^{15}N-labeled ammonia was prepared by reacting ^{15}N-labeled ammonium nitrate (from VEB Berlin-Chemie) with potassium hydroxide. 2,6-Diaminopurine (4) was prepared by reacting 2-amino-6-chloropurine (5) with ammonia in a sealed tube for 17 h at 100 °C.[4,5]

Amination Procedure. The amination reactions were carried out in the same manner as described in a previous paper.[22] The products were separated by preparative TLC with mixtures of methanol, chloroform, and water or methanol and chloroform in the presence of aqueous ammonia. The structure of 4-cyano-5-(cyanoamino)imidazole (3) was proved by the following: ^1H NMR (Me_2SO-d_6) δ 6.86 (s); ^{13}C NMR (Me_2SO-d_6) 129.6 (C-2, J = 209.5 Hz), 91.6 (C-4, J = 11 Hz); 153.0 (C-5), 119.4 and 122.7 ppm (NHC≡N and C≡N); UV λ_{max}(CH_3OH) 272 nm; IR (KBr) 2095, 2120, 2160, 2175 cm^{-1}.

(22) Kos, N. J.; van der Plas, H. C.; van Veldhuizen, A. *J. Org. Chem.* **1979**, *44*, 3140.

Acknowledgment. We are indebted to Mr. A. van Veldhuizen for measuring some of the NMR spectra and to Dr. C. A. Landheer, Mr. W. P. Combé, and Mr. C. J. Teunis for the mass spectroscopic data.

Registry No. 1, 5451-40-1; 2, 1839-18-5; 3, 85029-13-6; 4, 1904-98-9; 8, 85029-14-7; 9, 85029-15-8; 10, 30720-65-1; TMAH, 75-59-2; potassium amide, 17242-52-3.

Studies on the Syntheses of Sesquiterpene Lactones. 8.[1] Syntheses of Saussurea Lactone, 8-Deoxymelitensin, and 11,12-Dehydro-8-deoxymelitensin via a Novel Fragmentation Reaction[2]

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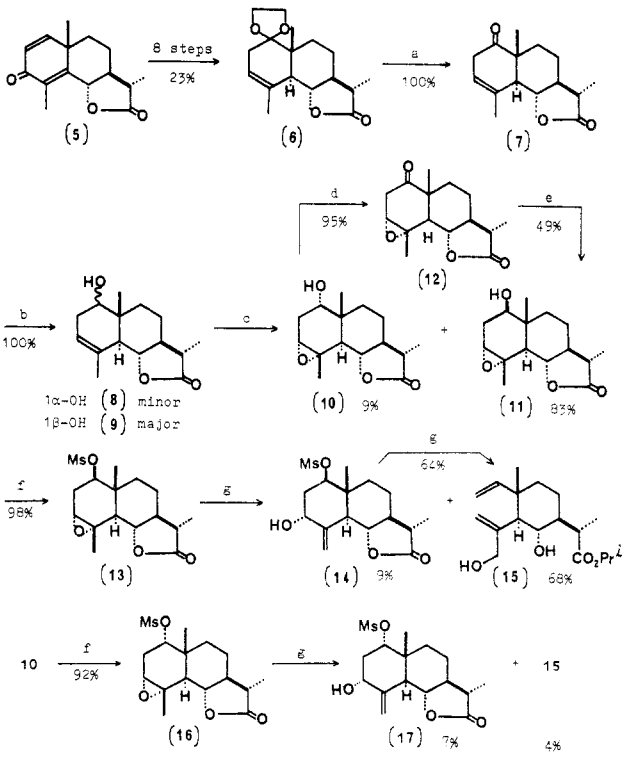
Saussurea lactone (4), 8-deoxymelitiensin (18), and 11,12-dehydro-8-deoxymelitensin (23) have been synthesized from (11*S*)-1,1-(ethylenedioxy)eudesm-3-eno-13,6α-lactone (6) in ten steps, seven steps, and nine steps, respectively. The key step involves a novel fragmentation reaction of (11*S*)-3α,4α-epoxy-1β-(mesyloxy)eudesmano-13,6α-lactone (13) with aluminum isopropoxide in refluxing toluene.

Elemanolides are a small group of natural products, comprising to date ca. 30 varieties.[3] With only a few exceptions the natural products of this class possess a functionality at C_{14} as shown in melitensin (1),[4,5] 11,12-dehydromelitensin (2),[6] and vernolepin (3).[7] In connection with the general synthetic strategy of these natural products, we envisioned an approach which consisted of the fragmentation reaction of appropriately functionalized epoxy mesylates such as compounds **A** and **B** by base as shown in Figure 1. In the present paper we report efficient syntheses of 8-deoxymelitensin (18) and 11,12-dehydro-8-deoxymelitensin (23), which are 8-deoxy derivatives of natural products, and the conversion of 18 to saussurea lactone (4)[8] to demonstrate the utility of this novel fragmentation reaction of an appropriately functionalized epoxy mesylate (13), which was conveniently prepared from α-santonin (5).

Results and Discussion

The starting material is the acetal 6 which can be prepared from α-santonin (5) in 23% yield in 8 steps.[9] Treatment of 6 with boiling 50% aqueous acetic acid for 1 h and 15 min gave the desired β,γ-unsaturated ketone 7 in quantitative yield (Scheme I). The structure of 7 was fully supported by the IR spectrum (1710 cm^{-1}) and the ^1H NMR spectrum [δ 5.59 (1 H, m, $w_{h/2}$ = 9.0 Hz, C_3–H)]. No epimerization of the double bond was observed under these reaction conditions.

Scheme I[a]



[a] (a) 50% AcOH aqueous solution, reflux; (b) LiAl(t-BuO)$_3$H; (c) MCPBA; (d) CrO_3·2Py, CH_2Cl_2; (e) $Zn(BH_3)_2$; (f) MsCl, Py; (g) Al(i-PrO)$_3$, toluene, reflux.

(1) Part VII of this series: M. Ando, A. Akahane, Y. Yamaoka, and K. Takase, *J. Org. Chem.*, **47**, 3909 (1982).
(2) A portion of this work has appeared in preliminary form: M. Ando, K. Tajima, and K. Takase, *Chem. Lett.*, 617 (1978).
(3) N. H. Fisher, E. J. Olivier, and H. D. Fisher, *Prog. Chem. Org. Nat. Prod.*, **38**, 214 (1979).
(4) A. G. González, J. M. Arteaga, J. Bermejo, and J. L. Bretón, *An. Quim.*, **67**, 1243 (1971).
(5) A. G. González, J. M. Arteaga, and J. L. Bretón, *An. Quim.*, **70**, 158 (1974).
(6) A. G. González, J. Bermejo, I. Cabrera, and G. M. Massanet, *An. Quim.*, **70**, 74 (1974).
(7) S. M. Kupchan, R. J. Hemingway, D. Werner, A. Karim, A. T. McPhail, and G. A. Sim, *J. Am. Chem. Soc.*, **90**, 3596 (1968).
(8) (a) Structure: A. S. Rao, A. Paul, D. Sadgopal, and S. C. Bhattacharyya, *Tetrahedron*, **13**, 319 (1961). (b) Synthesis: V. K. Honwad, E. Siscovic, and A. S. Rao, *Tetrahedron*, **23**, 1273 (1967). P. A. Grieco and M. Hishizawa, *J. Org. Chem.*, **42**, 1717 (1977).
(9) M. Ando, A. Akahane, and K. Takase, *Bull. Chem. Soc. Jpn.*, **51**, 283 (1978).

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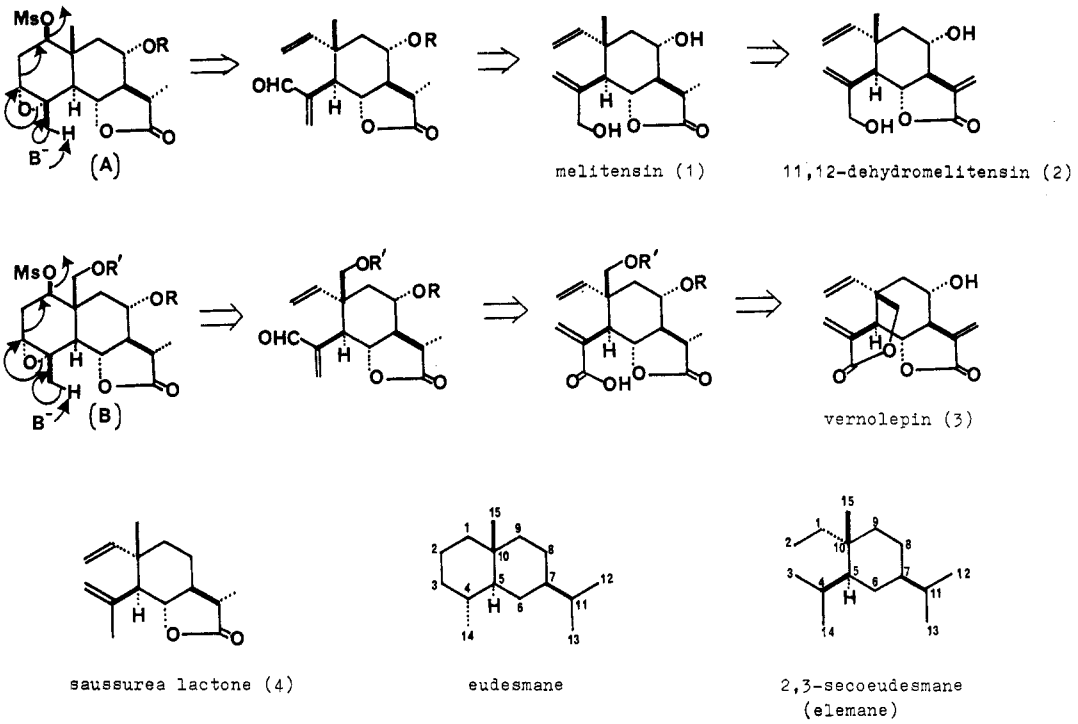


Figure 1.

Selective reduction of the C_1 carbonyl group of **7** with lithium tri-*tert*-butoxyaluminium hydride gave a ca. 1:8 mixture of 1α-alcohol **8** and 1β-alcohol **9** on the basis of analysis of the ^{1}H NMR spectrum. The β-equatorial configuration of the C_1 hydroxyl group in the major alcohol (**9**) was deduced from the ^{1}H NMR spectrum which showed a signal at δ 3.63 (1 H, dd, J = 7.0 and 10.0 Hz, C_1–H). Since the complete separation of **8** and **9** was difficult, we decided to employ this epimeric mixture in the next stage without any purification.

Epoxidation of the mixture of **8** and **9** with *m*-chloroperoxybenzoic acid gave the corresponding 3α,4α-epoxy 1α-alcohol **10** and 3α,4α-epoxy 1β-alcohol **11** in 9% and 83% yields, respectively. The former was converted to the latter by Collins oxidation and successive reduction of the resulting epoxy ketone (**12**) with zinc borohydride in 47% yield. The stereochemistry of **11** was fully supported by the ^{1}H NMR spectrum [δ 3.43 (1 H, ddd, J = 4.6, 6.6, and 10.0 Hz, C_1–H), 3.00 (1 H, dd, J = 0.8 and 3.3 Hz, C_3–H)][10,11] as well as the consideration that the reagent approached **9** from the less hindered α side. The stereochemistry of **10** was also supported by the ^{1}H NMR spectrum [δ 3.19 (1 H, m, $w_{h/2} \approx$ 11 Hz, C_1–H), 3.01 (1 H, m, $w_{h/2}$ = 4.4 Hz, C_3–H)][10,11] as well as the chemical transformation of **10** to **11**.

Mesylation of **11** with methanesulfonyl chloride in pyridine at room temperature gave a mesylate (**13**) in 98% yield. Analogous treatment of **10** gave a mesylate (**16**) in 92% yield.

Treatment of **13** with aluminum isopropoxide in boiling toluene under a nitrogen atmosphere for 72 h gave a hydroxy mesylate (**14**) and a fragmentation product (**15**) in 9% and 68% yields, respectively. In order to clarify the reaction pathway, this fragmentation reaction was followed by TLC.[12] Thus, in 12 h **13** was converted into **14** completely, and the resulting **14** was gradually changed into the desired fragmentation product (**15**). A reaction period longer than 72 h decreased the yield of **15** probably because of decomposition of **15** under these reaction conditions. Treatment of **14** under the same reaction conditions gave **15** in 64% yield as a sole product. The structure of **15** was fully supported by the IR spectrum (3590, 3420, and 1715 cm^{-1}) and the ^{1}H NMR spectrum [δ 1.23 (6 H, d, J = 6.2 Hz, $CH(CH_3)_2$), 3.66 (1 H, t, J = 10.5 Hz, C_6–H), 3.91 and 4.09 (1 H each, br d, J = 13.5 Hz, C_{14}–H), 4.87 and 4.90 (1 H each, AB part of ABX, C_2–H), 4.99 (1 H, m, $w_{h/2}$ = 2.5 Hz, C_3–H_a), 5.01 (1 H, m, septet, J = 6.2 Hz, $CH(CH_3)_2$), 5.38 (1 H, br s, C_3–H_b), 5.70 (1 H, X part of ABX, C_1–H)] as well as the subsequent transformations. The structure of **14** was also supported by the IR spectrum (3550, 3380, 1786, and 1757 cm^{-1}) and the ^{1}H NMR spectrum: δ 2.77 (1 H, br d, J = 10.0 Hz, C_5–H), 3.03 (3 H, s, OSO_2CH_3), 4.02 (1 H, br t, J = 10.0 Hz, C_6–H), 4.43 (1 H, m, $w_{h/2}$ = 7.0 Hz, C_3–H), 4.97 (1 H, dd, J = 5.0 and 11.0 Hz, C_1–H), 5.05 (1 H, m, $w_{h/2}$ = 4.0 Hz, C_{14}–H_a), 5.23 (1 H, m, $w_{h/2}$ = 3.0 Hz, C_{14}–H_b).

This fragmentation reaction can be rationalized as follows (Scheme II). The reaction was probably initiated by coordination of aluminum isopropoxide to the oxygen atom of the epoxide ring due to the strong affinity of the aluminum atom for oxygen and simultaneous opening of the epoxide ring.[13] Successive fragmentation of the resulting aluminum alkoxide (C) gave aldehyde (D). Reduction of D under the Meerwein–Ponndorf reduction conditions and successive ring opening and esterification of the γ-lactone moiety gave intermediate E. Products **14** and **15** were

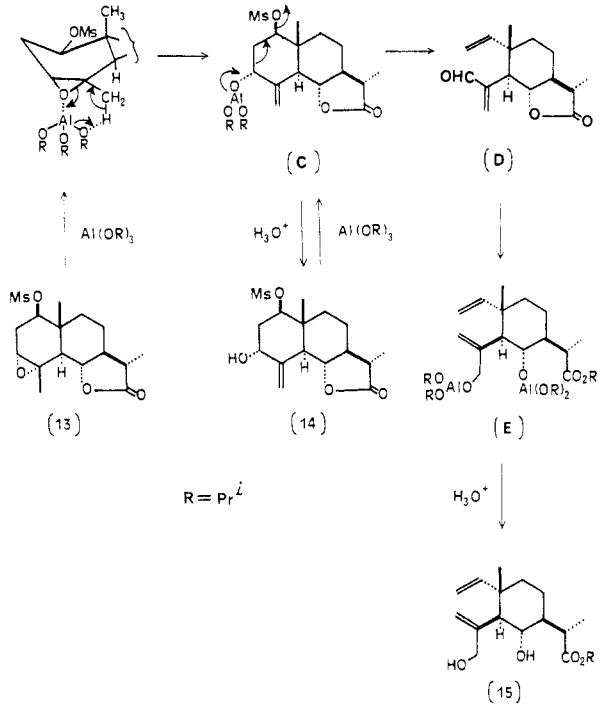
(10) N. S. Bhacca and D. H. Williams, "Applications of NMR spectroscopy in Organic Chemistry", Holden-Day, San Fransisco, 1964, pp 77–85, 100.

(11) The C_1–H resonance of **11** appeared at 0.24 ppm lower field than that of **10**. This observation also agreed with the assigned structures of **10** and **11**: N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Fransisco, 1964, pp 99–102; L. A. Paquette, W. E. Fristad, C. A. Schuman, M. A. Beno, and G. G. Christoph, *J. Am. Chem. Soc.*, **101** 4645 (1979); L. A. Maçaira, F. W. L. Machado, M. Garcia, and J. A. Rabi, *Tetrahedron Lett.*, **21**, 773 (1980); L. A. Maçaira, M. Garcia, and J. A. Rabi, *J. Org. Chem.*, **42**, 4207 (1977).

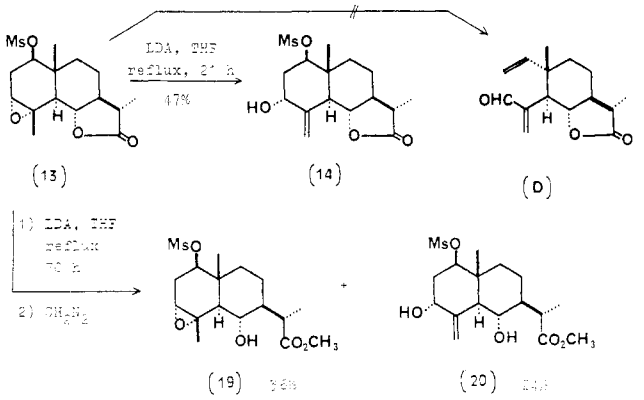
(12) The R_f values of **13**–**15** are 0.34, 0.25, and 0.30, respectively, on silica gel TLC [Kiesel gel GF_{254}, thickness 0.25 mm; EtOAc/$CHCl_3$ (1:1)].

(13) We have already reported the efficient conversion of epoxides to the corresponding allylic alcohols with aluminum isopropoxide in refluxing toluene: M. Ando, A. Akahane, and K. Takase, *Chem. Lett.*, **1978**, 727; M. Ando, A. Akahane, H. Yamaoka, and K. Takase, *J. Org. Chem.*, **47**, 3909 (1982).

Scheme II



Scheme III



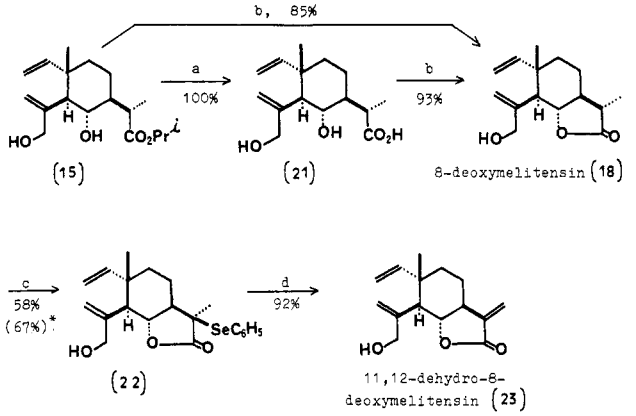
formed by hydrolysis of intermediates (C and E).

To examine the stereochemical requirements of this reaction, we studied the fragmentation reaction of **16**. Treatment of **16** with aluminum isopropoxide in refluxing toluene for 19 h gave a complex mixture, from which a hydroxy mesylate (**17**) and the fragmentation product **15** were isolated in only 7% and 4% yields, respectively. No starting material was recovered at this stage. Probably in this case the competitive 1,2-eliminations of the 1α(ax)-mesyloxy groups of **16** and the intermediate **17** decreased the yield of **15**.

The attempted fragmentation reaction of **13** to aldehyde D (Scheme III) with lithium diisopropylamide was unsuccessful. Thus treatment of **13** with lithium diisopropylamide in refluxing THF gave **14** in 47% yield as sole product (Scheme III). Prolonged reaction time (70 h) under the same reaction conditions gave a mixture of acidic products, which were separated after methylation with diazomethane to give methyl esters **19** and **20** in 36% and 24% yields, respectively.

Hydrolysis of **15** with 1 M potassium hydroxide in ethanol at 50 °C gave a carboxylic acid (**21**) in a quantitative yield (Scheme IV). Successive treatment of **21** with *p*-toluenesulfonic acid in boiling benzene for 2 h gave 8-deoxymelitensin (**18**) in 93% yield as a crystalline material,

Scheme IV[a]



[a] (a) 1 M KOH, EtOH, 50 °C; (b) *p*-TsOH, C_6H_6 reflux; (c) LDA, $C_6H_5SeSeC_6H_5$; the yield in parenthesis is based on the recovered starting material; (d) H_2O_2, AcOH.

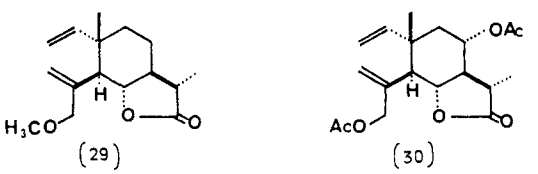
Table I. ^{1}H NMR Spectral Data Comparison between Melitensin (1) and 8-Deoxymelitensin (18)

atom	chemical shift, δ (in $CDCl_3$)	
	1[a]	18[b]
C_1-H	5.80 (q, J = 11, 17 Hz)	5.78 (q, J = 10.0, 17.5 Hz)
C_2-H	5.00	4.94 (dd, J = 1.0, 17.5 Hz), 4.98 (dd, J = 1.0, 10.0 Hz)
C_3-H	5.00 (s), 5.42 (t, J = 1 Hz)	4.95 (m), 5.36 (m, $w_{h/2}$ = 3.0 Hz)
C_5-H	2.34 (d, J = 11.5 Hz)	2.35 (d, J = 12.0 Hz)
C_6-H	4.20 (t, J = 11.5 Hz)	4.14 (dd, J = 10.0, 12.0 Hz)
C_8-H	4.00 (ddd, J = 4.5, 11, 11 Hz)	
C_{11}-H	2.60 (dq)	ca. 2.4 (m)
C_{11}-CH_3	1.38 (d, J = 7 Hz)	1.23 (d, J = 6.8 Hz)
C_{10}-CH_3	1.10 (s)	1.09 (s)
C_{14}-H	4.03 deformed AB system	4.01 (m)

[a] 60-MHz ^{1}H NMR data. [b] 100-MHz ^{1}H NMR data.

mp 104–105 °C. The direct transformation of **15** to **18** was also achieved by treatment with *p*-toluenesulfonic acid in boiling benzene for 2 h in 85% yield. The structure of **18** was fully supported by the IR spectrum (3590, 3510, and 1770 cm^{-1}) and comparison of the ^{1}H NMR spectrum data for melitensin (**1**) and **18** as shown in Table I. The ^{1}H NMR spectral data of **18** were in good accordance with those of melitensin (**1**) reported in the literature[14] except for the C_8-H, C_{11}-H, and C_{11}-CH_3 resonances. The downfield shift of the C_{11}-H and C_{11}-CH_3 resonances of **1** compared with those of **18** was resonably explained by the influence of the C_8 hydroxyl group of **1**.

For further confirmation of the structure **18**, we tried methylation and acetylation of **18**. Methylation of **18** with sodium hydride and methyl iodide in dimethylformamide at room temperature gave a methyl ether (**29**), whose



(14) A. G. González, J. M. Argeaga, and J. L. Bretón, *Pytochemistry*, 14, 2039 (1975).

Table II. ^{1}H NMR Spectral Data Comparison between Melitensin Diacetate (30) and 8-Deoxymelitensin Acetate (24)

	chemical shift, δ (in $CDCl_3$)	
atom	30[a]	24[b]
C_1-H	5.80 (q, J = 11, 17 Hz)	5.79 (q, J = 10.0, 18.0 Hz)
C_2-H	5.00	4.97 (dd, J = 1.0, 18.0 Hz), 5.05 (dd, J = 1.0, 10.0 Hz)
C_3-H	5.00 (s), 5.42 (t, J = 1 Hz)	5.02 (br s, $w_{h/2} \approx 2$ Hz), 5.37 (t, J = 1.5 Hz)
C_5-H	2.34 (d, J = 11.5 Hz)	2.29 (d, J = 11.5 Hz)
C_6-H	4.23 (t, J = 11.5 Hz)	4.12 (dd, J = 9.5 and 11.5 Hz)
C_8-H	5.10 (ddd, J = 4.5, 11, 11 Hz)	
C_{11}-H	2.60 (dq)	ca. 2.4 (m)
C_{11}-CH_3	1.28 (d, J = 7 Hz)	1.25 (d, J = 6.5 Hz, C_{11}-CH_3)
C_{10}-CH_3	1.18 (s)	1.11 (s)
C_{14}-H	4.52 (deformed AB system)	4.50 (m)

[a] 60 MHz ^{1}H NMR data. [b] 100 MHz ^{1}H NMR data.

Table III. ^{1}H NMR Spectral Data Comparison between 11,12-Dehydromelitensin (2) and 11,12-Dehydro-8-deoxymelitensin (23)

	chemical shift, δ (in $CDCl_3$)	
atom	2[a]	23[b]
C_1-H	5.80 (q, J = 11, 17 Hz)	5.79 (q, J = 10.5, 17.5 Hz)
C_2-H	5.00	4.95 (dd, J = 1.0, 17.5 Hz), 5.00 (dd, J = 1.0, 10.5 Hz)
C_3-H	4.95, 5.40	4.94 (br s), 5.39 (br s)
C_5-H		2.49 (d, J = 11.7 Hz)
C_6-H	4.15 (t, J = 11.5 Hz)	4.11 (dd, J = 10.7, 11.7 Hz)
C_8-H	4.05	
C_{12}-H	5.95 (d, J = 3 Hz), 6.12 (d, J = 3 Hz)	5.40 (d, J = 3.4 Hz), 6.05 (d, J = 3.2 Hz)
C_{10}-H	1.10 (s)	1.10 (s)
C_{14}-H	4.05	4.03 (br s)

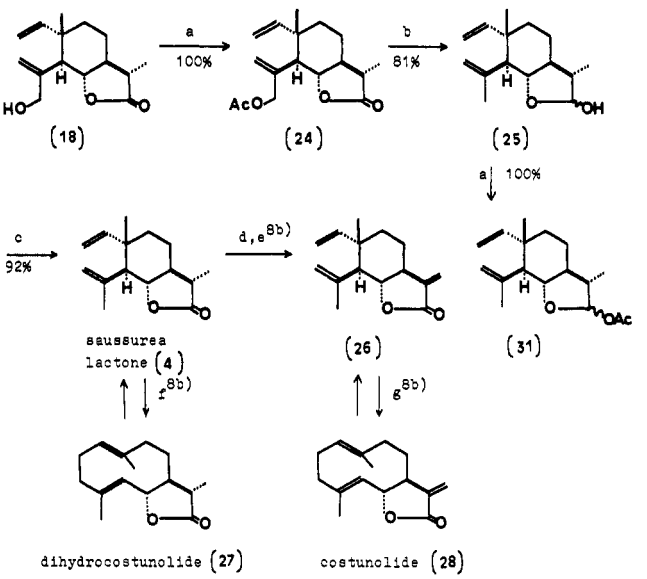
[a] 60-MHz ^{1}H NMR data. [b] 90-MHz ^{1}H NMR data.

structure was fully supported by the spectral data shown in the Experimental Section. Acetylation of 18 with acetic anhydride and pyridine gave an acetate (24). The ^{1}H NMR data of 24 was in good accordance with those of melitensin diacetate (30) reported in the literature[14] except for the C_8-H resonance (Table II).

Phenylselenenylation of 18 with lithium diisopropylamide and diphenyl diselenide afforded a phenylseleno lactone (22) in 67% yield. The oxidative syn elimination of 22 with hydrogen peroxide in tetrahydrofuran in the presence of acetic acid gave 11,12-dehydro-8-deoxymelitensin (23) as a colorless oil. The structure of 23 was fully supported by the IR spectrum (3600 and 1770 cm^{-1}) and comparison of the ^{1}H NMR spectral data for 11,12-dehydromelitensin (2) and 23. Thus, as shown in Table III, ^{1}H NMR spectral data of 23 were in good accordance with those of 11,12-dehydromelitensin (2) reported in the literature[5] except for C_8-H and one of the C_{12}-Hs. Since one of the C_{12}-Hs of 2 is located in the same side as the C_8 hydroxyl group, it is reasonable that its resonance appeared at 0.55 ppm lower field than that of 23.

Finally we tried the conversion of 24 to saussurea lactone (4). Reduction of 24 with lithium in liquid ammonia gave a hemiacetal (25) in 81% yield as a diastereomeric mixture of the C_{13} hydroxyl group (Scheme V). Acetylation of 25

Scheme V[a]



[a] (a) Ac_2O, Py; (b) Li, NH_3; (c) $CrO_3 \cdot 2Py$, CH_2Cl_2, 0 °C to room temperature; (d) LDA, $C_6H_5SeSeC_6H_5$; (e) H_2O_2, AcOH; (f) 210 °C, 5 min; (g) 200 °C.

with acetic anhydride in pyridine gave the corresponding acetate (31) as a diastereomeric mixture. The structures of 25 and 31 were confirmed by analysis of their IR and ^{1}H NMR spectral data shown in the Experimental Section, except for the C_{13} stereochemistries.

Oxidation of 25 by the Collins procedure gave a crystalline compound (4), whose melting point (146–147 °C) and $[\alpha]_D$ value (+65.4°) were identical with those of natural occurring saussurea lactone (mp 146–147 °C,[15,16] 148–149 °C;[8a] $[\alpha]_D$ +57°,[15] +62°,[16] +66°[8a]) reported in the literatures. The IR (Nujol) and ^{1}H NMR ($CDCl_3$, 60 MHz) spectra of synthetic 4 were superimposable on those of natural occurring saussurea lactone which were recorded in the literature.[8a,17]

The transformation of saussurea lactone to dihydrocostunolide and costunolide has already been accomplished by Grieco and Nishizawa via the Cope rearrangement.[8b]

Experimental Section

Melting points were determined in capillary tubes with a Yamato melting point apparatus. All melting points were uncorrected. IR spectra were determined on a Shimadzu IRG-1 spectrometer. NMR spectra were recorded with Hitachi R-24B (60 MHz), Varian HA-100 (100 MHz), and Varian EM-390 (90 MHz) spectrometers in $CDCl_3$ containing 1% Me_4Si as the internal standard. Mass spectra were recorded on a Hitachi RMU-6D spectrometer with a direct inlet system operating at 25 eV. Optical rotations were determined on a Perkin-Elmer 241 polarimeter.

Reactions were run under an atmosphere of nitrogen. Tetrahydrofuran (THF) and dimethoxyethane (DME) were distilled from lithium aluminium hydride. Hexamethylphosphoric triamide (HMPA), methylene chloride, and pyridine were distilled from calcium hydride. Diethyl ether, benzene, and toluene were dried over sodium wire. Kiesel gel 60 (Merck, finer than 230 mesh) was employed for column chromatography, and Kiesel gel 60 GF_{254} (Merck) was used for TLC or preparative TLC (thickness 0.25 mm).

(15) P. S. Rao and B. S. Varma, *J. Sci. Ind. Res., Sect. B*, 10, 166 (1951).
(16) P. S. Rao, B. S. Varma, N. R. Ghosh, and P. C. Dutta, *J. Sci. Ind. Res., Sect. B* 17, 228 (1958).
(17) H. Yoshioka, T. J. Mabry, B. N. Timmermann, "Sesquiterpene Lactones", University of Tokyo Press, Tokyo, 1973.

(11*S*)-1-Oxoeudesm-3-eno-13,6α-lactone (7). A mixture of (11*S*)-1,1-(ethylenedioxy)eudesm-3-eno-13,6α-lactone (**6**; 800 mg, 2.74 mmol) and a 50% aqueous solution of acetic acid (76 mL) was refluxed for 1 h and 15 min. The mixture was cooled, poured into a saturated aqueous solution of NaCl (100 mL), and extracted with ethyl acetate (2 × 100 mL). The combined extracts were washed successively with a saturated aqueous solution of $NaHCO_3$ (3 × 100 mL) and a saturated aqueous solution of NaCl (2 × 100 mL), dried (Na_2SO_4), and concentrated to give spectroscopically pure **7** (677 mg, 100%) as a crystalline material: mp 130–135 °C (lit.[18] mp 140–143 °C, 138–139 °C); IR (KBr) 1765, 1710 cm^{-1}; NMR (60 MHz) δ 1.13 (3 H, s, C_{10}–CH_3), 1.24 (3 H, d, J = 7.0 Hz, C_{11}–CH_3), 1.97 (3 H, m, C_4–CH_3), 2.93 (2 H, m, C_2–H), 4.11 (1 H, dd, J = 10.0, 11.0 Hz, C_6–H), 5.59 (1 H, m, $w_{h/2}$ = 9.0 Hz, C_3–H); $[\alpha]^{22}_D$ +63.6° (*c* 1.42, $CHCl_3$).

(11*S*)-1α-Hydroxyeudesm-3-eno-13,6α-lactone (8) and (11*S*)-1β-Hydroxyeudesm-3-eno-13,6α-lactone (9). To a stirred solution of **7** (575 mg, 2.32 mmol) in THF (58 mL) at 0 °C was added lithium tri-*tert*-butoxyaluminium hydride (1.74 g, 6.86 mmol). The solution was stirred for 2 h at 0 °C and then quenched by the addition of 0.6 M HCl (38 mL). The mixture was poured into a saturated aqueous solution of NaCl (250 mL) and extracted with ethyl acetate (3 × 100 mL). The combined extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give a crystalline crude product (588 mg, 100%) as a 1:8 mixture of **8** and **9**, which was used as the starting material of the next step.

The analytical sample of **9** was prepared in the following manner. The crude product (588 mg) was chromatographed over silica gel (30 g) and eluted with a mixture of chloroform and carbon tetrachloride (1:1).

The first run gave spectroscopically pure **9** (185 mg, 32%), which was subsequently recrystallized from ether to give colorless needles: mp 131.5–132 °C (lit.[19] mp 134.5 °C); IR (KBr) 3525, 1750 cm^{-1}; NMR (60 MHz) δ 0.89 (3 H, s, C_{10}–CH_3), 1.21 (3 H, d, J = 6.5 Hz, C_{11}–CH_3), 1.82 (3 H, br s, C_4–CH_3), 3.63 (1 H, dd, J = 7.0, 10.0 Hz, C_1–H), 3.97 (1 H, br t, $J \approx$ 10 Hz, C_6–H), 5.33 (1 H, m, $w_{h/2} \approx$ 8 Hz, C_3–H); $[\alpha]^{22}_D$ +66.3° (*c* 1.12, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.70; H, 8.82.

The second run gave a mixture of **8** and **9** (395 mg, 68%).

(11*S*)-3α,4α-Epoxy-1α-hydroxyeudesmano-13,6α-lactone (10) and (11*S*)-3α,4α-Epoxy-1β-hydroxyeudesmano-13,6α-lactone (11). A solution of a 1:8 mixture of **8** and **9** (416 mg, 1.66 mmol) and *m*-chloroperoxybenzoic acid (434 mg, purity 79%, 1.99 mmol) in methylene chloride (30 mL) was allowed to stand at room temperature for 106 h. The mixture was poured into an aqueous solution of KI and extracted with chloroform (3 × 30 mL). The combined extracts were washed successively with a 0.2 M aqueous solution of $Na_2S_2O_3$, a saturated aqueous solution of $NaHCO_3$, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give a crystalline crude product, which was subsequently chromatographed over silica gel (22 g) and eluted with a mixture of chloroform and carbon tetrachloride (1:1).

The first run gave 40 mg (9%) of spectroscopically pure **10** as a crystalline material, which was then recrystallized from ethanol to give colorless scales: mp 183–185 °C; IR (KBr) 3530, 1769 cm^{-1}; NMR (60 MHz), δ 0.88 (3 H, s, C_{10}–CH_3), 1.21 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 1.49 (3 H, s, C_4–CH_3), 3.01 (1 H, m, $w_{h/2}$ = 4.4 Hz, C_3–H), 3.19 (1 H, m, $w_{h/2} \approx$ 11 Hz, C_1–H), 3.93 (1 H, dd, J = 9.0, 11.0 Hz, C_6–H); $[\alpha]^{22}_D$ +97.4° (*c* 0.70, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.65; H, 8.33.

The second run gave 366 mg (83%) of spectroscopically pure **11** as a crystalline material, which was then recrystallized from ethanol to give colorless plates: mp 215–216 °C; IR (KBr) 3490, 1768 cm^{-1}; NMR (60 MHz) δ 0.93 (3 H, s, C_{10}–CH_3), 1.22 (3 H, d, J = 6.6 Hz, C_{11}–CH_3), 1.46 (3 H, s, C_4–CH_3), 1.73 (1 H, d, J = 4.6 Hz, OH), 2.46 (1 H, ddd, J = 0.8, 6.6, 15.5 Hz, $C_{2\alpha}$–H), 3.00 (1 H, dd, J = 0.8, 3.3 Hz, C_3–H), 3.43 (1 H, ddd, J = 4.6, 6.6, 10.0 Hz, C_1–H), 3.93 (1 H, dd, J = 9.0, 11.6 Hz, C_6–H); $[\alpha]^{22}_D$ +65.9° (*c* 0.18, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.81; H, 8.59.

(18) K. S. Rybalko and L. Dolejš, *Collect. Czech. Chem. Commun.*, **26**, 2909 (1961); T. A. Geissman and G. A. Ellestad, *J. Org. Chem.*, **27**, 1855 (1962).

(19) M. Ando and K. Takase, *Tetrahedron*, **33**, 2785 (1977).

Oxidation of 10. Formation of (11*S*)-3α,4α-Epoxy-1-oxoeudesmano-13,6α-lactone (12). Chromic anhydride (530 mg, 5.3 mmol) was added into a mixture of anhydrous methylene chloride (3 mL) and pyridine (860 μL, 10.6 mmol) at 0 °C and stirred for 10 min. Then **10** (57 mg, 0.21 mmol) dissolved in methylene chloride (8 mL) was added over 5 min, and the mixture was stirred at 0 °C for 12 h and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated aqueous solution of $NaHCO_3$, 0.4 M HCl, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give 54 mg (95%) of **12** as a crystalline material, which was subsequently recrystallized from ether to give colorless prisms: mp 148–151 °C; IR (KBr) 1770, 1712 cm^{-1}; NMR (60 MHz) δ 1.24 (3 H, d, J = 6.4 Hz, C_{11}–CH_3), 1.27 (3 H, s, C_{10}–CH_3), 1.59 (3 H, s, C_4–CH_3), 2.05 (1 H, d, J = 11.5 Hz, C_5–H), 2.79 (1 H, d, J = 1.6 Hz, $C_{2\alpha}$–H), 2.83 (1 H, d, J = 4.0 Hz, $C_{2\beta}$–H), 3.25 (1 H, dd, J = 1.6, 4.0 Hz, C_3–H), 4.06 (1 H, br t, J = 11.5 Hz, C_6–H); $[\alpha]^{22}_D$ +76.4° (*c* 0.17, $CHCl_3$). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.82; H, 7.71.

Reduction of 12 with Zinc Borohydride. To a stirred solution of **12** (54 mg, 0.20 mmol) in DME (3 mL) was added a 0.5 M solution of zinc borohydride in DME (8 mL, 4 mmol). The mixture was stirred for 1 h at room temperature, poured into a mixture of ice, saturated aqueous solution of NaCl, and 0.5 M HCl, and filtered. The filtrate was extracted with ethyl acetate (2 × 20 mL). The combined extracts were washed successively with a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product (53 mg), which was purified by TLC (EtOAc/$CHCl_3$, 2:8).

The first band (R_f 0.15) gave spectroscopically pure **10** (10 mg, 18%) as a crystalline material.

The second band (R_f 0.07) gave spectroscopically pure **11** (28 mg, 49%) as a crystalline material.

(11*S*)-3α,4α-Epoxy-1β-(mesyloxy)eudesmano-13,6α-lactone (13). To a stirred solution of **11** (271 mg, 1.02 mmol) in pyridine (1.7 mL) was added methanesulfonyl chloride (238 μL, 3.06 mmol). The mixture was allowed to stand at room temperature for 16.5 h, poured into water (35 mL), and extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed successively with 0.1 M HCl (35 mL), a saturated aqueous solution of $NaHCO_3$, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oil (365 mg). This was then chromatographed over silica gel (20 g) and eluted with a mixture of chloroform and carbon tetrachloride (1:1) to give spectroscopically pure **13** (345 mg, 98%), which was subsequently recrystallized from ether to give colorless prisms: mp 124–125 °C dec; IR ($CHCl_3$) 1780, 1168 cm^{-1}; MS, m/e (relative intensity) 344 (M^+, 9), 265 (54), 248 (35); NMR (60 MHz) δ 1.04 (3 H, s, C_{10}–CH_3), 1.23 (3 H, d, J = 6.5 Hz, C_{11}–CH_3), 1.47 (3 H, s, C_4–CH_3), 1.90 (1 H, d, J = 11.5 Hz, C_5–H), 2.08 (1 H, ddd, J = 3.6, 10.0, 15.0 Hz, $C_{2\beta}$–H), 2.74 (1 H, dd, J = 7.0, 15.0 Hz, $C_{2\alpha}$–H), 3.03 (3 H, s, OSO_2CH_3), 3.07 (1 H, d, J = 3.6 Hz, C_3–H), 3.93 (1 H, dd, J = 9.0, 11.6 Hz, C_6–H), 4.47 (1 H, dd, J = 7.0, 10.0 Hz, C_1–H); $[\alpha]^{22}_D$ +58.2° (*c* 0.70, $CHCl_3$). Anal. Calcd for $C_{16}H_{24}O_6S$: C, 55.79, H, 7.02. Found: C, 55.84; H, 7.07.

(11*S*)-3α,4α-Epoxy-1α-(mesyloxy)eudesmano-13,6α-lactone (16). The treatment of **10** in a manner analogous to the mesylation of **11** gave **16** as an oil: 92% yield; IR ($CHCl_3$) 1772, 1163 cm^{-1}; NMR (60 MHz) δ 1.01 (3 H, s, C_{10}–CH_3), 1.23 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 1.50 (3 H, s, C_4–CH_3), 2.93 (1 H, br d, J = 3.0 Hz, C_3–H), 3.06 (3 H, s, OSO_2CH_3), 3.92 (1 H, dd, J = 9.0, 12.0 Hz, C_6–H), 4.41 (1 H, m, C_1–H); $[\alpha]^{22}_D$ +83.2° (*c* 0.55, $CHCl_3$).

Fragmentation Reaction of 13. Formation of (11*S*)-3α-Hydroxy-1β-(mesyloxy)eudesm-4(14)-eno-13,6α-lactone (14) and Isopropyl (11*S*)-6α,14-Dihydroxy-2,3-secoeudesma-1,3-dien-13-oate (15). A mixture of **13** (133 mg, 0.39 mmol) and aluminum isopropoxide (630 mg, 3.08 mmol) in toluene (10 mL) was vigorously refluxed (bath temperature 125 °C) for 72 h. The solvent was removed from the reaction mixture under reduced pressure. The residue was stirred with a mixture of ethyl acetate (10 mL) and 2 M HCl (9.5 mL) until the residue was dissolved. The organic layer was separated, and the aqueous layer was further extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed successively with a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of NaCl, dried

(Na_2SO_4), and concentrated to give an oily material (120 mg). This was then chromatographed over silica gel impregnated with 10% $AgNO_3$ (5 g).

The fraction eluted with chloroform gave spectroscopically pure **14** (12 mg, 9%) as a crystalline material, which was recrystallized from ether to give colorless prisms: mp 177–177.5 °C; IR (KBr) 3550, 3380, 1786, 1757, 1165 cm^{-1}; NMR (60 MHz) δ 0.90 (3 H, s, C_{10}–CH_3) 1.23 (3 H, d, J = 6.5 Hz, C_{11}–CH_3), 2.77 (1 H, br d, J = 10.0 Hz, C_5–H), 3.03 (3 H, s, OSO_2CH_3), 4.02 (1 H, br t, J = 10.0 Hz, C_6–H), 4.43 (1 H, m, $w_{h/2}$ = 7.0 Hz, C_3–H), 4.97 (1 H, dd, J = 5.0, 11.0 Hz, C_1–H), 5.05 (1 H, m, $w_{h/2}$ = 4.0 Hz, C_{14}–H_a), 5.23 (1 H, m, $w_{h/2}$ = 3.0 Hz, C_{14}–H_b); $[\alpha]^{22}_D$ +64.7° (c 1.12, $CHCl_3$). Anal. Calcd for $C_{16}H_{24}O_6S$: C, 55.79; H, 7.02. Found: C, 55.76; H, 7.32.

The fraction eluted with ethyl acetate gave an oily mixture (104 mg), which was chromatographed over silica gel (5 g) and eluted with chloroform to give spectroscopically pure **15** (82 mg, 68%) as a colorless oil: IR ($CHCl_3$) 3590, 3420, 1715, 1105, 918 cm^{-1}; NMR (100 MHz; the assignment is based on the spin-decoupling experiments) δ 1.01 (3 H, s, C_{10}–CH_3), 1.13 (3 H, d, J = 7.0 Hz, C_{11}–CH_3), 1.23 (6 H, d, J = 6.2 Hz, $CH(CH_3)_2$), ca. 1.9 (1 H, m, C_7–H), 2.05 (1 H, d, J = 10.3 Hz, C_5–H), 2.90 (1 H, dq, J = 4.3, 7.0 Hz, C_{11}–H), 3.66 (1 H, t, J = 10.5 Hz, C_6–H), 3.91 (1 H, br d, J = 13.5 Hz, C_{14}–H_a), 4.09 (1 H, br d, J = 13.5 Hz, C_{14}–H_b), 4.87 (1 H, A part of ABX, C_2–H_a), 4.90 (1 H, B part of ABX, C_2–H_b), 4.99 (1 H, m, $w_{h/2}$ = 2.5 Hz, C_3–H_a), 5.01 (1 H, septet, J = 6.2 Hz, $CH(CH_3)_2$), 5.38 (1 H, br s, C_3–C_b), 5.70 (1 H, X part of ABX, C_1–H); $[\alpha]^{22}_D$ +9.9° (c 1.54, $CHCl_3$).

Fragmentation Reaction of 16. Formation of 15 and (11*S*)-3α-Hydroxy-1α-(mesyloxy)eudesm-4(14)-eno-13,6α-lactone (17). A mixture of **16** (50 mg, 0.15 mmol) and aluminum isopropoxide (250 mg, 1.22 mmol) in toluene (13 mL) was vigorously refluxed (bath temperature 130 °C) for 19 h. The reaction mixture was treated in the usual manner to give a complex mixture (55 mg) as an oil. This was then purified by the combination of the column chromatography on silica gel (3 g; $CHCl_3/CCl_4$, 1:1) and TLC ($CHCl_3$/EtOAc, 1:1) to give 2 mg (4%) of **15** and 3.5 mg (7%) of **17**. **17** (oil): NMR (100 MHz; the assignment is based on the spin-decoupling experiments) δ 0.91 (3 H, s, C_{10}–CH_3), 1.24 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 3.05 (1 H, br d, J = 10.0 Hz, C_5–H), 3.12 (3 H, s, OSO_2CH_3) 4.00 (1 H, dd, J = 10.0, 11.0 Hz, C_6–H), 4.36 (1 H, m, $w_{h/2}$ = 9.0 Hz, C_3–H), 4.52 (1 H, t, J = 3.0 Hz, C_1–H), 5.08 (1 H, m, $w_{h/2}$ = 3.5 Hz, C_{14}–H_a), 5.24 (1 H, m, $w_{h/2}$ = 3.5 Hz, C_{14}–H_b).

Fragmentation Reaction of 14. A mixture of **14** (20 mg, (0.06 mmol) and aluminum isopropoxide (100 mg, 0.49 mmol) in toluene (5 mL) was vigorously refluxed (bath temperature 125 °C) for 66 h. The reaction mixture was treated in the usual manner to give an oily material (24 mg). This was then chromatographed over silica gel (1 g) and eluted successively with a 1:1 mixture of chloroform and carbon tetrachloride (450 mL), chloroform (600 mL), and ethyl acetate (100 mL). The fraction eluted with chloroform gave **15** (11.5 mg, 64%).

Reaction of 13 with Lithium Diisopropylamide (LDA). (1) A mixture of **13** (15 mg, 0.04 mmol) and a 0.08 M THF solution of LDA (2.2 mL) was refluxed for 21 h, cooled, poured into 0.2 M HCl (10 mL), and extracted with ethyl acetate. The combined extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product (14 mg), which was subsequently purified by preparative TLC ($CHCl_3$/EtOAc, 1:1) to give 7 mg (47%) of **14** (R_f 0.32).

(2) A mixture of **13** (15 mg, 0.04 mmol) and a 0.08 M THF solution of LDA (2.2 mL) was refluxed for 70 h. The reaction mixture was treated in the above-mentioned manner to give oily material (18 mg), which was subsequently methylated with diazomethane to give an oily mixture. This was then separated by preparative TLC ($CHCl_3$/EtOAc, 1:1) to give 6 mg (36%) of methyl (11*S*)-3α,4α-epoxy-6α-hydroxy-1β-(mesyloxy)eudesman-13-oate (**19**, R_f 0.25) and 4 mg (24%) of methyl (11*S*)-3α,6α-dihydroxy-1β-(mesyloxy)eudesm-4(14)-en-13-oate (**20**, R_f 0.06). **19** (oil): IR ($CHCl_3$) 3450, 1720, 1175 cm^{-1}; NMR (60 MHz) δ 0.94 (3 H, s, C_{10}–CH_3), 1.15 (3 H, d, J = 7.0 Hz, C_{11}–CH_3), 1.56 (3 H, s, C_4–CH_3), 2.71 (1 H, dd, J = 6.8, 15.0 Hz, $C_{2\alpha}$–H), ca. 2.9 (1 H, m, C_3–H), 3.03 (3 H, s, OSO_2CH_3), ca. 3.5 (1 H, m, C_6–H), 3.73 (3 H, s, OCH_3), 4.33 (1 H, dd, J = 6.8, 9.8 Hz, C_1–H). **20** (oil): IR ($CHCl_3$), 3450, 1720, 1175 cm^{-1}; NMR (60 MHz) δ 0.78 (3 H, s, C_{10}–CH_3), 1.14 (3 H, d, J = 7.0 Hz, C_{11}–CH_3), 3.03 (3 H, s, OSO_2CH_3), 3.70 (3 H, s, OCH_3) 4.00 (1 H, t, J = 9.0 Hz, C_6–H), 4.40 (1 H, m, C_3–H), 4.90 (1 H, dd, J = 5.0, 11.0 Hz, C_1–H), 5.00 (1 H, m, C_{14}–H_a), 5.31 (1 H, m, C_{14}–H_b).

(11*S*)-6α,14-Dihydroxy-2,3-secoeudesma-1,3-dien-13-oic Acid (21). A mixture of **15** (68 mg, 0.22 mmol), 1 M KOH aqueous solution (0.5 mL), and ethanol (5 mL) was heated at 50–55 °C for 30 min and cooled. HCl (2 M, 0.4 mL) was added to the reaction mixture and stirred for 20 min. This was then poured into a saturated aqueous solution of NaCl and extracted with ethyl acetate (5 × 10 mL). The combined extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give **21** as an oil (59 mg, 100%), which was employed as the starting material of the next step without any purification. **21** (oil): IR ($CHCl_3$) 3400, 1700 cm^{-1}; NMR (100 MHz; the assignment is based on the spin-decoupling experiments) δ 1.01 (3 H, s, C_{10}–CH_3), 1.16 (3 H, d, J = 7.0 Hz, C_{11}–CH_3), 2.08 (1 H, d, J = 10.5 Hz, C_5–H), 2.85 (1 H, dq, J = 5.0, Hz, C_{11}–H), 3.66 (1 H, t, J = 10.5 Hz, C_6–H), 3.89 (1 H, d, J = 14.0 Hz, C_{14}–H_a), 4.06 (1 H, d, J = 14.0 Hz, C_{14}–H_b), 4.86 (1 H, A part of ABX, C_2–H_a), 4.90 (1 H, B part of ABX, C_2–H_b), 4.96 (1 H, m, C_3–H_a), 5.36 (1 H, m, C_3–H_b), 5.70 (1 H, X part of ABX, C_1–H).

Transformation of 21 to (11*S*)-14-Hydroxy-2,3-secoeudesma-1,3-dieno-13,6α-lactone (8-Deoxymelitensin, 18). A mixture of **21** (59 mg, 0.22 mmol), *p*-toluenesulfonic acid (6 mg), and benzene (50 mL) was refluxed in a flask equipped with a Dean–Stark column packed with molecular sieves for 2 h, cooled, and poured into ethyl acetate (20 mL). The mixture was washed successively with a saturated aqueous solution of $NaHCO_3$, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product. This was then chromatographed over silica gel (2.5 g) and eluted with a mixture of chloroform and carbon tetrachloride (1:1) to give spectroscopically pure **18** (51 mg, 93%), which was recrystallized from *n*-hexane to give colorless scales: mp 104–105 °C; IR (KBr) 3590, 3510, 1770 cm^{-1}; NMR (100 MHz; the assignment is based on the spin-decoupling experiments) δ 1.09 (3 H, s, C_{10}–CH_3), 1.23 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 2.35 (1 H, d, J = 12.0 Hz, C_5–H), 4.01 (2 H, m, C_{14}–H), 4.14 (1 H, dd, J = 10.0, 12.0 Hz, C_6–H), 4.94 (1 H, A part of ABX, C_2–H_a), 4.95 (1 H, m, C_3–H_a), 4.98 (1 H, B part of ABX, C_2–H_b), 5.36 (1 H, m, $w_{h/2}$ = 3.0 Hz, C_3–H_b), 5.78 (1 H, X part of ABX, C_1–H); $[\alpha]^{22}_D$ +52.4° (c 0.10, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.91; H, 8.92.

Direct Transformation of 15 to 18. A mixture of **15** (145 mg, 0.47 mmol), *p*-toluenesulfonic acid (17 mg), and benzene (140 mL) was refluxed for 2 h, cooled, poured into ethyl acetate (140 mL), and filtered. The filtrate was washed successively with a saturated aqueous solution of $NaHCO_3$ (100 mL) and a saturated aqueous solution of NaCl (100 mL), dried (Na_2SO_4), and concentrated to give an oily crude material, which was then chromatographed over silica gel (10 g) and eluted with a mixture of chloroform and carbon tetrachloride (1:1) to give spectroscopically pure **18** (99 mg, 85%) as a crystalline material.

14-Hydroxy-11β-(phenylseleno)-2,3-secoeudesma-1,3-dieno-13,6α-lactone (22). A solution of **18** (29.3 mg, 0.12 mmol) in THF (0.5 mL) containing HMPA (61 μL, 0.35 mmol) was slowly added over an 8-min period to a cooled (−78 °C) solution of lithium diisopropylamide [prepared from diisopropylamine (49 μL, 0.35 mmol) and 1.62 M butyllithium in hexane (217 μL, 0.35 mmol)] in THF (0.35 mL). After 30 min a solution of diphenyl diselenide (110 mg, 0.35 mmol) in THF (0.35 mL) was added at −78 °C. The reaction mixture was stirred at −78 °C for 30 min and then warmed to −20 °C where stirring was continued for an additional 1 h. The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL). The mixture was extracted with ethyl acetate (4 × 20 mL). The combined extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product, which was purified by preparative TLC ($CHCl_3$/EtOAc, 1:1).

The first band (R_f 0.64) gave diphenyl diselenide.

The second band (R_f 0.42) gave **22** (27.4 mg, 58%) as a colorless oil: IR ($CHCl_3$) 3600, 2945, 1770, 1640, 1440, 1380, 1120, 1075, 1025, 1010, 985, 920 cm^{-1}; NMR (90 MHz) δ 1.08 (3 H, s, C_{10}–CH_3), 1.56 (3 H, s, C_{11}–CH_3), 2.32 (1 H, d, J = 11.7 Hz, C_5–H), 3.97 (2 H, br s, C_{14}–H), 4.43 (1 H, dd, J = 11.7, 9.5 Hz, C_6–H), 4.81 (1 H, br s, C_3–H_a), 4.92 (1 H, A part of ABX, C_2–H_a), 4.97 (1 H, B

part of ABX, C_2–H_b), 5.31 (1 H, br s, C_3–H_b), 5.75 (1 H, X part of ABX, C_1–H), 7.17–7.40 (3 H, m, meta and para protons of C_6H_5), 7.56–7.68 (2 H, m, ortho protons of C_6H_5); $[\alpha]^{22}_D$ +70.8° (*c* 1.14, $CHCl_3$).

The third band (R_f 0.34) gave recovered **18** (3.9 mg, 13%).

14-Hydroxy-2,3-secoeudesma-1,3,11-trieno-13,6α-lactone (11,12-Dehydro-8-deoxymelitensin, 23). A solution of **22** (25.4 mg, 0.063 mmol) in THF (0.6 mL) containing acetic acid (9.5 μL, 0.17 mmol) was treated at 0 °C with 30% H_2O_2 (42 μL, 0.44 mmol). After the addition was complete, stirring was continued for additional 1 h at this temperature. The reaction mixture was poured into a cold saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily material, which was purified by preparative TLC (AcOEt/$CHCl_3$, 3:7) to give 14.3 mg (92%) of **23** (R_f 0.35) as a colorless oil: IR ($CHCl_3$) 3600, 3100, 2950, 1770, 1640, 1410, 1260, 1145, 1065, 1010, 985, 925 cm^{-1}; NMR (90 MHz) 1.10 (3 H, s, C_{10}–CH_3), 2.49 (1 H, d, J = 11.7 Hz, C_5–H), 4.03 (2 H, br s, C_{14}–H), 4.11 (1 H, dd, J = 10.7, 11.7 Hz, C_6–H), 4.94 (1 H, br s, C_3–H_a), 4.95 (1 H, A part of ABX, C_2–H_a), 5.00 (1 H, B part of ABX, C_2–H_b), 5.39 (1 H, br s, C_3–C_b), 5.40 (1 H, d, J = 3.4 Hz, C_{12}–H_a), 5.79 (1 H, X part of ABX, C_1–H), 6.05 (1 H, d, J = 3.4 Hz, C_{12}–H_b); $[\alpha]^{22}_D$ +36.8° (*c* 1.28, $CHCl_3$).

(11*S*)-14-Acetoxy-2,3-secoeudesma-1,3-dieno-13,6α-lactone (24). A mixture of **18** (21 mg, 0.084 mmol), pyridine (88 μL), and acetic anhydride (24 μL) was allowed to stand at room temperature for 38 h, poured into a saturated aqueous solution of NaCl (10 mL), and extracted with ether (2 × 10 mL). The combined extracts were washed successively with 1 M HCl (10 mL), a saturated aqueous solution of $NaHCO_3$ (10 mL), and a saturated aqueous solution of NaCl (2 × 10 mL), dried (Na_2SO_4), and concentrated to give an oily crude material, which was then chromatographed over silica gel and eluted with a mixture of chloroform and carbon tetrachloride (1:1) to give spectroscopically pure **24** (24 mg, 98%) as a crystalline material. This was then recrystallized from hexane to give colorless microcrystals: mp 41–42 °C; IR (KBr) 3100, 1778, 1740, 1005, 905 cm^{-1}; NMR (100 MHz; the assignment is based on the spin-decoupling experiments) δ 1.11 (3 H, s, C_{10}–CH_3), 1.25 (3 H, d, J = 6.5 Hz, C_{11}–CH_3), 2.08 (3 H, s, CH_3CO), 2.29 (1 H, d, J = 11.5 Hz, C_5–H), 4.12 (1 H, dd, J = 9.5, 11.5 Hz, C_6–H), 4.50 (2 H, m, C_{14}–H), 4.97 (1 H, A part of ABX, C_2–H_a), 5.02 (1 H, m, C_3–H_a), 5.05 (1 H, B part of ABX, C_2–H_b), 5.37 (1 H, m, C_3–H_b), 5.79 (1 H, X part of ABX, C_1–H); $[\alpha]^{22}_D$ +50.6° (*c* 0.31, $CHCl_3$). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.97; H, 8.35.

(11*S*)-6α,13-Epoxy-2,3-secoeudesma-1,3-dien-13-ol (25). The crude acetate **24** which was obtained from 34 mg (0.14 mmol) of **18** by the method mentioned above was employed in the following reaction without any purification.

Lithium (9.5 mg, 1.4 mmol) was added into dry liquid ammonia at −78 °C and stirred for a few minutes at this temperature, and then the solution of **24** in ether was added into the mixture. The deep blue solution was efficiently stirred at −78 °C for 30 min. Ammonium chloride (100 mg) was cautiously added to discharge the color. Ammonia was evaporated at room temperature, and the residue was dissolved in a mixture of ether (15 mL) and water (15 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (2 × 15 mL). The combined organic layer was washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product (42 mg), which was then chromatographed over silica gel and eluted with a mixture of chloroform and carbon tetrachloride (1:1) to give **25** (26 mg, 81% overall yield from **18**) as an epimeric mixture at C_{13}: IR ($CHCl_3$) 3600, 3430 cm^{-1}; NMR of the major isomer (100 MHz; the assignment is based on the spin-decoupling experiments) δ 1.05 (3 H, s, C_{10}–CH_3), 1.13 (3 H, d, J = 6.5 Hz, C_{11}–CH_3), 1.80 (3 H, m, C_4–CH_3), 2.08 (1 H, d, J = 11.0 Hz, C_5–H), 3.14 (1 H, m, OH), 3.98 (1 H, dd, J = 10.0, 11.0 Hz, C_6–H), 4.72 (1 H, m, C_3–H_a), 4.91 (1 H, A part of ABX, C_2–H_a), 4.93 (1 H, B part of ABX, C_2–H_b), 5.00 (1 H, m, C_3–H_b), 5.09 (1 H, br d, J = 4.5 Hz, C_{13}–H), 5.82 (1 H, X part of ABX, C_1–H).

Saussurea Lactone (4). Chromic anhydride (101 mg, 1.01 mmol) was added into a mixture of methylene chloride (1.2 mL) and pyridine (207 μL, 2.04 mmol) at 0 °C and stirred for 10 min. Then **25** (12 mg, 0.05 mmol) dissolved in methylene chloride (1.1 mL) was added over 10 min. The mixture was stirred at 0 °C for 5 h and at room temperature for 1 h, diluted with methylene chloride (20 mL), and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated aqueous solution of $NaHCO_3$, 2 M HCl, and a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give 11 mg (92%) of **4**: mp 146–147 °C (lit. mp 146–147 °C,[15,16] 148–149 °C[8a]); IR (Nujol) 1770 cm^{-1}; NMR (100 MHz; the assignment is based on spin-decoupling experiments) δ 1.09 (3 H, s, C_{10}–CH_3), 1.23 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 1.79 (3 H, m, $w_{h/2}$ = 3.0 Hz, C_4–CH_3), 2.24 (1 H, d, J = 11.0 Hz, C_5–H), 4.11 (1 H, dd, J = 10.0, 11.0 Hz, C_6–H), 4.70 (1 H, m, $w_{h/2}$ = 3.5 Hz, C_3–H_a), 5.03 (1 H, m, C_3–H_b), 4.94 (1 H, A part of ABX, C_2–H_a), 4.98 (1 H, B part of ABX, C_2–H_b), 5.82 (1 H, X part of ABX, C_1–H); $[\alpha]^{22}_D$ +65.4° (*c* 0.065, $CHCl_3$).

(11*S*)-14-Methoxy-2,3-secoeudesma-1,3-dieno-13,6α-lactone (29). Sodium hydride (50% dispersion in mineral oil, 30 mg, 0.63 mmol) was added to a 10-mL round-bottomed flask, and the mineral oil was removed by washing with pentane (2 × 2 mL). A solution of **18** (52 mg, 0.21 mmol) in dry DMF (5 mL) was added dropwise over 10 min to the flask. The mixture was stirred at room temperature for 30 min. MeI (98%, 66 μL, 1.04 mmol) was added to the stirred mixture at room temperature, and the stirring was continued at this temperature for 18 h. The mixture was then poured into a saturated aqueous solution of NaCl (10 mL) and extracted with ethyl acetate (5 × 10 mL). The combined extracts were washed successively with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product (46 mg), which was purified by preparative TLC ($CHCl_3$/EtOAc, 9:1).

The first band (R_f 0.44) gave **29** (33 mg, 67%) as a crystalline material: IR ($CHCl_3$) 3015, 1770, 1195, 1000, 915 cm^{-1}; NMR (90 MHz) δ 1.09 (3 H, s, C_{10}–CH_3), 1.23 (3 H, d, J = 6.6 Hz, C_{11}–CH_3), 2.33 (1 H, d, J = 11.7 Hz, C_5–H), 3.26 (3 H, s, OCH_3), 3.67 (1 H, d, J = 13.5 Hz, C_{14}–H_a), 3.99 (1 H, d, J = 13.5 Hz, C_{14}–H_b), 4.12 (1 H, dd, J = 9.5, 11.7 Hz, C_6–H), 4.93 (1 H, A part of ABX, C_2–H_a), 4.96 (1 H, B part of ABX, C_2–H_b), 4.96 (1 H, br s, C_3–H_a), 5.30 (1 H, br s, C_3–H_b), 5.79 (1 H, C_1–H, X part of ABX).

(11*S*)-13-Acetoxy-6α,13-epoxy-2,3-secoeudesma-1,3-diene (31). To a stirred solution of **25** (12 mg, 0.05 mmol) in pyridine (105 μL) was added acetic anhydride (29 μL, 0.3 mmol) at room temperature. The mixture was stirred for 27 h at room temperature and poured into a saturated aqueous solution of NaCl (10 mL). The mixture was extracted with ethyl acetate (2 × 10 mL). The combined extracts were washed successively with 1 M HCl (10 mL), a saturated aqueous solution of $NaHCO_3$ (10 mL), and a saturated aqueous solution of NaCl (10 mL), dried (Na_2SO_4), and concentrated to give **31** (14 mg, 100%) as an oil: NMR (60 MHz) δ 1.03 (3 H, s, C_{10}–CH_3), 1.15 (3 H, d, J = 6.8 Hz, C_{11}–CH_3), 1.77 (3 H, br s, C_4–CH_3), 2.04 (3 H, s, CH_3CO), 2.10 (1 H, J = 11.0 Hz, C_5–H), 3.90 (1 H, dd, J = 9.5, 11.5 Hz, C_6–H), 4.67 (1 H, br s, C_{14}–H_a), 4.88 (1 H, A part of ABX, C_2–H_a), 4.92 (1 H, B part of ABX, C_2–H_b), 4.96 (1 H, br s, C_{14}–H_b), 5.86 (1 H, X part of ABX, C_1–H), 5.86 (1 H, d, J = 4.0 Hz, C_{13}–H).

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