Seven Germacranolides, Eupaglehnins A, B, C, D, E, and F, and 2α-Acetoxyepitulipinolide from *Eupatorium glehni*

Motoo TORI,* Yoshiko TAKEICHI, Hiroe KUGA, Katsuyuki NAKASHIMA, and Masakazu SONO

Faculty of Pharmaceutical Sciences, Tokushima Bunri University; Yamashiro-cho, Tokushima 770–8514, Japan.
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Four new germacrane-type sesquiterpenoids with unsaturated acids as esters at the 8-position, two chlorine atom-containing lactones, 2α-acetoxyepitulipinolide, and 12 previously known compounds have been isolated from the MeOH extract of *Eupatorium glehni* (Compositae) and their structures have been determined on the basis of spectral data analyses.

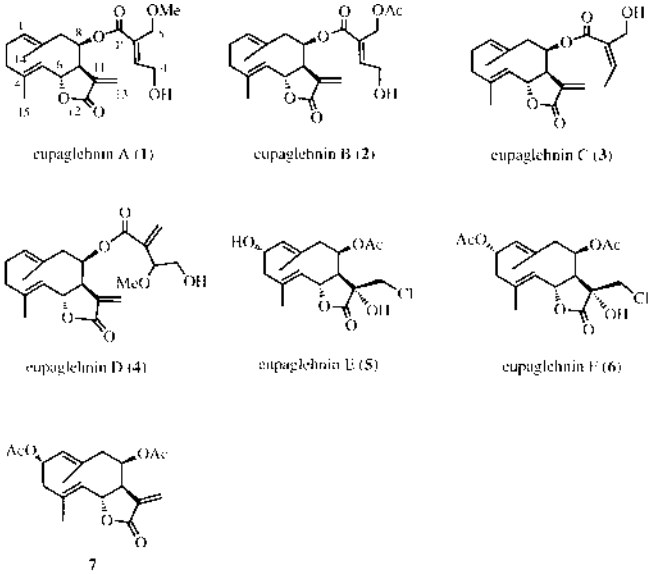
Key words Compositae; *Eupatorium glehni*; germacranolide; Eupaglehnin; sesquiterpene

Eupatorium glehni is found throughout Hokkaido, Honshu, and Shikoku Islands in Japan, especially at higher altitude in the southern parts, normally between 1000 and 1800 m. Kupchan and his group isolated eupaserrin and deacetyleupaserrin as antiluekemic sesquiterpenes from *Eupatorium semiserratum*, a plant belonging to the same genus, in 1973.[1] Later Takahashi and his group and others reported the isolation and biological activities of hiyodorilactones A—F from *Eupatorium sachalinense*,[2—5] of which the name was later changed to *E. glehni*.[6—8] We have been interested in biologically active terpenoids from Compositae[9—14] and collected *E. glehni*[6—8] in Tokushima and Hokkaido, Japan. From the ethyl acetate-soluble fraction of the methanol extract, we have found four new germacranolides with unsaturated esters at the 8-position, eupaglehnins A, B, C, and D, and two new chlorine atom-containing germacranolides, eupaglehnins E (**5**) and F (**6**),[13] as well as 2α-acetoxyepitulipinolide (**7**) for the first time from natural sources. This paper describes the structure elucidation of these terpenoids, mainly based on two-dimensional (2D) NMR techniques and biological activity.

The ethyl acetate-soluble fraction of the MeOH extract was subjected to silica gel column chromatography followed by Sephadex LH-20 ($CHCl_3$–MeOH, 1 : 1) and HPLC (Nucleosil 50-5, $CHCl_3$–EtOAc) to yield six new eupaglehnins (**1**—**6**), and **7**, as well as 12 previously known compounds.

Eupaglehnin A (**1**), $[\alpha]_D^{24}$ +55.3°, showed a quasimolecular ion peak at *m/z* 377 in the chemical ionization mass (CI-MS) spectrum, and the molecular formula was determined to be $C_{21}H_{29}O_6$ $[M+H]^+$ based on the CI-high resolution (HR)-MS spectrum. The ^{1}H-NMR spectrum showed the presence of two tri-substituted double bonds, an exomethylene, an α,β-unsaturated double bond, two oxymethyne protons, four methylene protons attached to the carbon bearing an oxygen function, and a methoxyl group (Table 1). The presence of a γ-lactone (1760 cm^{-1}), an ester (1710 cm^{-1}), and a hydroxyl group (3450 cm^{-1}) was indicated by the IR spectrum. From these spectral features as well as eight degrees of unsaturation, this molecule should have two rings, with one being the γ-lactone. The ^{1}H-detected heteronuclear multiple-bond connectivity (HMBC) spectrum (Fig. 1) clearly suggested the partial structures around C1–C10–C9, C3–C4–C5, C6–C7–C11(–C13)–C12, and C8–C1′. Since the connectivities for C1–C2–C3 and C5–C6–C7–C8–C9 were revealed by the ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum, the ring must be 10-membered, and thus the skeleton should be germacranolide. The proton at δ 5.17 assigned to H-6 had two coupling constants, one of which was due to a coupling with H-5 (9.9 Hz). The other one (8.5 Hz) was with H-7, implying the *trans* relationship of the lactone ring, which was supported by the nuclear Overhauser effect (NOESY) spectrum (*vide infra*). The proton at δ 7.03 attached to the C-3′ carbon appeared as a triplet, suggesting that the C-4′ must be a methylene bearing the hydroxyl group. The methoxyl group showed the correlation peak to the C-5′ carbon in the HMBC spectrum and H-5′ and H-4′ had an NOE correlation in the NOESY spectrum. Therefore the ester part at the C-8 position of compound **1** was determined to be *E*-4-hydroxy-2-methoxymethyl-2-butenoic acid. The NOESY spectrum showed that two methyl groups and H-6 were in the same orientation and that H-7, H-1, and H-5 were on the same side of the molecule opposite to the methyl groups. Therefore the germacradiene skeleton should be in the *E*,*E*-configuration and the gross conformation of the 10-membered ring must be as shown in Fig. 2. The structure of eupaglehnin A was established as depicted in structure **1**, corresponding to 5′-*O*-methylether derivative of eupatoriopicrin (**8**).

The spectral data of eupaglehnin B (**2**), $[\alpha]_D^{20}$ +52.5°, $C_{22}H_{28}O_7$ (by CI-HR-MS), were very similar to those of eupaglehnin A (**1**). The presence of an acetyl group (δ 2.00)



* To whom correspondence should be addressed. e-mail: tori@ph.bunri-u.ac.jp

Table 1. ^{1}H-NMR Data for Compounds **1**—**4** (600 MHz)

H	1	2	3	4
1	4.89 (dd, 11.3, 4.1)	4.91 (dd, 11.8, 4.4)	4.89 (dd, 11.3, 4.3)	4.91 (dd, 11.8, 4.4)
2	2.23 (m)	2.24 (m)	2.23 (m)	2.25 (m)
	2.36 (m)	2.33 (td, 12.1, 4.4)	2.32 (m)	2.33 (td, 12.0, 5.5)
3	2.12 (m)	2.11 (td, 11.5, 5.8)	2.10 (td, 11.5, 5.8)	2.11 (td, 11.5, 5.5)
	2.39 (m)	2.39 (m)	2.38 (m)	2.39 (m)
5	4.79 (d, 9.9)	4.79 (d, 9.6)	4.78 (br d, 9.6)	4.80 (br d, 9.9)
6	5.17 (dd, 9.9, 8.5)	5.20 (dd, 9.6, 8.5)	5.18 (dd, 9.6, 8.8)	5.15 (dd, 9.9, 8.8)
7	2.95 (dtd, 8.5, 3.3, 1.1)	2.96 (dtd, 8.5, 3.3, 1.1)	2.96 (m)	2.96 (dtd, 8.8, 3.3, 1.4)
8	5.81 (br d, 4.1)	5.85 (m)	5.85 (m)	5.82 (m)
9	2.33 (m)	2.38 (m)	2.37 (m)	2.38 (m)
	2.88 (dd, 14.6, 4.9)	2.88 (dd, 14.5, 4.9)	2.93 (dd, 14.5, 5.2)	2.87 (dd, 14.3, 4.9)
13	5.60 (d, 3.3)	5.60 (d, 3.6)	5.61 (d, 3.6)	5.59 (d, 3.3)
	6.30 (d, 3.6)	6.30 (d, 3.6)	6.33 (d, 3.6)	6.31 (d, 3.3)
14	1.48 (s)	1.49 (s)	1.48 (s)	1.49 (s)
15	1.78 (s)	1.78 (d, 1.4)	1.75 (s)	1.78 (d, 1.4)
3′	7.03 (t, 5.8)	7.07 (t, 5.9)	6.40 (qt, 7.1, 1.1)	4.22 (ddd, 7.1, 3.0, 1.1)
4′	4.42 (br t, 5.8)	4.45 (dt, 15.7, 5.2)	2.03 (dt, 7.1, 1.1)	3.46 (dd, 11.5, 7.1)
	—	4.53 (dt, 15.7, 5.2)	—	3.66 (dd, 11.5, 3.0)
5′	4.19 (d, 11.5)	4.80 (d, 12.1)	4.20 (d, 12.6)	5.96 (t, 1.1)
	4.22 (d, 11.5)	5.00 (d, 12.1)	4.27 (d, 12.6)	6.28 (d, 1.1)
OMe	3.32 (s)	—	—	3.32 (s)
OAc	—	2.00 (s)	—	—

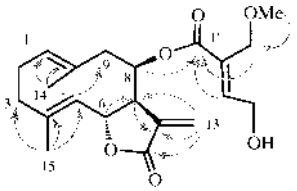


Fig. 1. Selected HMBC Correlations Detected for Eupaglehnin A (**1**)

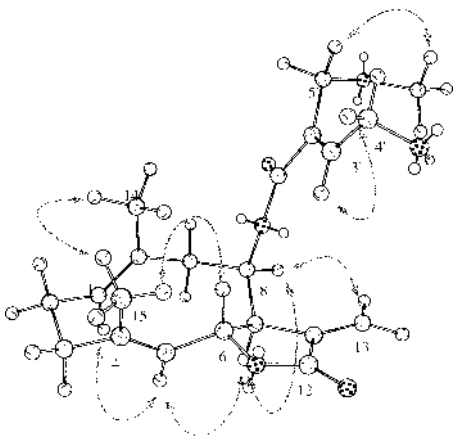


Fig. 2. Selected NOEs Detected by NOESY and the Conformation of Eupaglehnin (**1**)

and the absence of a methoxyl group in **2** was indicated by the ^{1}H-NMR spectrum (Table 1). The protons assigned to H-5′ (δ 4.19, 4.22) in compound **1** were shifted to δ 4.80 and 5.00, indicating that the acyl group is attached to the carbon bearing these protons. The connectivities of the 10-membered ring were revealed by the HMBC and COSY spectra, which are very similar to the results of compound **1**. Therefore compound **2** was determined to be 5′-*O*-acetyleupatoriopicrin with the aid of the NOESY spectrum.

The ^{1}H-NMR spectrum of eupaglehnin C (**3**), $[\alpha]_D^{20}$ +48.0°, $C_{20}H_{26}O_5$ (by CI-HR-MS), was very similar to those of eupaglehnins A (**1**) and B (**2**). However, there were three signals of methyl groups attached to the sp^2 carbon and a proton at the C-3′ position appeared at δ 6.40 as a quartet with a small triplet coupling in the ^{1}H-NMR spectrum of **3**. The other signals were almost the same as those of **2** except for the absence of the acetyl group and the hydroxymethylene group, suggesting that compound **3** is eupatolide 8-*O*-(5′-hydroxyangelate). The 2D NMR analysis clearly verified this assumption, and the stereochemistry was determined by the NOESY spectrum. The NOEs between H-14 and H-15, H-15 and H-6, H-14 and H-6, H-1 and H-5, H-5 and H-7, H-8 and H-7, H-8 and H-13a, and H-3′ and H-5′ were detected. Therefore the stereochemistry was determined as depicted in the formula, and the conformation was almost the same as that of compound **1**.

Eupaglehnin D (**4**), $[\alpha]_D^{20}$ +19.7°, $C_{21}H_{28}O_6$ (by CI-HR-MS), exhibited the signal of a methoxyl group and two sets of exomethylenes in the ^{1}H-NMR spectrum. The HMBC spectrum indicated that one exomethylene group at δ_H 5.59 and 6.31 was conjugated with the lactone carbonyl group (δ_C 169.4), and the other one at δ_H 5.96 and 6.28 with the ester carbonyl group (δ_C 164.8). The 2D NMR spectra indicated that the ester at C-8 is different from tiglate or angelate, and the germacranolide skeleton is the same as that of other eupaglehnins. The proton at δ_H 4.22 (H-3′) coupled with those at δ_H 3.46 and 3.66 (each dd) and the exomethylene protons at δ_H 5.96 and 6.28 (H-5′) coupled with the carbons at δ_C 80.5 (C-3′) and δ_C 164.8 (C-1′), suggesting that this ester should be 2-exomethylene-4-hydroxy-3-methoxybutyrate. Although the stereochemistry at 3′ was not clear, the structure was determined as depicted in formula **4**.

Eupaglehnin E (**5**), $[\alpha]_D^{24}$ +63.8°, exhibited quasimolecular ion peaks at *m/z* 361 $[M+2+H]^+$ and 359 $[M+H]^+$ (CI-MS) and the molecular formula was determined to be $C_{17}H_{23}O_6Cl$ by CI-HR-MS. The IR spectrum showed the presence of a lactone (1770 cm^{-1}) and an acetate (1740 cm^{-1}) as

Table 2. ^{1}H-NMR Data for Compounds **5**—**7** (600 MHz)

H	**5**	**6**	**7**
1	5.02 (br d, 11.0)	5.00 (d, 10.4)	4.98 (br d, 10.2)
2	4.80 (td, 11.0, 6.3)	5.69 (ddd, 16.5, 10.2, 6.3)	5.67 (td, 10.9, 5.8)
3	2.13 (t, 11.3)	2.22 (t, 11.3)	2.18 (t, 11.3)
	2.73 (dd, 11.3, 6.3)	2.73 (dd, 11.3, 6.3)	2.74 (dd, 11.3, 5.8)
5	4.92 (br d, 10.2)	4.96 (d, 10.7)	5.01 (br d, 9.9)
6	5.33 (t, 10.2)	5.34 (t, 10.0)	5.06 (dd, 9.9, 8.4)
7	2.58 (d, 10.2)	2.58 (d, 9.9)	2.92 (dtd, 8.4, 3.3, 0.8)
8	5.58 (dd, 6.3, 1.1)	5.58 (br d, 5.8)	5.74 (br d, 6.7)
9	2.21 (dd, 14.3, 1.1)	2.22 (t, 14.3)	2.31 (dd, 14.4, 2.2)
	2.85 (dd, 14.3, 6.3)	2.85 (dd, 14.3, 6.3)	2.81 (dd, 14.4, 6.7)
13	3.54 (d, 11.3)	3.55 (d, 11.5)	5.61 (d, 3.3)
	3.65 (d, 11.3)	3.65 (d, 11.5)	6.32 (d, 3.3)
14	1.59 (d, 1.1)	1.68 (d, 1.1)	1.64 (s)
15	1.75 (d, 1.4)	1.78 (d, 1.1)	1.82 (d, 1.4)
2-OAc	—	2.06 (s)	2.07 (s)
8-OAc	2.14 (s)	2.14 (s)	2.07 (s)

Table 3. ^{13}C-NMR Data for Compounds **1**—**7**

C	**1**[a]	**2**[a]	**3**[a]	**4**[b]	**5**[a]	**6**[a]	**7**[b]
1	130.8	130.9	130.7	131.0	134.5	130.4	129.8
2	26.2	26.2	26.2	26.2	68.8	70.7	70.9
3	39.4	39.4	39.4	39.4	48.4	44.7	44.9
4	142.5	142.6	142.6	142.5	141.3	140.1	141.9
5	127.3	127.3	127.3	127.3	129.5	130.1	129.6
6	75.6	75.6	75.9	75.5	74.5	74.4	74.8
7	52.8	52.7	52.7	52.8	58.5	58.5	52.7
8	72.5	72.6	72.1	72.3	69.8	69.5	70.9
9	44.0	44.0	43.9	44.0	44.3	44.2	43.7
10	134.2	134.0	134.3	133.9	133.8	135.7	136.1
11	136.6	136.6	136.7	136.7	77.0	77.0	136.6
12	169.6	169.5	169.5	169.4	174.7	174.7	169.3
13	121.2	121.2	121.2	121.0	44.0	43.9	120.8
14	19.0	19.0	18.8	19.0	20.0	19.9	19.8
15	17.5	17.5	17.5	17.5	18.1	17.9	18.4
1′	165.4	164.9	166.0	164.8	—	—	—
2′	129.3	126.8	131.4	137.0	—	—	—
3′	146.5	147.6	141.0	80.5	—	—	—
4′	59.6	59.6	15.9	65.3	—	—	—
5′	66.5	58.0	64.6	127.3	—	—	—
OMe	58.3	—	—	57.3	—	—	—
2-OAc	—	20.8[c]	—	—	—	21.2	20.8
	—	171.2[c]	—	—	—	170.6	170.1
8-OAc	—	—	—	—	21.3	21.2	21.1
	—	—	—	—	169.4	169.4	168.9

a) 150 MHz, *b*) 100 MHz, *c*) 5′-OAc.

well as a hydroxyl group (3450 cm^{-1}). The ^{13}C-NMR spectrum clearly exhibited 17 peaks, three methyl (18.1, 20.0, 21.3), three methylene (44.0, 44.3, 48.4), six methine (58.5, 68.8, 69.8, 74.5, 129.5, 134.5), and five quaternary carbons (77.0, 133.8, 141.3, 169.4, 174.7). Two carbonyl groups (a lactone and an acetate) and two olefins are obvious from the ^{1}H- and ^{13}C-NMR data (Tables 2, 3). These data suggest that this molecule contains one chlorine atom and two rings calculated from six degrees of unsaturation. In the HMBC spectrum the methyl group H-14 had correlations between carbons at C-1, C-10, and C-9. The methine proton H-8 had correlation peaks with C-10, C-9, C-7, C-6, C-11, and the acetyl carbon. The H-7 proton correlated to C-5, C-6, and C-11. The methyl group at H-15 had correlations between C-3, C-4, and C-5. These results indicate a partial structure through

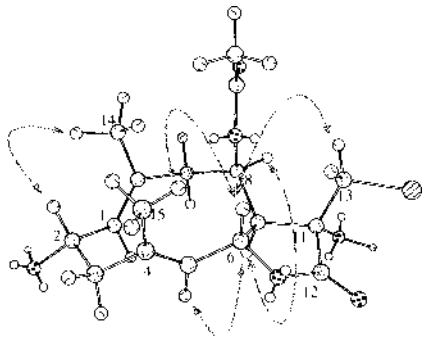
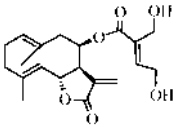


Fig. 3. Selected NOEs Detected by NOESY and the Conformation of Eupaglehnin E (**5**)

C3–C4–C5–C6–C7–C8–C9–C10–C1 as well as C11–C7. The linkage from C-1 to C-3 was revealed by the ^{1}H–^{1}H COSY spectrum. Therefore a 10-membered carbocycle fused with a butyrolactone at C-6 and C-7 was established, as well as the position of the acetyl group at C-8. The chlorine atom and the hydroxyl group must be at either C-11 or C-13. The chemical shift at C-11 was δ_C 77.0, while that at C-13 was δ_C 44.0, which indicates that the chlorine atom should be at C-13, although the protons at C-13 were found at δ_H 3.54 and 3.65 (each 1H, J=11.3 Hz). The stereochemistry was analyzed by the NOESY spectrum. The methyl group of H-14 had NOEs between H-2β and H-9β, and the methyl group of H-15 between H-3β and H-6β. NOEs between H-5 and H-7α, H-5 and H-3α, H-7α and H-8α, H-2β and H-3β, and H-1 and H-9α were also observed. The chloromethyl group at C-11 must have a β-orientation, because the NOE between H-6 and H-13 was observed in the NOESY spectrum. Thus the total structure was established as depicted in formula **5**.

Eupaglehnin F (**6**), $[\alpha]_D^{20}$ +40.0°, exhibited molecular ion peaks at m/z 402 $[M+2]^+$ and 400 $[M]^+$, $C_{19}H_{25}O_7Cl$ $[M]^+$ (by HR-MS). The ^{1}H-NMR spectrum is very similar to that of eupaglehnin E (**5**) except that compound **6** had two acetyl groups and one proton assignable to H-2 shifted to δ 5.69. Therefore it was very easy to assume that compound **6** is a 2-OAc derivative of compound **5**, which was confirmed by 2D NMR spectra. The NMR data are listed in the Tables 1 and 2. The stereochemistry of **6** was also established as depicted in



eupatoriopicrin (**8**)

the formula.

Compound **7** was easily determined to be 2α-acetoxyepitulipinolide[15,16] from the spectral data and was already known to be an acetylation product of 2α-hydroxyepitulipinolide (**9**).[17] This is, to the best of our knowledge, the first isolation of this diacetate from a natural source.[18]

The interesting thing is that we could not isolate hiyodorilactones[2,3] from *E. glehni* collected in Tokushima and Hokkaido. The name *E. glehni*, which was previously called *E. sachalinense*, was identified by Dr. Kawahara,[6] who studied the classification of *Eupatorium* by applying gene technology and reclassified the related species.[7,8] Thus the name *E. sachalinense* is no longer used in this field, although the plant should be the same as that studied by Takahashi's group in 1978.[19] They collected the plants in Nagano, at higher altitude than our collection sites.[19] However, for the time being, we have no data suggesting why we did not isolate hiyodorilactones, but instead found less oxygenated constituents. Furthermore, we have isolated two chlorine atom-containing compounds. Examples of chlorine atom-containing substances have been reported, although not very often, in terrestrial plants.[20—23] In our attempt to find cytotoxic compounds, eupatoriopicrin (**8**)[24—29] was the most effective (1.40 μg/ml), followed by eupaglehnin C (**3**) (2.19 μg/ml) against HeLa-S3. However, eupaglehnins E (**5**) and F (**6**) did not show cytotoxic activity, which is understandable because they had no exomethylene group. In preliminary experiments, eupatoriopicrin (**8**)[24—26] also showed apoptotic activity against Ha-60 cell lines, the details of which will be published in due course.

Experimental

General The IR spectra were measured with a JASCO FT/IR-5300 spectrophotometer. The ^{1}H-, ^{13}C-, and 2D NMR spectra were recorded with a Varian Unity 600 (600 MHz), a JEOL GX400 (400 MHz), or a Varian Unity 200 (200 MHz) spectrometer. The mass spectra including high-resolution mass spectra were measured with a JEOL JMS AX-500 spectrometer. Specific rotations were measured with a JASCO DIP-140. Chemcopak Nucleosil 50-5 was used for HPLC (JASCO pump system). Silica gel 60 (70—230 mesh, Merck) was used for column chromatography and silica gel 60 F_{254} plates (Merck) were used for TLC.

Plant Material *E. glehni* was collected in Ichiu-son village, Tokushima (1994, 1995) and in Obihiro city, Hokkaido (1995, 1996). Voucher specimens (TBU-MT-199401, -199501, -199502, and -199601) were deposited at the Herbarium of the Faculty of Pharmaceutical Sciences, Tokushima Bunri University. The plant was identified by Dr. Takayuki Kawahara, Hokkaido Research Center of Forestry and Forest Products Research Institute, Ministry of Agriculture, Forestry and Fisheries, Japan.[12—14]

Isolation The half-dried (overnight) plant (2.6 kg) collected in Tokushima was extracted with MeOH at room temperature for 3 weeks. The solvent was evaporated to afford a residue (145 g), which was partitioned between EtOAc and water–MeOH. The EtOAc-soluble fraction (56 g) was subjected to silica gel column chromatography (hexane : EtOAc in a gradient to EtOAc : MeOH in a gradient) to give fractions. Fractions were further separated by silica gel CC (hexane : EtOAc, gradient) and Sephadex LH-20 ($CHCl_3$: MeOH = 1 : 1) followed by HPLC ($CHCl_3$: EtOAc) to afford four new compounds: **1** (78.3 mg), **3** (14.5 mg), **5** (7.0 mg), **6** (11.7 mg), and 2α-acetoxyepitulipinolide (**7**, 665.5 mg),[15,16] as well as five previously known compounds, eupatoriopicrin (**8**, 1.2 g),[24—26] 2α-hydroxyepitulipinolide (**9**, 531.3 mg),[17] eupatolide (**10**, 305.8 mg),[30,31] 5′-deoxyeupatoriopicrin (**11**, 25.4 mg),[32] and eupatoriopicrin 4′-*O*-acetate (**12**, 694.2 mg).[33]

The methanol extract (368 g) of the aerial parts (half-dried, 6.3 kg) of *E. glehni* collected in Hokkaido was similarly treated to give the EtOAc-soluble fraction (139 g). The residue was similarly separated to afford two new compounds **2** (8.5 mg) and **4** (3.6 mg), as well as 10 previously known compounds, **8** (680.4 mg),[24—26] **10** (10.3 mg),[30,31] **11** (105.4 mg),[32] **12** (134.8 mg),[33] 4′-deoxyeupatoriopicrin (**13**, 509.5 mg),[34] eupaserrin (**14**, 4.6 mg),[1] deacetyleupaserrin (**15**, 9.3 mg),[1] 4′-deoxyhiyodorilactone E (**16**, 7.8 mg),[35] 4′-deoxyeupaformosanin (**17**, 94.0 mg),[35] and eupalinin-C (**18**, 67.2 mg).[36]

Eupaglehnin A (**1**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 1 and 3. Fourier transform (FT)-IR cm^{-1}: 3450, 1760, 1710, and 1660. CI-HR-MS (CH_4) *m/z*: 377.1976 $[M+H]^+$ (Calcd for $C_{21}H_{29}O_6$: 377.1964). CI-MS (CH_4) *m/z*: 377 $[M+H]^+$, 231, 230 (base), 215, 185, 129, and 97 (base). $[\alpha]_D^{24}$ +55.3° (*c*=0.86, EtOH). $[\theta]_{269\,nm}$ −280 (EtOH).

Eupaglehnin B (**2**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 1 and 3. FT-IR cm^{-1}: 3500, 1760, 1740, 1720, and 1660. CI-HR-MS (CH_4) *m/z*: 405.1909 $[M+H]^+$ (Calcd for $C_{22}H_{29}O_7$: 405.1914). CI-MS (CH_4) *m/z*: 405 $[M+H]^+$, 387, 335, 259, 231 (base), 213, 185, and 151. $[\alpha]_D^{20}$ +52.5° (*c*=0.5, $CHCl_3$). $[\theta]_{238\,nm}$ +33000, $[\theta]_{269\,nm}$ −6500 ($CHCl_3$).

Eupaglehnin C (**3**): Oil; ^{1}H- and ^{13}C-NMR spectra see Tables 1 and 3. FT-IR cm^{-1}: 3500, 1760, 1720, and 1660. HR-MS *m/z*: 346.1796 $[M]^+$ (Calcd for $C_{20}H_{26}O_5$: 346.1781). MS *m/z*: 346 $[M]^+$, 248, 230, 215, 202, amd 99 (base). $[\theta]_{242\,nm}$ +11000, $[\theta]_{271\,nm}$ −3200 ($CHCl_3$). $[\alpha]_D^{20}$ +48.0° (*c*=1.5, $CHCl_3$).

Eupaglehnin D (**4**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 1 and 3. FT-IR cm^{-1}: 3500, 1760, 1720, 1660, and 1630. CI-HR-MS (CH_4) *m/z*: 377.1974 $[M+H]^+$ (Calcd for $C_{21}H_{29}O_6$: 377.1965). CI-MS (CH_4) *m/z*: 377 $[M+H]^+$, 345, 249, 231 (base), 213, 203, 185, and 151. $[\alpha]_D^{20}$ +19.7° (*c*=0.39, $CHCl_3$).

Eupaglehnin E (**5**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 2 and 3. FT-IR cm^{-1}: 3450, 1770, 1740, and 1660. CI-HR-MS (CH_4) *m/z*: 359.1237 $[M+H]^+$ (Calcd for $C_{17}H_{24}O_6Cl$: 359.126). CI-MS (CH_4) *m/z*: 361 $[M+2+H]^+$, 359 $[M+H]^+$, 323, 301, 299, 283, 281 (base), 265, 263, 245, 227, 199, 177, 159, 95, and 61. $[\alpha]_D^{24}$ +63.8° (*c*=0.5, EtOH).

Eupaglehnin F (**6**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 2 and 3. FT-IR cm^{-1}: 3450, 1780, 1740, and 1670. CI-HR-MS (CH_4) *m/z*: 400.1287 (Calcd for $C_{19}H_{25}O_7Cl$: 400.1289). MS (EI) *m/z*: 402 $[M+2]^+$, 400 $[M]^+$, 360, 358, 342, 340, 300, 298, 282, 280, 231, 175 (base), and 157. $[\alpha]_D^{20}$ +40.0° (*c*=0.3, $CHCl_3$).

2α-Acetoxyepitulipinolide (**7**): Oil; ^{1}H- and ^{13}C-NMR spectra, see Tables 2 and 3. FT-IR cm^{-1}: 1765, 1740, and 1660. HR-MS *m/z*: 348.1578 (Calcd for $C_{19}H_{24}O_6$: 348.1572). MS (EI) *m/z*: 348 $[M]^+$, 306, 288, 246, 228 (base), and 213. $[\alpha]_D^{20}$ +70.4° (*c*=0.27, $CHCl_3$).

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