Structures of New Oplopane-Type Sesquiterpenoids from the Flower Buds of *Tussilago farfara* L.[1)]

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Five new oplopane-type sesquiterpenoids, 7β-senecioyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (1), 7β-angeloyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (2), 7β-(4-methylsenecioyloxy)oplopa-3(14)*E*,8(10)-dien-2-one (3), 1α-angeloyloxy-7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (4) and 1α,7β-di(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (5), were isolated from the flower buds of *Tussilago farfara* L. (Compositae). The structures of these compounds were elucidated on the basis of spectroscopic evidence.

Key words *Tussilago farfara*; Compositae; oplopane-type sesquiterpenoid

The flower buds of *Tussilago* (*T.*) *farfara* L. (Compositae) have been widely used for the treatment of coughs, bronchitis and asthmatic disorders in China.[2)] In previous papers, we reported the isolation and structural elucidation of the essential oil components,[3)] sesquiterpenoids,[4)] phenolic compounds[5)] and triterpenoids[1)] from the plant. Here, we report the isolation and structural elucidation of five new oplopane-type sesquiterpenoids, 7β-senecioyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (**1**), 7β-angeloyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (**2**), 7β-(4-methylsenecioyloxy)oplopa-3(14)*E*,8(10)-dien-2-one (**3**), 1α-angeloyloxy-7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (**4**) and 1α,7β-di(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (**5**). Extraction and isolation were carried out as described in the Experimental section.

Compound **1** was isolated as a colorless oil, $[\alpha]_D$ −97.6°. The molecular formula was determined to be $C_{20}H_{28}O_3$ by high-resolution (HR)-MS. The IR spectrum showed absorption bands due to an α,β-unsaturated ester (1715 cm^{-1}), an α,β-unsaturated ketone (1715 cm^{-1}) and a double bond (1650 cm^{-1}). The ^{1}H- (*vide* Experimental) and ^{13}C-NMR (Table 1) spectra were virtually identical to those of 7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (**6**), recently isolated from the flower buds of *T. farfara*, as an inhibitor of platelet aggregation caused by platelet activating factor,[2)] except for the presence of a senecioyl group[4)] instead of a 4-methylsenecioyl group in **6**. In the ^{1}H-detected heteronuclear multiple bond correlation (HMBC) spectrum, a cross peak was observed between the H-7 at δ_H 5.53 and the C-1′ at δ_C 165.7, confirming that the senecioyl group was attached to the oxygen at C-7. The stereochemistry of $\Delta^{3(14)}$ was shown to be *Z* by the nuclear Overhauser effect correlation spectroscopy (NOESY) spectrum, giving a cross peak between H-11 and H-14. The absolute configuration of oplopa-3(14)*Z*,8(10)-dien-2-one, which is the main skeleton of **1** has been established by Joseph–Nathan *et al.*[6)] On the basis of this evidence, the structure of **1** was determined to be 7β-senecioyloxyoplopa-3(14)*Z*,8(10)-dien-2-one.

Compound **2** was isolated as a colorless oil, $[\alpha]_D$ −104.5°. The molecular formula was determined to be $C_{20}H_{28}O_3$ by HR-MS. The IR spectrum showed absorptions due to an α,β-unsaturated ester (1714 cm^{-1}), an α,β-unsaturated ketone (1714 cm^{-1}) and a double bond (1646 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra of **2** were identical to those of **1** except for the appearance of signals ascribable to an angeloyl group[4)] instead of signals due to a senecioyl group in **1**. Thus, **2** was characterized as 7β-angeloyloxyoplopa-3(14)*Z*,8(10)-dien-2-one.

Compound **3** was isolated as a colorless oil, $[\alpha]_D$ −33.3°. The molecular formula was determined to be $C_{21}H_{30}O_3$ by HR-MS. The IR spectrum showed absorptions due to an α,β-unsaturated ester (1720 cm^{-1}), an α,β-unsaturated ketone (1720 cm^{-1}) and a double bond (1646 cm^{-1}). The ^{1}H-NMR spectrum was similar to that of **6**,[2)] although the ^{1}H-NMR spectrum showed that the olefinic methyl group (H_3-15) of **6** at δ_H 2.15 was shifted upfield to 1.90, and the trisubstituted olefinic proton (H-14) of **6** at δ_H 6.23 was shifted downfield to 6.53. The above results indicate that **3** is a $\Delta^{3(14)}E$ isomer of **6**.[7)] Based on this evidence, the structure of **3** was deter-

Table 1. ^{13}C-NMR Chemical Shifts of Compounds **1**—**5** (150 MHz, $CDCl_3$)

Carbon	1	2	3[a)]	4	5
1	41.0	41.1	39.6	72.4	71.8
2	206.4	206.3	205.3	200.0	200.0
3	141.1	140.9	142.2	139.0	139.1
4	50.8	50.8	51.3	44.9	44.8
5	39.9	40.4	37.7	40.4	40.6
6	30.7	30.8	29.9	29.8	29.9
7	73.1	73.9	72.6	73.4	73.5
8	146.1	145.8	146.2	140.9	140.9
9	41.7	42.0	41.3	45.8	45.7
10	110.0	110.4	110.2	112.7	113.5
11	27.0	27.0	29.5	27.5	27.5
12	21.3	21.3	21.3	21.3	21.3
13	15.3	15.3	16.0	15.4	15.5
14	132.4	132.8	128.5	137.0	137.0
15	14.6	14.6	14.6	15.1	15.1
1′	165.7	167.0	166.1	165.9	166.0
2′	116.3	128.2	114.6	114.5	114.6
3′	156.8	137.8	162.1	162.1	162.2
4′	27.4	15.9	33.8	33.8	33.8
5′	20.3	20.7	12.0	11.9	11.9
6′			18.9	18.9	18.9
1″				166.5	166.0
2″				127.3	114.6
3″				139.1	164.1
4″				15.9	33.9
5″				20.6	11.9
6″					19.1

a) Measured at 100 MHz.

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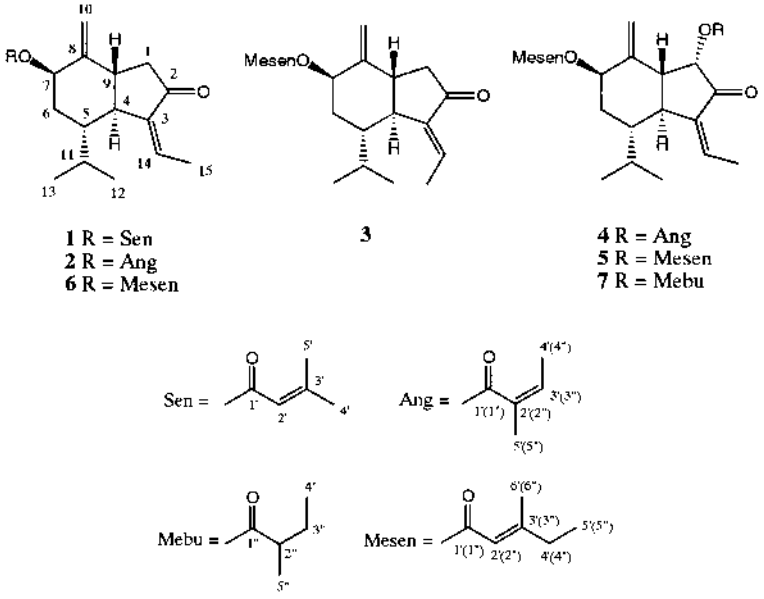

Chart 1

mined to be 7β-(4-methylsenecioyloxy)oplopa-3(14)*E*,8(10)-dien-2-one. This is the first report of the isolation of an oplopane derivative with a $\Delta^{3(14)}E$ configuration from the flower buds of *T. farfara*.

Compound **4** was isolated as a colorless oil, $[\alpha]_D$ −166.7°. The molecular formula was determined to be $C_{26}H_{36}O_5$ by HR-MS. The IR spectrum showed absorptions due to an α,β-unsaturated ester (1730 cm^{-1}), an α,β-unsaturated ketone (1708 cm^{-1}) and a double bond (1646 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra of **4** were similar to those of 1α-(2-methylbutyryloxy)-7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (**7**),[4] except for the presence of an angeloyl group[4] in place of a 2-methylbutyryl group in **7**. The oxygenated methine proton at δ_H 5.58 was assigned to H-1 by a ^{1}H–^{1}H shift correlation spectroscopy (^{1}H–^{1}H COSY) correlation between δ_H 5.58 and δ_H 2.70 (H-9). The oxygenated quaternary carbon at δ_C 166.5 was assigned to C-1″ by the HMBC correlation between δ_C 166.5 and δ_H 1.86 (H_3-5″). Furthermore, in the HMBC spectrum, a cross peak was observed between the H-1 and the C-1″, confirming that the angeloyl group was attached to the oxygen at C-1. The configuration of the angeloyloxyl group was shown to be α by the NOESY spectrum, giving a cross peak between H-1β and H-9β. On the basis of this evidence, the structure of **4** was determined to be 1α-angeloyloxy-7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one.

Compound **5** was isolated as a colorless oil, $[\alpha]_D$ −173.9°. The molecular formula was determined to be $C_{27}H_{38}O_5$ by HR-MS. The IR spectrum showed absorptions due to an α,β-unsaturated ester (1730 cm^{-1}), an α,β-unsaturated ketone (1710 cm^{-1}) and a double bond (1646 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra of **5** were similar to those of **4** except for the appearance of signals due to a 4-methylsenecioyl group[4] instead of signals due to an angeloyl group in **4**. Therefore, **5** was characterized as 1α,7β-di(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one. Compounds **4** and **5** are the first examples of the isolation of oplopane derivatives with an angeloyloxyl and 4-methylsenecioyloxyl groups at the C-1 positions, respectively, from the flower buds of *T. farfara*.

Experimental

General Procedures Optical rotations were determined with a JASCO DIP-360 digital polarimeter. IR spectra were recorded with a Perkin–Elmer FT-IR 1725X infrared spectrophotometer and UV spectra with a Beckman DU-64 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded with JEOL JNM-LA 600 (600 and 150 MHz, respectively) and JEOL JMN-LA 400 (400 and 100 MHz, respectively) spectrometers. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane as an internal standard (s, singlet; br s, broad singlet; d, doublet; dd, double doublet; ddd, double double doublet; t, triplet; q, quartet; dq, double quartet; qd, quartet doublet; qq, quartet quartet; m, multiplet). The electron ionization (EI)- and HR-MS were recorded on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (Merck; 230—400 mesh). Preparative HPLC was carried out on a Tosoh HPLC system (pump, CCPD; detector, RI-8010) using a TSK gel ODS-120T (7.8 mm i.d.×30 cm) column (Tosoh).

Plant Material The dried flower buds of *T. farfara* were purchased from Tochimoto Tenkaido Co., Ltd., Osaka, Japan in 1990.

Extraction and Isolation The dried flower 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 *n*-hexane–AcOEt (4 : 1—1 : 4), AcOEt and MeOH to afford 19 fractions (frs. 1—19). Fraction 5 was purified by preparative HPLC [MeOH–H_2O (4 : 1); flow rate, 1.5 ml/min; column temperature, 40 °C] to give a mixture of **1** and **2**, **3** (0.3 mg), **4** (0.4 mg) and **5** (0.2 mg). The mixture of **1** and **2** was purified by preparative HPLC [MeOH–H_2O (5 : 2); flow rate, 1.6 ml/min; column temperature, 40 °C] to give **1** (0.4 mg) and **2** (0.7 mg).

7β-Senecioyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (1) Colorless oil, $[\alpha]_D^{27}$ −97.6° (*c*=0.04, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715, 1650. UV λ_{max}^{MeOH} nm (log ε): 223 (4.3). HR-MS *m/z*: 316.2032 (M^+, Calcd for $C_{20}H_{28}O_3$; 316.2039). EI-MS *m/z*: 316 (M^+), 216 ($M^+-C_5H_8O_2$), 173 ($M^+-C_5H_8O_2-C_3H_7$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 0.81 (3H, d, *J*=7.0 Hz, H_3-13), 0.96 (3H, d, *J*=7.0 Hz, H_3-12), 1.89 (3H, d, *J*=1.5 Hz, H_3-4′), 2.12 (3H, d, *J*=7.3 Hz, H_3-15), 2.16 (3H, d, *J*=1.1 Hz, H_3-5′), 2.23 (1H, dd, *J*=16.8, 12.8 Hz, H-1α), 2.34 (1H, m, H-11), 2.39 (1H, dd, *J*=16.8, 6.2 Hz, H-1β), 2.59 (1H, m, H-9), 4.79 (1H, dd, *J*=2.2, 1.1 Hz, H-10a), 5.13 (1H, s, H-10b), 5.53 (1H, dd, *J*=3.3, 3.3 Hz, H-7), 5.67 (1H, dd, *J*=1.5, 1.1 Hz, H-2′), 6.22 (1H, q, *J*=7.3 Hz, H-14). ^{13}C- NMR (150 MHz, $CDCl_3$): see Table 1.

7β-Angeloyloxyoplopa-3(14)*Z*,8(10)-dien-2-one (2) Colorless oil, $[\alpha]_D^{28}$ −104.5° (*c*=0.07, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1714, 1646. UV λ_{max}^{MeOH} nm (log ε): 224 (4.1). HR-MS *m/z*: 316.2027 (M^+, Calcd for $C_{20}H_{28}O_3$; 316.2039). EI-MS *m/z*: 316 (M^+), 216 ($M^+-C_5H_8O_2$), 173 ($M^+-C_5H_8O_2-C_3H_7$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 0.82 (3H, d, *J*=7.0 Hz, H_3-13), 0.96 (3H, d, *J*=7.0 Hz, H_3-12), 1.88 (3H, dq, *J*=1.5, 1.5 Hz, H_3-5′), 1.98 (3H, dq, *J*=7.3, 1.5 Hz, H_3-4′), 2.13 (3H, dd, *J*=7.0, 2.2 Hz, H_3-15), 2.25 (1H, dd,

J=17.2, 13.2 Hz, H-1α), 2.36 (1H, m, H-11), 2.40 (1H, dd, J=17.2, 6.2 Hz, H-1β), 2.57 (1H, m, H-9), 4.82 (1H, dd, J=2.2, 1.1 Hz, H-10a), 5.16 (1H, s, H-10b), 5.61 (1H, dd, J=3.3, 2.9 Hz, H-7), 6.06 (1H, qq, J=7.3, 1.5 Hz, H-3′), 6.23 (1H, qd, J=7.3, 2.2 Hz, H-14). ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 1.

7β-(4-Methylsenecioyloxy)oplopa-3(14)*E*,8(10)-dien-2-one (3) Colorless oil, $[\alpha]_D^{25}$ −33.3° (c=0.03, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1646. UV λ_{max}^{MeOH} nm (log ε): 225 (4.0). HR-MS *m/z*: 330.2180 (M^+, Calcd for $C_{21}H_{30}O_3$; 330.2195). EI-MS *m/z*: 330 (M^+), 216 ($M^+-C_6H_{10}O_2$), 173 ($M^+-C_6H_{10}O_2-C_3H_7$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.86 (3H, d, J=6.8 Hz, H_3-13), 1.00 (3H, d, J=7.1 Hz, H_3-12), 1.07 (3H, t, J=7.3 Hz, H_3-5′), 1.90 (3H, dd, J=7.8, 2.0 Hz, H_3-15), 2.05 (1H, ddd, J=14.4, 4.4, 4.4 Hz, H-6β), 2.16 (3H, d, J=1.2 Hz, H_3-6′), 2.42 (1H, dd, J=17.3, 6.1 Hz, H-1β), 2.63 (1H, m, H-9), 4.84 (1H, d, J=1.5 Hz, H-10a), 5.16 (1H, dd, J=1.0, 1.0 Hz, H-10b), 5.57 (1H, dd, J=4.4, 3.7 Hz, H-7), 5.67 (1H, q, J=1.2 Hz, H-2′), 6.53 (1H, qd, J=7.8, 2.0 Hz, H-14). ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 1.

1α-Angeloyloxy-7β-(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (4) Colorless oil, $[\alpha]_D^{28}$ −166.7° (c=0.04, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730, 1708, 1644. UV λ_{max}^{MeOH} nm (log ε): 224 (4.5). HR-MS *m/z*: 428.2555 (M^+, Calcd for $C_{26}H_{36}O_5$; 428.2563). EI-MS *m/z*: 428 (M^+), 328 ($M^+-C_5H_8O_2$), 314 ($M^+-C_6H_{10}O_2$), 214 ($M^+-C_6H_{10}O_2-C_5H_8O_2$), 173 ($M^+-C_6H_{10}O_2-C_5H_8O_2-C_3H_7$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 0.87 (3H, d, J=7.0 Hz, H_3-13), 0.98 (3H, d, J=7.0 Hz, H_3-12), 1.07 (3H, t, J=7.3 Hz, H_3-5′), 1.86 (3H, dq, J=1.5, 1.5 Hz, H_3-5″), 1.96 (3H, dq, J=7.3, 1.5 Hz, H_3-4″), 2.15 (3H, d, J=1.1 Hz, H_3-6′), 2.16 (3H, d, J=7.3 Hz, H_3-15), 2.32 (1H, m, H-11), 2.70 (1H, br s, H-9), 4.83 (1H, s, H-10a), 5.18 (1H, s, H-10b), 5.52 (1H, dd, J=3.7 Hz, H-7), 5.58 (1H, d, J=3.3 Hz, H-1), 5.64 (1H, q, J=1.1 Hz, H-2′), 6.10 (1H, qq, J=7.3, 1.5 Hz, H-3″), 6.41 (1H, q, J=7.3 Hz, H-14). ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 1.

1α,7β-Di(4-methylsenecioyloxy)oplopa-3(14)*Z*,8(10)-dien-2-one (5) Colorless oil, $[\alpha]_D^{29}$ −173.9° (c=0.02, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1731, 1710, 1646. UV λ_{max}^{MeOH} nm (log ε): 222 (4.6). HR-MS *m/z*: 442.2694 (M^+, Calcd for $C_{27}H_{38}O_5$; 442.2719). EI-MS *m/z*: 442 (M^+), 328 ($M^+-C_6H_{10}O_2$), 214 ($M^+-C_6H_{10}O_2\times2$), 173 ($M^+-C_6H_{10}O_2\times2-C_3H_7$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 0.89 (3H, d, J=7.0 Hz, H_3-13), 0.97 (3H, d, J=7.0 Hz, H_3-12), 1.06 (3H, t, J=7.3 Hz, H_3-5″), 1.07 (3H, t, J=7.3 Hz, H_3-5′), 2.15 (3H, d, J=1.1 Hz, H_3-6′), 2.16 (3H, d, J=7.3 Hz, H_3-15), 2.17 (3H, d, J=1.1 Hz, H_3-6″), 4.84 (1H, dd, J=1.8, 1.1 Hz, H-10a), 5.17 (1H, s, H-10b), 5.53 (2H, m, H-1, H-7), 5.64 (2H, q, J=1.1 Hz, H-2′, H-2″), 6.40 (1H, q, J=7.3 Hz, H-14). ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 1.

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