consumption of the starting material. The mixture was filtered, and the GLC analysis of the filtrate revealed the formation of at least three products (1:24:75 ratio; 6% Carbowax 20M on 100/120 Gas Chrom Q, 120 °C). GC–mass spectral analysis established that all products were octahydro derivatives of **3**: CI GC–MS (CH_4) m/e (rel intensity) 281 ($M^+ + 1$, 1), 280 (M^+, 2), 279 ($M^+ - 1$, 9), 111 (100).

Hydrogenation of **4** (100 μg) under identical conditions resulted in the formation of a mixture of octahydro derivatives with the same GLC and GC–MS properties.

Acknowledgment. Generous gifts of cembrene A (Professor Sukh Dev, Maltichem Research Center) and of mukulol (Professor Sho Itô, Tôhoku University) are gratefully acknowledged. We thank Dr. R. M. C. Williams (Centre for Overseas Pest Research) for identification of the termite species. Partial support of this work by the NIH [Grant No. AI 12020 and Fellowship awards AI 05076 (G.D.P.) and CA 05646 (D.F.W.)] is acknowledged with pleasure.

Registry No. **1**, 66723-19-1; **2**, 69636-81-3; **3**, 31570-39-5; **3** octahydro derivative, 1786-12-5; **4**, 71213-92-8; **5**, 626-96-0; **6**, 71155-94-7; **7**, 138-86-3; geraniol, 106-24-1.

Isolation and Characterization of Peroxycostunolide (Verlotorin) and Peroxyparthenolide from *Magnolia grandiflora*. Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Costunolide and Related Compounds

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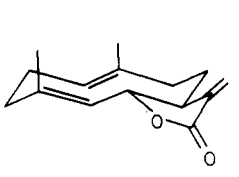
Recently, the hydroperoxy sesquiterpene lactones, peroxycostunolide (verlotorin) (**2**) and peroxyparthenolide (**9**), were reported[1] to occur in the leave of *Magnolia grandiflora* L. Their structure elucidation involved derivatization to the respective alcohols **4** and **11** and their acetates **7** and **12**, the methyl peroxides **5** and **14**, and the ketones **6** and **13**. The formation of **2** and **9** from costunolide (**1**) and parthenolide (**8**), respectively, by light-generated singlet oxygen confirmed the stereochemical assignments and established the configuration at the hydroperoxy-bearing carbon.

The experimental details of that work are described herein, with the ^1H NMR assignments of all new compounds compiled in Table I, while the ^{13}C NMR assignments for the above compounds along with those of costunolide (**1**) and parthenolide (**8**) are given in Tables II and III, respectively.

The assignment of the ^{13}C NMR signals for costunolide (**1**), peroxycostunolide (verlotorin) (**2**), parthenolide (**8**), peroxyparthenolide (**9**), and their derivatives (Tables II and III) was made from broad-band and off-resonance-decoupled spectra and by comparison with published data. The assignment of C-14 and C-13 in peroxycostunolide



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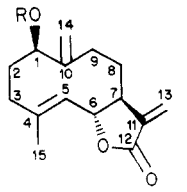
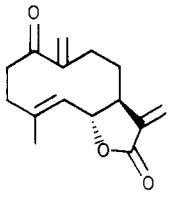


2, R = OH
4, R = H
5, R = OCH_3
7, R = $C(O)CH_3$



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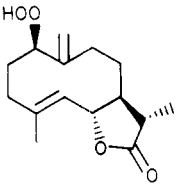

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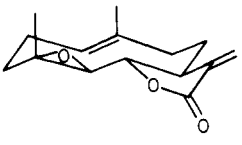
(verlotorin) (**2**) and peroxyparthenolide (**9**) was aided by



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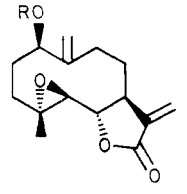
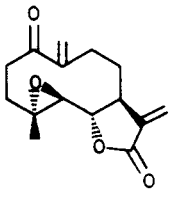


9, R = OH
11, R = H
12, R = $C(O)CH_3$
14, R = OCH_3



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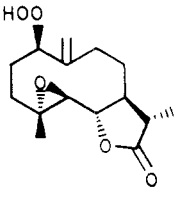

10

the ^{13}C NMR spectra of the corresponding 11,13-dihydro derivatives, which were obtained by photooxygenation of dihydrocostunolide (**15**) and dihydroparthenolide (**16**), respectively.[2] The C-7 and C-11 methine carbons in these compounds could not be readily assigned. The literature has conflicting information for designating these positions. While in some santonin derivatives[3] C-7 was assigned the lower field position after consideration of the β and γ effects, assignment was reversed for dihydrolaurenobiolide.[4] The chemical shift values of C-7 and C-11 of **3** (Table II) on comparison with those of **10** (Table III) require that the methine carbon signal at δ 42.0 in both compounds be due to C-11, as it is unlikely that the field position of this carbon would show a marked difference in these two compounds. The methine signal of C-7, on the other hand, would be expected to occur at a higher field position in **10**, due to the γ effect of the epoxide group. From this, the methine carbon signals at δ 47.8 (Table III) and 54.0 (Table II) were assigned to C-7 in **10** and **3**,

(1) F. S. El-Feraly, Y.-M. Chan, E. H. Fairchild, and R. W. Doskotch, *Tetrahedron Lett.*, 1973 (1977).

(2) These compounds were obtained by $NaBH_4$ reduction of costunolide (**1**) and parthenolide (**8**), respectively. The physical and spectral data of the products were identical with those reported for dihydrocostunolide (**15**) and dihydroparthenolide (**16**). See the book by H. Yoshioka, T. J. Mabry, and B. N. Timmermann, "Sesquiterpene Lactones Chemistry, NMR and Plant Distribution", University of Tokyo Press, Tokyo, 1973, p 143, and the paper by Govindachari et al., *Tetrahedron*, 21, 1509 (1965).

(3) P. S. Pregosin, E. W. Randall, and T. B. H. McMurry, *J. Chem. Soc., Trans. 1*, 299 (1972).

(4) K. Tori, I. Horibe, Y. Tamura, K. Kuriyama, H. Tada, and K. Takeda, *Tetrahedron Lett.*, 387 (1976).

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Table I. ^{1}H NMR Spectra of Peroxycostunolide (2) and Peroxyparthenolide (9) and Derivatives[a]

compd	H-1	H-5	H-6	H-13	H-14	H-15	miscellaneous
2[b]	4.04 dd (9.0, 3.5)	5.39 br d (8.9)	4.44 t (9.7)	6.03 d (3.2) 5.52 d (3.2)	5.18 br s 5.03 br s	1.70 d (1.3)	10.51 br s (OOH)[c]
3[e]	4.24 dd (8.0, 4.0)	5.40 br d (9.4)	4.58 t (9.6, 9.4)	1.19 d (6.8)	5.3 br s 5.13 br s	1.71 d (1.4)	10.68 br s (OOH)[c]
4[d]	3.94 br t (6.8)	~5.2[h]	4.2 t (10.2)	5.40 d (3.6) 6.29 d (3.6)	5.16 br s 4.83 br s	1.72 d (1.8)	
5[d]	4.41 dd (8.5, 4.0)	5.55 br d	4.57 t (9.2)	6.44 d (3.2) 5.70 d (3.2)	5.25 br s 5.45 br s	1.76 d (1.4)	4.0 s (OCH_3)
6[f]		5.08 br d (9.5)	4.32 t (9.5)	6.20 d (3.2) 5.48 d (3.2)	5.82 s 5.66 s	1.75 s	~3.1 m (H-7)
7[e]	masked by H-14	partially masked by H-13 (c)	4.27 t (9.6)	5.47 d (3.0) 5.96 d (3.6)	4.99 br s 5.20 br s	1.73 d (1.2)	1.95 s ($CH_3C(O)$-)
9[b]	4.33 dd (10.5, 4.2)	2.93 d (8.9)	3.92 t (9.2)	6.05 d (3.5) 5.60 d (3.5)	5.41 br s 5.28 br s	1.43 s	10.51 br s (OOH)
10[e]	4.23 br dd	2.79 d (9.6)	3.80 t (9.6)	1.37 d (6.6)	5.33 s 5.15 s	1.40 s	HOO- not observed
11[g]	4.48 br dd (10.0, 5.0)	3.13 d (9.0)	4.09 t (9.0)	6.31 d (3.0) 5.54 d (3.0)	5.45 br s 5.09 br s	1.55 s	2.34[h] s (OH)
12[d]	~5.2[h] m	2.87 t (8.4)	3.69 t (9.0)	6.20 d (3.0) ~5.47[h] d	5.45 s 5.06 br s	1.48 s	
13[d]		~2.9[h] d (9.5)	3.8 t (9.5)	5.76 d (3.0) 6.46 d (3.0)	6.28 s 5.13 br s	1.43 s	
14[d]	4.61 dd (10.0, 3.6)	3.02 d (8.2)	3.97[h] t (8.5)	6.46 d (3.0) 5.75 d (3.0)	5.63 s 5.40 s	1.53 s	3.99 s (OCH_3)

[a] Spectra were determined in the stated solvent at 60 or 90 MHz with Me_4Si as the internal standard. Chemical shifts are in ppm (δ), coupling constants J are in Hz given in parentheses, and multiplicities are designated by the following symbols: s = singlet, d = doublet, t = triplet, m = multiplet with center given, and br = broadened signal. [b] In acetone-d_6 at 90 MHz. [c] D_2O exchangeable. [d] In $CDCl_3$ at 60 MHz. [e] In acetone-d_6 at 60 MHz. [f] In $CDCl_3$ at 90 MHz. [g] In pyridine-d_5 at 60 MHz. [h] Partially obscured by other peaks.

Table II. ^{13}C NMR Spectra of Peroxycostunolide and Related Compounds[a]

carbon atom	1[b]	2[c]	3[c]	4[b]	5[b]	6[b]	7[b]
1	127.0	91.4	91.5	78.2	78.8	204.4	89.1
2	26.1[d]	34.0[d]	35.0[d]	32.6[d]	31.4[d]	35.6[d]	33.1[d]
3	39.4[d]	27.0[d]	28.2[d]	25.9[d]	25.9[d]	29.0[d]	26.8[d]
4	141.1	148.0	148.2	145.5	145.4	142.9	146.6
5	127.3	123.1	123.3	123.0	123.0	125.0	122.6
6	81.8	80.9	80.6	79.3	80.5	81.0	80.7
7	50.4	49.8	54.0	47.9	48.6	49.4	49.6
8	28.0[d]	28.3[d]	29.0[d]	30.0[d]	30.9[d]	28.2[d]	28.5[d]
9	40.9[d]	37.2[d]	37.4[d]	36.1[d]	36.3[d]	38.3[d]	37.0[d]
10	137.0	146.5	145.3	151.1	147.2	150.9	146.3
11	140.1	141.0	42.0	140.3	140.1	139.7	140.1
12	170.3	170.4	178.7	170.4	170.1	170.1	170.2
13	119.4	117.9	12.9	118.3	118.3	119.0	118.4
14	16.0	112.6	112.4	110.8	112.8	123.5	112.9
15	17.0	17.5	17.4	17.9	18.0	17.1	17.7
other carbons					21.2[e] 170.1[f]		62.4[g]

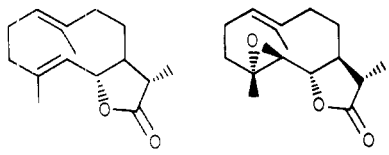
[a] Assignments of multiplets were made by single-frequency off-resonance spin decoupling. [b] In $CDCl_3$. [c] In Pyr-d_5. [d] Not designated, may be interchanged. [e] Acetate methyl. [f] Acetate carbonyl. [g] Methyl on the peroxy group.

Table III. ^{13}C NMR Spectra of Peroxyparthenolide and Related Compounds[a]

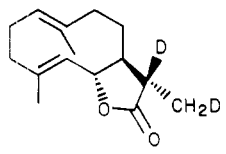
carbon atom	8[b]	9[c]	10[c]	11[c]	12[b]	13[b]	14[b]
1	125.3	91.2	91.2	78.1	79.1	203.3	88.9
2	24.2[d]	24.4[d]	25.7[d]	23.8[d]	23.8[d]	34.4[d]	34.0[d]
3	36.5[d]	27.3[d]	27.9[d]	31.3[d]	27.7[d]	30.8[d]	26.0[d]
4	61.5	60.7	60.6	60.8	60.2	59.2	60.4
5	66.4	63.9	64.0	64.3	63.7	65.3	63.7
6	82.5	80.2	80.2	80.4	79.8	81.5	79.9
7	47.7	44.4	47.8	43.5	43.3	45.0	44.0
8	30.2[d]	26.2[d]	26.3[d]	25.0[d]	25.6[d]	28.7[d]	25.9[d]
9	41.2[d]	34.4[d]	34.6[d]	34.6[d]	33.7[d]	35.7[d]	24.2[d]
10	134.7	145.2	145.4	150.2	144.0	149.8	144.3
11	139.5	140.5	42.0	140.8	139.4	139.2	139.5
12	169.3	169.8	178.4	169.8	169.6	169.1	169.3
13	121.0	118.8	12.9	118.5	119.4	120.1	119.4
14	17.3[e]	117.7	117.7	114.0	117.9	127.0	117.9
15	17.0[e]	18.3	18.2	18.8	18.5	17.5	18.3
other carbons					21.2[f] 169.2[g]		62.4[h]

[a] Assignments of multiplets were made by single-frequency off-resonance spin decoupling. [b] In $CDCl_3$. [c] In Pyd-d_5. [d,e] Not designated, may be interchanged. [f] Acetate methyl. [g] Acetate carbonyl. [h] Methyl on the peroxy group.

respectively. To confirm these assignments, costunolide (1) was reduced with $NaBD_4$ in deuterated methanol to give 11,13-dideuteriocostunolide (17). The ^{13}C NMR spectrum of the latter retained the lower field methine carbon signal at δ 54.8, but the higher field signal at δ 42.2 observed in the spectrum of dihydrocostunolide (15) had



15 16



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disappeared.

Comparison of the ^{13}C NMR spectra of peroxycostunolide (verlotorin) (2), peroxyparthenolide (9), and peroxyferolide[5] with their deoxy derivatives revealed a consistent downfield shift in the position of C-10 in going from the hydroperoxide series to the alcohol series. The magnitude of this shift was 4.6 ppm for peroxycostunolide (verlotorin) (2), 5.0 ppm for peroxyparthenolide (9), and 3.3 ppm for peroxyferolide.[5] In contrast, the C-14 signal showed a noticeable upfield shift (-1.8, -3.7, and -3.1 ppm, respectively). Acetylation of the deoxy peroxy compounds shifted C-10 upfield by an average of -5.0 ppm, while C-14 was shifted downfield by an average of 3.3 ppm, leaving the field position of C-1 virtually unchanged.

The upfield β shifts and downfield γ shifts which occur for the allylic hydroperoxides relative to the allylic alcohols are of diagnostic value and can be explained by delineating information already present in the literature[6] about allylic systems. When the oxygen atom is fixed at an anticlinal position with respect to the double bond, the through-space interaction between the π-type n orbital of the oxygen atom and the vacant $p\pi^*$ orbital results in a decrease of the electron density on the oxygen atom. The enhanced electronegativity of this oxygen atom, therefore, will cause the observed shift. While a hydroperoxy group or a hydroxy group would be expected to participate in this interaction, the extent of this interaction appears to be larger for the former than the latter.[7]

The shifts in the allylic acetate relative to the alcohols might involve other factors. They could be ascribed to direct interaction of the electronegative acetate group with the π electrons.[8] Such effect has no bearing on the field position of C-1,[8] but it, again, tends to shield the α carbon and deshield the β carbon of an allylic system. Recently, such acetylation-induced shifts have been well demonstrated in a series of allylic hydroxysterols.[9]

Experimental Section

Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. The UV spectra were determined in MeOH on a Beckman Model Acta III recording spectrophotometer, and IR spectra were obtained on either a Beckman IR-33 recording infrared spectrophotometer or a Perkin-Elmer 257 infrared spectrophotometer. ^1H NMR spectra were recorded on a Joel Model C-60 (60 MHz) nuclear magnetic spectrometer; the latter was also used for the ^{13}C NMR determinations (at 15.03 MHz). Some NMR spectra were also obtained using a Bruker HX-90E instrument (90 MHz) equipped with Fourier transform analysis. Mass spectra were measured on AEI MS-902 and MS-9, Finnigan 1015, and DuPont 21-492 mass spectrometers. Optical rotations were measured on a Perkin-Elmer 141 automatic polarimeter. Elemental analyses were done by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Silica gel G (E Merck) was used for TLC with 0.3% aqueous $KMnO_4$ as spray reagent.

Isolation of Peroxycostunolide (Verlotorin) (2). The dried powdered leaves of *Magnolia grandiflora* L. were percolated with EtOH. The residue remaining after removal of the solvent at reduced pressure was partitioned between 10% aqueous MeOH and hexane, and the 10% aqueous MeOH fraction was chromatographed on silica gel as already described.[10] A portion (580 mg) of the mother liquor left from the crystallization of costunolide (1) from the costunolide column fraction was chromatographed on a column (36.0 × 1.7 cm) of silica gel G packed in chloroform. The fractions obtained (2 mL each) were examined by TLC on silica gel G plates, using 8% EtOH in chloroform as the solvent system. The initial fractions contained pure costunolide (R_f 0.75, 200 mg). The fractions with the R_f value of 0.49 were combined and evaporated to leave 210 mg of a residue that crystallized readily from EtOH–Et_2O to form colorless prisms of peroxycostunolide (2): mp 141 °C (softens but decomposition temperature indeterminate); $[\alpha]^{25}_D$ +171° (*c* 0.20, acetone); UV end absorption (ϵ_{210} 9000); IR (KBr) bands at 3440 and 3350 (OH), 3090 (unconj. C=CH_2), 1745 (lactone C=O), and 1660 cm^{-1} (C=C); chemical ionization mass spectrum (isobutane) *m/e* 265 (12%, MH^+, $C_{15}H_{20}O_4$ requires 264), 249 (78%, $MH^+ - O$), 247 (60%, $MH^+ - H_2O$), and 231 (100%, $MH^+ - H_2O_2$).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.25; H, 7.77.

The mother liquor left from the crystallization of peroxycostunolide (2) showed a minor spot just behind that of peroxycostunolide (2), using the previously mentioned TLC system. The resolution was further improved with 20% acetone in $CHCl_3$ as the solvent system; the R_f value of peroxycostunolide (2) and the minor spot were 0.44 and 0.27, respectively. PLC with this system gave a product (9 mg from 77 mg of mother liquor) which was found to be identical with 4 (vide infra).

Isolation of Peroxyparthenolide (9). The mother liquor from the parthenolide column fraction[10] (0.287 g) was chromatographed on a column (1.5 × 14.0 cm) of 14 g of silica gel G packed in 1% EtOH in $CHCl_3$. Two-milliliter fractions were collected, and the composition of the eluate was monitored by TLC on silica gel G plates, using 8% EtOH in $CHCl_3$ as the solvent system. The early column fractions contained parthenolide (8), R_f 0.61, and upon evaporation 200 mg were recovered. The fractions containing spot R_f 0.21 were combined and upon evaporation yielded 45 mg of a solid residue that crystallized from acetone–Et_2O to give prisms of peroxyparthenolide (9): mp 190 °C dec; $[\alpha]^{25}_D$ +27° (*c* 0.21, acetone); UV end absorption (ϵ_{210} 8000); IR (KBr) bands at 3440 and 3350 (OH), 3090 (unconj. C=CH_2), 1748 (C=O), and 1660 cm^{-1} (C=C); chemical ionization mass spectrum (ammonia–methane) *m/e* 298 (86%, MNH_4^+, $C_{15}H_{20}O_5$ requires 280) and 282 (100%, $MNH_4^+ - O$).

Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.57; H, 7.08.

Deoxyperoxycostunolide (Artemorin) (4). A 50-mg sample of peroxycostunolide (2) was dissolved in 2 mL of acetone, and the solution was stirred for 15 min with 1.1 equiv (55 mg) of triphenylphosphine. The reaction mixture was evaporated to dryness, and the residue (120 mg) was chromatographed on a silica gel G column, using EtOAc–Et_2O (2:3) as eluent. Deoxyperoxycostunolide (4) was thus separated from the excess triphenylphosphine and from triphenylphosphine oxide and was obtained as colorless needles from ether: mp 120–121 °C (lit.[10]

(5) R. W. Doskotch, F. S. El-Feraly, E. H. Fairchild, and C.-T. Huang, *J. Org. Chem.*, **42**, 3614 (1977).

(6) Y. Senda, J.-i. Ishiyama, and S. Imaizumi, *Tetrahedron Lett.*, 1805 (1978).

(7) This is supported by the significant difference in chemical shift values of C-1 in the alcohol series and in the hydroperoxide series; in the latter C-1 absorbs about 13 ppm further downfield than the former.

(8) T. Yonemoto, *J. Magn. Reson.*, **13**, 153 (1974).

(9) M. Tsuda, E. J. Parish, and G. J. Schroepfer, *J. Org. Chem.*, **44**, 1282 (1979).

(10) F. S. El-Feraly and Y.-M. Chan, *J. Pharm. Sci.*, **67**, 347 (1978).

mp 115–117 °C for artemorin); $[\alpha]^{25}_D$ +89° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) bands at 3600 and 3500 (OH), 1760 (lactone C=O), 1670 and 1640 cm^{-1} (C=C); MS (EI) *m/e* 248 (6%, $M^{+\cdot}$) and 230 (91%, $M^{+\cdot} - H_2O$).

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.35, H, 7.92.

Methylperoxycostunolide (5). A 50-mg sample of peroxycostunolide (**2**) was dissolved in 1 mL of $CHCl_3$, and the solution was stirred for 17 h with 270 mg of CH_3I and 250 mg of Ag_2O. The mixture was then filtered, and the colorless filtrate on evaporation left an oily residue that crystallized readily from Et_2O–EtOH to give 32 mg of **5** as colorless needles: mp 104–105 °C; $[\alpha]^{25}_D$ +203° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) no OH bands, 1766 (lactone C=O), 1670 and 1646 cm^{-1} (C=C); MS, no parent ion peak in CI (isobutane) spectrum, but the EI spectrum showed peaks at *m/e* 278 (less than 1%, $M^{+\cdot}$) and *m/e* 231 (100%, $M^{+\cdot} - OOCH_3$).

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.31; H, 8.12.

Anhydroperoxycostunolide (6). A 100-mg sample of peroxycostunolide (**2**) was dissolved in 1.3 mL of Pyr, and 2.3 mL of Ac_2O was then added to the mixture which was stirred for 1 h (stirring for a longer time resulted in extensive polymerization). Ice was then added to the reaction mixture which was taken up in $CHCl_3$ and washed with 5% aqueous $NaHCO_3$. The chloroformic extract was then washed with H_2O, dilute HCl, and H_2O again, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue crystallized from Et_2O–EtOH to give 56 mg of colorless shiney needles of **6**: mp 123–124 °C (same as lit.[10] mp for dehydroartemorin); $[\alpha]^{25}_D$ +144° (*c* 0.16, $CHCl_3$); UV λ_{max} 233 nm (ϵ 4000) and shoulder at 300 nm (ϵ 68); IR ($CHCl_3$) no OH bands, 1770 (lactone C=O) and 1674 cm^{-1} (ketone C=O); MS (CI, isobutane), *m/e* 247 (100%, $M^{+\cdot}H$) and *m/e* 229 (54%, $M^{+\cdot}H - H_2O$).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.36. Found: C, 73.11; H, 7.47.

Acetyldeoxyperoxycostunolide (7). A 50-mg sample of **4** was dissolved in 2 mL of Pyr and 1 mL of Ac_2O, and the solution was stirred for 17 h. The reaction mixture was worked up as in the preceding experiment to give an oily reaction product that crystallized from Et_2O to give 30 mg of **7** as colorless prisms: mp 116–117 °C (lit.[10] mp 115–116 °C); $[\alpha]^{25}_D$ +196° (*c* 0.1, $CHCl_3$); IR (KBr) no OH bands, 1760 (lactone C=O) and 1720 cm^{-1} (acetate C=O); MS (EI), *m/e* 290 (less than 1%, $M^{+\cdot}$), 230 (100%, $M^{+\cdot}$ – HAC).

Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.25. H, 7.62.

Deoxyperoxyparthenolide (11). A 100-mg sample of peroxyparthenolide (**8**) was reduced with 1.1 equiv (110 mg) of triphenylphosphine as was described for **2** to yield 80 mg of **11** as colorless needles: mp 158–160 °C; $[\alpha]^{25}_D$ −11° (*c* 0.1, acetone); IR (KBr) bands at 3500 (OH), 1750 (lactone C=O), and 1665 cm^{-1} (C=C); MS (EI), *m/e* 264 (6%, $M^{+\cdot}$).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.81; H, 7.89.

Acetyldeoxyperoxyparthenolide (12). A 120-mg sample of **11** was acetylated as described above for the acetylation of **4** to give 90 mg of **12** which crystallized from Et_2O to give colorless prisms: mp 126–128 °C; $[\alpha]^{25}_D$ +40° (*c* 0.11, $CHCl_3$); IR ($CHCl_3$) bands at 1770 (lactone C=O) and 1730 cm^{-1} (acetate C=O); MS (CI, isobutane), *m/e* 307 (100%, $M^{+\cdot}H$), *m/e* 229 (41%, $M^{+\cdot}H - H_2O - CH_3COOH$).

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.64; H, 7.23. Found: C, 66.37; H, 7.25.

Anhydroperoxyparthenolide (13). A 60-mg sample of peroxyparthenolide (**9**) was treated with Pyr and Ac_2O as described for the formation of **6**. The reaction product was purified through a short column of silica gel G to give **13** as an unstable colorless oil that resisted crystallization: $[\alpha]^{25}_D$ +20° (*c* 0.16, $CHCl_3$); UV λ_{max} 228 nm (ϵ 4000) and shoulder at 310 nm (ϵ 38); IR ($CHCl_3$), no OH bands, 1775 (lactone C=O), and 1671 cm^{-1} (ketone C=O); MS (EI), *m/e* 262 (2%, $M^{+\cdot}$).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68, H, 6.91. Found: C, 68.77; H, 7.01.

Methylperoxyparthenolide (14). A 50-mg sample of peroxyparthenolide (**9**) was methylated with CH_3I and Ag_2O as described above for methylperoxycostunolide (**5**). The methylated product was obtained as colorless needles: mp 155 °C dec; $[\alpha]^{25}_D$ +34° (*c* 0.15, $CHCl_3$); IR ($CHCl_3$), no OH bands, 1770 (lactone C=O) and 1665 cm^{-1} (C=C); MS, no parent ion peak in EI or CI (isobutane) spectra; the EI spectrum showed peaks at *m/e* 263 (7%, $M^{+\cdot} - OCH_3$) and 247 (10%, $M^{+\cdot} - OOCH_3$).

Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.42, H, 7.72.

Photooxygenation of Costunolide (1) to 2. A 200-mg sample of **1** and 7 mg of methylene blue were dissolved in 10 mL of absolute EtOH placed in a Dudley bubbling tube connected to an oxygen source. Oxygen was gently passed through the solution. The reaction tube was placed into a 4 L silver-lined Dewar flask 10 cm from a Sylvania DWY 650 W quartz-halogen lamp. Cooling water passed into the Dewar maintained the temperature at 17 ± 1 °C. The reaction was monitored by TLC, and after 1 h all of **1** had reacted. The reaction mixture was worked up by evaporating the solvent, and the crystaline residue was dissolved in $CHCl_3$ and passed through a short column of silica gel 60 to remove the dye. Evaporation of the colorless filtrate and crystallization of the residue from Et_2O provided 163 mg of peroxycostunolide (**2**), identical (IR, UV, NMR, TLC, mp, and $[\alpha]_D$) with the natural material.

Photooxygenation of Parthenolide (8) to 9. Parthenolide (**8**) (200 mg) was photooxygenated as described for the photooxygenation of costunolide (**1**) to **2**. The product was crystallized from acetone–Et_2O to give peroxyparthenolide (**9**), identical with the natural material.

Peroxydihydrocostunolide (3). Dihydrocostunolide[2] (**15**) (250 mg) and methylene blue (10 mg) were dissolved in 25 mL of absolute EtOH, and the solution was photooxygenated as described above except that the reaction was allowed to go for 2 h. The dye-free reaction product was crystallized from Et_2O to give 190 mg of colorless needles of **3**: softening without melting at 111–113 °C; $[\alpha]^{25}_D$ +140° (*c* 0.24, acetone); IR (KBr) bands at 3495 (OH) and 1755 cm^{-1} (lactone C=O); MS (EI), *m/e* (2%, $M^{+\cdot}$), 248 (93%, $M^{+\cdot} - H_2O$), and 233 (41%, $M^{+\cdot} - HO_2$).

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.67; H, 8.33.

Peroxydihydroparthenolide (10). Dihydroparthenolide[2] (**16**) (250 mg) was subjected to photooxygenation as described above. The product was crystallized from Et_2O to give 195 mg of colorless needles of **10**: softening without melting at 112 °C; $[\alpha]^{25}_D$ +6° (*c* 0.22, acetone); IR (KBr) bands at 3370 (OH) and 1760 cm^{-1} (lactone C=O); MS (EI), *m/e* (10%, M^+O) 264 (55%, $M^{+\cdot} - H_2O$) and 249 (47%, $M^{+\cdot} - HO_2$).

Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.86. Found: C, 63.90; H, 7.81.

11,13-Dideuteriocostunolide (17). Costunolide (**1**) (300 mg) was dissolved in 10 mL of MeOH-d_4, and the solution was stirred at room temperature with 130 mg of $NaBD_4$. After 45 min, the mixture was acifidied with 10% HAc then extracted with $CHCl_3$. The chloroformic extract was washed with H_2O, 5% $NaHCO_3$, and H_2O again, dried over anhydrous Na_2SO_4, and evaporated to give an oily residue. Examination of this residue on TLC, using silica gel G and 7% EtOH in $CHCl_3$ as solvent, revealed one major spot R_f 0.75 and a minor more polar spot (R_f 0.15). Passage through a short column of silica gel G removed the more polar impurity, and the pure material was crystallized from *n*-hexane to give colorless needles (220 mg) of **19**, mp 75–76 °C. The ^1H NMR ($CDCl_3$) spectrum was essentially the same as that of dihydrocostunolide[2] (**15**) except for the presence of a broad 2-proton singlet at δ 1.23 due to H-13. The MS (EI) clearly showed the introduction of two deuterium atoms by exhibiting a molecular ion peak at *m/e* 236 (17%).

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