Isolation and Structures of Euphohelins, New Toxic Diterpenes from *Euphorbia Helioscopia* L.

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Five new toxic diterpenes, euphohelins A, B, C, D, and E, have been isolated from the plant *Euphorbia helioscopia* L., and their stereostructures have also been elucidated on the basis of their spectral data coupled with some chemical evidence: euphornin, the known toxic diterpene, has been successfully converted into euphohelin A.

In connection with highly-oxygenated diterpenes which have antitumor activity or promote cancer development in tumor formation, we examined toxic substances of the plants *Euphorbiaceae* and could isolate euphoscopin A (**1**),[1,2] euphornin (**2**),[3] euphohelioscopin A (**3**),[2] euphohelionone (**4**),[4] and others from the plant *Euphorbia helioscopia* L. (Todai-Gusa in Japanese), as seen in Fig. 1. Further investigation of toxic compounds in the same plant resulted in the isolation of five new diterpenes, euphohelins A, B, C, D, and E (**5**, **6**, **7**, **8**, and **9**) in addition to the known diterpenes (**1**, **2**, and **3**) and others.[1-3]

Isolation of Euphohelins A, B, C, D, and E. Fresh leaves and roots of the plant *Euphorbia helioscopia* L. collected in Kanagawa Prefecture in the middle of June were immersed in methanol at room temperature, and then the methanol extract was concentrated and shaken with ethyl acetate. The ethyl acetate extract was partitioned between 90% aqueous methanol and "isooctane". The methanol extract was roughly separated by column chromatography [silica gel (Merck 7734)] using a gradient solution of hexane and ethyl acetate. The fraction eluted only with ethyl acetate was further separated by repeating preparative TLC (Kieselgen PF_{254}) using hexane-ethyl acetate

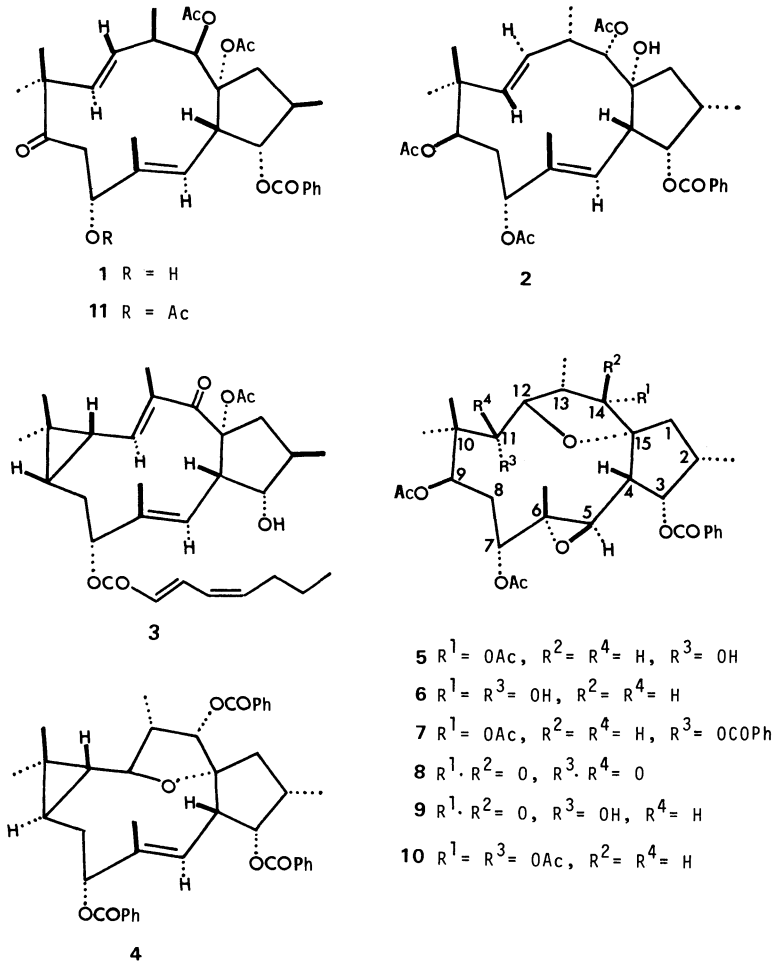


Fig. 1. Toxic diterpenes from *Euphorbia helioscopia* L.

Table 1. ^{1}H NMR Spectral data of euphohelins A (5), B (6), C (7), D (8), and E (9) and euphohelin a acetate (10) (δ from TMS)

Proton	5	6	7	8	9	10
C^1-H_2	1.91—2.23*	1.79—2.40*	1.93—2.63*	1.95—2.10*	1.93—1.98*	1.87—2.63*
C^2-H	2.10(m)	2.16—2.40*	1.93—2.63*	2.39—2.50*	2.36(m)	1.87—2.63*
C^3-H	5.63 (dd, J=6.5, 4.8 Hz)	5.63 (dd, J=5.6, 5.6 Hz)	5.66 (dd, J=6.3, 4.4 Hz)	5.74 (dd, J=6.0, 4.3 Hz)	5.74 (dd, J=6.1, 4.4 Hz)	5.65 (dd, J=6.6, 4.9 Hz)
C^4-H	2.33 (dd, J=9.9, 6.5 Hz)	2.16—2.40*	1.93—2.63*	2.39—2.50*	2.46 (dd, J=9.5, 6.1 Hz)	1.87—2.63*
C^5-H	3.66 (d, J=9.9 Hz)	3.66 (d, J=9.7 Hz)	3.70 (d, J=10 Hz)	3.73 (d, J=9.5 Hz)	3.68 (d, J=9.5 Hz)	3.66 (d, J=9.8 Hz)
C^7-H	5.06—5.10*	5.05 (dd, J=3.7, 3.4 Hz)	5.13—5.20*	5.02 (br. d, J= 5.9 Hz)	5.10 (dd, J=3.7, 3.4 Hz)	5.10 br. d, J= 5.4 Hz)
C^8-H_2	1.91—1.93*	1.79—1.94*	1.93—2.63*	1.95—2.10*	1.93—1.98*	1.87—2.62*
C^9-H	6.25 (dd, J=4, 4 Hz)	6.25 (dd, J=4.4, 3.9 Hz)	6.30 (br. d, J= 6.8 Hz)	6.59 (br. d, J= 7.8 Hz)	6.36 (dd, J=4.2, 3.9 Hz)	6.22 (br. d, J= 6.8 Hz)
C^{11}-H	3.30 (d, J=9.0 Hz)	3.22 (d, J=9.0 Hz)	5.13—5.20*		3.46 (d, J=8.8 Hz)	4.89 (d, J=9.5 Hz)
C^{12}-H	3.69*	3.65 (dd, J=9.0, 5.4 Hz)	4.05 (dd, J=9.3, 7.1 Hz)	4.67 (d, J=8.5 Hz)	3.95 (dd, J=8.8, 7.3 Hz)	3.87 (dd, J=9.5, 6.8 Hz)
C^{13}-H	2.51 (m)	2.16—2.40*	1.93—2.63*	2.77 (dq, J=8.5, 7.3 Hz)	2.35 (dq, J=7.3, 7.6 Hz)	1.87—2.63*
C^{14}-H	5.06—5.10*	4.06 (d, J=8.1 Hz)	5.13—5.20*			5.15 (d, J=7.3 Hz)
C^2-Me	1.07 (d, J=6.5 Hz)	1.18 (d, J=7.3 Hz)	0.88 (d, J=7.1 Hz)	1.10 (d, J=6.8 Hz)	1.05 (d, J=6.6 Hz)	0.97 (d, J=7.1 Hz)
C^6-Me	1.36 (s)	1.31 (s)	1.52 (s)	1.41 (s)	1.12 (s)	1.45 (s)
C^{10}-Me	0.93 (s)	0.92 (s)	0.81 (s)	0.97 (s)	0.96 (s)	0.77 (s)
C^{10}-Me′	0.93 (s)	0.92 (s)	1.12 (s)	1.11 (s)	1.01 (s)	1.00 (s)
C^{13}-Me	1.09 (d, J=7.2 Hz)	1.06 (d, J=6.6 Hz)	1.06 (d, J=5.6 Hz)	1.33 (d, J=7.3 Hz)	1.41 (d, J=7.6 Hz)	1.05 (d, J=5.9 Hz)
C^3-OCOPh	7.41—7.53 (3H, m) 8.20—8.25 (2H, m)	7.41—7.54 (3H, m) 8.20—8.25 (2H, m)	7.40—7.65 (3H, m) 8.19—8.24 (2H, m)	7.45—7.61 (3H, m) 8.23—8.33 (2H, m)	7.43—7.59 (3H, m) 8.26—8.31 (2H, m)	7.39—7.57 (3H, m) 8.18—8.24 (2H, m)
C^7-OAc	1.42 (s)	1.39 (s)	1.44 (s)	1.46 (s)	1.39 (s)	1.43 (s)
C^9-OAc	2.01 (s)	2.00 (s)	2.03 (s)	2.06 (s)	2.04 (s)	2.02 (s)
C^{11}-OAc						2.09 (s)
C^{14}-OAc	2.16 (s)		2.13 (s)			2.15 (s)
C^{11}-OCOPh			7.40—7.65 (3H, m) 8.02—8.06 (3H, m)			

* Overlapped with other signals.

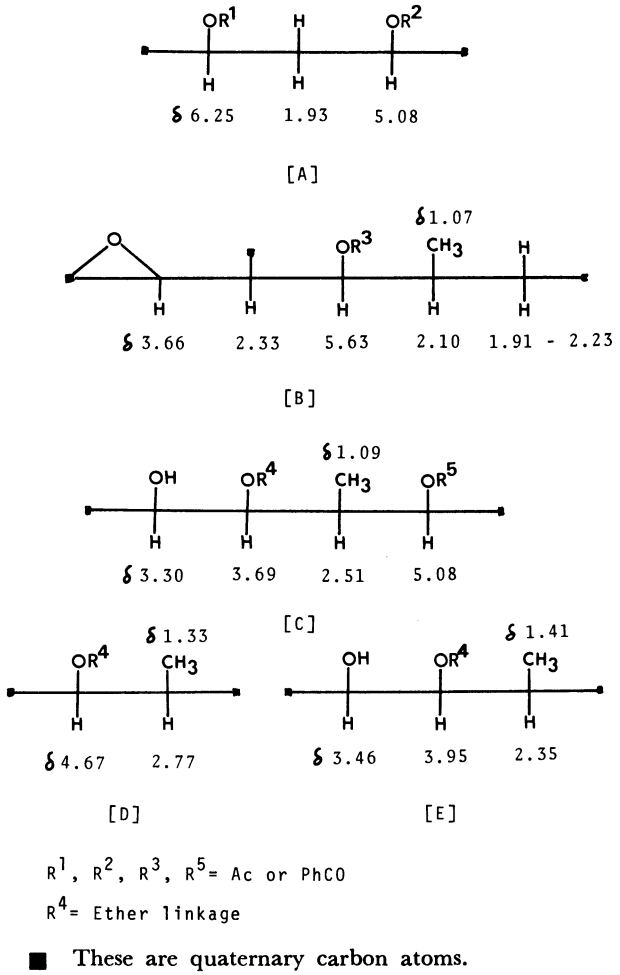
(2:1) to afford euphohelins A, B, C, D, and E (**5**, **6**, **7**, **8**, and **9**) in 0.038, 0.0035, 0.021, 0.061, and 0.0042% yields, based on the weight of the methanol extract, respectively, in addition to the known diterpenes.[1-3] The structure of these newly isolated diterpenes, which are shown in Fig. 1, have been unambiguously determined on the basis of their spectral data coupled with some chemical evidence.

The Structure of Euphohelin A (5). Euphohelin A with a molecular formula $C_{33}H_{44}O_{11}$ has the IR absorption bands at 3500, 1730, 1600, and 1580 cm^{-1}, and its ^1H and ^{13}C NMR spectral data are described in Tables 1 and 2. As seen in Table 1, euphohelin A (**5**) has one benzoyloxyl group [δ 7.41—7.53 (3H), 8.20—8.25 (2H)], three acetoxyl groups [δ 1.42 (C^7-OAc), 2.01 (C^9-OAc), 2.16 (C^{14}-OAc)] and five methyls [δ 0.93 (6H, s), 1.07 (3H, d, J=6.5 Hz), 1.09 (3H, d, J=7.2 Hz), 1.36 (3H, s)]. As judged from Table 2, furthermore, euphohelin A is regarded as a tetracyclic diterpene, because it has no sp^2 carbon atom except for ten sp^2 carbon atoms included in one benzoyloxyl and three acetoxyl groups. In addition, one of the four rings must be a trisubstituted epoxide ring on the basis of a gated decoupling experiment at δ 56.0 together with selected decoupling ones: the doublet at δ 56.0 due to the C^5 carbon atom, which has a characteristically large $^1J_{C\text{-}H}$ (178.8 Hz), is coupled with the proton (C^5-H) (δ 3.66). As seen in Table 1 and Fig. 2, a detailed analysis of the ^1H NMR spectrum of euphohelin A (**5**) by homonuclear spin decoupling experiments indicated the presence of partial structures [A], [B], and [C] and three tertiary methyls. In addition, euphohelin A has one secondary hydroxyl group, which is accommodated in [C] on the basis of the following observation: on acetylation of euphohelin A (**5**) with acetic anhydride–pyridine giving rise to the corresponding acetate (**10**), the doublet at δ 3.30 in **5** was shifted to δ 4.89 in **10**. Another important information about euphohelin A will be obtained from its ^1H NMR spectrum, as follows. One of the methyl singlets due to the three acetoxyl groups in **5** is observed in higher magnetic field (δ 1.42) rather than the remaining ones (δ 2.01

TABLE 2. ^{13}C NMR SPECTRAL DATA OF EUPHOHELINS A AND D (5 AND 8) (δ FROM TMS)

Carbon	5	8
1	40.5 (t)	43.1 (t)
2	37.4 (d)	37.4 (t)
3	76.3 (d)	77.0 (d)
4	51.0 (d)	50.8 (d)
5	56.0 (d)	54.5 (d)
6	58.7 (s)	58.3 (s)
7	70.3 (d)	69.4 (d)
8	29.7 (t)	30.6 (t)
9	71.5 (d)	69.6 (d)
10	43.2 (s)	54.8 (s)
11	78.1 (d)	208.5 (s)
12	85.3 (d)	85.4 (d)
13	41.2 (d)	42.6 (d)
14	79.5 (d)	217.7 (s)
15	90.3 (s)	89.0 (s)
Me	13.8 (q)	13.4 (q)
	14.1 (q)	15.2 (q)
	17.1 (q)	15.8 (q)
	17.3 (q)	16.9 (q)
	17.9 (q)	22.4 (q)*
AcO	19.9 (q)	19.9 (q)
	20.7 (q)	21.1 (q)
	21.2 (q)	
	169.5 (s)	169.2 (s)
	169.6 (s)	169.3 (s)
	170.4 (s)	
PhCOO	128.4 (d)**	128.4 (d)**
	130.1 (s) (d)**	129.8 (s)
	132.8 (d)	130.3 (d)**
		132.9 (d)
	165.8 (s)	165.7 (s)

* This signal is assigned tentatively. ** Corresponding to two protons.



■ These are quaternary carbon atoms.

Fig. 2. Partial structures of euphohelins.

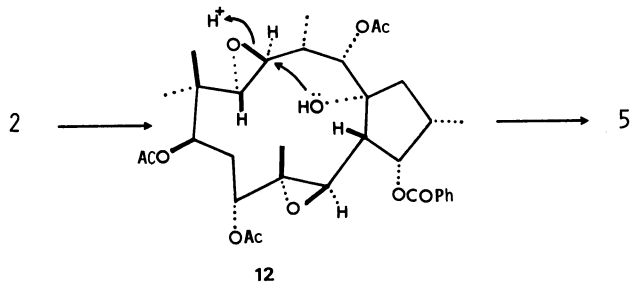


Fig. 3. Chemical conversion of euphornin (**2**) to euphohelin A (**5**).

and 2.16). This may be due to anisotropic effect of the benzoyloxyl group, as seen in the cases of euphornin (**2**)[3] and euphoscopin B (**11**).[1]

In the light of the above-mentioned results together with co-occurrence of euphoscopins A and B (**1** and **11**) and euphornin (**2**) and their ^{1}H NMR spectra, a tentative structure (**5**) is given to euphohelin A except for its stereochemistry (C^2-Me and C^{11}—C^{15}). Finally, the stereostructure of euphohelin A (**5**) was unambiguously determined in connection with euphornin (**2**), as follows.

Fortunately, euphornin (**2**), whose conformation strictly based on an X-ray crystallographic analysis, ^{1}H NMR spectrum, and molecular mechanics calculations,[3] was subjected to epoxidation using *m*-chloroperbenzoic acid in dichloromethane (room temp, 2 d) to give euphohelin A (**5**), 87% yield, through the corresponding diepoxide (**12**), as shown in Fig. 3., wherein one of the two epoxide rings was subsequently attacked by the hydroxyl group at C^{15}-position resulting in the formation of a tetrahydrofuran ring. Thus, the stereostructure of euphohelin A must be depicted as **5**, which is supported by its ^{1}H NMR spectrum: in consideration of the most plausible conformation, in which the acetoxyl group at C^7-position in **5** (δ 1.42) adopts the same situation as that in euphornin (**2**) and related diterpenes (δ 1.27—1.33), the two hydrogen atoms at C^{11}- and C^{12}-positions must be in a trans configuration having dihedral angle of 180° (J=9.0 Hz).

The Structure of Euphohelin B (6). Euphohelin B (**6**) with a molecular formula $C_{31}H_{42}O_{10}$ has the IR absorption bands at 3500, 1720, 1600, and 1580 cm^{-1}, and its ^{1}H NMR spectral data is also cited in Table 1. On a detailed comparison of the ^{1}H NMR spectra between euphohelins A and B, the NMR signal at δ 5.08 due to the proton (AcO-C^{14}-H) in **5** is not found in the latter, but instead a doublet is newly observed at δ 4.06, suggesting that euphohelin B (**6**) is a deacetyl derivative of euphohelin A (**5**) at C^{14}-position. Thus, euphohelin A was subjected to regioselective hydrolysis using one equivalent of KOH in methanol (room temp, 50 min) to afford euphohelin B (**6**) in 90% yield.

The Structure of Euphohelin C (7). Euphohelin C (**7**) has a molecular formula $C_{38}H_{46}O_{11}$ and its ^{1}H NMR spectrum indicates the presence of three acetoxyl and two benzoyloxyl groups. However, the IR spectrum of **7** has no absorption band assignable to a hydroxyl group. As seen in Table 1, the NMR signal at δ 3.30 (HO-C^{11}-H) in euphohelin A (**5**) is also not found in **7**, but instead the corresponding one is observed at δ 5.16, suggesting that euphohelin C has an additional benzoyloxyl group at C^{11}-position because the other corresponding signals are quite similar to one another. Thus, euphohelin A (**5**) was treated with benzoyl chloride in pyridine (room temp, overnight and then 60 °C, 1 h) to afford euphohelin C (**7**) in almost quantitative yield.

The Structure of Euphohelin D (8). The IR and ^{1}H NMR spectra of euphohelin D (**8**) having a molecular formula $C_{31}H_{38}O_{10}$ indicate the presence of one benzoyloxyl group and two acetoxyl groups (see Table 1), and any absorption band due to a hydroxyl group is not found in its IR spectrum. Furthermore, on the basis of detailed proton homonuclear spin decoupling and gated decoupling experiments, euphohelin D (**8**) has a trisubstituted epoxide ring (δ 54.5, $^1J_{C\text{-}H}$=178.8 Hz) and two partial structures [A] and [B], as seen in the case of euphohelin A (**5**). However, euphohelin D (**8**) with two carbonyl groups [δ 208.5 (s) and 217.7 (s)] possesses a partial structure [D] instead of [C] in **5** (see Fig. 2), suggesting that the two carbonyl groups are located at C^{11}- and C^{14}-positions. On Sarett oxidation at room temperature for 6 h, euphohelin B (**6**) was readily converted into euphohelin D (**8**) in 74% yield.

The Structure of Euphohelin E (9). On the basis of the IR and ^{1}H NMR spectra, euphohelin E (**9**) with a molecular formula $C_{31}H_{40}O_{10}$ has one secondary hydroxyl group [IR (film) 3500 cm^{-1}; δ 3.46 (1H, d, J=8.8 Hz)], two acetoxyl groups [δ 1.39 (3H, s) and 2.04 (3H, s)] and one benzoyloxyl group [δ 7.43—7.59 (3H, m) and 8.26—8.31 (2H, m)]. Further detailed proton homonuclear spin decoupling experiments of **9** indicate that it has a partial structure [E] instead of [C] in euphohelin A (**5**), in addition to the known moieties [A] and [B]. Thus, Sarett oxidation of euphohelin B (**6**) was carried out carefully at room temperature for 40 min to give rise to euphohelin E (**9**) in 65% yield, together with euphohelin D (**8**) in 18% yield.

Euphohelins, the highly-oxygenated diterpenes, belong to a small group of jatrophone-type ones,[5] and have been isolated only from the plant *Euphorbia helioscopia* L. collected in the middle of June and not found in April as well as early in May. Finally, from view points of their biogenesis and stereochemistry, it is quite interesting that euphohelins and the known macrocyclic diterpenes (**1**—**4**) co-occur in the same plant.

Experimental

All the melting points were uncorrected. ^1H and ^{13}C NMR spectra were taken on a JEOL JNM-FX 200 (199.5 MHz and 50.1 MHz) spectrometer, using $CDCl_3$ as solvent, unless otherwise stated. Chemical shifts are given in ppm from TMS as an internal standard. Coupling constants are given in Hz (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). IR spectra were recorded on a JASCO Model A-202 spectrophotometer. Mass spectra were obtained on a Hitachi M-80 mass spectrometer operating with an ionization energy (70 eV). Optical rotations were taken on a JASCO DIP-360 polarimeter. Preparative and analytical TLC were carried out on Kieselgel 60 PF_{254} (E. Merck A.G. Germany), unless otherwise stated.

Isolation of Euphohelins. Fresh leaves and roots of the plant *Euphorbia helioscopia* L. (*ca.* 5 kg), which were collected at Atsugi in Kanagawa Prefecture in the middle of June, were hashed with a shears and immersed in MeOH (20 L) at room temperature for 2 months, and then filtered. The filtrate was concentrated under reduced pressure below 40 °C to leave a greenish brown oil (*ca.* 110 g) which was partitioned between water and AcOEt. The AcOEt layer was dried over large amounts to anhydrous Na_2SO_4 and then concentrated under reduced pressure to leave a greenish brown oil (28.5 g), which was further partitioned between 90% aq MeOH and isooctane (isooctane layer, *ca.* 8.1 g). The 90% aq MeOH layer was concentrated under reduced pressure to leave a greenish brown oil (*ca.* 20.1 g) which was dissolved in small amounts of MeOH and adsorbed on activated charcoal (*ca.* 30 g), and then eluted with MeOH (1.5 L) and $CHCl_3$ (2.0 L) quickly. The eluate was concentrated under reduced pressure to leave a greenish brown oil (19.5 g) which was roughly separated by column chromatography on silica gel (Merck 7734) (500 g) using a gradient solution of hexane and AcOEt [hexane–AcOEt (5:1) 0.5 L, hexane–AcOEt (3:1) 2 L, AcOEt 2 L] to afford six fractions (Fr. **1**, 400 mg; Fr. **2**, 2200 mg; Fr. **3**, 320 mg; Fr. **4**, 1140 mg; Fr. **5**, 500 mg; Fr. **6**, 420 mg) after removal of the nonpolar fraction containing hydrocarbons using hexane–AcOEt (5:1) (3.5 L). The first fraction was mainly comprised of a lot of hydrocarbons. Analytical TLC of the fraction **2**—**5** using hexane–AcOEt (2:1) showed the spots corresponding to euphoscopins A and B, euphornin, euphohelioscopins A and B, and the related known diterpenes.[1-3] Therefore, further separation of these fractions has not been carried out.

The most polar fraction **6**, which showed several new spots on analytical TLC plate [hexane–AcOEt (2:1)], was separated by preparative TLC using hexane–AcOEt (2:1) to afford euphohelin D (**8**) (97 mg), euphohelin C (**7**) (23 mg), euphohelin E (**9**) (4.6 mg), euphohelin A (**5**) (42 mg), and euphohelin B (**6**) (3.9 mg) in the order of increasing polarity: **8** as a colorless oil: $[\alpha]_D^{27}$ +46.9° (*c* 2.21, $CHCl_3$); IR (film) 1745, 1720, 1600, 1580, and 1245 cm^{-1}; Found: *m/z* 570.2469. Calcd for $C_{31}H_{38}O_{10}$: M, 570.2462. **7** as a colorless oil: $[\alpha]_D^{27}$ +44.6° (*c* 1.24, $CHCl_3$); IR (film) 1740, 1720, 1600, and 1240 cm^{-1}; Found: *m/z* 720.3144. Calcd for $C_{40}H_{48}O_{12}$: M, 720.3143. **9** as a colorless oil: $[\alpha]_D^{27}$ +24.9° (*c* 0.57, $CHCl_3$); IR (film) 3500, 1735, 1720, 1595, 1580, and 1250 cm^{-1}; Found: *m/z* 572.2632. Calcd for $C_{31}H_{40}O_{10}$: M, 572.2619. **5** as a colorless oil: $[\alpha]_D^{27}$ +31.8° (*c* 1.55, $CHCl_3$); IR (film) 3500, 1730, 1600, 1580, and 1240br. cm^{-1}; Found: *m/z* 616.2893. Calcd for $C_{33}H_{44}O_{11}$: M, 616.2880. **6** as a colorless oil: $[\alpha]_D^{27}$ +25.8° (*c* 0.76, $CHCl_3$); IR (film) 3500br., 1720, 1600, 1580, 1275, and 1250 cm^{-1}; Found: *m/z* 574.2752. Calcd for $C_{31}H_{42}O_{10}$: M, 574.2775.

Acetylation of Euphohelin A (5). Euphohelin A (5 mg) was dissolved in Ac_2O (0.3 mL) and pyridine (0.6 mL) at room temperature and allowed to stand at the same temperature overnight. After decomposition of excess Ac_2O with MeOH, the reaction mixture was partitioned between water and AcOEt. The AcOEt layer was dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to give an oil, which was purified by preparative TLC using hexane–AcOEt (2:1) to afford euphohelin A acetate (**10**) (5.1 mg) as a colorless oil: IR (film) 1740, 1720sh, 1600, 1580, and 1235 cm^{-1}; Found: *m/z* 658.3006. Calcd for $C_{35}H_{46}O_{12}$: M, 658.2987.

Reaction of Euphornin (2) with m-*Chloroperbenzoic Acid.* To a solution of euphornin (11.2 mg) in dry dichloromethane (1 mL) was added, with stirring, *m*-chloroperbenzoic acid (13.1 mg) at room temperature. The reaction mixture was further stirred at room temperature for 2 d, and then diluted with aqueous sodium hydrogensulfite and extracted with AcOEt. The AcOEt extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to leave an oil, which was purified by preparative TLC [hexane–AcOEt (1:1)] to afford euphohelin A (**5**) (10.3 mg) (TLC, IR and ^1H NMR spectra).

Regioselective Hydrolysis of Euphornin A (5). To a solution of euphohelin A (10.5 mg) in MeOH (2 mL) was added, with stirring, a solution of KOH (1 mg) in MeOH (0.1 mL) at room temperature. The reaction solution was further stirred at the same temperature for 50 min. After addition of one drop of AcOH, the reaction solution was partitioned between water and AcOEt. The AcOEt layer was dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to give a colorless oil which was purified by preparative TLC [hexane–acetone (1:1)] to afford euphohelin B (**6**) (8.8 mg) (TLC, IR, and ^1H NMR spectra).

Reaction of Euphohelin A (5) with Benzoyl Chloride. A solution of euphohelin A (3.1 mg) and benzoyl chloride (1 drop) in pyridine (1 mL) was stirred at room temperature for 24 h, and then at 60 °C for 1 h. After addition of MeOH, the reaction mixture was diluted with water and extracted with AcOEt. The AcOEt solution was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to leave an oil, which was purified by preparative TLC [hexane–AcOEt (1:1)] to give euphohelin C (**7**) (3.4 mg) (TLC, IR, and ^1H NMR spectra).

Sarett Oxidation of Euphohelin B (6). To a solution of euphohelin B (8.5 mg) in pyridine (0.4 mL) was added, with stirring, excess amounts of CrO_3–pyridine complex. The reaction mixture was further stirred at room temperature for 6 h. The reaction mixture was diluted with small amounts of $CHCl_3$ and chromatographed on silica gel (5 g). Elution with $CHCl_3$ afforded an oil, which was purified by preparative TLC [hexane–AcOEt (1:1)] to give rise to euphohelin D (**8**) as a colorless oil (6.2 mg) (TLC, IR, and ^1H NMR spectra).

Under essentially the same conditions as described above, euphohelin B (8.6 mg) in pyridine (0.6 mL) was also oxi-

dized with excess amounts of CrO_3–pyridine complex at room temperature. However, the oxidation reaction was stopped only in 40 min. According to the above-mentioned procedure, the reaction mixture was chromatographed on silica gel (5 g) and eluted with $CHCl_3$ to give an oil, which was subjected to preparative TLC [hexane–AcOEt (1:1)] to afford euphohelin D (**8**) (1.5 mg) and euphohelin E (**9**) (5.5 mg) [TLC, IR, and ^1H NMR spectra).

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