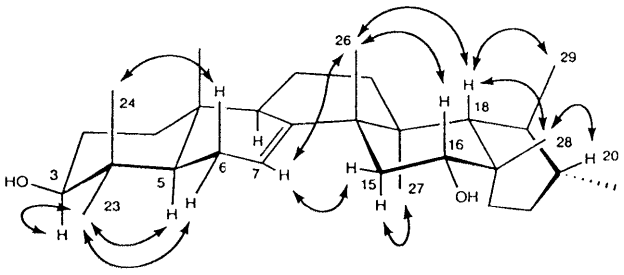


Fig. 3

was determined to be bauer-7-ene-3β,16α-diol.

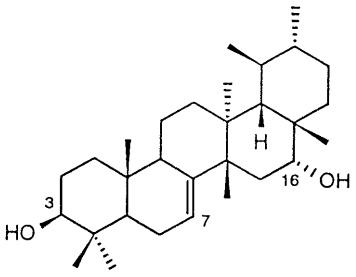
EXPERIMENTAL

General Procedure Melting point was determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were determined with a JASCO DIP-360 digital polarimeter. IR spectra with a Parkin-Elmer FT-IR 1725X infrared spectrophotometer, ^{1}H- and ^{13}C-NMR spectra with a JEOL JNM LA 600, JNM LA 400, JNM EX 270 spectrometer and EI- and HR-MS on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (Merck: 230 - 400 mesh) and preparative HPLC on a Tosoh HPLC system (pump; CCPD, detector; RI-8010).

Plant material Dried buds of *Tussilago farfara* were purchased from Tochimoto Tenkaido Co., Ltd., Osaka, Japan in 1990.

Extraction and isolation The dried buds of *T. farfara* (5.0 kg) were extracted with Et_2O at room temperature for one week. The Et_2O extract was subjected to steam distillation to give an essential oil (7.7 g) and residue (64.5 g). A part of this residue (23.5 g) was placed on a silica gel column and developed with benzene-AcOEt (9:1). The eluate was separated into 17 fractions (frs.1 - 17). Fr. 9 was purified by preparative HPLC (column;TSK gel ODS-120T, 7.8mmi.d.x 30cm; mobile phase, MeOH; column temperature, 40℃; flow rate, 1.0 ml/min; RI detector) to give **2** (1.4 mg) and **3** (1.9 mg). Fr. 15 was recrystallized from $CHCl_3$ to give **1** (1.6 mg).

Bauer-7-ene-3β,16α-diol (1) Colorless needles, mp. 282-285℃. $[\alpha]_D^{28}$ -25.6° (c =0.2, pyridine). IRν_{max} (KBr) cm^{-1} : 3329. HR-MS m/z : 442.3788 (M^+, Calcd for $C_{30}H_{50}O_2$; 442.3811). EI-MS m/z : 442 (M^+), 424 (M^+-H_2O), 406 (M^+-2H_2O), 273 (a), 255 (a$-H_2O$), 247 (b), 229 (b$-H_2O$), 221 (c), 203 (c$-H_2O$). ^{1}H-NMR ($CDCl_3$+CD_3OD (4:1), 600MHz) δ : 0.76 (3H, s, H_3-25), 0.85 (3H, s, H_3-24), 0.93 (3H, d, J=6.2Hz, H_3-30), 0.96 (3H, s, H_3-27), 0.97 (3H, s, H_3-23), 1.04 (3H, s, H_3-26), 1.08 (3H, d, J=7.0Hz, H_3-29), 1.22 (3H, s, H_3-28), 1.31 (2H, m, H-5, H-18), 1.53 (1H, dd, J=12.8, 12.8Hz, H-15α), 1.57 (1H, m, H-20), 1.71 (dd, J=12.8, 4.8Hz, H-15β), 1.98 (1H, m, H-6β), 2.14 (1H, m, H-6α), 3.21 (1H, dd, J=11.0, 4.8Hz, H-3), 3.62 (1H, dd, J=12.8, 4.8Hz, H-16), 5.45 (H, d, J=3.7Hz, H-7). ^{13}C-NMR ($CDCl_3$+CD_3OD (4:1), 100MHz) δ: 12.96 (C-25), 14.68 (C-24), 16.73 (C-11),



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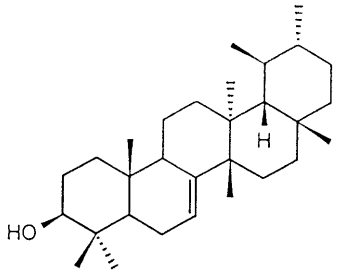

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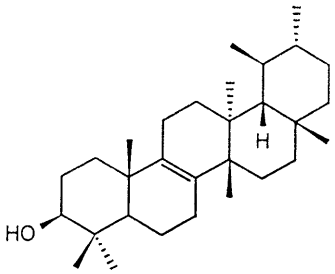

3

22.66 (C-30), 22.67 (C-27), 24.22 (C-22), 24.61 (C-6), 24.67 (C-26), 25.57 (C-29), 27.34 (C-2), 27.49 (C-23), 28.37 (C-21), 32.02 (C-12), 32.19 (C-19), 33.67 (C-28), 35.31 (C-10), 35.37 (C-20), 36.98 (C-1), 37.42 (C-15), 38.08 (C-13 or C-17), 38.09 (C-13 or C-17), 38.99 (C-4), 42.11 (C-14), 48.14 (C-9), 50.65 (C-5), 55.11 (C-18), 77.03 (C-16), 79.04 (C-3), 116.80 (C-7), 144.36 (C-8).

Bauerenol (2) Amorphous powder. $[\alpha]_D^{23}$ -21.7° (*c* = 0.1, $CHCl_3$); [lit.,[4]) $[\alpha]_D$ -25° ($CHCl_3$)]. IRν_{max} ($CHCl_3$) cm^{-1} : 3610, 3472. HR-MS *m/z* : 426.3852 (M^+, Calcd for $C_{30}H_{50}O$; 426.3861). EI-MS *m/z* : 426 (M^+), 411 (M^+-CH_3), 408 (M^+-2H_2O), 393 ($M^+-CH_3-H_2O$), 273, 259, 247, 229, 205. ^{1}H-NMR ($CDCl_3$, 270MHz) δ : 0.75 (3H, s, H_3-25), 0.86 (3H, s, H_3-24), 0.90 (3H, d, *J*=5.9Hz, H_3-30), 0.94 (3H, s, H_3-27), 0.97 (3H, s, H_3-23), 1.00 (3H, s, H_3-26), 1.04 (3H, s, H_3-28), 1.05 (3H, d, *J*=5.9Hz, H_3-29), 3.24 (1H, m, H-3), 5.45 (1H, br s, H-7); Acetate: ^{1}H-NMR ($CDCl_3$, 270MHz) δ : 0.77 (3H, s, H_3-25), 0.85 (3H, s, H_3-24), 0.91 (3H, d, *J*=5.8Hz, H_3-30), 0.93 (3H, s, H_3-27), 0.95 (3H, s, H_3-23), 1.00 (3H, s, H_3-26), 1.04 (3H, s, H_3-28), 1.05 (3H, d, *J*=5.9Hz, H_3-29), 2.05 (s, OAc), 4.52 (1H, dd, *J*=11.1, 4.8Hz, H-3), 5.41 (1H, br d, *J*=4.0Hz, H-7).

Isobauerenol (3) Amorphous powder. $[\alpha]_D^{22}$ +31.9° (*c* = 0.2, $CHCl_3$); [lit.,[5]) $[\alpha]_D$ +37.2°($CHCl_3$)]. IRν_{max} ($CHCl_3$) cm^{-1}: 3609, 3474. HR-MS *m/z* :426.3877 (M^+, Calcd for $C_{30}H_{50}O$; 426.3861). EI-MS *m/z* : 426 (M^+), 411 (M^+-CH_3), 408 (M^+-2H_2O), 393 ($M^+-CH_3-H_2O$), 273, 259, 247, 229, 205. ^{1}H-NMR ($CDCl_3$, 270MHz) δ : 0.80 (3H, s, H_3-24), 0.88 (3H, s, H_3-27), 0.90 (3H, d, *J*=5.9Hz, H_3-30), 0.95 (3H, s, H_3-25), 0.99 (3H, d, *J*=6.3Hz, H_3-29), 1.00 (6H, s, H_3-23, H_3-26), 1.05 (3H, s, H_3-28), 3.23 (1H, dd, *J*=10.7, 4.8Hz, H-3); Acetate: ^{1}H-NMR ($CDCl_3$, 270MHz) δ : 0.84 (3H, s, H_3-24), 0.87 (3H, s, H_3-27), 0.88 (3H, s, H_3-23), 0.90 (3H, d, *J*=5.9Hz, H_3-30), 0.98 (3H, s, H_3-25), 0.99 (3H, d, *J*=6.9Hz, H_3-29), 1.00 (3H, s, H_3-26), 1.05 (3H, s, H_3-28), 2.05 (s, OAc), 4.50 (1H, dd, *J*=11.4, 4.8Hz, H-3).

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