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Modification of α-Santonin. III. Synthesis of Dihydrocostunolide[1]

Yasuo Fujimoto, Takeshi Shimizu, Masayuki Ohmori, and Takashi Tatsuno

The Institute of Physical and Chemical Research (Rikagaku Kenkyusho)[2]

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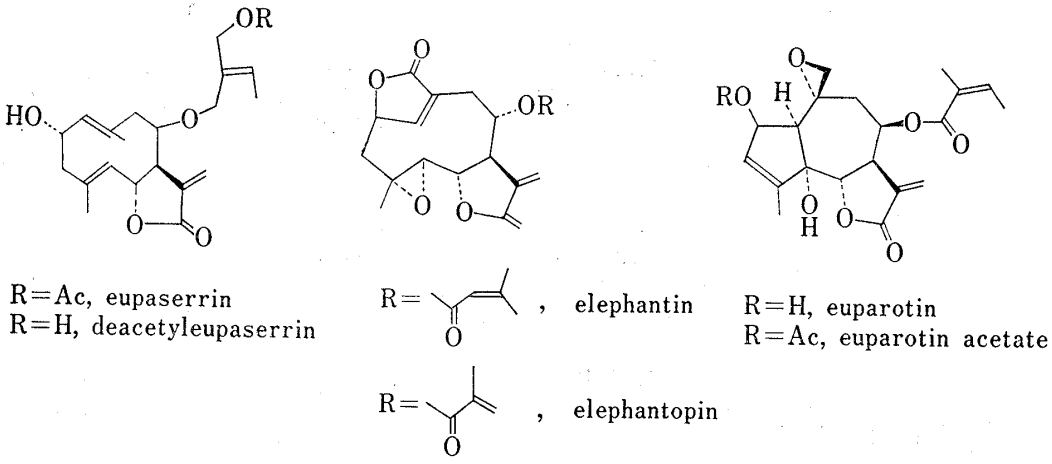
A new synthetic method for cyclodecanone intermediates (**33** and **38**) which are useful for the synthesis of not only germacranolide but guaianolide-type sesquiterpenoids is described. Synthesis of dihydrocostunolide, a typical germacranolide, is also described.

Keywords——sesquiterpenoid; α-santonin; germacranolide; guaianolide; dihydrocostunolide; chlorination; methanesulfonyl chloride; photolysis; cyclodecanone; hexahydronaphthalene

A number of germacranolide- and guaianolide-type sesquiterpenoids such as eupaserrin,[3a] euparotin,[3b] and elephantin,[3c] have been isolated from eupatorium and elephantopus species by Kupchan *et al.*[3] These sesquiterpenoids have been noted by their remarkable antitumor activities for leukemia p-388, 9-KB, and Walker 256.[4] Interesting pharmacological activities of these compounds prompted us to investigate a new synthetic method for germacranolide and guaianolide intermediates.



R=Ac, eupaserrin
R=H, deacetyleupaserrin

R= , elephantin

R= , elephantopin

R=H, euparotin
R=Ac, euparotin acetate

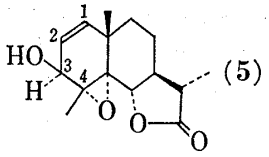
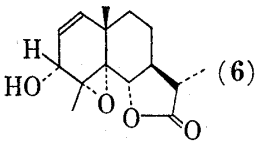
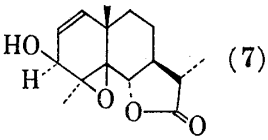
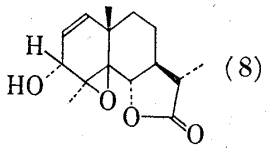
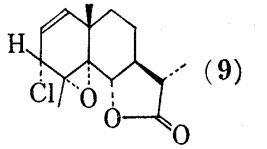
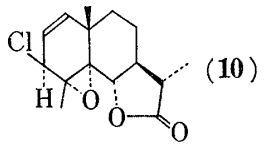
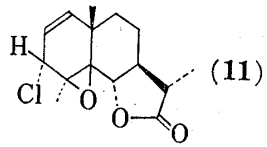
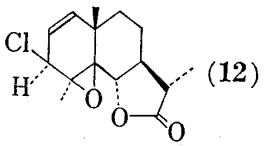
Chart 1

In this report, we describe a novel method for the preparation of cyclodecanone intermediate which is useful for the synthesis of not only germacranolide but quaianolide-type sesquiterpenoids starting from α-santonin, and further describe the synthesis of dihydroconstunolide,[5a,b] a typical germacranolide, isolated from costus root oil.

1) Part II: Y. Fujimoto, T. Shimizu, and T. Tatsuno, *Tetrahedron Lett.*, **1976**, 2041.
2) Location: *Wako-shi, Saitama 351, Japan.*
3) *a*) Eupaserrin: S.M. Kupchan, T. Fujita, M. Maruyama, and R.W. Briton, *J. Org. Chem.*, 38, 1260 (1973); *b*) Euparotin: S.M. Kupchan, J.C. Hemingway, J.M. Cassady, J.R. Cnox, A.T. McPhail, and G.A. Sim., *ibid.*, **89**, 465 (1976); *c*) Elephantin: S.M. Kupchan, Y. Aynehchi, M.M. Cassady, A.T. McPhail, G.M. Sim, H.K. Schnoes, and A.L. Burlingane, *J. Am. Chem. Soc.*, **88**, 3674 (1966).
4) S.M. Kupchan, A.M. Eakin, and A.M. Thomas, *J. Med. Chem.*, **14**, 1147 (1971) and references cited therein.
5) *a*) E.J. Corey and A.G. Hortmann, *J. Am. Chem. Soc.*, **87**, 5736 (1965); *b*) P.A. Grieco, and M. Nishizawa, *J. Org. Chem.*, **42**, 1717 (1977). After completion of our synthesis, Grieco and Nishizawa reported the synthesis of dihydrocostunolide.

Although epoxidation of α-santonin with perbenzoic acid and peracetic acid has been reported independently by three groups,[6-8] yields of α-epoxide (**1**) and β-epoxide (**2**) were not satisfactory for further transformation. We obtained α- and β-epoxides in 38.6% and 43.2% yields, respectively, together with small amounts of diepoxide (**3**)[8] and Baeyer–Villiger rearrangement product (**4**) by the action of *m*-chloroperbenzoic acid in the presence of 4,4′-thiobis(6-*t*-butyl-3-methylphenol) as a radical inhibitor.[9] Selective reduction of the

Table I. ^{1}H-NMR ($CDCl_3$, δ) Data of H-1, H-2, and H-3 of Allylic Alcohols and Allylic Chlorides

Compounds (No.)	H-1	H-2	H-3
 (**5**)	5.37 (d) $J_{1,2}$=10.0 Hz	5.65 (dd) $J_{2,1}$=10.0 Hz $J_{2,3}$=5.0 Hz	4.27 (d) $J_{3,2}$=5.0 Hz
 (**6**)	5.26 (dd) $J_{1,2}$=10.0 Hz $J_{2,3}$=2.0 Hz	5.46 (dd) $J_{2,1}$=10.0 Hz $J_{2,3}$=2.0 Hz	4.18 (ddd) $J_{3,OH}$=11.0 Hz $J_{3,1}$=2.0 Hz $J_{3,2}$=2.0 Hz
 (**7**)	5.22 (dd) $J_{1,2}$=10.5 Hz $J_{1,3}$=2.0 Hz	5.43 (dd) $J_{2,1}$=10.5 Hz $J_{2,3}$=2.0 Hz	4.12 (dd) $J_{3,1}$=2.0 Hz $J_{3,2}$=2.0 Hz
 (**8**)	5.27 (d) $J_{1,2}$=10.5 Hz	5.57 (dd) $J_{2,1}$=10.5 Hz $J_{2,3}$=5.0 Hz	4.20 (d) $J_{3,2}$=5.0 Hz
 (**9**)	5.32 (dd) $J_{1,2}$=10.0 Hz $J_{1,3}$=2.0 Hz	5.49 (dd) $J_{2,1}$=10.0 Hz $J_{2,3}$=2.0 Hz	4.51 (dd) $J_{3,2}$=2.0 Hz $J_{3,1}$=2.0 Hz
 (**10**)	5.34 (d) $J_{1,2}$=10.0 Hz	5.64 (dd) $J_{2,1}$=10.0 Hz $J_{2,3}$=5.5 Hz	4.55 (d) $J_{3,2}$=5.5 Hz
 (**11**)	5.24 (d) $J_{1,2}$=10.5 Hz	5.64 (dd) $J_{2,1}$=10.5 Hz $J_{2,3}$=5.0 Hz	4.56 (d) $J_{3,2}$=5.0 Hz
 (**12**)	5.29 (dd) $J_{1,2}$=10.0 Hz $J_{1,3}$=2.0 Hz	5.47 (dd) $J_{2,1}$=10.0 Hz $J_{2,3}$=2.0 Hz	4.70 (dd) $J_{3,1}$=2.0 Hz $J_{3,2}$=2.0 Hz

6) E. Wedekind and K. Tettweiler, *Ber.*, **64**, 1796 (1931).
7) J.B. Hedrickson and T.L. Bogard, *J. Chem. Soc.*, **1962**, 1678.
8) M. Yanagita, T. Hirose, and T. Okura, The 91st Annual Meeting of Pharmaceutical Society of Japan. Fukuoka, Apr. 1971.
9) Y. Kishi, M. Aratani, H. Tanino, T. Fukuyama, T. Goto, S. Inoue, S. Sugiura, and H. Kakoi, *J.C.S., Chem. Comm.*, **1972**, 64.

carbonyl group in **1** and **2** with lithium aluminum hydride in tetrahydrofuran at −78° afforded a mixture of the corresponding α- and β-alcohols, respectively (**5**, 16.7%; **6**, 65.6%; **7**, 65.9%; **8**, 15.6% yield). Configuration of the H-3 of the alcohols was assigned as shown in the structures (**5**, **6**, **7**, and **8**) from the considerations based on the coupling patterns[10] of H-3, H-2 and H-1, that is, the allylic coupling between H-3 and H-1 is only observed when the configuration of the H-3 is quasi axial orientation (see Table I).

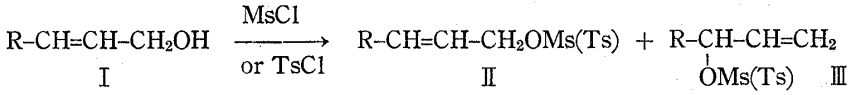


Chart 2

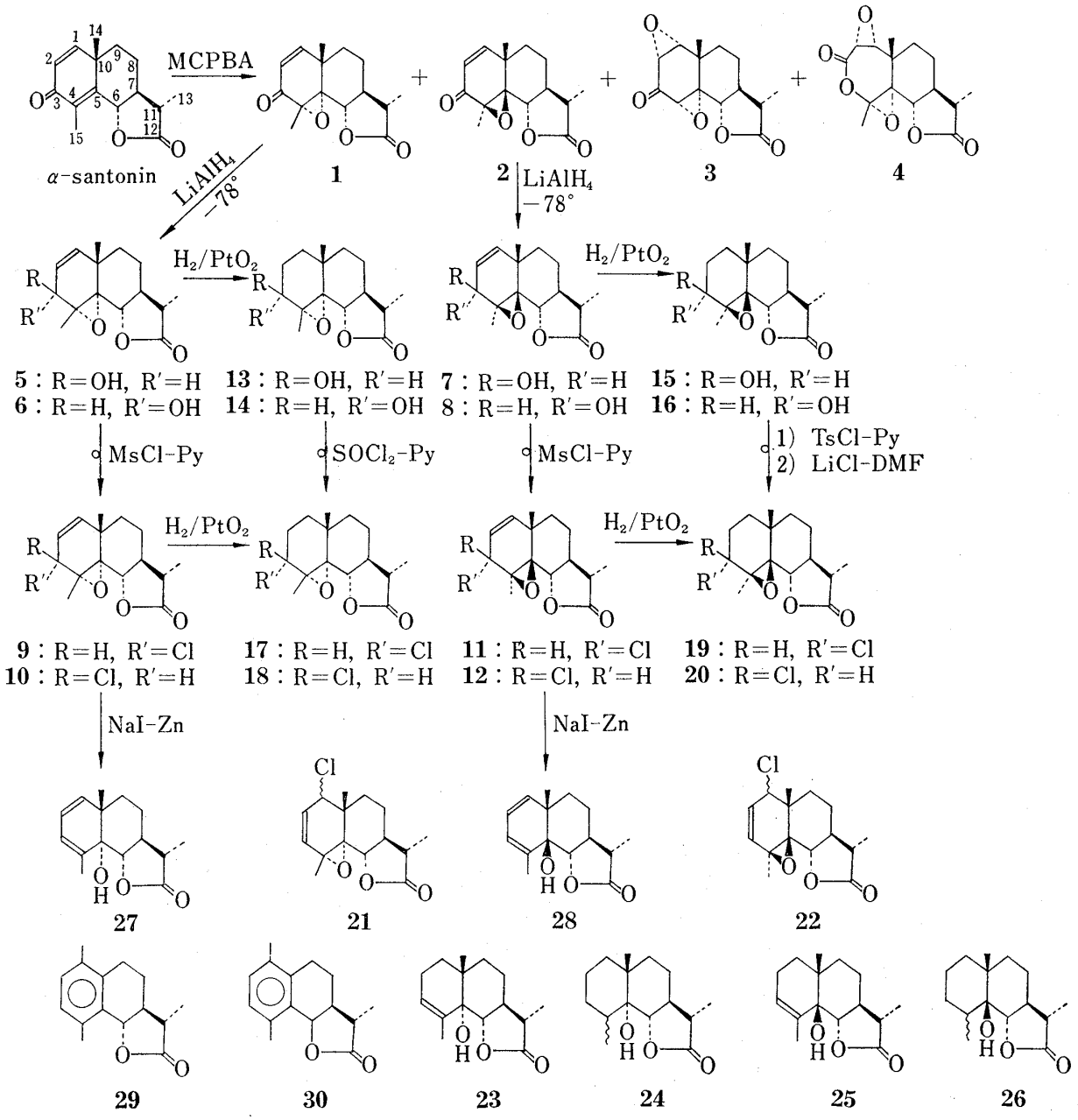


Chart 3

10) S. Sternhell, *Quart. Rev.*, **1969**, 236.

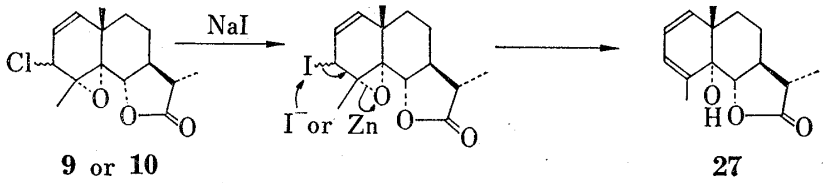
In general, it is well known that mesylation (or tosylation) of an allylic alcohol derivative (I) with methanesulfonyl chloride (MsCl) or *p*-toluenesulfonyl chloride (TsCl)-pyridine produces a mixture of the corresponding mesylate (or tosylate) (II) and the rearranged isomer (III). However, mesylation (or tosylation) of **6** with MsCl (or TsCl)–pyridine gave an unexpected chlorinated compound [**10**, 85.6% (MsCl); 79.8% (TsCl) yield] and any mesylated (or tosylated) compound was not obtained. By the same treatment, the other three alcohols (**5**, **7**, and **8**) were also converted stereospecifically into the corresponding chlorides (**9**, 92.3%; **11**, 98% and **12**, 90.8% yield) having the inverted configuration of H-3. Inversion of the configuration of H-3 during the chlorination of the alcohols (**5**, **6**, **7** and **8**) was verified by comparison of the coupling constants of H-3 in the original alcohols with those in the chlorides (**9**, **10**, **11** and **12**) (see Table I). The possibility of rearranged isomers (**21** and **22**) for the structure of the chlorinated compounds was excluded by the following experiments and the fact that the chloride (**10**) was also obtained from the compound (**6**) by the Meyers procedure[11] which is a facile and specific method for the conversion of allylic alcohols to the chlorides without rearrangement.

The alcohols (**5**, **6**, **7** and **8**) were hydrogenated over platinum to give the corresponding dihydro derivatives (**13**, **14**, **15** and **16**). Chlorination of **13** and **14** with thionyl chloride–pyridine gave the chlorides **17** and **18**, respectively. On the other hand, **15** and **16** afforded a complex mixture by the same treatment.

Thus, **15** and **16** were converted to the tosylates which were then chlorinated with lithium chloride–dimethylformamide to give the chlorides (**19** and **20**). These four chlorides (**17**, **18**, **19** and **20**) were also obtained together with small amounts of **23**,[12] **24**, **25** and **26** by catalytic reduction of the chlorides (**9**, **10**, **11** and **12**).

Treatment of the chloride (**9**) with sodium iodide in refluxing acetone for 5—7 hr gave a dienol (**27**) in 67% yield as well as small amounts of hyposantonin (**29**)[13] and isohyposantonin (**30**).[13]

It seems that the reaction proceeds along the pathway whereby the chloride is first converted to the iodo intermediate which is then attacked by an iodo anion to produce the dienol (Chart 4).



9 or **10** **27**

Chart 4

Therefore, it is expected thet the addition of an iodine-reducing agent such as zinc in this reaction system would accelerate the reaction rate and improve the yield of the dienol, since the rate determining step of this reaction may be the reductive cleavage of iodo-epoxide.

In fact, this expectation proved to be true and the dienols (**23** and **24**) were obtained in a high yield by treatment of the chlorides (**9**, **10**, **11** and **12**) with sodium iodide–zinc in refluxing acetone for 45—55 min. Direct dechlorination of **9** with zinc in refluxing acetone produced hyposantonin (**29**) and isohyposantonin (**30**) exclusively.

While the photolytic cleavage of hexahydronaphthalene derivatives[5a,14] usually yields a photostationary equilibrium mixture of the starting material and a cyclodecatriene, irradia-

11) E.W. Collington and A.I. Meyers, *J. Org. Chem.*, 36, 3044 (1971).
12) S.P. Pathak and G.H. Kulkarni, *Chem. and Ind.*, 1968, 913.
13) J. Simonsen and D.H.R. Barton, "The Terpenes," Vol. III, University Press, Cambridge, England 1961, p. 251.
14) W.G. Dauben, R.G. Williams, and R.D. Mckelvey, *J. Am. Chem. Soc.*, 95, 3932 (1973).

tion of the dienols (**27** and **28**) with a 7 W low pressure mercury lamp provided a diastereomeric mixture of dienones (**33**, 45.1%; **34**, 2.2%; **35**, 3.9% yield) together with guaianolide-type compound[15] (**37**, 23.7% yield), tetracyclic compound (**36**, 5.4% yield), and a conjugated

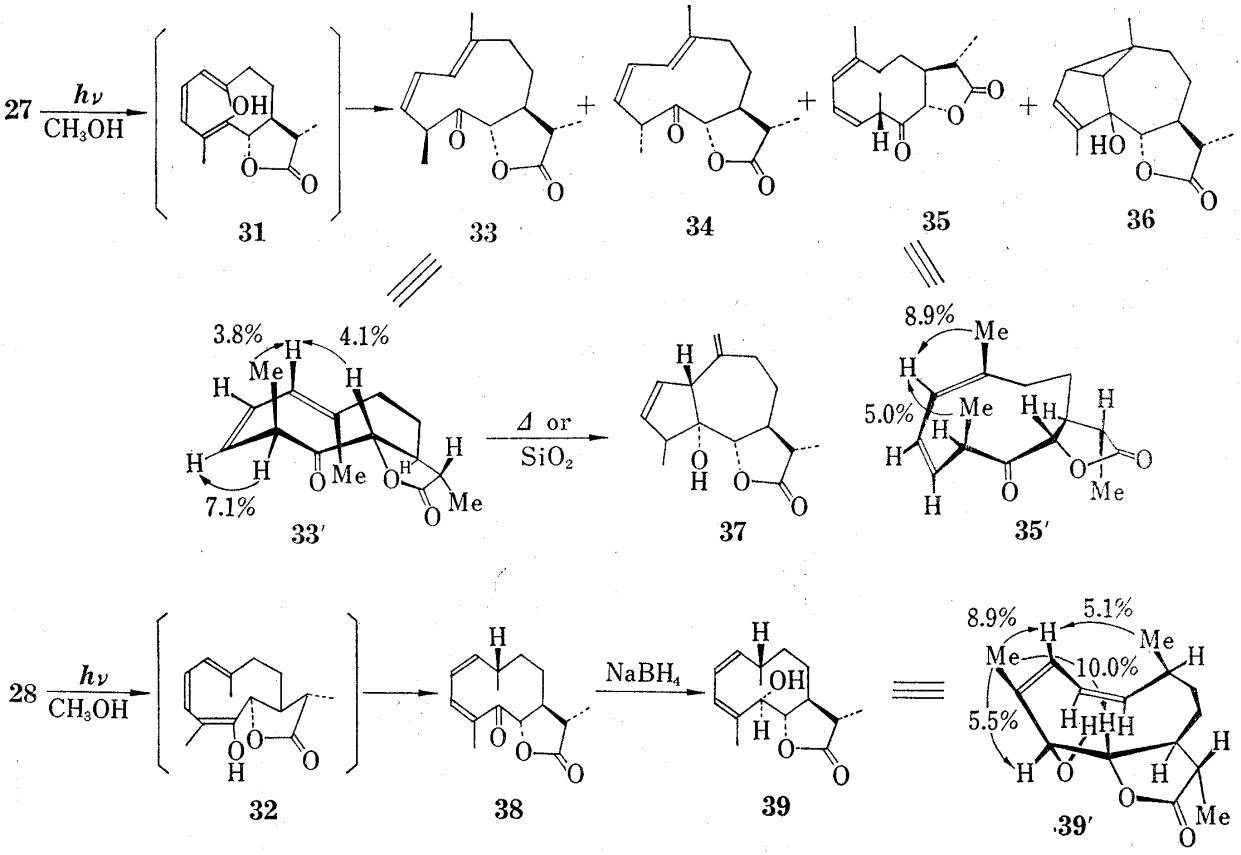


Chart 5

TABLE II. Physical Properties and Spectral Data of Cyclodecadienones

Compd. No.	mp (°C)	$[\alpha]_D^{22°}$	IR (KBr) cm^{-1}	UV λ_{max}^{MeOH} nm	^{1}H-NMR spectral data (100 MHz, δ, in $CDCl_3$) H-15	H-13	H-14	H-1	H-2	H-3	H-4	H-6
33	65°	−2.4°	1780 1715	214	1.36 (d) J=7.0	1.32 (d) J=7.0	1.56 (s)	5.69 (m)	6.03 (m)	5.45 (m) J=10.2 4.6 2.0	3.49 (m)	4.50 (d) J=7.5
34	90°	+31.4°	1782 1762(sh) 1720	203 215	1.26 (d) J=7.0	1.32 (d) J=6.5	1.70 (s)	5.57 (m)	5.49 (m)	5.43 (m) J=11.0 3.0 1.7	3.48 (m)	4.51 (d) J=7.5
35	147°	+222°	1770 1720	203 224	1.17 (d) J=6.5	1.23 (d) J=6.0	1.79 (s)	5.85 (m)	6.17 (m)	5.44 (m) J=10.0 10.0 1.8	3.73 (m) J=6.5 10.0	5.12 (d) J=2.0
38	120°		1780 1705	212 276.5	2.06 (s)	1.28 (d) J=6.5	0.93 (s)	5.30 (dd) J=11.0 11.0	5.73 (m)	5.86 (m)		4.75 (d) J=9.5

15) The compound (**37**) was mostly produced from **33** during isolation procedure, since high pressure liquid chromatographic analysis of the reaction mixture showed the presence of only a small amount of **37**.

dienone (**38**, 46.8% yield, UV λ_{max}^{MeOH} nm: 212, 276.5) respectively because the initially formed cyclodecatrienols (**31** and **32**) were transformed immediately to relatively stable dienones without equilibration.

The cyclodecadienone structures of the photolytic products were verified from their spectral data (Table II) and their chemical conversion. Treatment of **33** with refluxing benzene or mixing with silica gel gave **37** in a quantitative yield, whose stereochemistry was confirmed by X-ray analysis[16] as shown in the structure **37**.

From the nuclear overhauser effect (NOE) data shown on the structure **33'** and the easy transformation of **33** to **37**, it is presumed that the germacranolide-type compound (**33**) adopts the conformation **33'**. The configuration of C-1-C-10 double bond and C(4)–CH_3 in compound (**35**) was assumed to be structure **35'** from the measurement of the NOE. Structure of the compound (**36**) was confirmed by analysis of its ^{1}H-nuclear magnetic resonance (PMR) [1.75 (3H, broad singlet, vinyl methyl), 5.50 (1H, broad singlet, vinyl proton)] and ^{13}C-nuclear magnetic resonance (CMR) spectra [34.1 and 39.0 (doublet each), C-2 (or C-1) and C-1 (or C-2)].

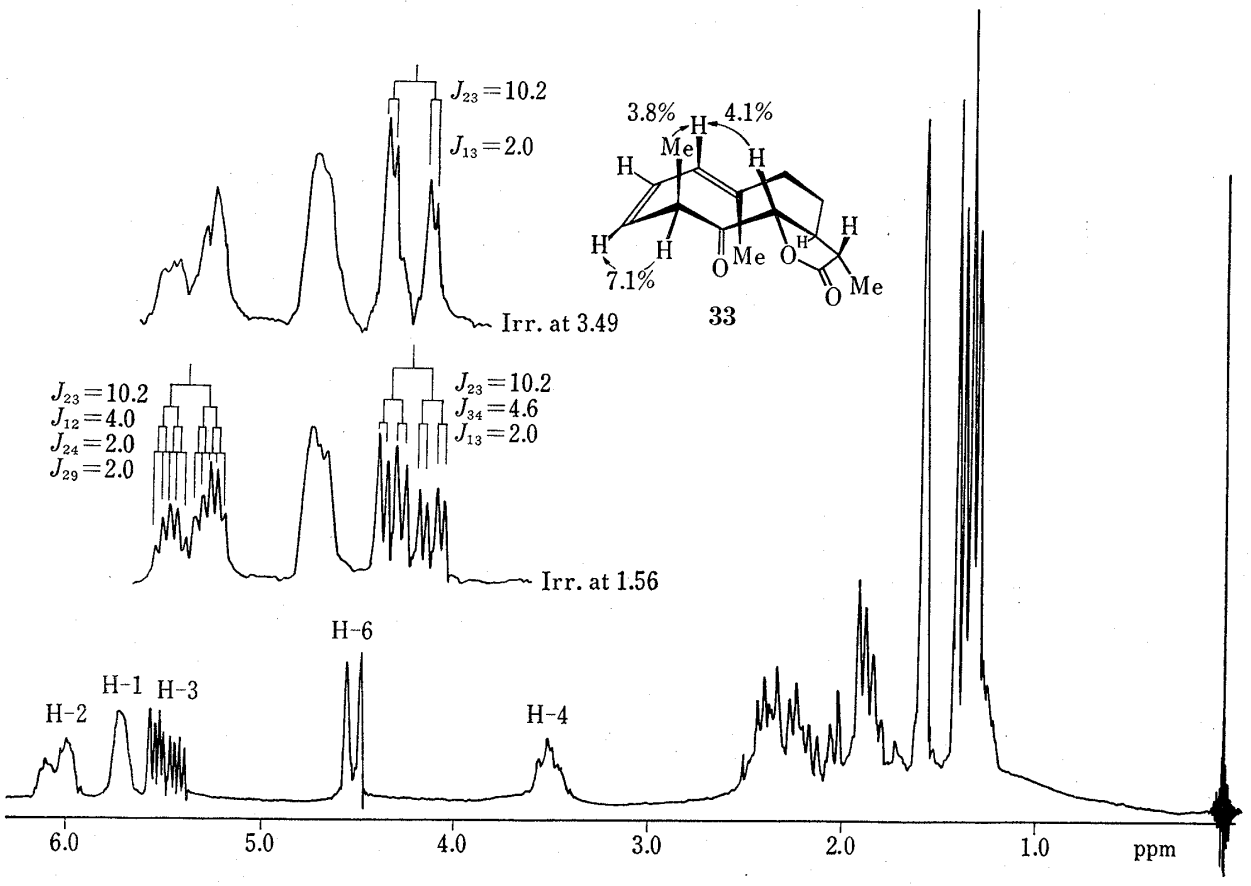


Fig. 1. ^{1}H-NMR Spectrum of Compound **33**

The stereostructures of compound (**38**) and its dihydro derivative (**39**) were confirmed from the PMR data (Table II) and the NOE data shown on the structure **39'**.

Hydrogenation of **33** over palladium on charcoal gave dihydro derivatives (**40**, 62.8%; **41**, 18.8% and **42**, 15.7% yield). The C-1-C-2 double bond of compound (**41**) was determined to be trans configuration by the coupling constant ($J_{1,2}$=16.0 Hz) between H-1 and H-2. Reduction of **40** with sodium borohydride produced an α-alcohol (**43**, 86.5% yield) by the attack of a hydride anion from the less hindered side.

16) T. Itoh, T. Shimizu, Y. Fujimoto, and T. Tatsuno, *Acta Cryst.* **B34**, 1978, 1009.

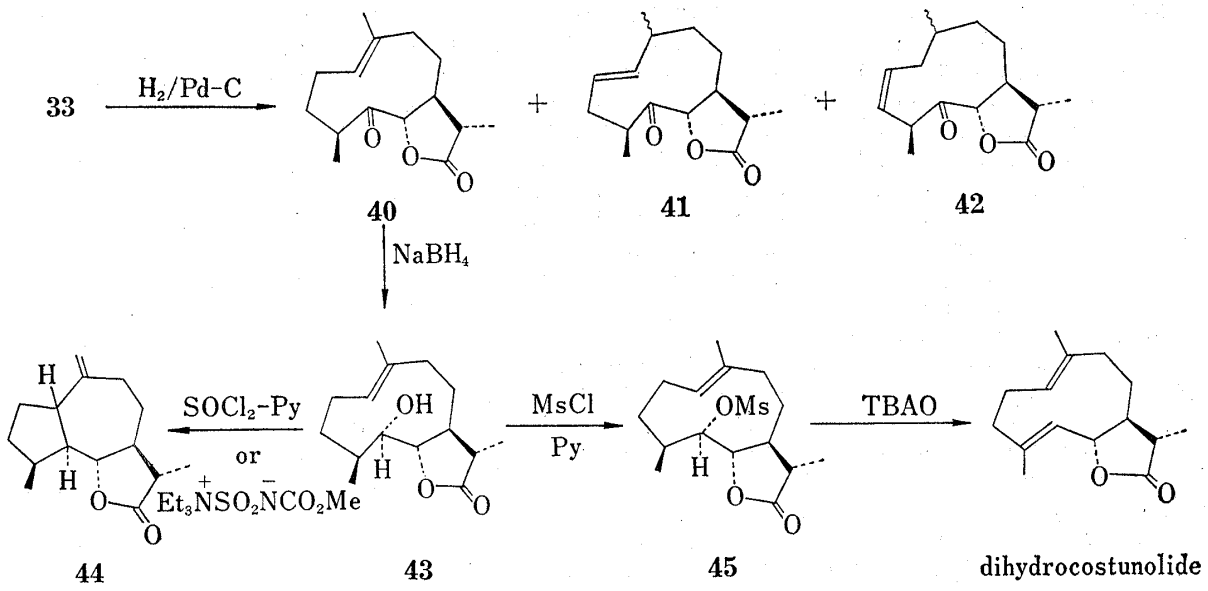


Chart 6

Dehydration of the alcohol (**43**) with thionyl chloride–pyridine or (carboxysulfamoyl)-triethylammonium hydroxide inner salt methyl ester[17] produced the compound (**44**) [36.4% or 80% yield, PMR: 4.83 (2H, singlet; exomethylene protons)] as a main product and dihydrocostunolide could not be detected on thin-layer chromatograms (TLC) or gas liquid chromatograms (GLC) of the reaction products. Thus, the alcohol (**43**) was converted to a mesylate[18] (**45**) which was then treated with tetra-butylammonium oxalate (TBAO)[19] to give dihydrocostunolide after purification by preparative TLC.

The synthesized dihydrocostunolide was identical with an authentic specimen in TLC, GLC, high pressure liquid chromatography and in mass spectrum (MS), infrared (IR), and PMR spectra.

Further work on transformation of cyclodecadienones (**33** and **38**) and guaianolide-type intermediate (**37**) to the natural products is now in progress.

Experimental

All melting points were uncorrected. IR spectra (cm^{-1}) of crystallized compounds were taken in KBr with Hitachi EPI-G2 spectrophotometer and ultraviolet (UV) spectra were recorded with Shimazu UV-200 spectrophotometer unless otherwise stated. PMR spectra (δ, 100 and 60 MHz) and CMR spectra were measured in $CDCl_3$ containing 1% tetramethylsilane as an internal standard with Varian HA-100, JEOL PMX-60 and JEOL FX-100 spectrometers respectively. Mass Spectra were recorded with Hitachi RMU-6M spectrometer.

Epoxidation of α-Santonin——A mixture of 49.2 g (0.2 mol) of α-santonin, 41.0 g (0.22 mol) of *m*-chloroperbenzoic acid (MCPBA) and 30 mg of 4,4′-thiobis-(6-*t*-butyl-3-methylphenol) in 300 ml of 1,2-dichloroethane was refluxed for 12 hr and then additional 12 g (0.07 mol) of MCPBA was added and the reflux was continued for further 12 hr. When cooled, precipitated *m*-chlorobenzoic acid was filtered off and the filtrate was washed with 1 N $NaHCO_3$ (50 ml×3) and saturated NaCl solution, and then dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residual oil was triturated with a small amount of ethanol for crystallization. Recrystallization from ethanol gave 18.3 g of α-epoxide (**1**). Evaporation of the mother liquor left an oil which was crystallized from benzene: AcOEt=3:1. Recrystallization from benzene–AcOEt gave 19.2 g of β-epoxide (**2**). The mother liquor was evaporated to dryness and the residual oil was adsorbed on silica gel and then eluted with benzene: AcOEt=10:1 to give 1.9 g of **1**, 3.0 g of **2**, 1.0 g of diepoxide (**3**), 0.3 g of diepoxy-lactone (**4**) and 4.0 g of α-santonin. **1**, 38.6% yield, mp 215° (lit.[6] 214°, lit.[7] 216°). **2**, 43.2% yield,

17) E.M. Burgess, H.R. Penton, Jr. and E.A. Taylor, *J. Org. Chem.*, **38**, 26 (1973).
18) In spite of the extensive efforts, the dihydrocostunolide was not obtained by treatment of mesylate (**45**) with 1,8-diazabiclo[5.4.0]undec-7-3n3 (DBU) or any other organic bases.
19) E.J. Corey and S. Terashima, *Tetrahedron Lett.*, **1972**, 111.

mp 158° (lit.[6] 157°). **3**, 1.8% yield, mp 234—235°. *Anal.* Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.45; H, 6.47. MS *m/e*: 278 (M^+). IR: 1778 (shoulder), 1770 (COO), 1690 (CO). PMR: 1.25 (3H, d, J=7.0 Hz, H-13), 1.65 (3H, s, H-14), 2.15 (3H, s, H-15), 3.22 (1H, d, J=4.0 Hz, H-1), 3.52 (1H, d, J=4.0, H-2), 4.33 (1H, d, J=10.0 Hz, H-6). **4**, 1% yield, mp 248°, colorless needles from $CHCl_3$. *Anal.* Calcd. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found: C, 61.12; H, 6.06. MS *m/e*: 294 (M^+). IR: 1780 (shoulder) and 1770 (γ-lactone), 1750 (7 membered lactone). PMR: 1.27 (3H, d, J=6.0 Hz, H-13), 1.44 (3H, s, H-14), 2.45 (3H, s, H-15), 2.94 (1H, d, J=3.6 Hz, H-1), 3.61 (1H, d, J=3.6 Hz, H-2), 4.42 (1H, d, J=10.0 Hz, H-6).

Reduction of α-Epoxide (1) and β-Epoxide (2) with $LiAlH_4$——A solution of 18.3 g (0.07 mol) of **1** or **2** in 400 ml of tetrahydrofuran (THF) was cooled with dry ice–acetone bath. A suspension of 1.33 g (0.035 mol) of $LiAlH_4$ in 100 ml of THF was added dropwise over a period of 1 hr under stirring. After 4 hr, the reaction mixture was poured into 800 ml of 50% potassium sodium tartrate solution and the organic layer was separated, and then the aqueous layer was extracted with AcOEt (100 ml×3). The combined organic extract was washed with saturated NaCl solution and dried over $MgSO_4$. Evaporation of the solvent left a solid which was separated by silica gel chromatography (benzene: AcOEt=5: 1). **5**, 16.7% yield, mp 202.5—203.5°, colorless needles from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.17; H, 7.66. IR: 3500 (OH), 1768 (CO). PMR: 1.25 (3H, d, J=6.0 Hz, H-13), 1.31 (3H, s, H-14), 1.75 (3H, s, H-15), 4.27 (1H, d, J=5.0 Hz, H-3), 4.49 (1H, d, J=10.0 Hz, H-6), 5.37 (1H, d, J=10.0 Hz, H-1), 5.65 (1H, dd, J=10.0, 5.0 Hz, H-2). **6**, 65.6% yield, mp 196—197°, colorless needles from ether. *Anal.* Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.25; H, 7.47. MS *m/e*: 264 (M^+). IR: 3450 (OH), 1780 (CO), 1660 (C=C). PMR: 1.14 (3H, s, H-14), 1.24 (3H, d, J=6.0 Hz, H-13), 1.78 (3H, s, H-15), 1.99 (1H, d, J=11.0 Hz, OH), 4.18 (1H, ddd, J=11.0, 2.0, 2.0 Hz, H-3), 4.47 (1H, d, J=10.0 Hz, H-6), 5.26 (1H, dd, J=10.0, 2.0 Hz, H-1), 5.46 (1H, dd, J=10.0, 2.0 Hz, H-2). **7**, 65.9% yield, mp 107°, colorless prisms from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.08; H, 7.72. IR: 3440 (OH), 1775 (CO). PMR: 1.20 (3H, s, H-14), 1.25 (3H, d, J=7.0 Hz, H-13), 1.74 (3H, s, H-15), 1.94 (1H, bs, OH), 4.12 (1H, dd, J=2.0, 2.0 Hz, H-3), 4.48 (1H, d, J=11.0 Hz, H-6), 5.22 (1H, dd, J=10.5, 2.0 Hz, H-1), 5.43 (1H, dd, J=10.5, 2.0 Hz, H-2). **8**, 15.6% yield, mp 158—160°, colorless needles from ether–petr. ether *Anal.* Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.07; H, 7.59. IR: 3480 (OH), 1780 and 1765 (shoulder) (CO), 1630 (C=C). PMR: 1.22 (3H, s, H-14), 1.25 (3H, d, J=6.0 Hz, H-13), 1.68 (3H, s, H-15), 1.87 (1H, bs, OH), 4.20 (1H, d, J=5.0 Hz, H-3), 4.51 (1H, d, J=10.0 Hz, H-6), 5.27 (1H, d, J=10.5 Hz, H-1), 5.57 (1H, dd, J=10.5, 5.0 Hz, H-2).

Chlorination of Alcohols (5, 6, 7 and 8) with MsCl (or TsCl)——Procedure A: To the solution of 132 mg (0.5 mmol) of alcohol in 0.5 ml of pyridine, 68.8 mg (0.6 mmol) of MsCl was added dropwise during 15 min. under stirring and ice cooling. After 4 hr, the mixture was poured into 10 ml of ice-water and extracted with AcOEt (20 ml×3). The organic layer was washed successively with 2 N HCl, 1 N $NaHCO_3$ and saturated NaCl solution, and then dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residual solid was recrystallized from ether–petr. ether.

Procedure B: A mixture of 132 mg (0.5 mmol) of alcohol (**6**) and 191 mg (1.0 mmol) of TsCl in 1.0 ml of pyridine was stirred at room temperature for 3 hr. The reaction mixture was worked up as above. **9**, 92.3% yield, mp 189—191°, colorless needles from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{19}ClO_3$: C, 63.70; H, 6.72. Found: C, 63.78; H, 6.81. MS *m/e*: 282 (M^+). IR: 1790 (CO), 1660 (C=C). PMR: 1.17 (3H, s, H-14), 1.23 (3H, d, J=6.5 Hz, H-13), 1.82 (3H, s, H-15), 4.49 (1H, d, J=10.0 Hz, H-6), 4.71 (1H, dd, J=2.0, 2.0 Hz, H-3), 5.32 (1H, dd, J=10.0, 2.0 Hz, H-1), 5.49 (1H, dd, J=10.0, 2.0 Hz, H-2). **10**, 85.6% yield (procedure A), 79.8 yield (procedure B), mp 189°, colorless leaflets from ether. *Anal.* Calcd. for $C_{15}H_{19}ClO_3$: C, 63.70; H, 6.72. Found: C, 63.68; H, 6.60. MS *m/e*: 282 (M^+). IR: 1783 and 1775 (shoulder) (CO), 1665 (C=C). PMR: 1.24 (3H, d, J=6.0 Hz, H-13), 1.36 (3H, s, H-14), 1.82 (3H, s, H-15), 4.52 (1H, d, J=10.0 Hz, H-6), 4.55 (1H, d, J=5.5 Hz, H-3), 5.34 (1H, d, J=10.0 Hz, H-1), 5.64 (1H, dd, J=10.0, 5.5 Hz, H-2). **11**, 98.0% yield, mp 176—178°, colorless leaflets from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{19}ClO_3$: C, 63.70; H, 6.72. Found: C, 64.02; H, 6.91. IR: 1785 and 1765 (w) (CO), 1662 (w) (C=C). PMR: 1.26 (3H, s, H-14), 1.30 (3H, d, J=6.0 Hz, H-13), 1.80 (3H, s, H-15), 4.52 (1H, d, J=11.0 Hz, H-6), 4.56 (1H, d, J=5.0 Hz, H-3), 5.24 (1H, d, J=10.5 Hz, H-1), 5.64 (1H, dd, J=10.5, 5.0 Hz, H-2). **12**, 90.8% yield, mp 219—221°, colorless prisms from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{19}ClO_3$: C, 63.70; H, 6.72. Found: C, 63.62; H, 6.75. IR: 1770 (CO). PMR: 1.26 (3H, s, H-14), 1.26 (3H, d, J=7.0 Hz, H-13), 1.79 (3H, s, H-15), 4.49 (1H, d, J=10.5 Hz, H-6), 4.70 (1H, dd, J=2.0, 2.0 Hz, H-3), 5.29 (1H, dd, J=10.0, 2.0 Hz, H-1), 5.47 (1H, dd, J=10.0, 2.0 Hz, H-2).

Hydrogenation of Alcohols (5, 6, 7 and 8)——Reduction Procedure: A mixture of 132 mg (0.5 mmol) of alcohol, 13 mg of platinum oxide and 10 ml of AcOEt was stirred at ordinary pressure in a hydrogen atmosphere. After 40 min, the reaction mixture was filtered and the solvent was evaporated to dryness. The residual solid was recrystallized from ether–petr. ether or ether–hexane. **13**, 85% yield, mp 156—157°, colorless plates from ether–hexane. *Anal.* Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.70; H, 8.36. MS *m/e*: 266 (M^+). IR: 3540 (OH), 1765 (CO). PMR: 1.22 (3H, s, H-14), 1.23 (3H, d, J=6.5 Hz, H-13), 1.65 (3H, s, H-15), 2.18 (1H, bs, OH), 3.84 (1H, ddd, J=7.6, 7.6, 2.0 Hz, H-3), 4.34 (1H, d, J=10.0 Hz, H-6). **14**, 88% yield, mp 139—140°, colorless needles from petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.51; H, 8.20. MS *m/e*: 266 (M^+). IR: 3500 (OH), 1780 (CO). PMR: 1.16

(3H, s, H-14), 1.24 (3H, d, J=6.0 Hz, H-13), 1.70 (3H, s, H-15), 3.80 (1H, m, H-3), 4.35 (1H, d, J=10.0 Hz, H-6). **15**, ~80.0% yield, mp 191—193°, colorless prisms from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.61; H, 8.32. IR: 3420 (OH), 1775 and 1760 (shoulder) (CO). PMR (60 MHz, $CDCl_3$): 1.19 (3H, s, H-14), 1.27 (3H, d, J=7.0 Hz, H-13), 1.65 (3H, s, H-15), 3.80 (1H, m, H-3), 4.50 (1H, d, J=10.0 Hz, H-6). **16**, 72% yield, mp 175—177°, colorless prisms from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.57; H, 8.32. IR: 3500 (OH), 1770 (CO). PMR (60 MHz, $CDCl_3$): 1.13 (3H, s, H-14), 1.25 (3H, d, J=8.0 Hz, H-13), 1.63 (3H, s, H-15), 3.88 (1H, dd, J=5.0, 5.0 Hz, H-3), 4.47 (1H, d, J=10.0 Hz, H-6).

Catalytic Reduction of Chlorides (9, 10, 11 and 12)——General procedure: A mixture of 141 mg (0.5 mmol) of chloride, 14 mg of PtO_2 and 5 ml of AcOEt was stirred at ordinary pressure in a hydrogen atmosphere. The catalyst was filtered off and the filtrate was concentrated to dryness. The residual solid was submitted to the preparative TLC on silica gel for separation of the reduction products.

Reduction Products of **9**: **17**, 49.0% yield, mp 147.5—148.5°, colorless prisms from ether–hexane. *Anal.* Calcd. for $C_{15}H_{21}ClO_3$; C, 63.26; H, 7.43. Found: C, 63.53; H, 7.35. MS *m/e*: 284 (M^+). IR: 1780 (CO). PMR (60 MHz, $CDCl_3$): 1.16 (3H, s, H-14), 1.21 (3H, d, J=6.0 Hz, H-13), 1.67 (3H, s, H-15), 4.25 (1H, m, H-3), 4.34 (1H, d, J=9.0 Hz, H-6). **23**, 16.8% yield, mp 164—167°, (lit[12] 178°). **24**, 15.7% yield, mp 179—180°, colorless needles from ether. *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.73; H, 9.67. MS *m/e*: 252 (M^+). IR: 3500 (OH), 1768 (CO). PMR: 1.12 (3H, d, J=6.0 Hz, H-15), 1.17 (3H, s, H-14), 1.22 (3H, d, J=6.0 Hz, H-13), 4.23 (1H, d, J=10.0 Hz, H-6). **9**, 14.9% recovery.

Reduction Products of **10**: **18**, 11.6% yield, mp 163—165°, colorless needles from ether. *Anal.* Calcd. for $C_{15}H_{21}ClO_3$: C, 63.26; H, 7.43. Found: C, 62.97; H, 7.42. IR: 1775 and 1765 (shoulder) (CO). PMR (60 MHz, $CDCl_3$): 1.22 (3H, d, J=6.0 Hz, H-13), 1.25 (3H, s, H-14), 1.73 (3H, s, H-15), 4.15 (1H, dd, J= 7.8, 7.8 Hz, H-3), 4.36 (1H, d, J=9.6 Hz, H-6). **23**, 20.8% yield. **24**, 31.9% yield. **10**, 9.6% recovery.

Reduction Products of **11**: **19**, 16.9% yield, mp 204° colorless needles from ether. *Anal.* Calcd. for $C_{15}H_{21}ClO_3$: C, 63.26; H, 7.43. Found C, 63.17; H, 7.46. IR: 1780 and 1765 (CO). PMR (60 MHz, $CDCl_3$): 1.20 (3H, s, H-14), 1.28 (3H, d, J=8.0 Hz, H-13), 1.73 (3H, s, H-15), 4.30 (1H, dd, J=2.0, 2.0 Hz, H-3), 4.40 (1H, d, J=10.0 Hz, H-6). **25**, 26.0% yield, mp 101—102°, colorless leaflets from benzene–petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.86; H, 8.86. MS *m/e*: 250 (M^+). IR: 3450 (OH), 1770 (CO). PMR (60 MHz, $CDCl_3$): 1.12 (3H, s, H-14), 1.22 (3H, d, J=7.0 Hz, H-13), 1.80 (3H, s, H-15), 4.30 (1H, d, J=10.0 Hz, H-6), 5.60 (1H, m, H-3). **26**, 23.0% yield, mp 135—137°, colorless prisms from petr. ether. *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.47; H, 9.55. MS *m/e*: 252 (M^+). IR: 3480 (OH), 1760 (CO). PMR (60 MHz, $CDCl_3$): 1.07 (3H, s, H-14), 1.23 (3H, d, J=6.0 Hz, H-13 or H-15), 1.24 (3H, d, J=7.0 Hz, H-15 or H-13), 4.17 (1H, d, J=12.0 Hz, H-6).

Reduction Products of **12**: **20**, 49.6% yield, mp 225—227°, colorless prisms from ether. *Anal.* Calcd. for $C_{15}H_{21}ClO_3$: C, 63.26; H, 7.43. Found: C, 63.26; H, 7.39. IR: 1770 (CO). PMR (60 MHz, $CDCl_3$): 1.20 (3H, s, H-14), 1.27 (3H, d, J=7.0 Hz, H-13), 1.66 (3H, s, H-15), 4.25 (1H, dd, J=4.0, 4.0 Hz, H-3), 4.50 (1H, d, J=10.0 Hz, H-6). **25**, 16.0% yield. **26**, 16.6% yield.

Chlorination of 13 with $SOCl_2$–Pyridine——To a stirred solution of 133 mg (0.5 mmol) of **13**, 0.1 ml of pyridine in 3 ml of $CHCl_3$, 77.5 mg (0.65 mmol) of $SOCl_2$ was added dropwise under ice cooling. After 1 hr, the reaction mixture was poured into ice water and extracted with $CHCl_3$. The combined organic layer was washed successively with 2 N HCl, 1 N $NaHCO_3$, saturated NaCl solution and dried over $MgSO_4$. Evaporation of the solvent left an oil which was purified by preparative TLC to give 40 mg (28.2% yield) of **17**.

Chlorination of 14 with $SOCl_2$–Pyridine——The reaction was carried out by the same manner described above. **18**, 45 mg (31.7% yield).

Chlorination of 15——To a stirred solution of 125 mg (0.47 mmol) of **15** in 5 ml of pyridine, 185 mg (0.94 mmol) of TsCl was added under ice cooling. The reaction mixture was stirred overnight at room temperature. Work up by usual manner gave 135 mg (68% yield) of tosylate which without purification was converted to the chloride (**19**) as follows. A mixture of 100 mg (0.24 mmol) of tosylate and 2 mg (0.48 mmol) of LiCl in 6 ml of dimethylformamide (DMF) was stirred at 65—70° for 14 hr. After cooling, the reaction mixture was poured into water and extracted with AcOEt. The extract was washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was submitted to the preparative TLC (benzene: AcOEt=5: 1) to give 50 mg (74% yield) of **19**.

Chlorination of 16——The reaction was carried out as above. Tosylate (crude), 73% yield, **20**, 85% yield from tosylate.

Dienol (27)——A mixture of 141 mg (0.5 mmol) of **9** or **10**, 325 mg (5 mmol) of zinc powder and 450 mg (3 mmol) of NaI in 4 ml of acetone was refluxed for 45 min under vigorous stirring. The reaction mixture was centrifuged to remove excess NaI and zinc powder. The solvent was evaporated *in vacuo* and the residue was dissolved in AcOEt and then washed with aqueous $Na_2S_2O_3$ and saturated NaCl solution. The organic layer was dried over $MgSO_4$ and evaporated to dryness. The resulting solid was purified by preparative TLC (benzene: AcOEt=5: 1) and then recrystallized from benzene–pentane to give 118 mg (95% yield) of **27**. mp 118—119°, colorless prisms. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.71; H, 7.91. MS *m/e*: 248 (M^+). IR: 3500 (OH), 1760 (CO). UV λ_{max}^{MeOH} nm: 263. PMR: 1.13 (3H, s, H-14),

1.20 (3H, d, J=6.5 Hz, H-13), 2.02 (3H, s, H-15), 2.12 (1H, bs, OH), 4.19 (1H, d, J=11 Hz, H-6), 5.51 (1H, dd, J=9.0, 1.5 Hz, H-1), 5.73 (1H, dd, J=5.0, 1.5 Hz, H-3), 5.93 (1H, dd, J=9.0, 5.0 Hz, H-2).

Dienol (28)——A mixture of **11** and **12** was treated to give **28** according to the procedure described above. ~95% yield, colorless oil. MS *m/e*: 248 (M^+). IR ν_{max}^{NaCl}: 3450 (OH), 1770 (CO). UV λ_{max}^{MeOH} nm: 263. PMR: 1.25 (3H, d, J=7.5 Hz, H-13), 1.30 (3H, s, H-14), 1.94 (3H, s, H-15), 4.28 (1H, d, J=11.0 Hz, H-6), 5.42 (1H, dd, J=8.5, 2.0 Hz, H-1), 5.75 (1H, m, H-3), 5.88 (1H, m, H-2).

Photolysis of Dienol (27)——A solution of 500 mg of dienol (**27**) in 220 ml of MeOH was irradiated with 7w low-pressure mercury lamp for 8 hr at 20—30° under bubbling of an argon stream. Evaporation of the solvent left an oil which was chromatographed over silica gel. Elution with benzene: AcOEt=5: 1 gave 210 mg of **33**, 10 mg of **34**, 18 mg of **35**, 110 mg of **37**, 25 mg of **36** and 35 mg of starting material. **33**, 45.1% yield, mp 64.5—65°, colorless needles from ether–pentane. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.76; H, 8.13. MS *m/e*: 248 (M^+). IR, UV and PMR spectral data: see Table II. **34**, 2.2% yield, mp 87—89°, colorless needles from AcOEt–pentane. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.01; H, 8.09. MS *m/e*: 248 (M^+), IR, UV and PMR spectral data: see Table II. **35**, 3.9% yield, mp 147°, colorless prisms from ether–pentane. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.51; H, 8.12. MS *m/e*: 248 (M^+). IR, UV and PMR spectral data: see Table II. **36**, 5.4% yield, mp 160—161°, colorless needles from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.37; H, 8.05. MS *m/e*: 248 (M^+). IR: 3450 (OH), 1760 (CO). UV λ_{max}^{MeOH} nm: 215. PMR: 1.10 (3H, s, H-14), 1.27 (3H, d, J=6.5 Hz, H-13), 1.75 (3H, s, H-15), 3.14 (1H, bs, OH), 3.88 (1H, d, J=10.0 Hz, H-6), 5.50 (1H, bs, H-3). CMR: 31.8 (s, C-10), 34.1 and 39.0 (d, each, C-1 and C-2, or C-2 and C-1), 79.5 (d, C-6), 83.3 (s, C-5), 127.2 (d, C-3), 144.7 (s, C-4), 177.1 (s, C-12). **37**, 23.7% yield, mp 119—120°, colorless needles from ether–petr. ether or colorless prisms from ether. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.34; H, 7.81. MS *m/e*: 248 (M^+). IR: 3450 (OH), 1770 (CO), 1630 and 890 (C=C). PMR: 1.06 (3H, d, J=7.0 Hz, H-15), 1.26 (3H, d, J=7.0 Hz, H-13), 2.16 (1H, bs, OH), 2.96 (1H, m, J=2.8, 1.0, 7.8 Hz, H-4), 3.50 (1H, bs, H-1), 4.03 (1H, d, J=9.8 Hz, H-6), 5.01 and 5.18 (1H each, bs, H-14), 5.50 (1H, ddd, J=5.6, 1.5, 1.0 Hz, H-2), 5.97 (1H, m, J=5.6, 2.8, 2.8 Hz, H-3).

Photolysis of Dienol (28)——The reaction was carried out as described above. **38**, 46.8% yield, mp 119—120°, colorless prisms from acetone–hexane. *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: 72.58; H, 7.91. IR, UV and PMR spectral data: see Table II.

Preparation of Guaianolide (37) from Compound (33)——Method A: A solution of 5 mg of **33** in 2 ml of benzene was refluxed for 48 hr. Evaporation of the solvent gave 5 mg of **37** as colorless crystals.

Method B: A mixture of 5 mg of **33**, 20 mg of silica gel in 2 ml of benzene: ethyl acetate=5: 1 was stirred for a week at room temperature. Filtration and evaporation of the solvent gave 5 mg of **37** as colorless crystals.

Reduction of Conjugated Dienone (38) with $NaBH_4$——To a stirred solution of 49.6 mg (0.2 mmol) of **38** in 2 ml of MeOH, 3.8 mg (0.1 mmol) of $NaBH_4$ was added at room temperature. After 30 min, the solvent was concentrated *in vacuo* and the residual oil was diluted with water and extracted with AcOEt. The organic layer was washed with saturated NaCl solution and dried over $MgSO_4$. Evaporation of the solvent left a solid which was purified by preparative TLC (benzene: AcOEt=5: 1) and recrystallized from ether–petr. ether to give 43 mg (86% yield) of **39**. mp 136—137°, colorless needles. *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.87; H, 8.82. IR: 3450 (OH), 1755 (CO). UV λ_{max}^{MeOH} nm: 220. PMR: 0.96 (3H, d, J=7.0 Hz, H-14), 1.30 (3H, d, J=7.0 Hz, H-13), 1.82 (3H, bs, H-15), 4.11 (1H, dd, J=9.0, 2.0 Hz, H-6), 4.49 (1H, bs, H-5), 5.19 (1H, ddd, J=11.0, 9.0, 2.0 Hz, H-1), 6.22 (1H, m, H-3), 6.45 (1H, m, H-2). CMR: 73.8 (d, C-5), 83.5 (d, C-6), 126.5 (d, C-2), 126.9 (d, C-3), 134.3 (s, C-4), 136.7 (d, C-1), 179.1 (s, C-12).

Hydrogenation of Compound (33)——A mixture of 530 mg (2.14 mmol) of **33** and 40 mg of 10% palladium on charcoal in 10 ml of AcOEt at oridinary pressure for 3 hr in a hydrogen atmosphere. Filtration and evaporation of the solvent left an oil which was adsorbed on silica gel. Elution with benzene: AcOEt=10: 1 gave 76 mg (14.2%) of **41**, 340 mg (63.7%) of **40** and 91 mg (17.0%) of **42**. **41**, mp 152—153°, colorless needles from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 70.18; H, 8.57. IR: 1775 (γ-lactone), 1705 (CO). PMR: 0.95 (3H, d, J=6.8 Hz, H-14), 1.12 (3H, d, J=6.8 Hz, H-15), 1.31 (3H, d, J=6.8 Hz, H-13), 3.08 (1H, m, H-4), 4.12 (1H, d, J=10.0 Hz, H-6), 5.04 (1H, dd, J=16.0, 8.2 Hz, H-1), 5.44 (1H, ddd, J=16.0, 9.0, 5.5 Hz, H-2). **40**, mp 76—77°, colorless prisms from ether–petr. ether. *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.02; H, 8.86. IR: 1770 and 1760 (shoulder) (γ-lactone), 1695 (CO). PMR (60 MHz, $CDCl_3$): 1.23 and 1.32 [(3H each, d, J=7.0 and 6.5 Hz, H-13 (or H-15) and H-15 (or H-13)], 1.66 (3H, s, H-14), 4.66 (1H, d, J=7.2 Hz, H-6), 5.04 (1H, dd, J=7.0, 7.0 Hz, H-1). **42**, mp 110—111°, colorless needles from ether–petr. ether, *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.74; H, 8.84. IR: 1770 (γ-lactone), 1722 (CO). PMR: 1.09 (3H, d, J=6.2 Hz, H-14), 1.19 (3H, d, J=6.5 Hz, H-13), 1.20 (3H, d, J=6.5 Hz, H-15), 2.82 (1H, ddd, J=10.5, 10.5, 5.0 Hz, H-1), 3.57 (1H, dq, J=10.5, 6.5 Hz, H-4), 5.25 (1H, d, J=7.5 Hz, H-6), 5.48 (1H, dd, J=10.5, 10.5 Hz, H-3), 5.82 (1H, ddd, J=10.5, 10.5, 5.0 Hz, H-2).

Reduction of 40 with $NaBH_4$——A mixture of 32 mg (1.128 mmol) of **40** and 2.43 mg (0.06 mmol) of $NaBH_4$ in 2 ml of methanol was stirred at room temperature for 2 hr. The reaction mixture was diluted

with water and neutralized with 2 N HCl, and then extracted with AcOEt (10 ml×3). The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residual oil was submitted to the preparative TLC (benzene: AcOEt=5: 2) to give 27.5 mg (85.5% yield) of **43**. mp 115—117°, colorless prisms from petr. ether. *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.39; H, 9.62. IR: 3380 (OH), 1755 (shoulder) and 1745 (CO). PMR: 1.01 (3H, d, J=6.8 Hz, H-15), 1.32 (3H, d, J=7.5 Hz, H-13), 1.65 (3H, s, H-14), 3.43 (1H, dd, J=5.8, 2.0 Hz, H-5), 4.23 (1H, dd, J=5.0, 2.0 Hz, H-6), 5.35 (1H, m, H-1).

Compound (44)——Method A: To a stirred solution of 50.4 mg (0.2 mmol) of alcohol (**43**) and 0.3 ml of pyridine in 1 ml of $CHCl_3$ was added 48 mg (0.4 mmol) of $SOCl_2$ under ice cooling. After 1.5 hr, additional 48 mg of $SOCl_2$ was added and it was kept for 4 hr under stirring and ice cooling. The reaction mixture was poured into ice water and extracted with AcOEt. The combined extract was washed successively with 2 N HCl, 1 N $NaHCO_3$ and saturated NaCl solution, and then dried over $MgSO_4$. Evaporation of the solvent left 54 mg of a brown oil which was separated by preparative TLC (benzene: AcOEt=5: 1) to give 17 mg (36.4%) of **44** as a colorless oil and 16 mg of unseparable crystalline mixture which was positive for Beilstein test. **44**, MS *m/e*: 234 (M^+). IR ($CHCl_3$): 1775 (CO), 1645 (C=C). PMR (60 MHz, $CDCl_3$): 1.16 (3H, d, J=5.0 Hz, H-15), 1.23 (3H, d, J=6.0 Hz, H-13), 4.30 (1H, dd, J=9.0, 9.0 Hz, H-6), 4.83 (2H, s, H-14). CMR ($CDCl_3$): 84.0 (d, C-6), 108.5 (t, C-14), 149.6 (s, C-10), 178.5 (s, C-12).

Method B: A mixture of 12.6 mg (0.05 mmol) of **43** and 35.6 mg (0.15 mmol) of (carboxysulfamoyl)-triethylammonium hydroxide inner salt methyl ester in 3 ml of benzene was stirred at room temperature for 1 hr under a nitrogen atmosphere, and then the reaction temperature was raised to 50° and it was maintained at that temperature for 6 hr. After usual work up, the crude oil was submitted to the silica gel chromatography to gave **44** (80% yield) as a pale yellow oil which showed the spectroscopic properties identical with those of an authentic specimen.

Mesylation of 43——To a stirred solution of 33 mg (0.13 mmol) of **43** and 0.5 ml of pyridine in 1 ml of $CHCl_3$, 29.8 mg (0.26 mmol) of MsCl was added dropwise under ice cooling. After 2.5 hr, the reaction mixture was poured into ice water and extracted with AcOEt. The combined extract was washed successively with 2 N HCl, 1 N $NaHCO_3$ and saturated NaCl solution, and then dried over $MgSO_4$. Evaporation of the solvent left a solid which was recrystallized from ether–petr. ether to give 42.5 mg (98.5%) of **45**. mp 137—138°, colorless prisms. *Anal.* Calcd. for $C_{16}H_{26}O_5S$: C, 58.17; H, 7.93. Found: C, 58.15; H, 7.85. IR: 1775 (CO), 1360 and 1180 (SO_2). PMR: 1.04 (3H, d, J=7.0 Hz, H-15), 1.29 (3H, d, J=7.5 Hz, H-13), 1.73 (3H, s, H-14), 3.09 (3H, s, SO_2Me), 4.29 (1H, dd, J=9.0, 2.0 Hz, H-6), 4.82 (1H, dd, J=2.0, 1.0 Hz, H-5), 5.21 (1H, m, H-1).

Dihydrocostunolide——A mixture of 32 mg (0.095 mmol) of **45**, 114 mg (0.20 mmol) of TBAO and 4 ml of acetone was stirred at 65° (bath temperature) in a nitrogen atmosphere. After 48 hr and 96 hr, each 32 mg of TBAO was added and the stirring was further continued for 24 hr.

The reaction mixture was poured into water and extracted with AcOEt (20 ml×3). The organic layer was dried over $MgSO_4$ and evaporated to dryness under reduced pressure. The residual oil was purified by preparative TLC (benzene: AcOEt=5: 1) to give 9 mg (39.6%) of dihydrocostunolide $[\alpha]_D^{18}$ +105.2° ($CHCl_3$, c=0.37) {lit.[5a] $[\alpha]_D^{18}$ +113.6° ($CHCl_3$, c=3.0)}.

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