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# Biogenetically Patterned Transformation of Eudesmanolide to Eremophilanolide. I. Angular Methyl Migration of 5α,6α-Epoxy-dihydroalantolactone

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As a continuation of our study on the biogenetically patterned transformation leading to the natural terpenoids, conversion of an eudesmanolide directing to the related eremophilanolide was investigated and the object was accomplished.

After several attempts, treatment of 5α,6α-epoxy-dihydroalantolactone (**15**) with HCOOH–acetone (1 : 2) at reflux was found to afford eight products (A—H). Among them, two major products (products A and B) and one minor product (product D), which were obtained in a combined yield of 46%, were elucidated to be the desired eremophilanolides (**17**, **18**, and **23**) on the basis of the physicochemical evidence and the chemical conversion of **23** to tetrahydroligularenolide (**34**). The structure of the product C was assigned **20** on the basis of its physical properties and the chemical derivation. Afterwards, a better reaction condition transforming **15** to give **17** and **18** in a combined 68% yield was found.

The carbon framework (**2**) of eremophilane-type sesquiterpenes does not satisfy the classical isoprene rule, but it has been mentioned to be constructed from an eudesmane-type precursor (**1**) *via* a 1,2-shift of an angular methyl function.[2] Recently, it was demonstrated in a biosynthetic study of *Petasites hybridus* L. that petasin (**4**) was in fact biosynthesized from mevalonic lactone *via* an eudesmanoid intermediate (**3**).[3] On the other hand, a terminal epoxide was shown to function as an important initiating site in the biological formation of triterpenoid skeleton.[4]

With these concept and evidence for the background, the chemical conversion of eudesmane-type compounds directing to the eremophilane-type counterparts has been a subject of much interest and many attempts have been made but without success.[5] The acid treatment of some eudesmane-type epoxides were also reported, but none of them resulted in the formation of eremophilane-type derivatives.[6]

As a continuative study on the biogenetically patterned transformation leading to the natural terpenoids,[7] we have been working with a hope of the direct chemical conversion of

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2) *a*) R. Robinson, "The Structural Relations of Natural Products," Clarendon, Oxford, 1955, p. 12; *b*) J.B. Hendrickson, *Tetrahedron*, **7**, 82 (1959); *c*) L.H. Zalkow, F.X. Markley, and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 6354 (1960); *d*) W. Parker, J.S. Roberts, and R. Ramage, *Quart. Rev.*, **21**, 331 (1967).

3) C.J.W. Brooks and R.A.B. Keates, *Phytochemistry*, **11**, 3235 (1972).

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5) *a*) C.H. Heathcock and T.R. Kelly, *Tetrahedron*, **24**, 3753 (1968); *b*) G. Mehta, G.L. Chetty, U.R. Nayak, and S. Dev, *ibid.*, **24**, 3775 (1968); *c*) H.W. Whitelock, Jr. and A.H. Olson, *J. Am. Chem. Soc.*, **92**, 5383 (1970); *d*) D.J. Dunham and R.G. Lawton, *ibid.*, **93**, 2075 (1971); *e*) J.W. Huffman, *J. Org. Chem.*, **37**, 2736 (1972).

6) *a*) P. Vita-Finzi, Y. Kashman, E. Glotter, and D. Lavie, *Tetrahedron*, **24**, 5847 (1968); *b*) H. Hikino, T. Kohama, and T. Takemoto, *ibid.*, **25**, 1037 (1969).

7) *a*) I. Kitagawa, K. Kitazawa, and I. Yosioka, *Tetrahedron*, **28**, 907 (1972); *b*) I. Kitagawa, K. Kitazawa, K. Aoyama, M. Asanuma, and I. Yosioka, *ibid.*, **28**, 923 (1972).

eudesmane-type compounds to their eremophilane-type analogs, and after several attempts, the desired transformation has been accomplished as detailed in the present paper.

**Acid Treatment of Eudesmane-type Compounds**[8]

At the beginning, $\gamma$-eudesmol (**5**) and 5$\alpha$-hydroxy-11-benzoyloxy-selinane (**9**) were treated under several acid conditions. Photosensitized oxygenation of **5** followed by $LiAlH_4$ reduction afforded two fairly labile diols **6** and **7**, the assignment of both was made on the basis of their physicochemical properties (terminal methylenes shown by infrared (IR) and proton magnetic resonance (PMR) spectra) and they were discriminated each other by the angular methyl chemical shifts ($\delta$ 0.87 in **6** and $\delta$ 1.04 in **7**; the methyl in the latter being deshielded by a *cis* vicinal hydroxyl). Catalytic hydrogenation of **6** gave a crystalline diol **8** as a single product which on benzoylation was converted to **9**. For comparison purpose, **7** was similarly subjected to catalytic hydrogenation and in this case were obtained two diols **10** and **11** which were isomeric at C-4 but the assignment was not made. Acid treatment (*e.g.* conc. $H_2SO_4$–ether or HCOOH) of **5** furnished only $\gamma$- or $\delta$-selinene (**12**, **13**), while treatment of **9** with $POCl_3$–pyridine followed by $LiAlH_4$ reduction yielded **5** and on treatment of **9** with $BF_3$-etherate was identified **13** as a major product.

Next, since the eudesmane 4,5-epoxides were already shown not to give the desired eremophilane derivatives under the acid conditions,[5a,6] 5$\alpha$,6$\alpha$-epoxy-dihydroalantolactone (**15**)[6a] prepared from dihydroalantolactone (**14**) was chosen as a starting material. After some preliminary examinations by treating **15** under a variety of acid conditions (*e.g.* $BF_3$–etherate, AcOH, $CF_3COOH$–$CHCl_3$, $H_2SO_4$–AcOH, *p*-TsOH–EtOH, and HCOOH–acetone)

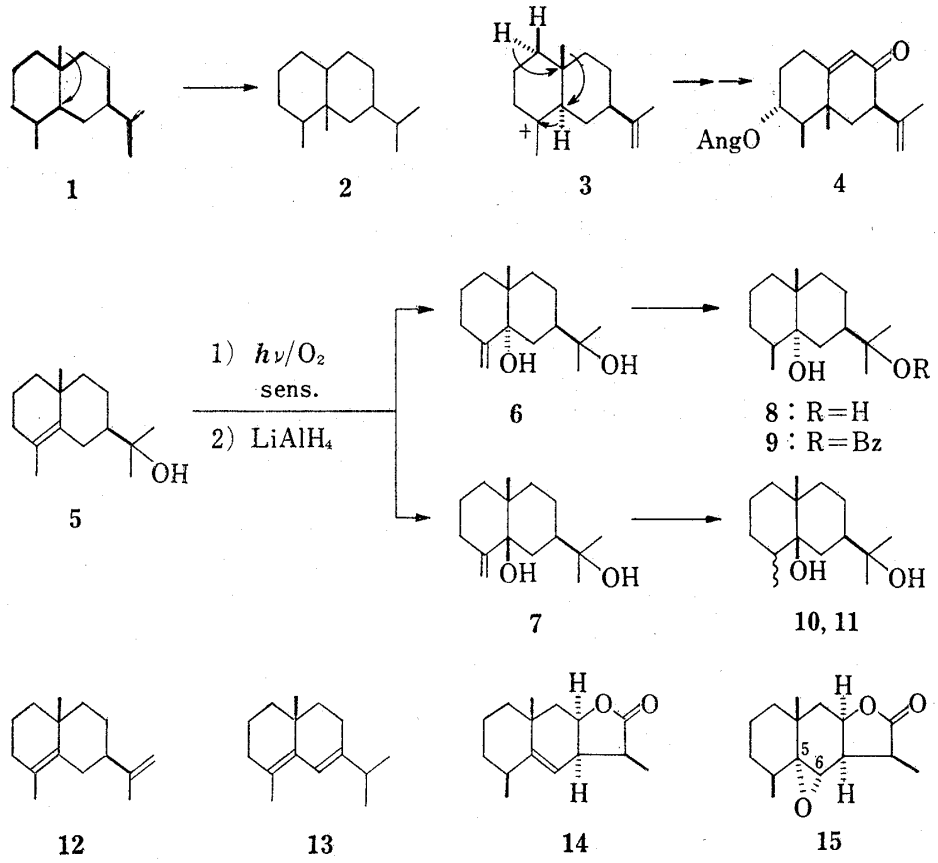



Chart 1

8) I. Kitagawa, Y. Yamazoe, R. Takeda, and I. Yosioka, *Tetrahedron Letters*, **1972**, 4843 (Preliminary communication).

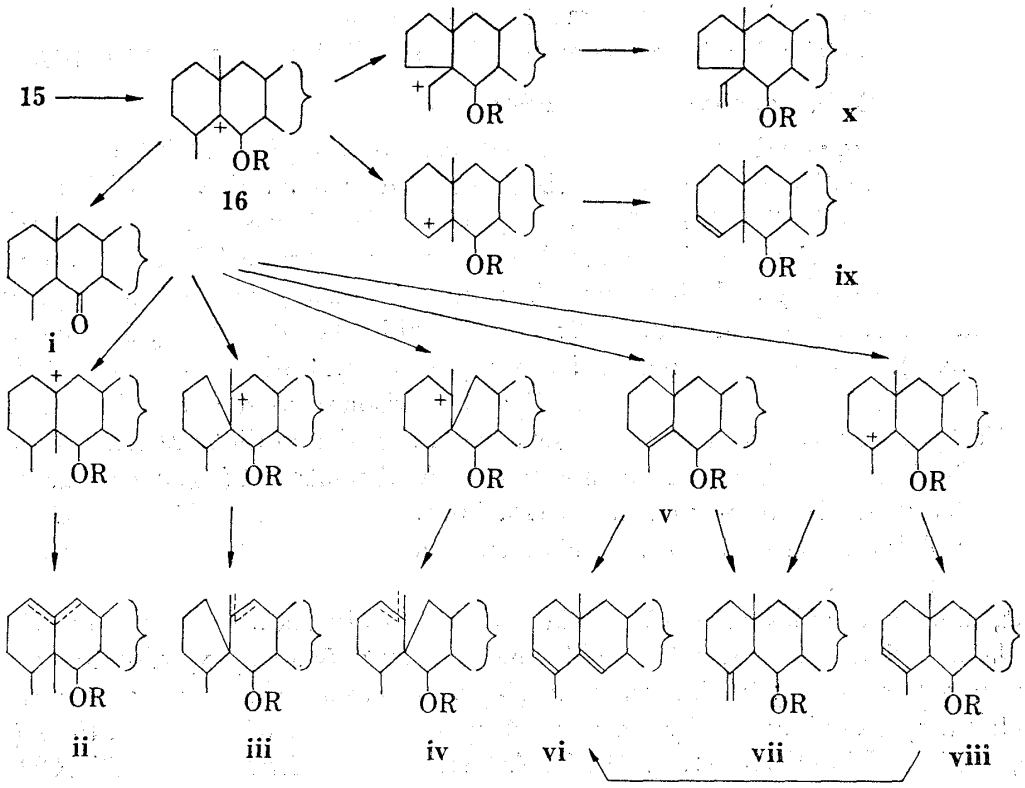


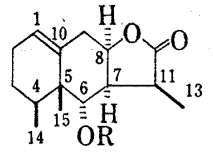

Chart 2

with the monitoring by gas–liquid chromatography (GLC) and thin-layer chromatography (TLC), it was found that treatment with HCOOH–acetone (1: 2) gave a satisfactory result.

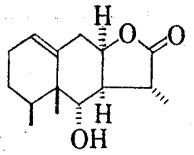
On acid treatment of **15**, the compounds of types **i**—**x** would formally be anticipated through a cation **16**, and so far eight products, *i.e.*: product A (10%), B (34%), C (2.2%), D (2.0%), E (0.5%), F (3.4%), G (2.4%), and H (0.3%), were isolated and four of them (A—D) elucidated as having types **ii** and **vii** carbon skeletons as described below.

Product A (**17**) possesses a $\gamma$-lactone, a formate, a double bond and no hydroxyl function as shown by its IR spectrum. The PMR spectrum (Table I) shows the presence of one vinyl proton, two methine protons which are respectively geminal to formyloxy and lactone moieties, two secondary and one tertiary methyls, and the absence of a vinyl methyl and a terminal methylene function. It is therefore presumed that the product A holds a type **ii** carbon skeleton and a partial structure **xi** becomes plausible on the basis of the spin decoupling experiments as shown in Table II. Among them, it is noted that irradiation at $\delta$ 5.24 (6-H) brought out only a change of signal pattern at $\delta$ 2.74 (7-H) thus disclosing C-5 to be quaternary. Since two secondary methyl functions of **15** are considered to be preserved in the product A, and since the signal pattern of 8-H ($\delta$ 4.64) of product A is alike to that of **14**, product B (**18**), and product B acetate (**19**) (*vide infra*), the partial structure **xi** is extended to **17** (without stereochemistry). In addition to mechanistic considerations, the Dreiding model examinations keeping in mind two coupling constants $J_{6,7}$ (4 Hz) and $J_{7,11}$ (10 Hz) finally lead to a formulation of product A as **17**. The conformation of ring B and the configuration at C-11 will be discussed later.

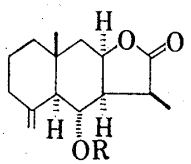
Product B (**18**) contains a hydroxyl and a $\gamma$-lactone function as revealed by its IR spectrum. It exhibits a similar PMR spectrum to that of **17** (Table I) but lacking a formate function of the latter. A monoacetate (**19**) obtained by acetylation of the product B also shows a quite similar PMR spectrum to that of **17** (Table I) apart from an acyl function. Hydrolysis of **17** with $K_2CO_3$–MeOH gave the product B while formylation of the latter restored **17**, thus the structure **18** is assigned to the product B. On alkaline hydrolysis of **17**, a con-



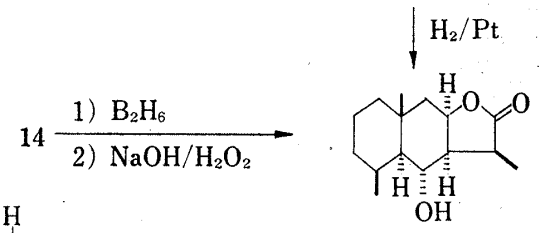
17 : R=CHO (product A)
18 : R=H (product B)
19 : R=Ac



23 : (product D)



20 : R=H (product C)
21 : R=Ac



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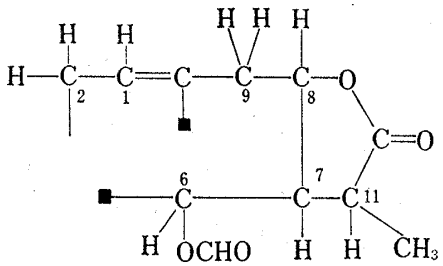


xi ■ denotes a quaternary carbon

Chart 3

TABLE I. PMR Data ($\delta$ values) of **17**, **18**, **19**, and **23** (Coupling Constants in Parentheses are given in Hz)

| | **17** (100 MHz) | **18** (90 MHz) | **19** (90 MHz) | **23** (90 MHz) |
|---|---|---|---|---|
| 1-H | 5.51 (m) | 5.48 (t-like) | 5.46 (m) | 5.70 (m) |
| 6-H | 5.24 (d, 4) | 3.88 (d.d, 9 and 6)[a] | 5.11 (d, 5) | 3.90 (d, 4) |
| 7-H | 2.74 (m) | —[b] | —[b] | 2.56 (m) |
| 8-H | 4.64 (d.t, 5 and 6) | 4.51 (q, 7) | 4.59 (q-like, 5) | 4.67 (d.t, 7 and 10) |
| 9-$H_2$ | 2.74 (m) | —[b] | —[b] | —[b] |
| 11-H | 2.98 (d.q, 7 and 10)[c] | 2.91 (m)[d] | —[b] | 2.84 (m)[e] |
| 4-Me | 0.82 (d, 6) | 1.05 (d, 5.5) | 0.83 (d, 6) | 0.95 (d, 7) |
| 5-Me | 0.96 (s) | 1.01 (s) | 0.95 (s) | 1.02 (s) |
| 11-Me | 1.36 (d, 7) | 1.37 (d, 7) | 1.31 (d, 7) | 1.32 (d, 7) |
| others | 8.06 (1H, s, formyl) | — | 2.04 (3H, s, acetyl) | 1.81 (1H, br.s, OH) |

*a*) altered to d ($J$=9 Hz) on $D_2O$ addition
*b*) unassigned due to overlapping of the signals
*c*) altered to d ($J$=10 Hz) on irradiation at $\delta$ 1.36
*d*) altered to d ($J$=9 Hz) on irradiation at $\delta$ 1.37
*e*) altered to d ($J$=12 Hz) on irradiation at $\delta$ 1.32

comitant partial epimerization at C-11 giving the product D (*vide infra*) was observed as shown by GLC.

Product C (**20**) possesses a terminal methylene function other than a hydroxyl and a $\gamma$-lactone function as shown by its IR spectrum. The PMR spectrum shows the presence of a terminal methylene ($\delta$ 5.04 and 4.66, 1H each, s-like), three methine protons which are respectively geminal to a lactone moiety ($\delta$ 4.56, d.t, $J$=3 and 5 Hz, 8-H), a secondary methyl ($\delta$ 2.88, quintet, $J$=7 Hz, 11-H), and a hydroxyl ($\delta$ 3.79, d.d, $J$=11 and 10 Hz, 6-H), one secondary methyl ($\delta$ 1.38, d, $J$=7 Hz, 11-Me), and one tertiary methyl ($\delta$ 0.83, s, 10-Me).

Table II. Spin Decoupling Experiments of **17** (90 MHz)

| Decoupled proton ($\delta$) | Irradiated at $\delta$ | | | | | |
|---|---|---|---|---|---|---|
| | 5.51 (1-H) | 2.05 (2-$H_2$) | 5.24 (6-H) | 2.74 (7-H; 9-$H_2$) | 4.64 (8-H) | 1.36 (11-Me) |
| 1-H (5.51, m) | — | broad singlet ($W_{h/2}$=4) | | triplet ($J$=4) | | |
| 2-$H_2$ (2.05, m) | varied | — | | | | |
| 6-H (5.24, d) | | | — | singlet | | |
| 7-H (2.74, m) | *a*) | | varied | — | varied | |
| 8-H (4.64, d.t) | | | | singlet-like | — | |
| 9-$H_2$ (2.74, m) | varied | | *a*) | — | varied | |
| 11-H (2.98, d.q) | | | | | | doublet ($J$=10) |

*a*) varied simultaneously due to overlapping

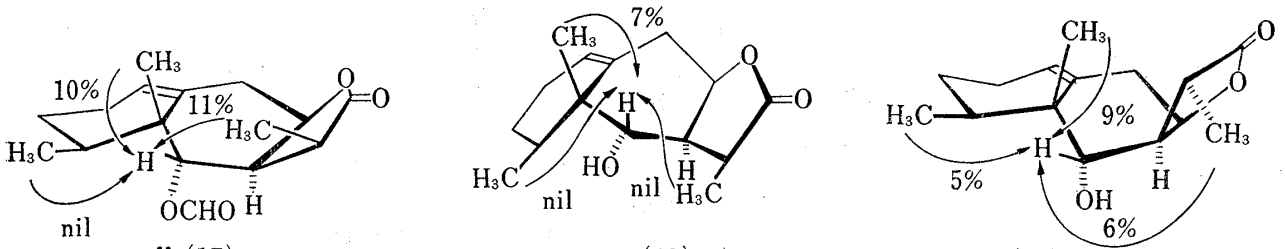
On acetylation the product C gave a monoacetate (**21**), which was shown by its IR and PMR spectra to possess the same functions as the product C except a change of a hydroxyl to an acetoxyl function. Therefore, the product C is assumed to be a compound of type **vii** and the structure **20** has eventually been established by preparing a dihydro derivative (**22**) of the product C through hydroboration of dihydroalantolactone (**14**). The preservation of 11$\beta$-Me configuration of **14** during the alakaline $H_2O_2$ treatment in the hydroboration of **14** giving **22** was assured by a blank test treating **14** with NaOH–$H_2O_2$ under the same reaction conditions.

Product D (**23**) possesses a hydroxyl and a $\gamma$-lactone function as shown by its IR spectrum. The PMR spectrum of the product D (Table I) is quite similar to that of **18** except the signal patterns ascribable to 6-H and 11-H. The spin decoupling experiments (Table III) on the signals due to 6-H, 7-H, 8-H, 11-H, and 11-Me substantiate the assignments given in Table I. Here again a doublet at $\delta$ 3.90 assignable to 6-H changed to a singlet upon irradiation at $\delta$ 2.56 (7-H) thus confirming C-5 to be quaternary. The accumulated physical evidence leads to assume the product D being an 11-epimer of **18**, and the assumption was verified by a quantitative isomerization of **18** on $K_2CO_3$–toluene treatment at reflux to the product D whose structure thus proved to be **23**. It has become clear at the same time that the product D (**23**) is a thermodynamically more favored isomer than the product B (**18**).

Table III. Spin Decoupling Experiments of **23** (90 MHz)

| Decoupled proton ($\delta$) | Irradiated at $\delta$ | | | |
|---|---|---|---|---|
| | 1.32 (11-Me) | 2.56 (7-H) | 2.84 (11-H) | 3.90 (6-H) |
| 6-H (3.90, d) | | singlet | | — |
| 7-H (2.56, m) | | — | | varied |
| 8-H (4.67, d.t) | | broad singlet | | |
| 11-H (2.84, m) | doublet ($J$=12) | | — | |
| 11-Me (1.32, d) | — | | singlet | |

Thus far, it has been elucidated on the basis of physicochemical evidence that three reaction products (**17**, **18**, **23**) obtained in a 46% combined yield are aimed eremophilanolides. The structures of the remaining minor products (E–H) are currently under investigation. Since several eremophilane-type derivatives are known to show the significant intramolecular




xii (17) xiii (18) xiv (23)

($J_{6,7}=4$Hz, B ring : chair-like) ($J_{6,7}=9$Hz, B ring : boat) ($J_{6,7}=4$Hz, B ring : chair)

Chart 4

nuclear Overhauser effects (NOE) between 6-H and the methyl functions,[9] the present compounds **17**, **18**, and **23** were subjected to the NOE analyses. As depicted by the perspective formulations **xii** (**17**), **xiii** (**18**), **xiv** (**23**), enhancement of the signal area of 6-H in **17**, **18**, and **23** was observed upon irradiation of either one of the methyl signals concerned and the values of percentage enhancement are in reasonable accord with the inspections using a Dreiding model and with considerations of the coupling constants between 6-H and 7-H. On the other hand, no NOE was observed between 6-H and the methyl functions in the eudesmanolide derivatives **20** and **22** as expected.

**Conversion of 23 to Tetrahydroligularenolide (34)[10]**

In order to prove chemically the eremophilane carbon framework of the above described rearrangement products (**17**, **18**, **23**), their conversion to a known natural eremophilane or its allied compounds has been attempted and the object has been accomplished as described below.

First, for example, a conversion of **18** to tetrahydroligularenolide (**34**)[11] was endeavored. Since base treatment of a mesylation product of a dihydro derivative (**24**), prepared from **18**, yielded an unidentified rearranged product (due to an unfavorable relative configuration of 6-MsO and 7-H for elimination), a preparation of a 6-epimer of **24** was attempted. However, reduction of a ketone (**25**) either with $NaBH_4$ or Al (iso-Pro)$_3$ always regenerated **24**, which, according to the Dreiding model inspection, is probably due to steric congestion of the rear side of the carbonyl function against the both reagents. Furthermore, several attempts to remove 6-keto function of **25** (*e.g.* $TsNHNH_2/LiAlH_4$, 1.2-ethanedithiol-$BF_3$/Raney Ni *etc.*) were in vain, but a similar effort treating 6-keto derivative (**26**) of **18** under the modified Huang-Minlon conditions[12] yielded a nitrogen containing product. The product possesses a molecular formula $C_{15}H_{22}ON_2$ (high mass) and contains a pyridazone moiety as revealed by its ultraviolet (UV) and IR spectra. The PMR spectrum of the product shows the presence of >NH ($\delta$ 11.85, br), one olefinic proton ($\delta$ 5.57, t-like, 1-H), one vinylic and one tertiary methyls ($\delta$ 2.04, s, 11-Me and $\delta$ 1.22, s, 5-Me), and one secondary methyl ($\delta$ 1.14 ,d, $J=6$ Hz, 4-Me). These physical properties are in accord with a formulation of the product as **27**, which

9) *a*) Y. Ishizaki, Y. Tanahashi, T. Takahashi, and K. Tori, *Chem. Comm.*, **1969**, 551; *b*) T. Tada, H. Nagano, E. Shirasaki, H. Komatsu, Y. Tanahashi, Y. Moriyama, T. Takahashi, and M. Fukuyama, The 15th Symposium on Natural Products Chemistry, Symposium Paper, p. 223 (Nagoya, Oct., 1971); *c*) C. Kabuto, N. Takada, S. Maeda, and Y. Kitahara, *Chemistry Letters* (Tokyo), **1973**, 371.

10) I. Kitagawa, H. Shibuya, Y. Yamazoe, H. Takeno, and I. Yosioka, *Tetrahedron Letters*, **1974**, 111 (Preliminary communication).

11) *a*) Y. Ishizaki, Y. Tanahashi, T. Takahashi, and K. Tori, *Tetrahedron*, **26**, 5387 (1970); *b*) T. Tatee and T. Takahashi, *Chemistry Letters* (Tokyo), **1973**, 929; *c*) E. Piers and M.B. Geraghty, *Can. J. Chem.*, **51**, 2166 (1973).

12) W. Nagata and H. Itazaki, *Chem. & Ind.*, **1964**, 1194.

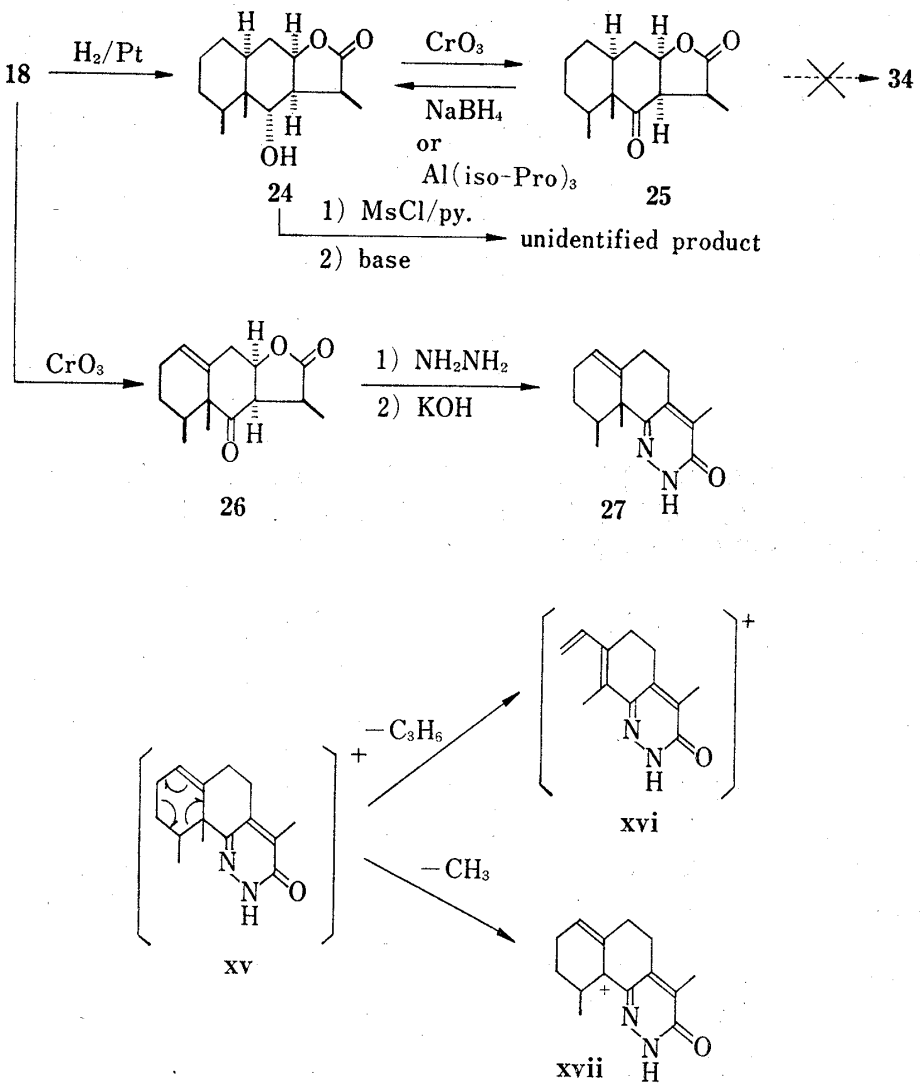



Chart 5

has been corroborated by a high resolution mass spectrum in which a base peak and a prominent ion peak are observed and formulated as **xvi** and **xvii** respectively. It is pointed out here that the location of a double bond at C-1 (10) has been substantiated by a reverse Diels-Alder type fragmentation of the ring A which gives the base peak **xvi**.

Because the 11$\beta$-Me function appeared responsible for the direction of reduction of 6-keto function in **25** (always giving **24**) on the basis of the Dreiding model examinations referring the coupling constants $J_{6,7}$ and $J_{7,11}$ and the B ring conformation in **18**, **23**, **24**, and **25**, and because $NaBH_4$ reduction of **26** gave an undesired mixture, the 11$\alpha$-Me isomer **23** was taken as a starting compound for the conversion.

Chromium trioxide oxidation of **23** gave almost quantitatively a keto-lactone (**28**) whose IR (1775, 1718, 1676 $cm^{-1}$) and PMR (Table IV) spectra support the formulation. Reduction of **28** with $NaBH_4$ yielded a 6-epimer of **23** in an excellent yield as expected. The structure **29** has been assigned on the basis of its physical properties (IR: 3650, 1770, 1610 $cm^{-1}$ and PMR: Table IV), among which the coupling constant $J_{6,7}$ (3 Hz) figures out the stereochemical correlation of 6$\alpha$-H and 7$\alpha$-H in a B-ring chair-like conformation. Catalytic hydrogenation of **29** over Pd-C furnished two products in 64 and 33% yields, but the minor product was further revealed to be a mixture of two lactones. The major product, formulated as **30** on the basis of its physical properties (IR: 3460, 1768 $cm^{-1}$ and PMR: Table IV), was mesylated and treated with collidine successively. A resulting fairly labile product (**33**) was then, without

further purification because of its facile partial isomerization to a final product even upon careful isolation, treated with $K_2CO_3$–toluene at reflux to give a final product which was proved identical with tetrahydroligularenolide (**34**) in all respects including the specific rotation. Since two minor hydrogenation products of **29** were readily convertible each other during the careful chromatographic procedure, their separation was abandoned and they were assigned as a 1: 4 mixture of **31** and **32** on the basis of PMR data (see Experimental).

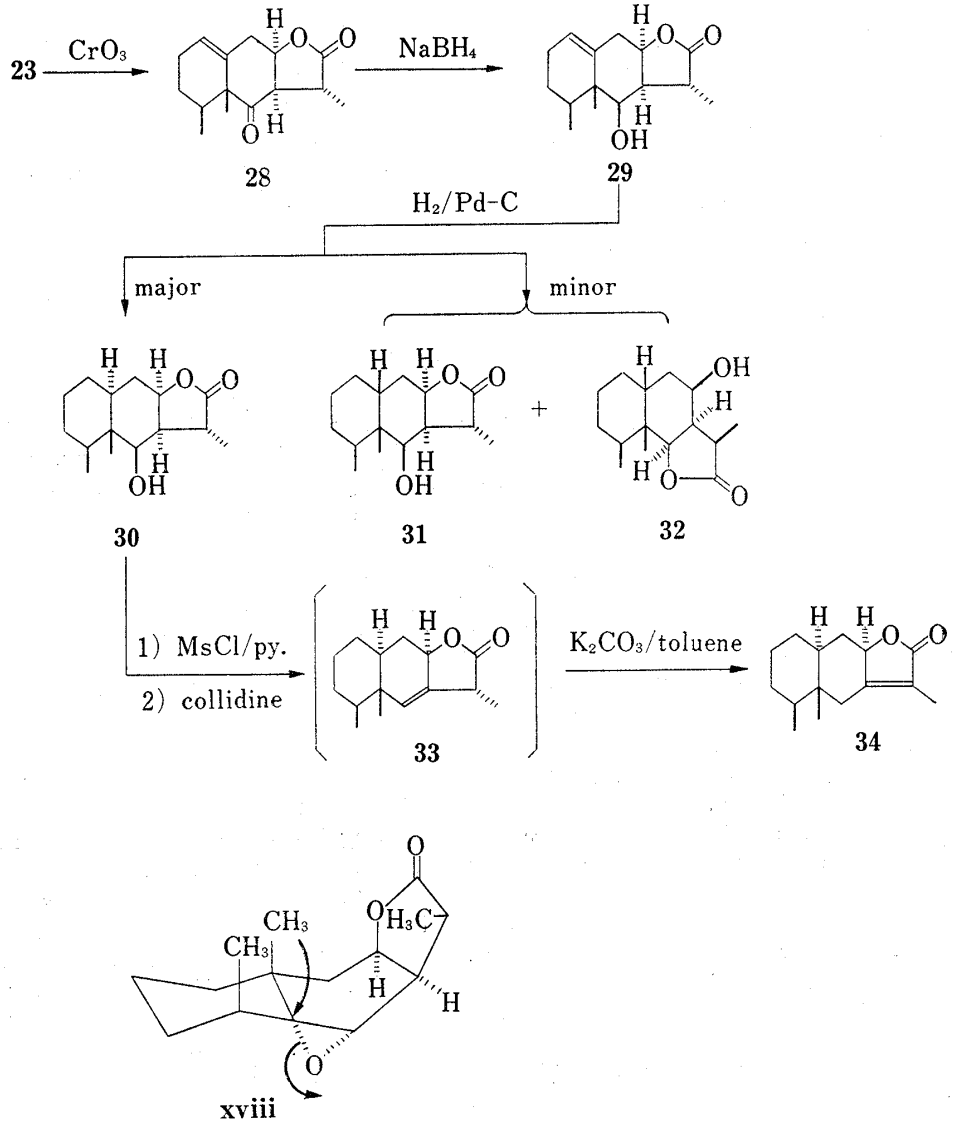



Chart 6

TABLE IV. PMR Data of **28**, **29**, and **30** (90 MHz)

| | **28** | **29** | **30**[a] |
|---|---|---|---|
| 1-H | 5.72 (m) | 5.40 (m) | — |
| 6-H | — | 3.81 (d, 3) | 3.38 (d, 7) |
| 7-H | 2.91 (d.d, 3 and 8) | —[b] | 2.22 (d.t, 7 and 12) |
| 8-H | 4.83 (q-like, 8) | 4.81 (q-like, 7) | 4.12 (d.t, 7 and 11) |
| 11-H | 3.29 (d.q, 3 and 7) | —[b] | 2.64 (d.q, 7 and 12) |
| 4-Me | 0.89 (d, 6.5) | 0.93 (d, 6.5) | 1.13 (d, 6.5) |
| 5-Me | 1.07 (s) | 0.98 (s) | 0.68 (s) |
| 11-Me | 1.30 (d, 7) | 1.32 (d, 7) | 1.31 (d, 7) |

*a*) measured in $CDCl_3+C_6D_6$ (1:1) *b*) unclear due to overlapping

As described above, the product A (**17**) and B (**18**) could be converted quantitatively to the product D (**23**), it follows therefore that the final derivation starting from **23** completes the conversion of dihydroalantolactone (**14**) to tetrahydroligularenolide (**34**) in a 15% overall yield. Very recently, it has been found that HCOOH–acetone (2: 1 mixture) treatment of **15** at reflux gave **17** and **18** in 52 and 16% yields. Consequently, it is conceivably expected that the present conversion would provide a new synthetic route of eremophilane-type sesquiterpenoid *via* a precursory eudesmane-type compound.

As for a reason of the facile 1,2-shift of the angular methyl in **15** through a biogenetically patterned pathway, a release of strain would be considered responsible, since as disclosed in an X-ray structure study of 13$\beta$-*p*-bromo-phenylthio-11$\alpha$,13-dihydropulchellin C diacetate,[13] the ring B of **15** is presumed to possess a boat-like conformation due to the presence of a *cis*-$\gamma$-lactone and consequently the 5$\alpha$,6$\alpha$-epoxide function is presumed to be in a favorable disposition for the angular methyl migration as depicted in **xviii** in which three methyl functions are in the congested proximity. The presumption will be a subject of further investigation.

## Experimental[14]

**Photooxygenation of 5 followed by $LiAlH_4$ Reduction giving 6 and 7**——A solution of **5** (1.0 g) and hematoporphyrin (100 mg) in dry pyridine (250 ml) was irradiated with a 30 W low pressure mercury lamp (Eikosha PIL-30) for 20 hr with a slow stream of oxygen bubbled through the irradiation solution. After dilution with ether, the reaction mixture was treated with active charcoal (2 g) while warming and evaporated *in vacuo* to give a crude hydroperoxide (1.1 g), which was dissolved in dry ether (30 ml) and poured into a mixture of $LiAlH_4$ (1.0 g)–dry ether (50 ml) at 0°. The total mixture was stirred for 2 hr at room temperature, treated with water and 5% HCl successively, and extracted with ether. Usual working-up of the ether extract gave a mixture of two diols (1.0 g), which was purified by a $AgNO_3$–$SiO_2$ column eluting with $CH_2Cl_2$ to give **6** (340 mg) and **7** (360 mg) successively. **6**, colorless glassy, $[\alpha]_D$ +122.0° ($c$=1.0, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3600, 3470 (OH), 1644, 900 (C=$CH_2$). PMR (60 MHz): 0.87 (3H, s, 10-Me), 1.22 (6H, s, two 11-Me's), 4.70, 4.81 (1H each, br.s, with fine splitting, >C=$CH_2$). High resolution Mass Spectrum $m/e$: 238.192 ($M^+$). Calcd. for $C_{15}H_{26}O_2$: 238.193. **7**, colorless glassy, $[\alpha]_D$ −28.7° ($c$=1.0, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3610, 3470 (OH), 1640, 906 (C=$CH_2$). PMR (60 MHz): 1.04 (3H, s, 10-Me), 1.25 (6H, s, two 11-Me's), 4.93, 4.96 (1H each, br.s, >C=$CH_2$). High resolution Mass Spectrum $m/e$: 238.193 ($M^+$). Calcd. for $C_{15}H_{26}O_2$: 238.193.

**Catalytic Hydrogenation of 6 followed by Benzoylation giving 9**——A solution of **6** (225 mg) in MeOH (25 ml) was hydrogenated over $PtO_2$ (200 mg) at room temperature for 2 hr. A crude product (255 mg) obtained after evaporation of the filtrate was purified by a $AgNO_3$–$SiO_2$ column eluting with $CH_2Cl_2$ and crystallized from *n*-hexane to give colorless needles of a dihydro derivative (**8**), mp 115—116°, $[\alpha]_D$ +41.9° ($c$=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.88; H, 11.51. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3630, 3490 (OH). PMR (60 MHz): 1.05 (3H, d, $J$=7, 4-Me), 1.07 (3H, s, 10-Me), 1.20 (6H, s, two 11-Me's). To a solution of **8** (500 mg) in dry pyridine (10 ml) was added benzoyl chloride (1 ml) and the total mixture was left standing at room temperature for 2 days, poured into ice-water, and extracted with ether. The ether extract, after successive washing with 10% NaOH, 5% HCl, 5% $NaHCO_3$, and water, was dried and evaporated to give a crude benzoate (700 mg), which was purified by $SiO_2$ column chromatography eluting with $CH_2Cl_2$–benzene (1: 1). A pure sample of **9** was obtained as colorless glassy substance (550 mg), $[\alpha]_D$

13) M. Curie and G.A. Sim, *J. Chem. Soc. Perkin II*, **1973**, 400.

14) The following instruments were used for obtaining the physical data: mp (Yanagimoto Micro-melting point Appratus; recorded uncorrected); specific rotation (Rex Photoelectric Polarimeter NEP-2, measured at room temperature with 1=1 dm); IR spectra (Hitachi IR Spectrometer EPI-G3 or EPI-S2); UV spectra (Shimadzu MPS-50L UV Spectrometer); mass spectra (Hitachi RMU-6D Mass Spectrometer); high resolution mass spectra (JEOL JMS-01SG Mass Spectrometer); PMR spectra (Hitachi R-22 or R-20A, or Varian HA-100 NMR Spectrometer, in $CDCl_3$ and $Me_4Si$ as an internal standard). The chemical shifts are given in $\delta$ value and coupling constants ($J$) and half-height band width ($W_{h/2}$) are in Hz. For GLC, Hitachi Model 063 or Varian 90P (for preparative) Gas Chromatograph was used under the following conditions: 3% or 10% SE-30 on chromosorb W (12 m×3 mm), HB 2000 Golay (45 m×0.25 mm), or carbowax 20M (10 ft×1/4 inch); the carrier gas ($N_2$ or He) flow rate: 40—50 ml/min, 0.9 ml/min, or 10 ml/min; temp: 150° or 170°. For TLC, silica gel D-5 (Camag) or $HF_{254}$ (Merck) was used and detection by 1% $Ce(SO_4)_2$ in 10% $H_2SO_4$ with heating or by UV fluorescence. For column chromatography, silica gel (Merck. 0.05—0.2 mm) was used.

+28.7° ($c$=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.88; H, 9.50. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3610 (w, OH), 1712, 1285, 709 (benzoate). PMR (60 MHz): 1.06 (3H, d, $J$=7, 4-Me), 1.14 (3H, s, 10-Me), 1.64 (6H, s, two 11-Me's), 7.27—8.18 (5H, m, phenyl).

**Catalytic Hydrogenation of 7**——A solution of **7** (270 mg) in MeOH (25 ml) was hydrogenated over $PtO_2$ (250 mg) at room temperature for 3 hr. A product (297 mg) obtained after evaporation of the filtrate was purified by a $AgNO_3$–$SiO_2$ column eluting with $CH_2Cl_2$ to give two dihydro derivatives (**10**, 126 mg, and **11**, 60 mg) respectively. **10**, mp 123—124.5°, $[\alpha]_D$ −48.0° ($c$=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.73; H, 11.44. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3625, 3300 (br) (OH). PMR (60 MHz): 0.93 (3H, d, $J$=7, 4-Me), 0.97 (3H, s, 10-Me), 1.28 (6H, s, two 11-Me's). **11**, mp 73.5—74.0°, $[\alpha]_D$ +37.4° ($c$=0.8, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3640, 3510 (OH). PMR (60 MHz): 0.86 (3H, d, $J$=7, 4-Me), 0.98 (3H, s, 10-Me), 1.19 (6H, s, two 11-Me's). High resolution Mass Spectrum $m/e$: 240.208 ($M^+$). Calcd. for $C_{15}H_{28}O_2$: 240.209.

**Acid Treatment of 5**——1) To an ice-cooled solution of **5** (100 mg) in ether (2 ml) was added conc. $H_2SO_4$ (0.1 ml) and the total solution was left standing at room temperature for 2 hr, poured into ice-water, neutralized with 5% $NaHCO_3$. The ether layer was taken up, washed with water, and treated in a usual manner to give a product (84 mg). A major product was isolated in a pure form by preparative GLC and identified with $\gamma$-selinene (**12**) by TLC, GLC, and IR (film).

2) A solution of **5** (250 mg) in 99% HCOOH (5 ml) was refluxed for 30 min. After neutralization with 5% $NaHCO_3$, the reaction mixture was extracted with ether and the ether extract was treated in a usual manner to give a product (200 mg), whose major component was isolated in a pure form by preparative GLC and identified with $\delta$-selinene (**13**) by TLC, GLC, and IR (film).

**Treatment of 9 with $POCl_3$-pyridine followed by $LiAlH_4$ Reduction**——To an ice-cooled solution of **9** (80 mg) in dry pyridine (4 ml) was added $POCl_3$ (0.4 ml) and the total solution was left standing overnight at room temperature, poured into ice-water, and extracted with ether. The ether layer was washed with 5% $NaHCO_3$ and water successively and worked up in a usual manner to give a product (65 mg), which, without purification, was dissolved in dry ether (10 ml) and poured into an ice-cooled stirred solution of $LiAlH_4$ (100 mg)–dry ether (10 ml) and the total mixture was stirred for further 2 hr at room temperature. After working up of the reaction mixture in a usual manner, a product was purified by preparative TLC to give 40 mg of a pure material which was identified with $\gamma$-eudesmol (**5**) by TLC, GLC, IR (film), and PMR.

**Treatment of 9 with $BF_3$-etherate**——To an ice-cooled solution of **9** (70 mg) in dry ether (2 ml) was added $BF_3$-etherate (0.2 ml) and the total solution was stirred for 30 min, poured into ice-water, and extracted with ether. The ether extract was washed with 5% $NaHCO_3$ and water successively, and worked up in a usual manner to give a product (40 mg). A major product was obtained in a pure form by preparative GLC and identified with $\delta$-selinene (**13**) by GLC, IR (film), and PMR.

**Epoxidation of Dihydroalantolactone (14)**——To a solution of **14** (6.0 g) in $CH_2Cl_2$ (300 ml) was added dropwise a solution of $m$-chloroperbenzoic acid (5.8 g) in $CH_2Cl_2$ (220 ml) and the total solution was kept stirring at room temperature for 30 min and treated with aq. 10% $Na_2SO_3$ until the organic layer became negative for KI-starch test. The $CH_2Cl_2$ solution was then neutralized with aq. 5% $NaHCO_3$, washed with water, dried over $MgSO_4$ and evaporated *in vacuo*. A residue thus obtained was crystallized from $n$-hexane–ether to give colorless needles of 5$\alpha$,6$\alpha$-epoxy-dihydroalantolactone (**15**) (5.5 g), mp 191.5—193°, $[\alpha]_D$ −30.9° ($c$=1.0, pyridine). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.17; H, 9.10. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1760 (sh), 1749. PMR (90 MHz): 1.11 (3H, d, $J$=6, 4-Me), 1.19 (3H, s, 10-Me), 1.38 (3H, d, $J$=7, 11-Me), 2.85 (1H, br.s, $W_{h/2}$=3, 6-H), 3.05 (1H, t, $J$=5, 7-H), 4.58 (1H, quintet-like, $J$=3, 8-H). Mass Spectrum $m/e$ (%): 250 ($M^+$, 8), 126 (100). The compound was identified with authentic **15**[6a] by direct comparison.

**Treatment of 5$\alpha$,6$\alpha$-Epoxy-dihydroalantolactone (15) with HCOOH-Acetone (1: 2)**——A solution of **15** (7.9 g) in freshly distilled acetone (400 ml) was treated with 99% HCOOH (200 ml) and the total solution was refluxed for 10 hr. After cooling, the reaction mixture was diluted with water (400 ml), neutralized with aq. 10% KOH and concentrated *in vacuo* to remove acetone. The resulting aqueous emulsion was extracted with ether three times and the ether extract was washed with water and treated in a usual manner to give a colorless oily product (8.0 g), which was chromatographed on a silica gel (400 g) column developing with $n$-hexane and $n$-hexane–ether (4: 1) and the fractions containing the products A-H were repeatedly subjected to silica gel column chromatography and preparative TLC developing with $CHCl_3$–ether (5: 2) or $n$-hexane–$CHCl_3$–MeOH (16: 44: 1) and the combined respective yields were as follows: product A (**17**), 888 mg (10%); product B (**18**), 2.68 g (34%); product C (**20**), 174 mg (2.2%); product D (**23**), 158 mg (2.0%); product E, 47 mg (0.5%); product F, 269 mg (3.4%); product G, 176 mg (2.4%); product H, 26 mg (0.3%).

Product A (**17**), mp 114—116°, colorless needles ($n$-hexane–acetone), $[\alpha]_D$ −0.7° ($c$=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{24}O_4$: C, 69.04; H, 7.97. Found: C, 69.07; H, 8.15. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1768, 1715, 1640. PMR (100 MHz): as given in Table I. Mass Spectrum $m/e$ (%): 278 ($M^+$, 0.7), 41 (100).

Product B (**18**), mp 113—114.5°, colorless needles ($n$-hexane–acetone), $[\alpha]_D$ −68.4° ($c$=1.8, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.87; H, 8.66. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3620, 3540, 1766. PMR (90 MHz): as given in Table I. Mass Spectrum $m/e$ (%): 250 ($M^+$, 3), 158 (100).

Product C (**20**), mp 131.5—133°, colorless needles ($n$-hexane–acetone), $[\alpha]_D$ −32.9° ($c$=1.31, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.06; H, 8.55. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3480, 1754, 1638, 901. PMR (90 MHz): 0.83 (3H, s, 10-Me), 1.38 (3H, d, $J$=7, 11-Me), 2.88 (1H, quintet, $J$=7, 11-H), 3.79

(1H, d.d, $J$=10 and 11, 6-H), 4.56 (1H, d.t, $J$=3 and 5, 8-H), 4.66, 5.04 (1H each, s-like, >C=$CH_2$). Mass Spectrum *m/e* (%): 250 ($M^+$, 6), 147 (100).

Product D (23), colorless glassy, $[\alpha]_D$ −50.0° ($c$=0.33, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3560, 1768, 1665. PMR (90 MHz): as given in Table I. Mass Spectrum *m/e* (%): 250 ($M^+$, 3), 41 (100). High resolution Mass Spectrum *m/e*: 250.157 ($M^+$). Calcd. for $C_{15}H_{22}O_3$: 250.157.

**Treatment of 5α,6α-Epoxy-dihydroalantolactone (15) with HCOOH–Acetone (2: 1)**——A solution of **15** (100 mg) in freshly distilled acetone (7 ml) and 99% HCOOH (14 ml) was refluxed for 5 hr and after cooling, the reaction mixture was neutralized with 5% KOH–MeOH, diluted with water (20 ml), and concentrated *in vacuo* to remove acetone and MeOH. A solid residue was then extracted with ether (30 ml×3) and the ether extract was washed with water and treated in a usual manner to give a colorless oily product (93 mg), which was subjected to preparative TLC (sliica gel Camag D-5) developing with $CHCl_3$–ether (5: 2) to give product A (**17**, 58 mg) and B (**18**, 16 mg) as the major products (totally 68% yield).

**Acetylation of Product B (18)**——A solution of **18** (80 mg) in pyridine (3 ml) and $Ac_2O$ (4 ml) was left standing at 31° overnight, poured into ice-water, and extracted with ether. After usual work-up, the ether extract furnished a product which was purified by preparative TLC ($CHCl_3$–acetone=10: 1) to give an acetate (**19**) as colorless needles (23 mg) of mp 117—118° (ether–*n*-hexane), $[\alpha]_D$ −16.3° ($c$=2.34, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.45; H, 8.31. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1767, 1725, 1655. PMR (90 MHz): as given in Table I.

**Hydrolysis of Product A (17)**——To a solution of **17** (20 mg) in anhydrous MeOH (5 ml) was added dry $K_2CO_3$ (5 mg) and the total mixture was refluxed for 30 sec, filtered to remove $K_2CO_3$, and evaporated *in vacuo* to give a product (9 mg) which was purified by preparative TLC ($CHCl_3$: ether=5: 2) and identified with product B (**18**) by TLC ($CHCl_3$: ether=5: 2; *n*-hexane: ether=1: 1), GLC (SE-30), and IR ($CHCl_3$).

**Formylation of Product B (18)**——A solution of **18** (50 mg) in freshly distilled acetone (10 ml) and 99% HCOOH (5 ml) was refluxed for 2 hr, diluted with water, neutralized with KOH, and concentrated *in vacuo* to remove acetone. An aqueous emulsion was then extracted with ether and the ether extract was treated in a usual manner. A product was purified by preparative TLC ($CHCl_3$: ether=5: 2) to give a formete (30 mg) being identical with **17** by TLC ($CHCl_3$:ether=5: 2; *n*-hexane: ether=1: 1), GLC (SE-30), and IR ($CHCl_3$).

**Acetylation of Product C (20)**——A solution of **20** (33 mg) in pyridine (1 ml) and $Ac_2O$ (1 ml) was refluxed for 4 hr, treated with ice-water, and extracted with ether. After usual work-up, a product was crystallized from *n*-hexane–acetone to furnish colorless needles of an acetate (**21**), mp 188—189°, $[\alpha]_D$ −38.2° ($c$=1.5, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.51; H, 8.15. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1770, 1728. PMR (100 MHz): 0.85 (3H, s, 10-Me), 1.25 (3H, d, $J$=5, 11-Me), 1.93 (3H, s, OAc), 4.52 (1H, d.t, $J$=2.3 and 1.0, 8-H), 4.84 (1H, m, 6-H), 4.71, 4.82 (1H each, s-like, >C=$CH_2$).

**Hydroboration of Dihydroalantolactone (14)**——To a solution of **14** (173 mg) in dry tetrahydrofuran (5 ml) was introduced $B_2H_6$ generated from $NaBH_4$ (300 mg) and $BF_3$–etherate (2.5 ml) and the reaction mixture was left standing at room temperature for 20 hr. The reaction mixture was then treated with ice to decompose excess $B_2H_6$ and added dropwise with 3N NaOH (3 ml) and 30% $H_2O_2$ (3 ml), left standing at room temperature for 2 hr, neutralized with aq. 5% $H_2SO_4$, extracted with $CHCl_3$. The $CHCl_3$ extract, after working-up in a usual way, was evaporated *in vacuo* and a residue was crystallized from benzene to give colorless needles of **22** (40 mg), mp 154.5—156°, $[\alpha]_D$ −71.2° ($c$=0.85, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 70.93; H, 9.18. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3465, 1743. PMR (90 MHz): 0.94 (3H, d, $J$=6, 4-Me), 0.99 (3H, s, 10-Me), 1.40 (3H, d, $J$=7, 11-Me), 2.87 (1H, quintet, $J$=7, 11-H), 3.71 (1H, d.d, $J$=9 and 11, 6-H), 4.55 (1H, d.t, $J$=2 and 4, 8-H).

**Catalytic Hydrogenation of Product C (20)**——A solution of **20** (12 mg) in EtOH (5 ml) was hydrogenated over $PtO_2$ (5 mg) for 3 hr, filtered, and concentrated *in vacuo* to give a residue which was crystallized from benzene to furnish a product (10 mg) being identical with **22** prepared above by mixed mp, TLC ($CHCl_3$: ether=3: 2), and IR (KBr).

**Isomerization of Product B (18) with $K_2CO_3$–Toluene**——A mixture of **18** (380 mg) in dry toluene (45 ml) containing dry $K_2CO_3$ (3.0 g) was refluxed with stirring in an oil bath for 7 hr. After cooling, the mixture was filtered to remove $K_2CO_3$ and concentrated *in vacuo* to give a colorless oily product (370 mg), which was found to be a pure sample of product D (**23**) as identified by TLC ($CHCl_3$: ether=5: 2; *n*-hexane: ether=2: 7; benzene: AcOEt=5: 2), GLC (3% SE-30), IR, PMR, and $[\alpha]_D$.

**NOE Experiments**——NOE experiments were undertaken with a Hitachi R-22 NMR spectrometer operating at 90 MHz in the frequency-swept and external $CF_3COOH$-locked mode, for the degassed solution in $CDCl_3$. NOE values were obtained as percentage increases in the integrated signal intensities (accuracies within ±2%).

**Catalytic Hydrogenation of Product B (18)**——A solution of **18** (134 mg) in EtOH (9 ml) was hydrogenated over $PtO_2$ (28mg) with stirring at room temperature for 5 hr. After filtration, a reaction mixture was evaporated *in vacuo* and a residue was crystallized from ether and then from *n*-hexane–acetone to furnish colorless needles of **24** (112 mg), mp 180.5—181°, $[\alpha]_D$ −2.0° ($c$=0.92, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.43; H, 9.53. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3460, 1751. PMR (90 MHz); 0.99 (3H, d, $J$=7, 4-Me),

1.03 (3H, s, 5-Me), 1.35 (3H, d, $J$=7, 11-Me), 2.92 (1H, quintet, $J$=7, 11-H), 3.29 (1H, d, $J$=11, 6-H), 5.56 (1H, m, 8-H).

**Oxidation of 24 giving 25**——1) With $Na_2Cr_2O_7 \cdot 2H_2O$: To a stirred solution of **24** (51 mg) in glacial AcOH (5 ml) was added dropwise a solution of $Na_2Cr_2O_7 \cdot 2H_2O$ (26 mg) in glacial AcOH (3 ml) and the total mixture was kept stirring for 2 hr, added with an additional amount of $Na_2Cr_2O_7 \cdot 2H_2O$ (20 mg) and stirred for further 2 hr. After diluting with ice-water, the reaction mixture was extracted with ether and the ether extract was washed with water, and worked up in a usual manner. A product was crystallized from *n*-hexane–ether to furnish colorless needles of **25** (36 mg) which was further recrystallized from *n*-hexane–acetone to give colorless needles of mp 111.5—112°, $[\alpha]_D$ −14.7° ($c$=0.57, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.96; H, 8.86. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1758, 1658. PMR (90 MHz): 0.70 (3H, d, $J$=7, 4-Me), 1.06 (3H, s, 5-Me), 1.53 (3H, d, $J$=7, 11-Me), 2.74 (1H, quintet, $J$=7, 11-H), 3.15 (1H, d.d, $J$=7 and 4.5, 7-H), 4.76 (1H, d.t, $J$=4.5 and 2, 8-H).

2) With Jones Reagent: To a stirred solution of **24** (40 mg) in acetone (3 ml) was added 0.5 ml of Jones reagent (prepared from $CrO_3$: 270 mg, $H_2SO_4$: 2.3 ml, and water: 10 ml) and the total mixture was kept stirring at room temperature for 30 min. After diluting with water, the reaction mixture was extracted with ether and the ether extract, after usual work-up, furnished a product, which was crystallized from ether–*n*-hexane to give a pure material (33 mg) being identical with **25** obtained above by TLC ($CHCl_3$: ether=7: 3).

**Reduction of 25 with $NaBH_4$ or Al (iso-PrO)$_3$**——1) To a solution of **25** (33 mg) in EtOH (10 ml) was added $NaBH_4$ (15 mg) and the mixture was stirred at room temperature for 2 hr, treated with aq. 5% $H_2SO_4$, diluted with water and extracted with ether. The ether extract, after usual work-up, gave a product, which was purified by a silica gel column eluting successively with *n*-hexane and benzene–ether (1: 1) and a product (23 mg) thus obtained was identified with **24** by mixed mp and TLC.

2) A solution of **25** (10 mg) in anhydrous iso-PrOH (5 ml) was treated with aluminium isopropoxide (10 mg) and heated in an oil bath (100°) for 5 hr. After usual work-up, a resulting major product was identified with **24** by TLC ($CHCl_3$: ether=3: 2).

**Chromium Trioxide Oxidation of Product B (18)**——To a stirred solution of **18** (70 mg) in acetone (5 ml) was added dropwise 1 ml of Jones reagent (prepared as above) and the total mixture was kept stirring at room temperature for 45 min, diluted with ice-water and extracted with ether. After usual work-up, the ether extract yielded a product, which was purified by preparative TLC ($CHCl_3$: ether=3: 2) to furnish **26** (35 mg), colorless glassy, $[\alpha]_D$ −102.2° ($c$=2.17, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1768, 1722, 1674. PMR (90 MHz): 0.84 (3H, d, $J$=6.5, 4-Me), 1.02 (3H, s, 5-Me), 1.47 (3H, d, $J$=7, 11-Me), 3.42 (1H, t, $J$=7.5, 7-H), 4.71 (1H, q, $J$=7.5, 8-H), 5.66 (1H, t, with further splitting, 1-H). High resolution Mass Spectrum $m/e$: 248.141 ($M^+$). Calcd. for $C_{15}H_{20}O_3$: 248.141.

**Treatment of 26 under Modified Huang-Minlon Conditions**[12]——A solution of **26** (57 mg) in triethyleneglycol (5 ml) was treated with hydrazine dihydrochloride (700 mg) and 98.5% hydrazine (2.7 ml) and the total mixture was heated at reflux in an oil bath (130°) for 3 hr. After addition of KOH (800 mg), the reaction mixture was heated with a downward condenser while raising the bath temperature from 130° to 210° and heated further at 220° for 3 hr. After cooling, the reaction mixture was adjusted to pH 4 with aq. 5% $H_2SO_4$ and extracted with ether. The ether extract was then treated as usual and a product was washed with a small amount of ether to furnish **27** (27 mg), amorphous. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3425, 3130 (br), 1640, 1592. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 290 (2380). PMR (60 MHz): as given in the text. Mass Spectrum $m/e$ (%): 244 ($M^+$, 29), 202 (100). High resolution Mass Spectrum $m/e$: 244.157 ($M^+$); 229.133 (xvii); 202.112 (xvi). Calcd. for $C_{15}H_{20}ON_2$: 244.158; $C_{14}H_{17}ON_2$: 229.134; $C_{12}H_{14}ON_2$: 202.111.

**Chromium Trioxide Oxidation of Product D (23)**——To a stirred solution of **23** (360 mg) in acetone (17 ml) was added dropwise 25 drops of Jones reagent and the total mixture was kept stirring at room temperature for 45 min, poured into ice-water, and extracted with ether. After successive washing with 5% $NaHCO_3$ and water followed by usual work-up, the ether extract gave a redisue (350 mg), which was purified by silica gel (10 g) column chromatography eluting with $CHCl_3$ to furnish a pure product (**28**, 345 mg), colorless needles of mp 85—86° (*n*-hexane–acetone), $[\alpha]_D$ −129.0° ($c$=0.26, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.49; H, 8.12. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1775, 1718, 1676. PMR (90 MHz): as given in Table IV. Mass Spectrum $m/e$ (%): 248 ($M^+$, 10), 41 (100).

**Reduction of 28 with $NaBH_4$**——To an ice-cooled stirred solution of **28** (180 mg) in MeOH (1.5 ml) was added $NaBH_4$ (65 mg) in small portions. The total mixture was kept stirring at 0° for 30 min, treated with 5% $H_2SO_4$ (3 drops), and diluted with ice-water, and extracted with ether. After usual work-up, a residue obtained by evaporation of ether was crystallized from ether to furnish colorless needles of **29** (150 mg), mp 155°, $[\alpha]_D$ −40.8° ($c$=0.1, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.96; H, 8.79. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3650, 1770, 1610. PMR (90 MHz): as given in Table IV. Mass Spectrum $m/e$ (%): 250 ($M^+$, 3), 158 (100).

**Catalytic Hydrogenation of 29**——A solution of **29** (60 mg) in 95% EtOH (20 ml) was hydrogenated over 5% Pd-C (45 mg) at room temperature for 1 hr. After removing the catalyst by filtration, a filtrate was evaporated to dryness to give a white powder (59 mg), which was purified by preparative TLC (silica gel Camag D-5; benzene: AcOEt=5: 2) to furnish **30** (37 mg) and a mixture of **31** and **32** (20 mg). Colorless

needles of **30**, mp 175—176° (*n*-hexane), $[\alpha]_D$ −26.5° ($c$=0.55, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.38; H, 9.59. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3640, 1768. PMR (90 MHz): as given in Table IV. Mass Spectrum *m/e* (%): 234 ($M^+-H_2O$, highest peak, 2), 109 (100). The mixture of **31** and **32** was subjected to preparative TLC (silica gel Camag D-5 or alumina Merck type T), however it was found that two compounds were convertible each other even upon the careful preparative TLC separation. The composition of the equilibrated mixture was determined by PMR analysis and the structures were assigned on the basis of PMR data (90 MHz). **31** (linear lactone), PMR: 0.68 (3H, d, $J$=5.5, 4-Me), 1.00 (3H, s, 5-Me), 1.31 (3H, d, $J$=7, 11-Me), 3.69 (1H, d-like, $J$=4, 6-H), 4.76 (1H, m, 8-H). **32** (angular lactone), PMR: 0.82 (3H, d, $J$=6, 4-Me), 1.12 (3H, s, 5-Me), 1.38 (3H, d, $J$=7, 11-Me), 4.10 (1H, m, 8-H), 4.23 (1H, d, $J$=4, 6-H).

**Conversion of 30 to Tetrahydroligularenolide (34)**——A solution of **30** (15 mg) in dry pyridine (2 ml) was treated with MsCl (5 drops) and left standing at room temperature overnight. After pouring into ice-water, the reaction mixture was extracted with $CHCl_3$ and the $CHCl_3$ extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Evaporation of the solvent gave a mesylate (17 mg), IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1765, 1331, 1169, which was dissolved in 2,4,6-collidine (5 ml) and refluxed for 2 hr. After cooling, the reaction mixture was treated with ice-water, and extracted with ether. The ether extract was then washed successively with 5% HCl, 5% $NaHCO_3$, and water, and treated in a usual manner to give **33** (12 mg), which, without further purification, was dissolved in dry toluene (3 ml), treated with $K_2CO_3$ (20 mg), and heated at reflux for 5 hr. After filtration for removing $K_2CO_3$, a filtrate was evaporated to dryness to give colorless needles (10 mg), mp 114.5—115.5°, $[\alpha]_D$ −97° ($c$=0.057, MeOH). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1751, 1691. PMR (90 MHz): 0.58 (3H, s, 5-Me), 0.91 (3H, d, $J$=6, 4-Me), 1.79 (3H, t, $J$=2, 11-Me), 2.78 (1H, d, $J$=13, 6$\beta$-H), 4.59 (1H, m, $W_{h/2}$=18, 8-H). The final product was identified with authentic tetrahydroligularenolide (**34**) by mixed mp, IR, TLC (*n*-hexane–ether=5: 3; *n*-hexane: $CHCl_3$=1: 1; benzene: AcOEt=5: 1), GLC (3% SE-30), and $[\alpha]_D$.

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