Two New Cyclopentenone Derivatives and a New Cyclooctadienone Derivative from *Erigeron annuus* (L.) Pers., *Erigeron philadelphicus* L., and *Erigeron sumatrensis* Retz.

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Received March 6, 2003; accepted March 30, 2003

Two new cyclopentenone derivatives, erigerenones A (1) and B (2), and a new cyclooctadienone derivative, erigerenone C (3), were isolated from the aerial parts of *Erigeron philadelphicus* L. Compound 2 was also isolated from the aerial parts of *Erigeron annuus* (L.) Pers. and *Erigeron sumatrensis* Retz. The structures of 1—3 were elucidated on the basis of their spectral data.

Key words *Erigeron annuus*; *Erigeron philadelphicus*; *Erigeron sumatrensis*; Compositae; cyclopentenone derivative; cyclooctadienone derivative

The genus *Erigeron* is a common group of Compositae plants, and *Erigeron annuus* (L.) Pers. (*himejyon* in Japanese), *Erigeron philadelphicus* L. (*harujion* in Japanese) and *Erigeron sumatrensis* Retz. (*oarechinogiku* in Japanese) are now, as naturalized weeds, widely distributed throughout urban and rural areas of Japan.[1] Among these, *E. annuus* has been used as an hypoglycemic drug in China.[2] The constituents of *E. annuus*, *E. philadelphicus*, and *E. sumatrensis* have been previously investigated and shown to contain monoterpenoids,[3] sesquiterpenoids,[3] diterpenoid,[4] polyacetylenic compounds,[5] and γ-pyrone derivatives.[1] Recently we reported the isolation and structural elucidation of norisoprenoids,[6] sesquiterpenoids,[7] diterpenoids,[7] triterpenoids,[8] and sterols[8] from the aerial parts and roots of *E. annuus*, *E. philadelphicus*, and *E. sumatrensis*. As part of our continuing study of the constituents of the genus *Erigeron* plants, we now report the isolation and structural elucidation of two new cyclopentenone derivatives, erigerenons A (**1**) and B (**2**), and a new cyclooctadienone derivative, erigerenone C (**3**), from the aerial parts of *E. annuus*, *E. philadelphicus*, and *E. sumatrensis*.

Compound **1** was isolated as a colorless oil, $[\alpha]_D$ +7.3°. The molecular formula was determined to be $C_{12}H_{16}O_4$ by high-resolution (HR)-electron ionization (EI)-MS. The IR spectrum showed the presence of ester (1735 cm^{-1}) and α,β-unsaturated ketone (1691, 1596 cm^{-1}) functionalities. The UV spectrum also suggested the presence of an α,β-unsaturated ketone (λ_{max}=237 nm). The ^{1}H- (Table 1) and ^{13}C-NMR spectra (Table 2), obtained with the aid of distortionless enhancement by polarization transfer (DEPT) and ^{1}H-detected heteronuclear multiple quantum coherence (HMQC) spectra, showed signals due to a methyl [δ_H 1.70 (3H, H_3-10); δ_C 13.1 (C-10)], a methylene [δ_H 2.58 (1H, H_a-2), 2.77 (1H, H_b-2); δ_C 33.8 (C-2)], two methines [δ_H 2.56 (1H, H-3), 3.68 (1H, H-7); δ_C 44.8 (C-7), 49.9 (C-3)], two methoxyl groups [δ_H 3.67 (3H, CH_3O-1), 3.84 (3H, CH_3O-6); δ_C 51.7 (CH_3O-1), 59.0 (CH_3O-6)], a trisubstituted double bond [δ_H 5.32 (1H, H-5); δ_C 102.9 (C-5), 190.3 (C-6)], a disubstituted double bond [δ_H 5.24 (1H, H-8), 5.74 (1H, H-9); δ_C 127.6 (C-8), 128.5 (C-9)], and two carbonyl carbons [δ_C 172.3 (C-1), 204.2 (C-4)]. The gross structure of **1** was elucidated by analyses of two-dimensional (2D) NMR data including ^{1}H–^{1}H shift correlation spectroscopy (^{1}H–^{1}H COSY) and ^{1}H-detected heteronuclear multiple bond connectivity (HMBC) spectra (Fig. 1). The ^{1}H–^{1}H COSY spectrum of **1** implied connectivities for H_2-2—H-3, H-3—H-7, H-7—H-8, H-8—H-9, and H-9—H_3-10. Interpretation of the HMBC spectrum revealed correlations from H_2-2 to C-1 and C-4; H-5 to C-3 and C-7; H-7 to C-6; CH_3O-1 to C-1; and CH_3O-6 to C-6. Thus the gross structure of **1** was deduced to be as shown in Fig. 1. The relative stereochemistry at C-3 and C-7 was established by comparing the proton coupling constant between H-3 and H-7 with analogous couplings observed for other cyclopentenones.[9,10] In cyclopentene rings, a vicinal coupling constant of 5—6 Hz normally indicates a *cis* relationship, while a coupling constant of *ca.* 2 Hz suggests a *trans* relationship.[11] These observations have been extended to cyclopentenone rings and a similar correlation has been observed.[9,10] Thus, in the case of **1**, the small coupling constant of 2.2 Hz is suggestive of a *trans* relationship between H-3 and H-7. The geometry of the Δ^8-double bond was deduced to be *Z* from ^{1}H–^{1}H coupling constant (J=11.0 Hz) between H-8 and H-9. On the basis of the above data, the structure of **1** was represented as shown in the formula.

Compound **2** was isolated as a colorless oil, $[\alpha]_D$ +7.9°. The molecular formula was determined to be $C_{12}H_{18}O_4$ by HR-EI-MS. The ^{1}H- and ^{13}C-NMR spectra of **2** resembled those of **1**, except for the presence of two methylene groups [δ_H 1.51 (1H, H_a-8), 1.75 (1H, H_b-8), 1.33 (2H, H_2-9); δ_C 19.5 (C-9), 33.8 (C-8)] instead of a disubstituted double bond in **1**. The molecular formula of **2** suggested that **2** was a dihydro derivative of **1**. The ^{1}H–^{1}H COSY spectrum of **2** implied

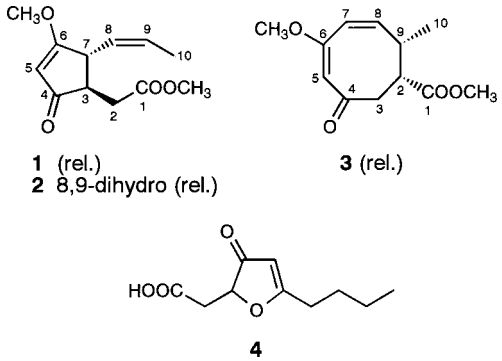

Chart 1

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Table 1. ^{1}H-NMR Chemical Shifts of Compounds **1**—**3** ($CDCl_3$, 400 MHz)

Proton	**1**[a]	**2**	**3**
2	a 2.58 dd (20.5, 8.1)[b] b 2.77 dd (20.5, 8.8)	a 2.53 dd (20.2, 8.1) b 27.5 dd (20.2, 8.8)	3.16 ddd (13.2, 5.6, 3.9)
3	2.56 m	2.51 m	α 3.30 dd (13.2, 11.0) β 2.40 ddd (11.0, 3.9, 1.5)
5	5.32 d (1.1)	5.27 d (0.7)	5.49 br s
7	3.68 ddd (9.9, 2.2, 1.1)	2.64 ddd (5.4, 5.1, 2.4)	6.19 dd (11.7, 0.7)
8	5.24 ddq (11.0, 9.9, 1.8)	a 1.51 m b 1.75 m	6.16 dd (12.7, 11.7)
9	5.74 dqd (11.0, 7.0, 1.1)	1.33[c] m	2.92 m
10	1.70 dd (7.0, 1.8)	0.93 t (7.3)	1.11 d (6.6)
CH_3O-1	3.67 s	3.68 s	3.69 s
CH_3O-6	3.84 s	3.84 s	3.66 s

a) Measured at 600 MHz. *b*) Coupling constants (*J* in Hz) are given in parentheses. *c*) 2H.

Table 2. ^{13}C-NMR Chemical Shifts of Compounds **1**—**3** ($CDCl_3$, 100 MHz)

Carbon	**1**[a]	**2**	**3**
1	172.3	172.4	172.8
2	33.8	35.3	54.0
3	49.9	48.0	41.9
4	204.2	204.9	199.9
5	102.9	102.8	107.2
6	190.3	192.0	166.6
7	44.8	46.3	125.4
8	127.6	33.8	145.0
9	128.5	19.5	34.6
10	13.1	14.2	17.6
CH_3O-1	51.7	51.7	51.6
CH_3O-6	59.0	58.7	56.0

a) Measured at 150 MHz.

connectivities for H-7—H_2-8, H_2-8—H_2-9, and H_2-9—H_3-10. The relative stereochemistry at C-3 and C-7 was deduced to be *trans* from the ^{1}H–^{1}H coupling constant (J=2.4 Hz) between H-3 and H-7.[9—11] Thus compound **2** was an 8,9-dihydro derivative of **1**. From the above data, the structure of **2** was represented as shown in the formula.

Compound **3** was isolated as a colorless oil, $[\alpha]_D$ +4.2°. The molecular formula was determined to be $C_{12}H_{16}O_4$ by HR-EI-MS. The IR spectrum showed the presence of ester (1731 cm^{-1}) and α,β-γ,δ-unsaturated ketone (1627, 1592 cm^{-1}) functionalities. The UV spectrum also suggested the presence of an α,β-γ,δ-unsaturated ketone (λ_{max}= 279 nm). The ^{1}H- and ^{13}C-NMR spectra showed signals due to a secondary methyl [δ_H 1.11 (3H, H_3-10); δ_C 17.6 (C-10)], a methylene [δ_H 2.40 (1H, H_β-3), 3.30 (1H, H_α-3); δ_C 41.9 (C-3)], two methines [δ_H 2.92 (1H, H-9), 3.16 (1H, H-2); δ_C 34.6 (C-9), 54.0 (C-2)], two methoxyl groups [δ_H 3.66 (3H, CH_3O-6), 3.69 (3H, CH_3O-1); δ_C 51.6 (CH_3O-1), 56.0 (CH_3O-6)], a trisubstituted double bond [δ_H 5.49 (1H, H-5); δ_C 107.2 (C-5), 166.6 (C-6)], a disubstituted double bond [δ_H 6.16 (1H, H-8), 6.19 (1H, H-7); δ_C 125.4 (C-7), 145.0 (C-8)], and two carbonyl carbons [δ_C 172.8 (C-1), 199.9 (C-4)]. The gross structure of **3** was elucidated by analyses of 2D NMR data including ^{1}H–^{1}H COSY and HMBC spectra (Fig. 2). The ^{1}H–^{1}H COSY spectrum of **3** implied connectivities for H-2—H-3, H-2—H-9, H-7—H-8, H-8—H-9, and H-9—H_3-10. Interpretation of the HMBC spectrum revealed correlations from H_2-3 to C-1 and C-4; H-5 to C-3, C-4, C-6 and C-7; CH_3O-1 to C-1; and CH_3O-6 to C-6. Thus the gross structure of **3** was deduced to be as shown in Fig. 2. The relative stereochemistry at C-2 and C-9 was established as follows (Fig. 3). In the ^{1}H-NMR spectrum, the long-range coupling observed between H_β-3 and H-5 (J=1.5 Hz) indicated that the bonds between them are W-shaped. The magnitude of $J_{2,3\alpha}$=13.2 and $J_{2,3\beta}$=3.9 Hz suggested that H-2 and H_α-3, H-2 and H_β-3 were located in *anti* and *gauche* arrangements, respectively. Thus the relative stereochemistry at C-2 was determined to be *R**. The magnitude of $J_{8,9}$=12.7 Hz suggested that H-8 and H-9 were located in an *anti* arrangement. In the difference nuclear Overhauser effect (NOE) experiments, irradiation at δ 1.11 (H_3-10) caused NOE enhancement in the signals of the H-2, H-8, and H-9. The ^{1}H–^{1}H coupling constant (J=12.7 Hz) between H-8 and H-9, and the observation of NOE from the H_3-10 methyl group to H-8 implied that the relative stereochemistry at C-9 was *S**. The geometry of the Δ^5-double bond was shown to be *E*. Accordingly, irradiation at δ 5.49 (H-5) caused NOE enhancement in the signal of the CH_3O-6. The *Z* configuration of the Δ^7-double bond was shown by the ^{1}H–^{1}H coupling constant (J=11.7 Hz) between

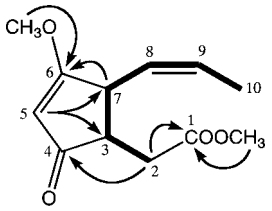

Fig. 1. ^{1}H–^{1}H COSY (Bold Lines) and HMBC (Arrows) Correlations for **1**

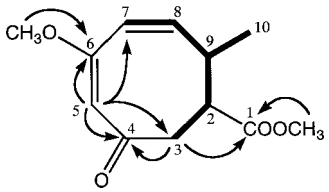

Fig. 2. ^{1}H–^{1}H COSY (Bold Lines) and HMBC (Arrows) Correlations for **3**

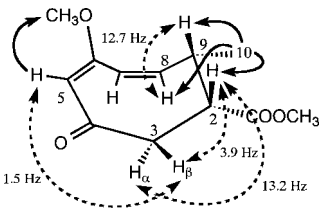

Fig. 3. Selected *J*-Values (Dotted-Line Arrows) and Significant NOEs (Full-Line Arrows) in **3**

H-7 and H-8. On the basis of the above data, the structure of **3** was represented as shown in the formula.

In conclusion, we described here the isolation and structure elucidation of erigerenones A (**1**), B (**2**), and C (**3**) from the aerial parts of *E. annuus*, *E. philadelphicus*, and *E. sumatrensis*. Although dibenzocyclooctadienone lignans such as steganone[12] and benzocyclooctadienone sesquiterpenes such as isoparvifolinone[13] are known, compound **3** is, to the best of our knowledge, the first example of a naturally occurring cyclooctadienone derivative without the fused phenyl system.

The framework of compounds **1**—**3** resembles that of (5-butyl-3-oxo-2,3-dihydrofuran-2-yl)-acetic acid (**4**), which was recently isolated from *E. annuus*.[14] This implies that compounds **1**—**4** may be formed by similar biosynthetic processes.

Experimental

General Procedures Optical rotations were determined using a JASCO DIP-360 digital polarimeter. IR spectra were recorded with a Perkin-Elmer FT-IR 1725X IR spectrophotometer and UV spectra on a Beckman DU-64 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded using JEOL JNM-LA 600 (600 and 150 MHz, respectively) and JEOL JNM-LA 400 (400 and 100 MHz, respectively) spectrometers. Chemical shifts are given on a δ (ppm) scale, with tetramethylsilane as an internal standard. The HR-EI-MS were recorded on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (230—400 mesh, Merck). Preparative HPLC was carried out on a Tosoh HPLC system (pump, CCPM; detector, RI-8020 and UV-8020) using TSKgel ODS-120T (7.8 mm i.d.×30 cm) column (Tosoh).

Plant Material The aerial parts of *E. annuus* were collected in Sendai City, Miyagi Prefecture, Japan, in July 2001; those of *E. philadelphicus* in Sendai City in April 2002; and those of *E. sumatrensis* in Sendai City in October 2000.

Extraction and Isolation *E. annuus*: The aerial parts of *E. annuus* (5.3 kg) were extracted with MeOH at room temperature for 2 weeks. The MeOH extract was concentrated under reduced pressure and the residue was suspended in a small excess of water. This suspension was extracted with $CHCl_3$. The $CHCl_3$-soluble fraction was concentrated under reduced pressure to afford a residue (79.4 g). A part of this residue (67.0 g) was chromatographed on a silica gel column using hexane–EtOAc (7 : 1—1 : 7) and $CHCl_3$–MeOH (9 : 1—1 : 1) to afford 62 fractions. Fraction 19 was purified by preparative HPLC [column temperature, 40 °C; mobile phase, MeOH–H_2O (1 : 1); flow rate, 1.5 ml/min; RI detector] to give **2** (0.5 mg).

E. philadelphicus: The aerial parts of *E. philadelphicus* (2.5 kg) were extracted with MeOH at room temperature for 2 weeks. The MeOH extract was concentrated under reduced pressure and the residue was suspended in a small excess of water. This suspension was extracted with $CHCl_3$. The $CHCl_3$-soluble fraction was concentrated under reduced pressure to afford a residue (24.0 g). This residue was chromatographed on a silica gel column using hexanen–EtOAc (7 : 1—1 : 7) and $CHCl_3$–MeOH (9 : 1—1 : 1) to afford 47 fractions. Fraction 11 was purified by preparative HPLC [column temperature, 40 °C; mobile phase, MeOH–H_2O (1 : 1); flow rate, 1.5 ml/min; RI detector] to give **3** (2.4 mg). Fraction 17 was purified by preparative HPLC [column temperature, 40 °C; mobile phase, MeOH–H_2O (1 : 1); flow rate, 1.5 ml/min; UV detector, 230 nm] to give **1** (1.5 mg) and **2** (0.4 mg).

E. sumatrensis: The aerial parts of *E. sumatrensis* (4.0 kg) were extracted with MeOH at room temperature for 2 weeks. The MeOH extract was concentrated under reduced pressure and the residue was suspended in a small excess of water. This suspension was extracted with $CHCl_3$. The $CHCl_3$-soluble fraction was concentrated under reduced pressure to afford a residue (80.7 g). A part of this residue (50.0 g) was chromatographed on a silica gel column using hexane–EtOAc (7 : 1—1 : 7) and $CHCl_3$–MeOH (9 : 1—1 : 1) to afford 60 fractions. Fraction 18 was purified by preparative HPLC [column temperature, 40 °C; mobile phase, MeOH–H_2O (1 : 1); flow rate, 1.5 ml/min; RI detector] to give **2** (2.5 mg).

Erigerenone A (**1**): Colorless oil. $[\alpha]_D^{24}$ +7.3° (c=0.14, MeOH). UV λ_{max} MeOH nm (log ε): 237 (4.2). IR ν_{max} $CHCl_3$ cm^{-1}: 1735, 1691, 1596. HR-EI-MS m/z: 224.1063 (M^+, Calcd for $C_{12}H_{16}O_4$: 224.1049). ^{1}H-NMR (600 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 2.

Erigerenone B (**2**): Colorless oil. $[\alpha]_D^{26}$ +7.9° (c=0.25, MeOH). UV λ_{max} MeOH nm (log ε): 238 (4.1). IR ν_{max} $CHCl_3$ cm^{-1}: 1735, 1688, 1593. HR-EI-MS m/z: 226.1178 (M^+, Calcd for $C_{12}H_{18}O_4$: 226.1205). ^{1}H-NMR (400 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 2.

Erigerenone C (**3**): Colorless oil. $[\alpha]_D^{22}$ +4.2° (c=0.24, MeOH). UV λ_{max} MeOH nm (log ε): 279 (3.8). IR ν_{max} $CHCl_3$ cm^{-1}: 1731, 1627, 1592. HR-EI-MS m/z: 224.1055 (M^+, Calcd for $C_{12}H_{16}O_4$: 224.1049). ^{1}H-NMR (400 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 2.

Acknowledgments We are grateful to Mr. S. Sato and Mr. T. Matsuki of this university for providing the mass and NMR spectra.

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