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New Sesquiterpene Dilactone from *Pertya glabrescens*

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A germacranolide, namely pertilide (I), mp 186—187°C (dec.), $[\alpha]_D^{20}$ +1.4°, $C_{15}H_{16}O_4$, was isolated from the leaves of *Pertya glabrescens* Sch.Bip. (Compositae).

I yielded the 4,5-epoxide (IV) on peracid oxidation, and the 1(10),3-dien-14-oic acid (III) on catalytic hydrogenation. Chemical and spectroscopic studies (especially NMDR experiments on I, III and IV) led to the proposal for I of the structure formulated as I (devoid of its stereochemistry) in Chart 1. The results of X-ray crystallographic analysis of I and its dibromide (VI) established the stereochemistry of I as [1(10)*Z*,4*E*]-(3*R*,7*R*,8*S*)-germacra-1(10),4,11(13)-triene-12,8: 14,3-diolide.

Keywords——*Pertya glabrescens*; Compositae; sesquiterpene; germacranolide; germacrane dilactone; X-ray crystallographic analysis; pertilide

In the course of our chemical investigations on *Pertya* plants (Compositae), we have reported the isolation and characterization of *O*-methyl pertyol,[1] 3β-methoxy-24-methyllanosta-9(11),25-diene[2] and glucozaluzanin C[3] from the underground parts of *Pertya robusta* (Maxim.) Beauv.

In this paper we report the isolation and structure determination of a sesquiterpene dilactone, designated as pertilide (I), from the leaves of *Pertya glabrescens* Sch. B_{IP}.[5] The structure of this compound was elucidated on the basis of chemical and spectral evidence,[4] and the stereostructure of I has been confirmed by crystal X-ray analysis.[6]

Pertilide (I), $C_{15}H_{16}O_4$, mp 186—187°C (dec.),[7] $[\alpha]_D^{20}$ +1.4°, showed absorption bands at 1767, 1752, and 1660 cm^{-1} due to unsaturated lactones and gave no hydroxyl absorption in its infrared (IR) spectrum. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of I showed fifteen carbon signals comprising six olefinic carbons (>C=×3, =CH_2×1, –CH=×2), two lactone carbonyls, two methines joined to oxygen atoms, three methylene carbons, a methine carbon, and a methyl group. These data indicated the presence of two lactone rings and three double bonds in the molecule. Taking into consideration its functional groups, the molecular formula of pertilide (I) required that it must be monocarbocyclic.

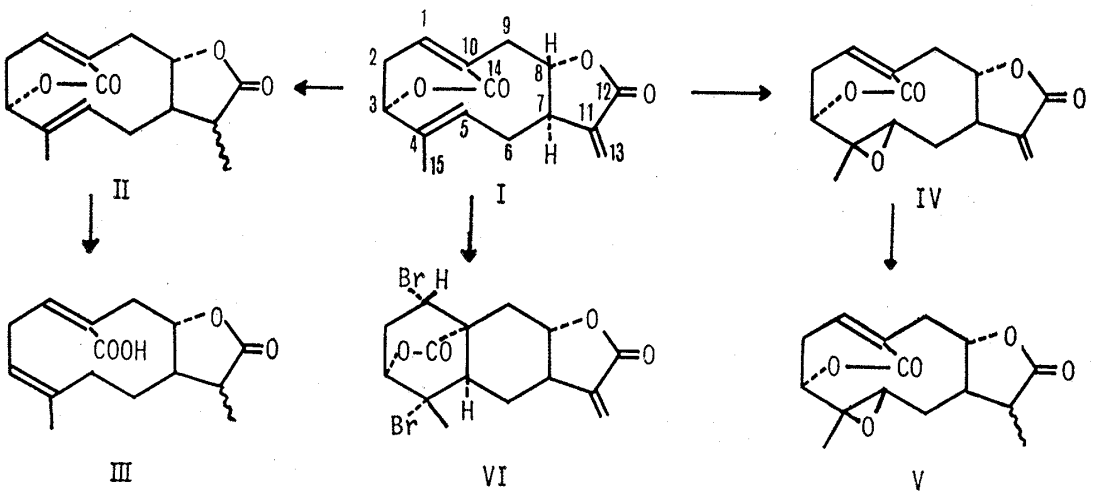


Chart 1

The ^{1}H-NMR spectrum[8] of pertilide (Table I) exhibited two doublets in lower field at δ_H 5.16 ppm (J=2.9 Hz) and δ_H 6.12 ppm (J=3.4 Hz) corresponding to the olefinic protons of the exo-cyclic methylene group conjugated with a *trans*-fused γ-lactone.[11] These signals vanished in a dihydro derivative (II), $C_{15}H_{18}O_4$, mp 148—153°C (dec.),[7] $[\alpha]_D^{18}$ −36.8°, obtained by partial hydrogenation of I, while on the other hand a new secondary methyl signal appeared at δ_H 1.29 ppm (J=6.8 Hz)[9] in II. Other features of the ^{1}H-NMR[8] of pertilide included two olefinic protons at δ_H 5.30 and 5.59 ppm, two protons at δ_H 3.23 and 4.61 ppm (each on a carbon bearing the ether oxygen of a lactone group (lactone proton)), and a slightly broadened vinyl methyl singlet at δ_H 0.98 ppm. These ^{1}H-NMR data correspond very well with the ^{13}C-NMR spectral data.

Table I. ^{1}H-NMR Data[a] and Results of NMDR Experiments

Compounds	I			II	III	IV
Solvents	C_6D_6	C_6D_6–$CDCl_3$ (1:1)	$CDCl_3$	$CDCl_3$	$CDCl_3$	C_5D_5N
1-H	5.19 br d[f] (7)	5.59 br d (7)	6.24[f]	6.22 br d (6)	6.20 dd (4, 12)	6.90 m
2-H	[d]	[d]	[d]	[d]	Ha: 3.94 br ddd (5, 12, 14) Hb: 2.26 br ddd (2, 4, 10, 14)	[d]
3-H	4.39 br s[g]	4.61 br s[g]	5.10 br s[g]	5.17 br s[g]	5.65 br dd (5, 10)	4.80 br s[h]
5-H	5.25 br d[f] (12)	5.30 br d (12)	5.46 br d (12)	5.38 br d (11)	[d]	3.20 br d (1, 11)
6-H	[d]	[d]	[d]	[d]	[d]	Ha: 2.35 br d (1, 3, 14) Hb: 1.40 dt (11, 14)
7-H	2.30 m[e,f]	2.50 m[e,f]	2.90 m[e,f]	[d]	[d]	2.85 m[e]
8-H	3.00 m[f]	3.23 ddd (4, 7, 10)	3.64 br dd (8, 9)	3.68 dt (7, 8)	4.52 ddd (5, 7, 11)	4.04 q (7)
9-H	[d]	2.6—2.8 m[b,f]	[d]	2.84 br d[b] (7)	Ha: 2.04[e,f] Hb: 3.30 br dd (2, 5, 13)	3.00 br d[b] (7)
13-H	Ha: 4.86 d (3.2) Hb: 6.10 d (3.7)	Ha: 5.16 d (2.9) Hb: 6.12 d (3.4)	Ha: 5.63 d (2.9) Hb: 6.30 d (3.4)	1.29 d[c] (6.8)	1.25 d[c] (7.1)	Ha: 5.65 d (2.9) Hb: 6.34 d (3.4)
15-H	0.68 br s[c]	0.98 br s[c]	1.45 br s[c]	1.44 br s[c]	1.67 br s[c]	1.28 s[c]
Inference		$J_{1,3}\fallingdotseq 2$ $J_{1,9}\fallingdotseq 1$ $J_{5,15}\fallingdotseq 1$ $J_{7,13a}=2.9$ $J_{7,13b}=3.4$ $J_{7,8}=7$ $J_{8,9a}=10$ $J_{8,9b}=4$ $J_{9a,9b}\fallingdotseq 13$		$J_{7,8}=8$ $J_{8,9}=7$	$J_{1,2a}=12$ $J_{1,2b}=4$ $J_{2,2b}=14$ $J_{2a,15}\fallingdotseq 1$ $J_{2a,3}=5$ $J_{2b,3}=10$ $J_{2b,9b}=2$ $J_{7,8}=7$ $J_{8,9a}=11$ $J_{8,9b}=5$ $J_{9a,9b}=13$	$J_{1,3}\fallingdotseq 2$ $J_{5,6a}=1$ $J_{5,6b}=11$ $J_{6a,6b}=14$ $J_{6a,7}=3$ $J_{6b,7}=11$ $J_{7,8}=7$ $J_{8,9}=7$ $J_{7,13a}=2.9$ $J_{7,13b}=3.4$

a) Coupling constants (J values) are shown in parentheses and expressed in Hz.
b) Intensity two protons.
c) Intensity three protons.
d) These signals could not be assigned because of overlapping with other signals.
e) These chemical shifts were only determined by NMDR experiments.
f) The exact chemical shifts and coupling constants could not be determined because of overlapping of the signals.
g) $W_{1/2}$ value : about 10 Hz.
h) $W_{1/2}$ value : about 8 Hz.

By spin decoupling (NMDR) experiments[8] on I (Table I), the presence of the partial structure A in Fig. 1 was demonstrated as follows. The proton on C-7 resonates at δ_H 2.50 ppm as a multiplet. Irradiation at the frequency of 7-H converted the terminal methylene (13-H_2) signals into singlets, collapsed a double double doublet (J=4, J=7, J=10 Hz) at δ_H 3.23 ppm into a double doublet (J=4, J=10Hz), and affected the methylene region (δ_H 1.5—2.0 ppm). From this finding, the signal at δ_H 3.23 ppm was assigned to the γ-lactone proton (8-H) and its splitting pattern indicated that the γ-lactone proton has three vicinal protons. Irradiation at δ_H 3.23 ppm (8-H) affected the multiplet at δ_H 2.50 ppm (7-H) and a two-proton multiplet at δ_H 2.6—2.8 ppm. Conversely, irradiation at δ_H 2.6—2.8 ppm collapsed the 8-H signal to a doublet (J=7), leaving the rest of the spectrum mostly unaffected.[13] From these findings, two protons observed as the multiplet at δ_H 2.6—2.8 ppm are adjacent to 8-H, *i.e.*, methylene protons at C-9, which were in turn adjacent to a quaternary center of a non-protonated double bond carbon. Consequently the partial structure A was established in the molecule I.

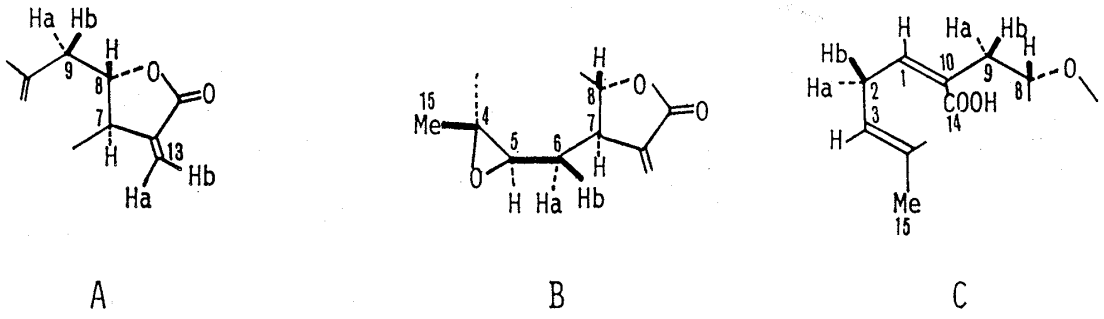


Fig. 1

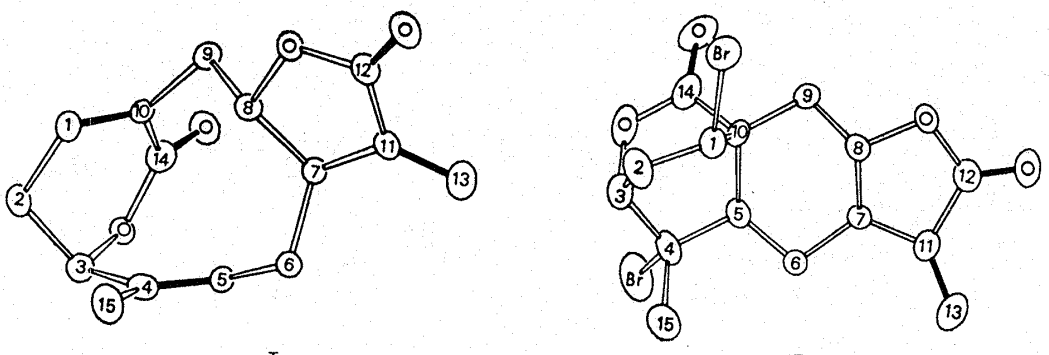
Epoxidation of I with *m*-chloroperbenzoic acid in chloroform furnished a monoepoxide (IV), $C_{15}H_{16}O_5$, mp 230—235°C (dec.),[7] $[\alpha]_D^{20}$ −133.0°, which was also obtained by treatment of I with *tert*-butyl chromate or bromine in chloroform[14] (see experimental section). The NMDR experiments on IV (Table I)[10] disclosed the partial structure B in Fig. 1. Irradiation at the frequency of 7-H at δ_H 2.85 ppm converted signals due to 13-Ha and 13-Hb into singlets, collapsed a quartet (J=7 Hz) at δ_H 4.04 ppm (8-H) into a triplet, changed a double triplet (J=11, J=14 Hz) at δ_H 1.40 ppm (6-Hb) into a double doublet (J=11, J=14 Hz), and changed a broadened doublet (J=1, J=3, J=14 Hz) at δ_H 2.35 ppm (6-Ha) into a less broadened doublet (J=1, J=14 Hz). Irradiation at the frequency of a proton attached to the epoxide ring carbon at δ_H 3.20 ppm (a slightly broadened doublet (J=1, J=11 Hz)) converted the double triplet (J=11, J=14 Hz) at δ_H 1.40 ppm (6-Hb) into a double doublet (J=11, J=14 Hz) and sharpened the broadened doublet (J=1, J=3, J=14 Hz) at δ_H 2.35 ppm (6-Ha) into a double doublet (J=3, J=14 Hz). These experiments showed that the protons 7-H and 6-Hb as well as 6-Hb and 5-H are arranged in a *trans*-diaxial relationship, and that two signals observed at δ_H 1.40[15] and 2.35 ppm are ascribable to geminal protons at C-6.

A non-conjugated double bond is usually epoxidized in preference to a conjugated one. Therefore in pertilide (I) the isolated double bond between C_4–C_5 was preferentially oxidized to give IV having the partial structure B. This conclusion was also supported by the facts that the epoxidation of I caused disappearance of the olefinic proton signal at δ_H 5.30 ppm[8] and that the epoxidation converted the vinylic methyl signal (δ_H 1.45 ppm)[9] into a sharper singlet at higher field (δ_H 1.23 ppm).[9] In other words, C-15 was concluded to be a methyl carbon in pertilide (I), while C-14 was concluded to be the carbonyl carbon of the other lactone (δ-lactone). Taking into consideration partial structure A and B, we presumed pertilide (I) to be a new substance belonging to the germacranolide series of sesquiterpenes.

Hydrogenation of pertilide (I) for half an hour with 10% Pd-C catalyst afforded the 11,13-dihydro derivative (II) described above. Further reduction of I for an additional half an

hour afforded a tetrahydro derivative (III), $C_{15}H_{20}O_4$, mp 211—212°C (dec.), $[\alpha]_D^{18}$ −232.8° as a main product; it is soluble in aqueous sodium bicarbonate. III showed bands at 3400—2900 and 1690 cm^{-1} due to a carboxylic group in its IR spectrum. In the ^{13}C-NMR spectrum of III, in comparison with that of II, a signal at δ_C 87.5 ppm of II ascribable to a methine bound to the ether oxygen of the δ-lactone[16] disappeared, and a new triplet due to a methylene appeared, although two trisubstituted double bonds still remained. The NMDR experiments[9] on III revealed that two protons observed at δ_H 3.94 and 2.26 ppm are geminal ones (J=14 Hz) at C-2 and that each of these protons couples with two olefinic protons observed at δ_H 5.65 (3-H) and 6.20 ppm (1-H) with the coupling constants shown in Table I.[18] The formation of this 1,4-diene structure (described as partial structure C in Fig. 1) from pertilide (I) was reasonably explained by assuming hydrogenolysis of the allylic oxygen–carbon bond[17] involving concomitant migration of the double bond at C-4 to C-3. Taking into consideration the hydrogenolysis mechanism, we concluded that the ether oxygen of the δ-lactone is attached to C-3 in the molecule I.

On the basis of all the above spectral and chemical results, the structure of pertilide was established as I in Chart 1 (devoid of its stereochemistry).[4]



I VI

Fig. 2

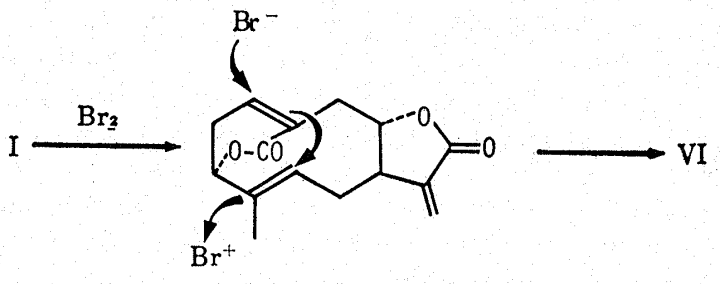
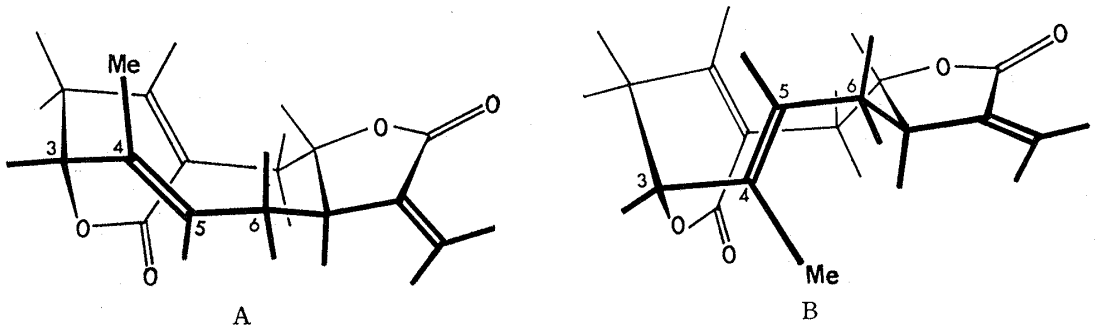


Chart 2

Since it seemed difficult to give a chemical proof of its stereostructure, pertilide (I) was subjected to X-ray crystallographic analysis. The resulting molecular structure is shown as I or its antipode in Fig. 2.[6] In order to establish the absolute configuration by the heavy atom method, we tried to prepare a heavy atom-containing derivative of pertilide (I). After several unsuccessful attempts, we treated pertilide (I) with bromine in chloroform to yield the monoepoxide (IV). This conversion probably proceeds *via* a bromohydrin intermediate[14] from which the monoepoxide (IV) is formed through S_{Ni} reaction. In absolute chloroform medium, an analogous bromination of I was carried out and gave a complex mixture of reaction products, from which a dibromide (VI), mp 251—252°C (dec.), $[\alpha]_D^{15}$ 0° was isolated. The complete structure of the dibromide (VI) as determined by X-ray crystallographic analysis[19]

is illustrated in Fig. 2; this work proved the absolute configurations of pertilide (I) in the asymmetric centers at C-3, -7, and -8. In conclusion, pertilide is [1(10)*Z*, 4*E*]-(3*R*, 7*R*, 8*S*)-germacra-1(10),4,11(13)-triene-12,8: 14,3-diolide. Sesquiterpene lactones possessing the *trans*, *trans*-cyclodeca-1,5-diene system are known to undergo acid-catalyzed *trans*-annular ring closure into eudesmanolides with *trans* ring juncture.[20] A possible transformation mechanism of I into VI on treatment with bromine is shown in Chart 2. In this reaction, since the δ-lactone of pertilide (I) prevented the rotation of the C_1–C_{10} double bond group, it gave an eudesmanolide (VI) which has a unique *cis* ring juncture.

A Dreiding model of I showed two possible conformational forms (A and B in Fig. 3). They are rotational isomers of the C-4(5) double bond group around the C_3-C_4 and C_5-C_6 sigma bonds. Since the epoxidation of I exclusively yielded the epoxide (IV), a stereospecific epoxidation occurred on a definite conformer A or B of I. As attack of the peracid on the double bond takes place from the less hindered side of the molecule (I) and the epoxide IV has 5α-H orientation as already described, pertilide must be present in the reaction solution as the conformer A, which is the same conformer as that in the solid state elucidated by X-ray analysis. The bromination reaction to form the dibromide (VI) from pertilide (I) also seems to proceed on the conformer A through the reaction mechanism suggested in Chart 2.



A B

Fig. 3

Two α,β-unsaturated lactone chromophores, unsaturated γ- and δ-lactones, are present in pertilide (I). Beecham[21] has suggested that the sign of the Cotton effect for α,β-unsaturated lactone chromophores is determined by the C=C–C=O group chirality. The difference $\Delta[\theta]$ −8800 calculated on the basis of the molecular ellipticity of I minus that of the dihydro derivative (II) at 250 nm in their circular dichroism (CD) curves accords with Beecham's suggestion of a negative Cotton effect for the C_{13}=C_{11}–C_{12}=O torsion angle of −4° in the solid state of I. The negative Cotton effect at 260 nm of 11,13-dihydro-epoxide (V), mp 203—208°C (dec.), $[\alpha]_D^{12}$ −106.7° is also compatible with Beecham's suggestion, provided that the α,β-unsaturated δ-lactone system of V has the same conformation as in the case of pertilide (torsion angle of C_1=C_{10}–C_{14}=O, +150°).

Experimental

All melting points were taken on a Shimadzu micro melting point determination apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-181 automatic polarimeter in a 1 dm tube. NMR spectra were recorded with a JEOL FX-100 spectrometer with tetramethylsilane as the internal standard, and $CDCl_3$ was used as the solvent unless otherwise stated. Chemical shifts are given on the δ scale (ppm) and coupling constants (J values) are expressed in Hz. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. CD spectra were measured with a JASCO J-40 in a 1 cm tube. Mass spectra (MS) were recorded with a JEOL JMS-D 300 machine. IR spectra were obtained with a Shimadzu IR-400 and a Hitachi IR-215 spectrometer. Thin-layer chromatography (TLC) was performed on Kiesel gel 60 F_{254} pre-coated plates (Merck) and detection was carried out by UV absorption measurement at 254 nm and by spraying 10% H_2SO_4 followed by heating.

Isolation of Pertilide (I)——The leaves of *Pertya glabrescens* were collected in Ohme City, Tokyo, in May 1979. The air-dried and powdered leaves (4.1 kg) were extracted six times with MeOH for 3 h each under reflux. The total MeOH solution was concentrated as far as possible under reduced pressure. The dark green residue (1.0 kg) was dissolved again in MeOH (2.2 l) and water (7.3 l) was added to the MeOH solution. The solution was allowed to stand at room temperature for a day, then the precipitated matter was removed by filtration. The filtrate was concentrated under reduced pressure in order to evaporate off the MeOH dissolved in it. The residual water solution (6 l) was successively extracted, once with hexane (5 l), five times with EtOAc (total 20 l) and three times with BuOH (total 10 l) in a separatory funnel. The hexane, EtOAc, and BuOH extractives, after removal of the solvent, weighed 3.1, 82.6, and 193.6 g respectively.

The EtOAc extract (82.6 g) was chromatographed on silica gel. The eluate with benzene–EtOAc (4: 1) was again chromatographed with benzene–EtOAc (9: 1), affording crude pertilide (1.1 g). Pertilide (I), colorless needles from acetone–isopropyl ether, mp 186—187°C (dec.),[7] $[\alpha]_{589}^{20}$ +1.4°, $[\alpha]_{577}^{20}$ +0.3°, $[\alpha]_{546}^{20}$ −3.4°, $[\alpha]_{435}^{20}$ −48.6°, $[\alpha]_{365}^{20}$ −195.1° (c=1.5, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 68.99; H, 6.40. CI-MS (CH_4) m/e: 261 (M^++1). UV λ^{EtOH} nm (ε): 210 (16100). CD (c=0.002, EtOH) $[\theta]^{20}$ (nm): +45000 (213) (positive maximum), −37000 (245) (negative maximum), −36300 (250). NMR δ_C: 16.0 (CH_3–), 29.5, 32.7, 35.8 (>CH_2–), 48.0 (>CH–), 78.9, 88.1 (>CH–O–), 122.1 (CH_2=), 129.1, 130.8 (–CH=), 132.4, 135.5, 138.0 (>C=), 168.8, 167.3 (C=O).

Dihydro Derivative (II)——A solution of I (170 mg) in 20 ml of EtOAc–EtOH (1: 1) was hydrogenated for 30 min at atmospheric pressure in the presence of 10% Pd-C (40 mg). After removal of the catalyst by filtration, the solvent was evaporated off *in vacuo*. The residue was chromatographed over silica gel. Elution with benzene–EtOAc (2: 1) afforded the dihydro derivative (II) as colorless needles (110 mg), mp 148—153°C (dec.)[7] (hexane–acetone), $[\alpha]_D^{18}$ −36.8° (c=0.6, $CHCl_3$). CI-MS (CH_4) m/e: 263 (M^++1). UV λ_{max}^{EtOH} nm (ε): 210 (6000). CD (c=0.003, EtOH) $[\theta]^{18}$ (nm): +11000 (210), −34600 (240) (negative maximum), −27500 (250). NMR δ_C: 14.2, 15.9 (CH_3–), 29.7, 32.4, 35.7 (–CH_2–), 41.8, 52.5 (>CH–), 78.9, 87.5 (>CH–O–), 129.4, 129.9 (–CH=), 132.3, 134.7 (>C=), 167.3, 177.2 (C=O).

Further elution with the same solvent afforded colorless needles (23 mg), mp 210—212°C (dec.) (hexane–acetone) which were identical (IR and TLC) with III.

Tetrahydro Derivative (III)——I (280 mg) was hydrogenated for about 1 h in the same manner as described above. The reaction products were dissolved in EtOAc (30 ml) and extracted with 5% $NaHCO_3$ solution (6 ml×4). The alkaline solution was acidified with dil. HCl, then the separated materials were extracted with EtOAc (10 ml×4). The EtOAc layer was dried and concentrated. The residue was purified by silica gel chromatography using benzene–EtOAc–AcOH (95: 5: 0.5) as a solvent. Recrystallization from acetone–isopropyl ether furnished the tetrahydro derivative (III) (50 mg), mp 211—212°C (dec.), $[\alpha]_D^{18}$ −232.8° (c=0.34, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.52; H, 7.85. CI-MS (CH_4) m/e: 265 (M^++1). UV λ_{max}^{EtOH} nm (ε): 215 (4200). CD (c=0.01, EtOH) $[\theta]^{18}$ (nm): −65000 (245) (negative maximum). NMR δ_C: 15.0, 22.7 (CH_3–), 28.6, 31.2, 41.2, 43.0 (–CH_2–), 29.4, 44.4 (>CH–), 85.5 (>CH–O–), 122.6, 140.1 (>C=), 122.7, 150.7 (–CH=), 172.8, 178.2 (C=O).

Epoxide (IV)——i) IV from I with *m*-Chloroperbenzoic Acid: *m*-Chloroperbenzoic acid (40 mg) was added to a solution of I (35 mg) in $CHCl_3$ (5 ml), and the mixture was allowed to stand for 2 h at room temperature. The solution was washed with 5% $NaHCO_3$, then with H_2O, and dried over $MgSO_4$. The solvent was evaporated off. The residue (49 mg) was crystallized from acetone–isopropyl ether, affording the epoxide (IV), mp 230—235°C (dec.),[7] $[\alpha]_D^{20}$ −133.0° (c=0.6, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.03; H, 5.87. CI-MS (CH_4) m/e: 277 (M^++1). UV λ^{EtOH} nm (ε): 210 (14000). NMR δ_C (C_5D_5N): 18.7 (CH_3–), 28.7, 29.2, 34.9 (–CH_2–), 44.5 (>CH–), 64.7 (>C–O–), 61.3, 78.1, 87.0 (>CH–O–), 121.9 (CH_2=), 130.5, 138.6 (>C=), 139.6 (–CH=), 166.9, 168.9 (C=O). δ_H: 1.23 (3H, s, 15-H), 1.42 (1H, dt, J=10, J=14, 6-Hb), 3.88 (1H, q, J=7.1, 8-H), 4.71 (1H, br s, 3-H), 5.65 (1H, d, J=2.9, 13-Ha), 6.35 (1H, d, J=3.7, 13-Hb), 6.75 (1H, br d, J=7, 1-H).

ii) IV from I with *tert*-Butyl Chromate: *tert*-Butyl chromate was prepared in CCl_4 (13 ml) from *tert*-BuOH (5 ml) and CrO_3 (2 g).[12] A solution of *tert*-butyl chromate in CCl_4 (2 ml), Ac_2O (1.5 ml), and AcOH (1.5 ml) was added to a solution of I (150 mg) in benzene (3 ml), and the mixture was stirred for half an hour at room temperature. Next, 30% aqueous oxalic acid (10 ml) was added at 0°C. After further addition of powdered oxalic acid (0.5 g), the solution was stirred for 30 min at room temperature, then extracted with $CHCl_3$ (10 ml×3). The solution in $CHCl_3$ was washed with 5% $NaHCO_3$ and with water, dried over $MgSO_4$, and concentrated to dryness. The residue was purified by silica gel chromatography using benzene–EtOAc (3: 1) as a solvent. Crystallization from acetone–isopropyl ether afforded colorless needles (49 mg), mp 231—234°C (dec.),[7] which were found to be identical with the epoxide (IV) by TLC, IR, and MS comparisons.

iii) IV from I with Bromine:[14] A solution of I (10 mg) in $CHCl_3$ (4 ml) was treated with several drops of 10% bromine in $CHCl_3$ and shaken vigorously for 5 min. After concentration of the reaction mixture under reduced pressure at room temperature, the residue (10 mg) was crystallized from MeOH to yield colorless needles, mp 234—236°C (dec.),[7] which were found to be identical with the epoxide (IV) by TLC, IR, and MS comparisons.

Dihydro Epoxide (V)——A solution of IV (23.5 mg) in 8 ml of EtOAc was hydrogenated in the presence of 22 mg of 5% Pd-C at atmospheric pressure for 35 min. The solution was filtered and the filtrate was

concentrated to dryness. The residue was purified by silica gel chromatography using benzene–EtOAc (2: 1) as a solvent. Recrystallization from acetone–isopropyl ether afforded V (11.8 mg), mp 203—208°C (dec.), $[\alpha]_D^{12}$ −106.7° (c=0.25, $CHCl_3$). MS m/e: 278 (M^+). UV λ_{max}^{EtOH} nm (ε) 217 (5100). CD (c=0.02, EtOH) $[\theta]^{12}$ nm: −59000 (220) (negative maximum), −8600 (260). NMR δ_H: 1.23 (3H, s, 15-H), 1.30 (3H, d, J= 6.8, 13-H), 3.88 (1H, dt, J=6, J=9, 8-H), 4.71 (1H, br s, 3-H), 6.70 (1H, br d, J=6, 1-H).

Dibromide (VI)——A solution of I (50 mg) in absolute $CHCl_3$ (20 ml) was treated with several drops of 10% bromine in absolute $CHCl_3$ and shaken for 5 min. After concentration of the reaction mixture under reduced pressure at room temperature, the residue was chromatographed over silica gel. Elution with benzene–EtOAc (9: 1) gave the dibromide (VI) (7 mg), mp 251—252°C (dec.) (acetone), $[\alpha]_D^{15}$ 0° (c=0.1, pyridine). Beilstein test: + (green). MS m/e: 339, 341 (M^+−Br). NMR δ_H (C_5D_5N): 1.91 (3H, s, 15-H), 5.37 (1H, d, J=2.9, 13-Ha) 6.22 (1H, d, J=3.2, 13-Hb).

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References and Notes

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