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BIOMIMETIC TRANSFORMATIONS OF PARTHENOLIDE

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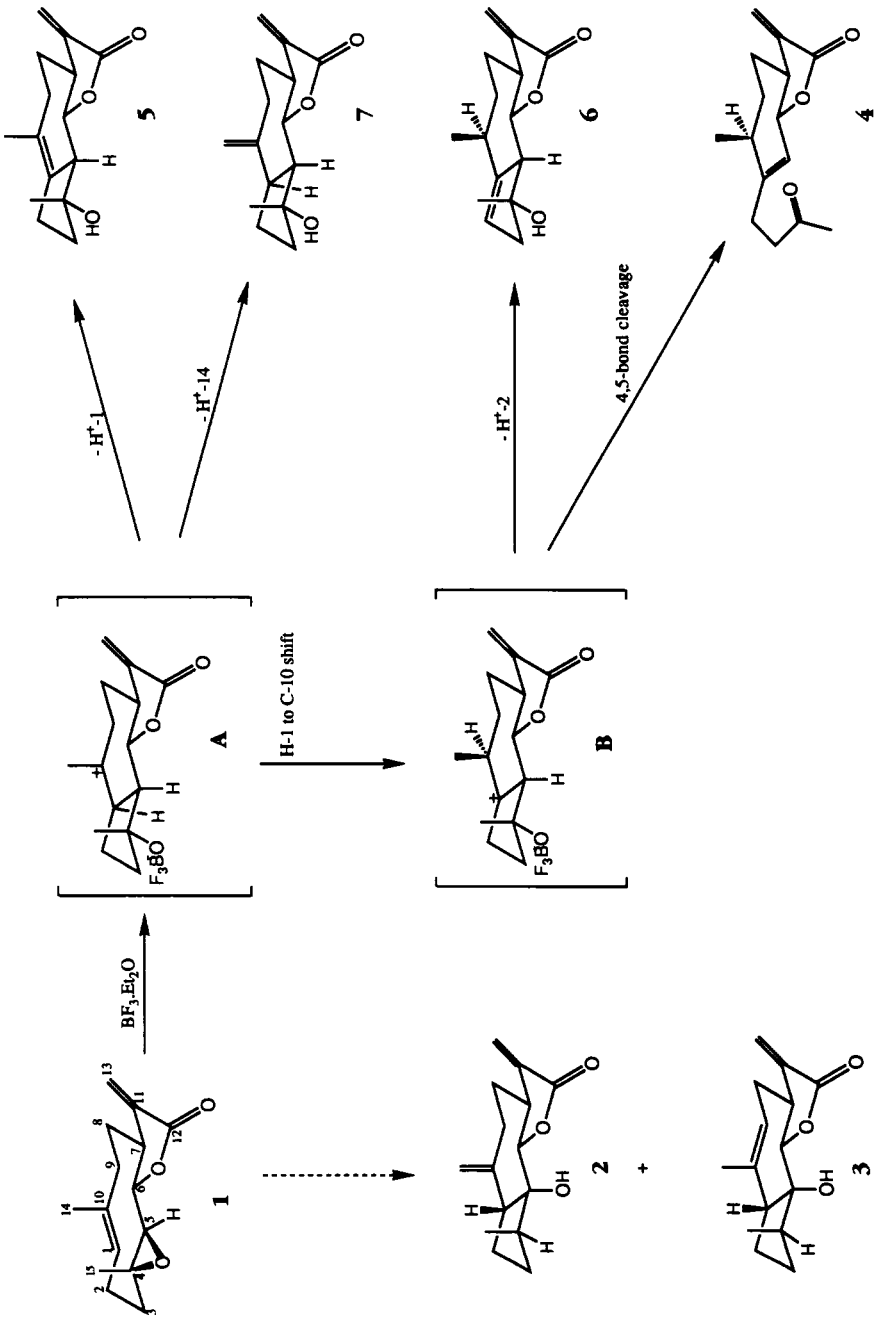
ABSTRACT.—An investigation of BF_3-mediated rearrangements of parthenolide [**1**] provided micheliolide [**5**] as a major product. Minor reaction products included 10(14)-dehydro-5α-hydroxy-*trans*-guaianolide [**2**], 9,10-dehydro-5α-hydroxy-*trans*-guaianolide [**3**], the xanthanolide 2-desoxy-6-*epi*-parthemollin [**4**], 1,2-dehydro-4α-hydroxyguaianolide [**6**], 11,13-dehydrocompressanolide [**7**], and bicyclo[6.2.0]dec-10(14)-en-12,6-olide [**8**]. Their mechanisms of formation were interpreted as rearrangements involving carbocation intermediates.

In recent years, the well-known 4,5-epoxygermacranolide, parthenolide [**1**], has attracted considerable attention for two major reasons. A biogenetic hypothesis (1) proposes that it plays a central role in the biosynthesis of guaianolide- and seco-guaianolide (xanthanolide)-type sesquiterpene lactones. Furthermore, parthenolide exhibits a wide spectrum of biological activities which include cytotoxic, antibacterial, and antifungal activity (2), and it causes experimental allergic contact dermatitis in humans (3). Recent reports on its anti-inflammatory activity (4), anti-rheumatoid-arthritis activity (5), and its action as the active principle in European feverfew (*Tanacetum parthenium*), which is in popular use for the prophylactic treatment of migraine headaches (6,7), have generated renewed interest in this sesquiterpene lactone.

For several centuries, European feverfew (*T. parthenium*) has been used for the prophylactic treatment of migraine. We have recently analyzed three feverfew products, which are locally sold in health food stores for the prophylaxis of migraine (B. Pascual-Teresa and N.H. Fischer, unpublished). Only in one product, which was advertised as European feverfew, was parthenolide detected. In the other two samples no parthenolide was found. Part of the existing problem of varying product quality seems to be related to the fact that the name feverfew is often used for different plant species, depending on the country or region. For instance, in the Southeastern United States the common feverfew refers to members of the genus *Parthenium* (Asteraceae, Heliantheae). Recently, two placebo-controlled trials established the potential of feverfew as a prophylactic against migraine (6,7) with reduction of the frequency and severity of migraine attacks and in the degree of vomiting. Since parthenolide [**1**] is the predominant sesquiterpene lactone in European feverfew and a potent inhibitor of human platelet aggregation and degranulation (8), it is considered to be its major antimigraine principle (9).

Our interest in parthenolide is twofold. First, biomimetic transformations of key sesquiterpene lactones allow for testing biogenetic proposals by indirect chemical evidence based on mechanistic arguments (10). Second, recent findings in our laboratory have shown that germacranolide-type sesquiterpene lactones act as potent germination stimulants of witchweed (*Striga asiatica*) (11), a parasite of major crop plants (corn, wheat, sorghum, rice, millet, and sugar cane), which causes severe reductions in yields of major staple crops in Africa and Asia (12). A potential method of witchweed control involves the use of germination stimulants to promote seed germination in the absence of a suitable host, which results in death of the witchweed seedling. Parthenolide [**1**] induced germination of witchweed (42–54%) over a broad concentration range from 10^{-5} to 10^{-9} M (11).



SCHEME 1. BF_3-Initiated rearrangements of parthenolide [1].

Parthenolide [**1**] is assumed to be a key intermediate in the formation of guaianolide-type sesquiterpene lactones (1). Due to the ease of intramolecular cyclization of **1**, these cyclization products could possibly play a role in the bioactivity as well. In order to test the major cyclization products for activity against migraine headache and germination stimulation of *Striga*, we performed the BF_3-mediated cyclization of parthenolide. Structure-activity studies within this series will hopefully lead to a better understanding of the mechanism of action and the specific structural requirements for their bioactivities.

RESULTS AND DISCUSSION

Parthenolide [**1**] was isolated from local *Magnolia grandiflora* L. (Magnoliaceae) (13). Its structure had been previously described by spectral (13–15) and X-ray analysis (16), and its nmr spectra were unambiguously assigned using modern 2D nmr methods (17). Cyclization of parthenolide [**1**] using BF_3 in C_6H_6 provided micheliolide [**5**] (18) as the major product, four other guaianolides, and a xanthanolide and a bicyclo[6.2.0]decanolide **8** as minor compounds (Scheme 1).

The structure of micheliolide [**5**] was unambiguously established by comparison of its spectroscopic data with those reported in the literature (15). Since the ^{13}C-nmr spectrum of **5** had not been previously reported, the data assigned on the basis of its 2D ^1H-^1H and 2D ^1H-^{13}C COSY analyses are included in Table 2.

11,13-Dehydrocompressanolide [**7**] exhibited a ^1H-nmr spectrum similar to that of compressanolide (10,15), except for the lactonic exocyclic methylene absorptions. The ^1H and ^{13}C assignments, which were obtained by ^1H-^1H and ^1H-^{13}C- correlation experiments, are summarized in Tables 1 and 2, repectively.

Inspection of the ^1H-nmr spectrum of guaianolide **6** indicated the presence of an olefinic proton at δ 5.44, a three-proton singlet assigned to the 4-Me (δ 1.31) geminal to a hydroxyl group, and another methyl absorption which appeared as a doublet at δ 1.13. The ^{13}C-nmr spectrum exhibited two olefinic signals at δ 123.0 and 145.5 due to a methine and a quaternary carbon, respectively. Application of the 2D ^1H-^1H COSY combined with the inverse 2D ^1H-^{13}C correlation method (19) established that the double bond was at the C-1(2) position, which was further confirmed by inverse long-range ^1H-^{13}C correlation (HMBC) (20).

2-Desoxy-6-*epi*-parthemollin [**4**] had strong ir absorption bands at 1711 (ketone) and 1767 cm^{-1} (α,β-unsaturated γ-lactone). The eims showed a parent peak at *m/z* 248 and a base peak at *m/z* 190 $[M-C_3H_6O]^+$ and exhibited major peaks at *m/z* 230 $[M-H_2O]^+$, 215 $[M-Me-H_2O]^+$, 206 $[M-C_2H_2O]^+$, and 175 $[M-C_3H_6O-Me]^+$. The presence of a methyl ketone moiety was supported by a three-proton singlet at δ 2.17 and a ^{13}C-nmr signal (q) at δ 30.0. Since the spectroscopic data, with the exception of the methylene lactone portion, were very similar to those of the corresponding 11βH,13-dihydrocompound (10), stereostructure **4** was assigned to this xanthanolide.

Inspection of the ^1H-nmr spectrum of guaianolide **2** showed H-6 as a doublet at δ 4.01 ($J=9.8$ Hz), suggesting that no proton was present at C-5. In addition, the spectrum lacked the characteristic absorption for the C-4 methyl group geminal to the hydroxyl as in compounds **5**, **6**, and **7**. Instead, two olefinic proton signals at δ 5.06 and δ 5.14, as well as a carbon absorption due to an oxygen-bearing quaternary carbon (C-5, δ 78.9), were observed. The methylene group could be attached to either the C-4 or C-10 position. Using the ^1H-^1H COSY and NOESY experiments, the attachment could be unambiguously established. One of the exocyclic olefinic methylene protons (δ 5.14) exhibited nOe with H-9, and the other (δ 5.06) with H-2, and weaker interactions were

TABLE 1. ^{1}H-nmr Chemical Shifts of Compounds **1–8** in $CDCl_3$.

Proton	Compound							
	1	**2**[a]	**3**	**4**	**5**	**6**	**7**	**8**
H-1	5.21 (dd, 11.6, 2.4)	2.43 (dd, 11.6, 7.9)	2.65 (dd, 9.8, 9.2)	—	—	—	3.02 (ddd, 12.1, 8.7, 8.7)	2.82 (dd, 11, 9.8)
H-2	2.35–2.48	2.02 (dddd, 12.2, 12.2, 10.4, 7.9)	2.00 (m)	2.32 (m)	2.21 (m)	5.44	1.76–1.86	2.10 (m)
H-2′	2.11–2.24	1.77 (m)	2.14 (m)	2.32 (m)	2.39 (ddd, 15.9, 8.5, 8.5)	—	1.76–1.86	1.93 (m)
H-3	1.25 m	1.28 (dddd, 14, 12.2, 8.5, 3.1)	1.28 (m)	2.56 (m)	1.82 (m)	2.57 (dd, 15.9, 2.4)	1.76–1.86	1.67 (m)
H-3′	2.11–2.24	2.26 (m o)	2.23 (m)	2.56 (m)	1.77 (m)	2.32 (dd, 15.9, 1.3)	1.89 (m o)	1.95 (m)
H-4	—	2.38 (m o)	2.27 (m)	—	—	—	—	—
H-5	2.78 (d, 8.5)	—	—	5.67 (d, 2.2)	2.73 (d, 10.3)	2.91 (d, 11.0)	2.37 (dd, 11.9, 11.9)	3.72 (d, 9.8)
H-6	3.86 (dd, 9.2, 8.5)	4.01 (d, 9.8)	4.01 (d, 10.5)	4.75 (dd, 10.3, 2.2)	3.81 (t, 10.3)	4.23 (dd, 11.0, 9.6)	4.05 (dd, 11.4, 11.3)	4.13 (dd, 9.8, 9.8)
H-7	2.78 (m o)	2.96 (ddddd, 11, 9.8, 7.3, 3.7, 3.1)	3.02 (ddddd, 10.5, 9.2, 3.3, 3.1)	2.50 (m)	2.65 (m)	2.98 (ddddd, 11, 6.7, 3.7, 3.1)	2.76 (ddddd, 11.3, 8.6, 3.2, 3.2, 3)	2.91 (ddddd, 11.6, 9.8, 6.1, 3.7, 3.1)
H-8	1.74 (m)	1.58 (dddd, 14, 11.9, 9.2, 6.7)	2.48 (ddd, 15.4, 9.2, 1.7)	2.13 (m)	2.09 (dddd, 13.6, 10, 3.9, 2.3)	2.22 (dddd, 16.5, 10.4, 6.7, 3.1)	1.38 (m)	1.59 (m)
H-8′	2.11–2.24	2.19 (dddd, 14, 9.2, 7.3, 3.7)	1.95 (m)	2.29 (m)	1.35 (m)	1.58 (dddd, 14, 10.4, 6.7, 3.1)	2.25 (dddd, 13.2, 7.3, 3.7, 3.7)	2.11 (m)
H-9	2.11–2.24	2.35 (m o)	5.81	1.70 (m)	2.25 (m)	1.39 (m)	1.93	2.16 (m)
H-9′	2.35–2.48	2.61 (ddd, 14.7, 9.2, 6.7)		1.76 (m)	2.25 (m)	1.74 (m)	2.68 (ddd, 13, 3.8, 3.8)	2.57 (ddd, 14.6, 8.5, 2.4)
H-10	—	—	—	—	—	2.32 (m o)	—	—
H-13	6.34 (d, 3.7)	6.21 (d, 3.7)	6.18 (d, 3.3)	6.17 (d, 3.2)	6.21 (d, 3.5)	6.21 (d, 3.7)	6.23 (d, 3.6)	6.31 (d, 3.7)
H-13	5.62 (d, 3.1)	5.47 (d, 3.1)	5.47 (d, 3.1)	5.46 (d, 3.1)	5.50 (d, 3.2)	5.51 (d, 3.1)	5.52 (d, 3.1)	5.58 (d, 3.1)
H-14	1.72 (br s)	5.14 (br s) 5.06 (br s)	1.82 (br s)	1.09 (d, 7.4)	1.68 (br s)	1.13 (d, 7.3)	5.00 (br s) 4.97 (br s)	5.02 (br s) 4.79 (br s)
H-15	1.31 (s)	1.06 (d, 7.3)	1.07 (d, 6.9)	2.18 (s)	1.30 (s)	1.41 (s)	1.31 (s)	1.09 (s)

[a] ^{1}H-nmr chemical shifts of the trichloroacetyl isocyanate derivative (only the shifts > δ 0.05 are given): δ 1.34 (H-3), 3.38 (H-4), 4.20 (H-6), 3.22 (H-7), 2.43 (H-9α), 1.23 (H-15).

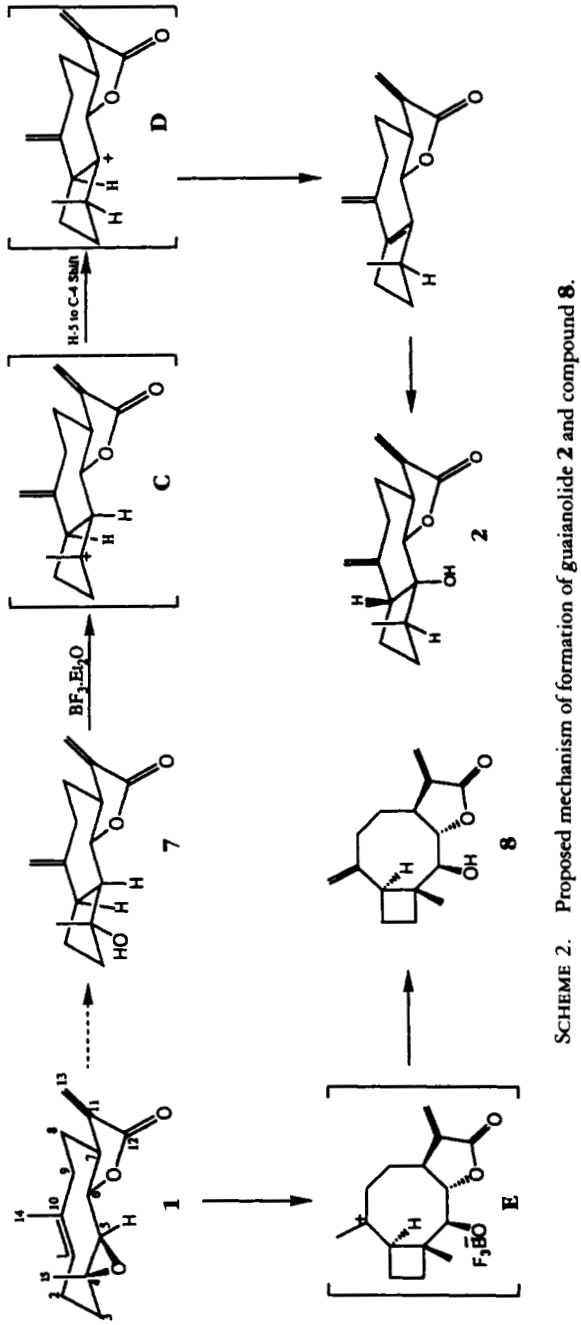
observed with H-1, H-2′, and H-8. The methyl signal (H-15) showed nOe with H-1, H-3β, H-2β, and H-6. This information suggested that the exocyclic methylene is in the 10(14) position. Inverse long-range ^{1}H-^{13}C correlation (20) showed coupling of the 4-Me protons to C-3, C-4, and C-5, and the exocyclic methylene protons (H-14) were coupled to C-1 and C-9. This was in full agreement with a guaianolide structure bearing a 10(14)-methylene group. Assignment of the configuration of the C-5 hydroxyl group in **2** was based on mechanistic as well as ^{1}H-nmr spectral arguments. Guaianolides with a 5β-oxygen function cause a distinct downfield shift of the lactonic H-6β to ca. 5 ppm (21), but in guaianolide **2** H-6 appeared at δ 4.01. Based on the above arguments, a C-5α hydroxyl group was suggested. This was strongly supported by ^{1}H-nmr chemical shift data of the trichloroacetyl carbamate derivative (22) of **2**, in which the signal of H-4 appeared at δ 3.38 (see Table 1). This dramatic downfield shift of H-4 from δ 2.38 in **2** to 3.38 in its carbamate derivative together with an effect of Δ δ 0.26 upon H-7α clearly indicated an α orientation of the C-5 hydroxyl group in **2**.

Compound **3** exhibited a ^{1}H-nmr spectrum similar to that of guaianolide **2**. The major difference between **2** and **3** was that **3** lacked the signals for the exocyclic methylene protons at C-14. Instead, absorptions for a methyl group on a double bond at δ 1.82 and an olefinic proton at δ 5.81 appeared in compound **3**. The ^{1}H-^{1}H COSY spectrum of **3** indicated coupling between the olefinic proton (H-9) and H-8, which in turn was coupled to H-7. Furthermore, the distinct H-6 doublet at δ 4.01 showed nOe with H-1 and the 4-Me protons, suggesting that H-1 and the 4-Me group are β-oriented, as is H-6. Based on the above data, stereostructure **3** was assigned to this compound.

The spectral data of compound **8** suggested a ring skeleton very similar to the previously described bicyclo[6.2.0]decanolides (10,23). The eims of **8** exhibited a parent peak at *m/z* 248 and strong ir absorptions for hydroxyl at 3478 cm^{-1} and an α,β-unsaturated γ-lactone at 1764 cm^{-1}. The COSY spectrum indicated that H-5 to H-9 corresponded to a structural arrangement also found in the starting parthenolide [**1**]. Since H-5 only coupled to the lactonic H-6, C-4 had to be a quaternary carbon. This was supported by a quaternary carbon signal at 42.7, which was part of a cyclobutane ring, as established by comparison of the ^{13}C-nmr resonances of similar four-membered ring

TABLE 2. ^{13}C-nmr Assignments for Compounds **1–8** in $CDCl_3$.

Carbon	Compound							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
C-1	125.2 d	49.2 d	46.0 d	146.0 s	131.9 s	145.5 s	44.0 d	43.1 d
C-2	24.1 t	26.5 t	30.9 t	33.1 t	35.0 t	123.0 d	26.2 t	21.3 t
C-3	36.3 t	30.8 t	25.1 t	41.7 t	38.3 t	32.8 t	40.2 t	31.8 t
C-4	61.5 s	43.3 d	40.1 d	207.7 s	80.3 s	81.7 s	79.7 s	42.7 s
C-5	66.3 d	78.9 s	80.4 s	123.8 d	58.7 d	64.0 d	55.7 d	83.6 d
C-6	82.4 d	86.4 d	88.4 d	81.4 d	84.5 d	81.0 d	84.1 d	85.3 d
C-7	47.6 d	38.1 d	45.0 d	47.8 d	49.6 d	43.9 d	47.3 d	44.8 d
C-8	30.6 t	24.7 t	26.5 t	30.9 t	25.8 t	25.9 t	31.4 t	31.7 t
C-9	41.1 t	34.9 t	123.8 d	24.0 t	30.1 t	31.6 t	39.3 t	38.7 t
C-10	134.6 s	144.1 s	137.4 s	37.6 d	130.9 s	46.0 d	148.0 s	147.2 s
C-11	139.2 s	139.8 s	139.4 s	140.0 s	138.8 s	139.8 s	138.7 s	131.9 s
C-12	169.2 s	170.2 s	170.2 s	169.8 s	169.8 s	170.0 s	169.7 s	168.6 s
C-13	121.1 t	119.6 t	118.4 t	118.8 t	119.5 t	120.1 t	120.8 t	121.7 t
C-14	16.9 q	114.9 t	19.0 q	15.8 q	22.7 q	20.9 q	112.6 t	113.2 t
C-15	17.2 q	19.0 q	25.4 q	30.0 q	23.9 q	24.5 q	23.9 q	15.4 q



SCHEME 2. Proposed mechanism of formation of guaianolide **2** and compound **8**.

lactones (10,23). Another coupling sequence (H-1 to H-3) supported the arrangement of H-1 and two pairs of geminally coupled protons (H-2 and H-3) which must be part of the cyclobutane moiety in **8**. Two olefinic proton absorptions at 4.79 and 5.02 together with arrangement of H-1 and two pairs of geminally coupled protons (H-2 and H-3) must be part of the cyclobutane moiety in **8**. Two olefinic proton absorptions at 4.79 and 5.02 together with two carbon signals, a triplet at 113.2 and a singlet at 147.2, suggested an olefinic 10 (14) bond. The above data of **8** compare very favorably with previously reported spectral values for an analogue ring skeleton (23). Formation of compound **8** from parthenolide is outlined in Scheme 2.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Thomas Hoover apparatus and are uncorrected. Spectra were recorded on the following instruments: nmr, Bruker AM 400 (400 MHz), Bruker WP 200 (200 MHz); ir, Perkin Elmer 1760X FT-IR; ms, HP-5985 gc-ms-ds. Hplc separations were performed on a Hewlett-Packard 1090 liquid chromatograph equipped with diode array detector, and the detection channel was set at 230 nm. The column was a 10-μm Rsil C18 (250 × 10 mm i.d., Alltech). The separations were performed at ambient temperature with a flow rate of 2.0 ml/min. Two solvents were used: hplc-grade MeOH and distilled, deionized H_2O. Compounds were eluted isocratically with 55% of MeOH. Parthenolide [**1**] was isolated from local Grand Magnolia (*M. grandiflora*) by a previously described method (24). The plant material was collected on May 26, 1992, in East Baton Rouge Parish, Louisiana (N.H. Fischer No 440; voucher deposited at LSU).

BF_3-CATALYZED REARRANGEMENT OF PARTHENOLIDE [**1**].—A solution of **1** (722 mg) in 20 ml of C_6H_6 was treated with 140 μl of freshly distilled BF_3-etherate (25,26). The resulting mixture was allowed to stand at room temperature for 45 min; then EtOAc (20 ml) was added and the mixture extracted with 5% aqueous $NaHCO_3$ (200 ml), washed with H_2O (300 ml), dried ($MgSO_4$), and evaporated in vacuo to give 474 mg of a crude mixture. The gummy material was chromatographed in Lobar column size B (Si gel 60G, E. Merck), using mixtures of hexane/EtOAc. Rechromatography by hplc of fractions 34–37 gave pure **4** (6.3 mg) and **8** (1.2 mg). Recrystallization of fractions 40–50 using hexane/EtOAc yielded pure **5** (94 mg). Hplc of fractions 55–64 provided pure **6** (8.2 mg), and fractions 82–99 gave 12 mg of **7**.

Parthenolide [**1**].—$C_{15}H_{20}O_3$; mol wt 248; colorless crystals; mp 105–108° [lit. (14) mp 115°]; eims *m/z* (% rel. int.) $[M]^+$ 248 (0.5), $[M-Me]^+$ 233 (2.5), $[M-H_2O]^+$ 230 (2.1), $[M-Me-H_2O]^+$ 215 (3.8), $[M-Me-CO]^+$ 205 (4.7), $[M-C_3H_6O]^+$ 190 (29.4), 175 (16.7), 163 (22.6), $[M-C_3H_4O-Me-H_2O]^+$ 159 (11.7), 149, 147, 145 (25.6), 131, 121, 119, $[C_9H_9]^+$ 117, 109 (24.2), 107 (24.0), 105 (26.6), 97, 95 (46.1), 93 (31.8), 91 (32.8), 81 (51.4), 79 (38.1), 77 (20.6), 69, 67, 55 (37.0), $[C_4H_5]^+$ 53 (55.5), $[MeCO]^+$ 43 (100.0); ir ν max (neat) 1768 (α,β-unsaturated γ-lactone), 1601, 1462, 1263, 1098.

10(14)-Dehydro-5α-hydroxy-trans-guaianolide [**2**].—Compound **2**: $C_{15}H_{20}O_3$; mol wt 248; crystals; mp 129–131°; eims *m/z* (% rel. int.) $[M]^+$ 248 (62.3), $[M-Me]^+$ 233 (4.8), $[M-H_2O]^+$ 230 (12.8), $[M-Me-H_2O]^+$ 215 (8.4), $[M-Me-CO]^+$ 205 (42.5), 192 (13.6), 187 (13.4), 177 (15.5), 163 (17.5), 150 (24.4), 131 (28.2), 109 (29.4), 107 (33.9), 105 (35.9), 91 (62.3), 81 (76), 79 (73.2), 77 (48.8), 69 (45.9), 67 (60.4), 55 (79.8), $[C_4H_5]^+$ 53 (93.2), 41 (100); ir ν max (neat) 3517 (OH), 1765 (α,β-unsaturated γ-lactone), 1461, 1408, 1261.

9,10-Dehydro-5α-hydroxy-trans-guaianolide [**3**].—Compound **3**: $C_{15}H_{20}O_3$; mol wt 248; gum; eims *m/z* (% rel. int.) $[M]^+$ 248 (11.5), $[M-Me]^+$ 233 (6.5), $[M-H_2O]^+$ 230 (100.0), $[M-Me-H_2O]^+$ 215 (20.4), $[M-C_2H_2O]^+$ 206 (4.9), $[M-Me-CO]^+$ 205 (14.2), $[M-H_2O-CO]^+$ 202 (17.1), 191 (20.0), 187 (18.8), 163 (20.3), $[M-C_3H_4O-Me-H_2O]^+$ 159 (20.0), 150 (69.4), 145 (20.7), 136 (20.1), 133 (16.3), 131 (17.5), 121 (47.2), $[C_9H_9]^+$ 117 (17.5), 109 (32.9), 107 (32.7), 105 (23.9), 95 (30.9), 93 (31.4), 91 (36.2), 81 (58.2), 79 (44.4), 77 (29.2), 69 (25.6), 67 (27.2), 55 (38.0), $[C_4H_5]^+$ 53 (27.1), $[MeCO]^+$ 43 (21.8), 41 (38.3).

2-Desoxy-6-epi-parthemollin [**4**].—Compound **4**: $C_{15}H_{20}O_3$; mol wt 248; gum; eims *m/z* (% rel. int.) $[M]^+$ 248 (1.0), $[M-Me]^+$ 233 (1.2), $[M-H_2O]^+$ 230 (9.0), $[M-Me-H_2O]^+$ 215 (3.8), $[M-C_2H_2O]^+$ 206 (8.4), $[M-C_3H_6O]^+$ 190 (100), $[M-C_3H_6O-Me]^+$ 175 (10.8), 145 (12.9), 131 (9.1), 109 (5.9), 107 (6.7), 105 (11.6), 91 (12.3), 81 (8.0), 79 (9.8), 77 (8.4), 67 (8.5), 55 (8.5), $[C_4H_5]^+$ 53 (10.6), $[MeCO]^+$ 43 (46); ir ν max (neat) 1767 (α,β-unsaturated γ-lactone), 1711 (C=O), 1453, 1365, 1000.

Micheliolide [**5**].—Compound **5**: $C_{15}H_{20}O_3$; mol wt 248; colorless crystals; mp 142–145° [lit. (15)

mp 141°]; eims *m/z* (% rel. int.) $[M]^+$ 248 (12.8), $[M-Me]^+$ 233 (9.0), $[M-H_2O]^+$ 230 (36.8), $[M-Me-H_2O]^+$ 215 (29.2), $[M-C_3H_6O]^+$ 190 (79.7), $[M-C_3H_6O-Me]^+$ 175 (28.5), $[M-C_3H_6O-Me-H_2O]^+$ 157 (6.9), 145 (66.6), 105 (46.1), 91 (40.6), $[C_4H_5]^+$ 53 (38.6), $[MeCO]^+$ 43 (100); ir ν max (neat) 3541 (OH), 1763 (α,β-unsaturated γ-lactone), 1260, 992, 950.

1,2-Dehydro-4α-hydroxyguaianolide [**6**].—Compound **6**: $C_{15}H_{20}O_3$; mol wt 248; gum; eims *m/z* (% rel. int.) $[M]^+$ 248 (6.2), $[M-Me]^+$ 233 (5.6), $[M-H_2O]^+$ 230 (25.5), $[M-Me-H_2O]^+$ 215 (9.8), $[M-C_2H_2O]^+$ 206 (17.0), $[M-H_2O-CO]^+$ 202 (23.5), $[M-C_3H_6O]^+$ 190 (81.4), 160 (21.8), $[M-C_3H_4O-Me-H_2O]^+$ 159 (24.5), 145 (26.4), 131 (21.2), 105 (25.8), 91 (31.2), 79 (24.9), 77 (20.1), 55 (22.8), 53 $[C_4H_5]^+$ (22.1), $[MeCO]^+$ 43 (100), 41 (23.4); ir ν max (neat) 3520 (OH), 1766 (α,β-unsaturated γ-lactone) 1653, 1458, 1260, 1139, 999, 756.

11,13-Dehydrocompressanolide [**7**].—Compound **7**: $C_{15}H_{20}O_3$; mol wt 248; gum; eims *m/z* (% rel. int.) $[M]^+$ 248 (2.7), $[M-Me]^+$ 233 (5.8), $[M-H_2O]^+$ 230 (20.1), $[M-Me-H_2O]^+$ 215 (7.9), $[M-C_3H_6O]^+$ 190 (26.6), 175 (8.9), $[M-C_3H_4O-Me-H_2O]^+$ 159 (8.8), 150 (18.3), 145 (24.2), 131 (17.5), $[C_9H_9]^+$ 117 (15.8), 105 (26.5), 91 (38.1), 71 (50.9), $[C_4H_5]^+$ 53 (35.6), $[MeCO]^+$ 43 (100); ir ν max (neat) 3588 (OH), 1766 (α,β-unsaturated γ-lactone), 1644, 1459, 1258, 911, 735.

Bicyclo[6.2.0]dec-10(14)-en-12,6-olide [**8**].—Compound **8**: $C_{15}H_{22}O_2$; mol wt 248; gum; eims *m/z* (% rel. int.) $[M]^+$ 248 (1.8), $[M-H]^+$ 247 (11.5), $[M-Me]^+$ 233 (20), $[M-H_2O]^+$ 230 (21), $[M-Me-H_2O]^+$ 215 (5.8), 202 (23.2), 133 (11.1), 131 (21.4), 129 (22.2), 117 (62.4), 105 (21.5), 97 (40.5), 91 (100), 83 (36.6), 81 (41.3), 71 (40), 55 (76.2), 43 (81.5); ir ν max (neat) 3478 (OH), 1764 (α,β-unsaturated γ-lactone), 1638, 1454, 1273, 1136, 993, 733.

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